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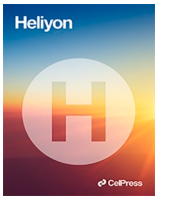

Research article

# Health-related quality of life in children with childhood acute myeloid leukemia in China: A five-year prospective study

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ABSTRACT

*Purpose:* This study aims to identify the key factors influencing health-related quality of life (HRQoL) of pediatric acute myeloid leukemia (AML) patients following their initial diagnosis and examine their impact on the five-year survival prognosis.

*Methods:* A chart review and follow-up were conducted for children with AML who participated in a prospective cohort study between 2017 and 2020. We identified factors influencing HRQoL through Pediatric Quality of Life Inventory™ (PedsQL™ 4.0), PedsQL™ Cancer Module 3.0 (CM 3.0) and PedsQL™ Family Impact Module 2.0 (FIM 2.0), as well as assessed the impact of impaired HRQoL on the overall outcomes of patients.

*Results:* Sixty-four subjects enrolled in the study had complete HRQoL outcome data, and 61 of them completed the 5-year follow-up. In CM 3.0, age was positively associated with parental proxy reports ($p = 0.040$), whereas divorced families were negatively associated with child self-reports ($p = 0.045$). A positive medical history correlates with FIM 2.0 ($p = 0.025$). Residence ($p = 0.046$), the occupation of caregivers ($p = 0.014$), disease severity ($p = 0.024$), and the only child ($p = 0.029$) exhibited statistically significant associations with the impairment of HRQoL. Impaired HRQoL scores shown by the PedsQL™4.0 parent proxy report ($p = 0.013$) and FIM 2.0 ($p = 0.011$) were associated with a reduced 5-year survival rate.

*Conclusions:* This study demonstrated that early impairment of HRQoL in pediatric acute myeloid leukemia patients has predictive value for long-term prognosis. Once validated, these findings may provide some guidance to clinicians treating children with AML.

## 1. Introduction

Acute myeloid leukemia (AML), a clonal and aberrantly differentiated hematopoietic malignancy, is characterized by the accumulation of abnormal cells in the bone marrow, blood, and possibly other organs [1]. Pediatric AML comprises approximately 15–20 % of all pediatric leukemia worldwide [2]. AML is associated with lower five-year event free survival rates and reduced quality of life compared to other leukemia. However, recent decades have witnessed remarkable improvements in the prognosis of children with AML, with current long-term survival rates reaching approximately 70 % [3]. Consequently, there has been a shift in focus towards

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optimizing health-related quality of life (HRQoL) for pediatric AML patients and their family's following diagnosis and treatment [4]. Numerous studies have shown the negative effect of AML on patients' quality of life [5].

A growing body of evidence suggests that the intensity of treatment can seriously affect patients' HRQoL [6–8]. Moreover, patients with secondary or relapsed AML at the time of study initiation exhibited considerably impaired HRQoL compared to those with de novo AML [8]. It was found that changes in patients' quality of life were associated with long-term survival across various diseases, with diminished quality of life indicating a poor prognosis for patients [9–11]. Similarly, poor HRQoL at the time of patient diagnosis has been associated with reduced survival rates in cases of AML [12]. However, there remains a scarcity of studies investigating the factors affecting HRQoL in children with AML after initial diagnosis, and there is a notable lack of long-term prognostic data. Consequently, an AML cohort was established to address these knowledge gaps, with a specific focus on exploring the potential impact of impaired quality of life on patients' long-term survival. The study hypothesized that the impairment of quality of life would have a negative effect on the long-term survival of AML patients.

## 2. Methods

### 2.1. Patients

A prospective study was conducted, enrolling a total of 67 pediatric patients diagnosed with AML and their respective parents at Children's Hospital of Nanjing Medical University, between August 2017 and December 2020. Patients with cognitive impairments, limited literacy skills, or other chronic illnesses such as trisomy 21 syndrome and metabolic disorders or documented history of a pervasive developmental disorder, autism, or a nonverbal presentation that would impede the ability to complete questionnaires were excluded from this study.

### 2.2. Procedures

The identification of eligible participants was carried out by the medical team, who performed a preliminary assessment through electronic chart review. Subsequently, research staff met with the children within three days of their AML diagnosis, providing a detailed explanation of the study objectives and procedures. Informed consent from parents and assent from the children were obtained during this meeting. Children aged 7 years old and older were asked to independently complete self-report versions with minimal or no interference from parents. To ensure data accuracy, the collected data was meticulously checked by two individuals before being entered into the database. The follow-up was completed in January 2024, with the primary endpoint of death.

### 2.3. Measures

Demographic information for children and parents (e.g., age, sex, race, annual family income, relation to the child) was collected using a standard demographic questionnaire. Additionally, medical and disease-related data were abstracted via electronic chart review. In this study, the impairment threshold was set at one standard deviation below the mean of the total number of samples [13]. Based on this threshold, patients were categorized into groups with either impaired or unimpaired quality of life.

The assessment of children's HRQoL was assessed utilizing both child self-report and parent-proxy reports, employing the validated Pediatric Quality of Life Inventory™ General Core Module (PedsQL™4.0), PedsQL™ Family Impact Module (FIM 2.0) and PedsQL™ Cancer Module (CM 3.0). PedsQL™ was initially developed by Varni et al., in 1987 [14], and consists of a universal core scale designed to assess the common aspects of quality of life, as well as specific disease module tailored to measure the quality of life of children with different diseases.

The PedsQL™ 4.0 Generic Core Scales include separate versions for child self-report and parent proxy-report, tailored to specific age ranges. It consists of 4 scales assessing physical functioning, emotional functioning, social functioning, and school functioning [15,16]. In addition, the CM 3.0, specifically designed for pediatric cancer patients, was employed to measure HRQoL dimensions pertinent to this population [17]. The scale assesses 8 scales through pain and hurt, nausea, procedural anxiety, treatment anxiety, worry, cognitive problems, perceived physical appearance, and communication. The FIM 2.0 has 36 items and was used to assess respondents' functioning in eight areas: physical functioning, emotional functioning, social functioning, cognitive functioning, communication, worry, daily activities and family relationships [13].

### 2.4. Statistical analysis

All analyses were conducted with SPSS 27.0 software. Patient characteristics were analyzed descriptively for the total study sample. The influencing factors were taken as independent variables and the comprehensive score of quality of life was taken as dependent variables for statistical analysis. Cronbach's α coefficient assessed internal consistency (>0.7 considered good reliability). For numerical variables, T tests were performed. For nominal/ordinal variables, Pearson's chi-square tests were performed. If the conditions for linear regression analysis are not met, the Fisher exact test is performed. Linear regression was used for multifactor analysis, and results were reported with a 95 % confidence interval. Kaplan-Meier survival curves and the log-rank test assessed the relationship between scale scores and prognosis. The Cox regression model calculated P-values, considering death events in Kaplan-Meier analysis. $P < 0.05$ was deemed significant.

## 3. Results

### 3.1. Participant characteristics

Table 1 summarizes baseline characteristics. The median age of participants was 7.3 years old. Due to the age criteria for independent questionnaire completion, the children were divided into two age groups. The score of each module is shown in Table 2. Among the participants, seven patients were younger than two years old, so only the FIM 2.0 was completed. At baseline, all parents on behalf of their children completed the parent version while only 41 patients were old enough to complete the self-report scale independently. One child refused to fill out the PedsQL™ 4.0 self-report scale. Therefore, 40 patients completed the PedsQL™ 4.0 scale, and 41 patients completed the CM 3.0.

### 3.2. HRQoL scores

Comparative results are summarized in Table 2. PedsQL™ 4.0 child/agent reports both achieved the highest score for Social Functioning and the lowest score for School Functioning However, parental assessments consistently yielded lower scores across all dimensions compared to those provided by the children, with the most pronounced disparity in the School Functioning dimension (6.63).

In CM 3.0, the lowest scores were all found in Procedural Anxiety. Unlike PedsQL™ 4.0, Communication scored the highest on the children's self-report (81.71 ± 20.85), while Pain and Hurt scored the highest on the parent ratings.

As can be seen from the results of the PedsQL™ 4.0 and CM 3.0, although the scores of parent proxy report in most dimensions (11/12) were generally lower than the scores of child self-report, the Cronbach's alpha of each scale was greater than 0.7 (0.87–0.92), indicating a good consistency between parent rating and child self-rating scale. To some extent, the results of parental evaluation can replace children's self-evaluation.

### 3.3. Validation and reliability

Validity assessment was based on the Pearson's correlation between child self-report and parent proxy report. Internal consistency

**Table 1**
Clinical characteristics of the AML patient cohort.

| Characteristics | | n | % |
|---|---|---|---|
| Age | ≤7 | 31 | 48.4 |
| | >7 | 33 | 51.6 |
| Gender | Male | 32 | 50 |
| | Female | 32 | 50 |
| Disease typing | AML ( Non-M3 ) | 48 | 75 |
| | AML ( M3 ) | 16 | 25 |
| Disease severity | LR/IR | 41 | 64.1 |
| | HR | 23 | 35.9 |
| Body type | E/O | 14 | 15.6 |
| | Normal | 50 | 78.1 |
| Only child | Yes | 35 | 54.7 |
| | No | 29 | 45.3 |
| Residence | City | 36 | 56.3 |
| | Village | 28 | 43.7 |
| WBC (10^9/L) | ≤50 | 15 | 23.4 |
| | >50 | 49 | 76.6 |
| HB (g/L) | ≤90 | 36 | 56.3 |
| | >90 | 28 | 43.7 |
| PLT (10^9/L) | ≤30 | 22 | 34.4 |
| | >30 | 42 | 65.6 |
| Caregiver | Mother | 26 | 40.6 |
| | Grandfather | 2 | 3.1 |
| | Father | 34 | 53.2 |
| | Grandmother | 2 | 3.1 |
| Caregivers' occupation | Yes | 22 | 34.4 |
| | No | 42 | 65.6 |
| Divorced family | Yes | 5 | 7.8 |
| | No | 59 | 92.2 |
| Medical & Health | Yes | 51 | 79.7 |
| | No | 13 | 20.3 |
| PF | Yes | 11 | 17.2 |
| | No | 53 | 82.8 |

Abbreviation: AML: acute myelocytic leukemia; WBC: white blood cell; HB: hemoglobin; PLT: platelet count; LR: low risk; IR: intermediate risk; HR: high risk; E/O: Emaciation/Overweight; PF: past medical history and family medical history.

**Table 2**
Scores, reliability, and prognostic impact of HRQoL impairment on prognosis in PedsQL™ child/proxy groups.

| HRQoL Scales | N | Scores | | | Reliability | | OS | |
|---|---|---|---|---|---|---|---|---|
| | | Mean values (SD) | MINI | MAX | Cronbach's alpha | ICC | $x^2$ | *P* |
| **PedsQL™ 4.0** | | | | | | | | |
| ***Child self-report*** | | | | | 0.92 | 0.82 | | |
| Total score | 40 | 81.84 (19.29) | 2.27 | 100.00 | | | 0.732 | 0.392 |
| Physical functioning | 40 | 80.23 (23.63) | 0.00 | 100.00 | | | 0.732 | 0.392 |
| Emotional functioning | 40 | 80.25 (22.39) | 0.00 | 100.00 | | | 1.383 | 0.240 |
| Social functioning | 40 | 87.75 (20.94) | 0.00 | 100.00 | | | 0.316 | 0.574 |
| School functioning | 40 | 79.38 (22.48) | 10.00 | 100.00 | | | 1.127 | 0.288 |
| ***Parent proxy report*** | | | | | 0.87 | | | |
| Total score | 57 | 76.14 (17.13) | 9.78 | 100.00 | | | **6.339** | **0.012** |
| Physical functioning | 57 | 75.11 (21.36) | 6.25 | 100.00 | | | 1.949 | 0.163 |
| Emotional functioning | 57 | 75.48 (21.17) | 5.00 | 100.00 | | | 1.526 | 0.217 |
| Social functioning | 57 | 82.30 (19.02) | 10.00 | 100.00 | | | 2.651 | 0.103 |
| School functioning | 52 | 72.75 (21.66) | 20.00 | 100.00 | | | **3.943** | **0.047** |
| **CM 3.0** | | | | | | | | |
| ***Child self-report*** | | | | | 0.87 | 0.80 | | |
| Total score | 41 | 73.03 (18.58) | 31.48 | 100.00 | | | | |
| Pain and hurt | 41 | 81.10 (23.07) | 25.00 | 100.00 | | | | |
| Nausea | 41 | 70.31 (23.43) | 20.00 | 100.00 | | | | |
| Procedural anxiety | 41 | 64.84 (32.19) | 0.00 | 100.00 | | | | |
| Treatment anxiety | 41 | 67.89 (29.61) | 0.00 | 100.00 | | | | |
| Worry | 41 | 67.48 (30.61) | 0.00 | 100.00 | | | | |
| Cognitive problems | 41 | 75.31 (23.10) | 10.00 | 100.00 | | | | |
| Perceived physical appearance | 41 | 80.49 (21.78) | 33.33 | 100.00 | | | | |
| Communication | 41 | 81.71 (20.85) | 50.00 | 100.00 | | | | |
| ***Parent proxy report*** | | | | | 0.88 | | | |
| Total score | 57 | 66.67 (18.75) | 22.83 | 100.00 | | | | |
| Pain and hurt | 55 | 82.27 (18.43) | 37.50 | 100.00 | | | | |
| Nausea | 55 | 64.70 (24.75) | 0 | 100.00 | | | | |
| Procedural anxiety | 56 | 45.39 (30.36) | 0 | 100.00 | | | | |
| Treatment anxiety | 56 | 64.14 (28.95) | 0 | 100.00 | | | | |
| Worry | 56 | 56.84 (35.22) | 0 | 100.00 | | | | |
| Cognitive problems | 56 | 68.22 (26.83) | 0 | 100.00 | | | | |
| Perceived physical appearance | 56 | 76.93 (21.84) | 25.00 | 100.00 | | | | |
| Communication | 56 | 77.83 (22.60) | 16.67 | 100.00 | | | | |
| **FIM 2.0** | | | | | 0.92 | | | |
| Total score | 64 | 64.76 (18.05) | 18.24 | 100.00 | | | 0.847 | 0.357 |
| Parent HRQoL summary | 64 | 65.27 (22.97) | 16.25 | 100.00 | | | 2.377 | 0.123 |
| Physical functioning | 64 | 69.79 (25.50) | 0 | 100.00 | | | 0.653 | 0.419 |
| Emotional functioning | 64 | 63.01 (26.82) | 0 | 100 | | | 0.643 | 0.423 |
| Social functioning | 64 | 66.92 (26.98) | 0 | 100.00 | | | 0 | 0.990 |
| Cognitive functioning | 64 | 65.31 (23.07) | 20.00 | 100.00 | | | 0.404 | 0.525 |
| Communication | 63 | 74.34 (22.86) | 16.67 | 100.00 | | | 0.171 | 0.679 |
| Worry | 64 | 43.98 (26.58) | 0 | 100.00 | | | 0.447 | 0.504 |
| Family summary | 64 | 67.99 (22.11) | 4.69 | 100.00 | | | 1.425 | 0.233 |
| Daily activities | 64 | 54.88 (31.36) | 0 | 100.00 | | | **8.327** | **0.004** |
| Family relationships | 64 | 75.86 (24.42) | 0 | 100.00 | | | 0.095 | 0.728 |

Abbreviation: HRQoL: Health-related Quality of Life; PedsQL™: pediatric quality of life inventory™; CM: cancer module; FIM: family impact module; SD: Standard Deviation; ICC: intraclass correlation coefficient; OS: Overall survival.

reliability was demonstrated with Cronbach's alpha for all scales above the acceptable level of 0.87 (range: 0.87–0.92). As Table 2 shows, there was also a substantial concordance between the children's summary scores and the parent proxy report scores for the two measures (ICC for PedsQL™ 4.0 is 0.82, ICC for CM 3.0 is 0.80).

### *3.4. Correlation analysis of HRQoL scores*

One-way analysis of variance (One-ANOVA) was used to analyze factors affecting quality of life. As shown in Table 3, the total scale score of PedsQL™ 4.0 child self-report was related to only child ($p = 0.040$) and caregivers' occupation ($p = 0.026$). Moreover, the total scale score of PedsQL™ 4.0 parent-proxy report scores was related to disease severity ($p = 0.041$), only child ($p = 0.042$), and Medical & Health ($p = 0.034$). For the CM 3.0, divorced family was correlated with children's self-report scores ($p = 0.036$), while age ($p = 0.035$) and HB ($p = 0.046$) were correlated with parent proxy report scores. The total scale score of FIM 2.0 demonstrates a connection with caregivers' occupation ($p = 0.048$) and PF (past medical history and family medical history) ($p = 0.013$). Multiple linear regression analyses were conducted to examine the associations between HRQoL and score. The correlation between variables and scale scores is shown in Table 4. The only child was positively correlated with PedsQL™ 4.0 parent proxy report score ($\beta = 0.29$, $p = 0.025$). For the CM 3.0, divorced families were negatively correlated with children's self-report scores ($\beta = -0.31$, $p = 0.045$), while

**Table 3**
Factors associated with summary score.

| Variable | | PedsQL™4.0 | | | | | | CM 3.0 | | | | | | FIM 2.0 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Child self-report | | | Parent proxy report | | | Child self-report | | | Parent proxy report | | | | | |
| | | N | Mean ± SD | *P* | N | Mean ± SD | *P* | N | Mean ± SD | *P* | N | Mean ± SD | *P* | N | Mean ± SD | *P* |
| Child age | <7 | 8 | 79.30 ± 19.11 | 0.683 | 24 | 75.91 ± 16.31 | 0.913 | 11 | 67.06 ± 22.09 | 0.217 | 24 | 60.14 ± 18.81 | **0.035** | 31 | 64.82 ± 21.02 | 0.793 |
| | ≥7 | 32 | 82.47 ± 17.58 | | 33 | 76.43 ± 18.44 | | 30 | 75.22 ± 17.00 | | 33 | 70.78 ± 18.06 | | 33 | 63.62 ± 15.14 | |
| Child gender | Male | 20 | 84.25 ± 14.16 | 0.436 | 27 | 78.03 ± 13.57 | 0.450 | 21 | 76.46 ± 18.52 | 0.230 | 27 | 70.60 ± 17.46 | 0.106 | 32 | 61.65 ± 15.60 | 0.263 |
| | Female | 20 | 79.42 ± 23.47 | | 30 | 74.58 ± 20.38 | | 20 | 69.43 ± 18.40 | | 30 | 62 . 44 ± 19.72 | | 32 | 66.75 ± 20.20 | |
| Disease typing | Non-M3 | 28 | 82.15 ± 20.43 | 0.849 | 41 | 78.49 ± 18.95 | 0.623 | 28 | 72.65 ± 18.33 | 0.849 | 41 | 64.86 ± 18.95 | 0.362 | 16 | 62.38 ± 18.64 | 0.646 |
| | M3 | 12 | 80.90 ± 16.42 | | 16 | 78.05 ± 13.05 | | 13 | 73.86 ± 19.82 | | 16 | 70.01 ± 19.11 | | 48 | 64.80 ± 18.06 | |
| Disease severity | LR/IR | 25 | 83.44 ± 15.97 | 0.486 | 36 | 79.79 ± 23.00 | **0.041** | 25 | 72.90 ± 18.72 | 0.956 | 36 | 67.24 ± 18.57 | 0.630 | 41 | 62.34 ± 18.45 | 0.277 |
| | HR | 16 | 79.12 ± 23.41 | | 21 | 70.07 ± 22.17 | | 16 | 73.23 ± 18.96 | | 21 | 64.70 ± 20.00 | | 23 | 67.50 ± 17.34 | |
| Body type | E/O | 8 | 82.83 ± 18.67 | 0.874 | 12 | 72.10 ± 20.53 | 0.362 | 9 | 63.78 ± 23.48 | 0.091 | 12 | 63.16 ± 22.62 | 0.524 | 14 | 59.12 ± 15.29 | 0.237 |
| | Normal | 32 | 81.59 ± 19.93 | | 45 | 77.31 ± 16.59 | | 32 | 75.63 ± 16.46 | | 45 | 67.14 ± 18.07 | | 50 | 65.62 ± 18.69 | |
| Only child | Yes | 21 | 75.94 ± 20.19 | **0.040** | 29 | 71.62 ± 16.69 | **0.042** | 20 | 71.37 ± 18.18 | 0.584 | 29 | 63.75 ± 17.64 | 0.305 | 34 | 62.81 ± 18.51 | 0.519 |
| | No | 19 | 88.36 ± 16.37 | | 28 | 80.97 ± 17.16 | | 21 | 74.61 ± 19.25 | | 28 | 68.95 ± 20.24 | | 30 | 65.77 ± 17.78 | |
| Residence | City | 21 | 77.42 ± 23.34 | 0.129 | 31 | 74.62 ± 17.90 | 0.456 | 21 | 70.35 ± 19.70 | 0.350 | 31 | 65.31 ± 18.88 | 0.671 | 36 | 62.75 ± 17.66 | 0.471 |
| | Village | 19 | 86.73 ± 12.35 | | 26 | 78.11 ± 16.98 | | 20 | 75.85 ± 17.38 | | 26 | 67.49 ± 19.39 | | 28 | 66.06 ± 18.78 | |
| WBC(10^9/L) | <50 | 28 | 83.27 ± 15.13 | 0.481 | 43 | 76.56 ± 15.29 | 0.795 | 32 | 74.39 ± 16.46 | 0.385 | 43 | 67.22 ± 18.66 | 0.527 | 16 | 63.16 ± 18.54 | 0.793 |
| | ≥50 | 12 | 78.50 ± 27.20 | | 14 | 75.15 ± 24.37 | | 9 | 68.21 ± 25.33 | | 14 | 63.49 ± 20.34 | | 48 | 64.55 ± 18.13 | |
| HB(g/L) | <90 | 27 | 83.03 ± 21.25 | 0.557 | 35 | 78.70 ± 18.30 | 0.176 | 25 | 74.07 ± 20.15 | 0.642 | 35 | 70.26 ± 18.87 | **0.046** | 36 | 67.22 ± 17.01 | 0.131 |
| | ≥90 | 13 | 79.36 ± 14.85 | | 22 | 72.25 ± 15.51 | | 16 | 71.22 ± 15.98 | | 22 | 60.01 ± 17.76 | | 28 | 60.32 ± 18.99 | |
| PLT(10^9/L) | <30 | 17 | 78.93 ± 24.95 | 0.420 | 21 | 76.30 ± 20.63 | 0.977 | 16 | 72.23 ± 22.12 | 0.828 | 21 | 67.94 ± 21.41 | 0.623 | 22 | 61.30 ± 19.03 | 0.357 |
| | ≥30 | 23 | 83.99 ± 13.98 | | 36 | 76.16 ± 15.57 | | 25 | 73.54 ± 16.39 | | 36 | 65.35 ± 17.64 | | 42 | 65.72 ± 17.62 | |
| Caregivers' occupation | Yes | 14 | 72.70 ± 24.24 | **0.026** | 18 | 70.95 ± 22.30 | 0.122 | 14 | 70.52 ± 19.44 | 0.541 | 18 | 64.80 ± 20.13 | 0.689 | 22 | 58.03 ± 18.09 | **0.048** |
| | No | 26 | 86.76 ± 14.06 | | 39 | 78.64 ± 14.34 | | 27 | 74.33 ± 18.35 | | 39 | 66.99 ± 18.64 | | 42 | 67.43 ± 17.44 | |
| Divorced family | Yes | 3 | 85.01 ± 3.84 | 0.772 | 5 | 71.73 ± 26.43 | 0.552 | 3 | 94.44 ± 7.44 | **0.036** | 5 | 70.11 ± 30.01 | 0.673 | 5 | 68.54 ± 19.85 | 0.581 |
| | No | 37 | 81.58 ± 20.03 | | 52 | 76.64 ± 16.62 | | 38 | 71.34 ± 18.17 | | 52 | 65.94 ± 17.97 | | 59 | 63.83 ± 18.07 | |
| Medical & Health | Yes | 35 | 82.19 ± 19.49 | 0.762 | 46 | 78.58 ± 16.50 | **0.034** | 35 | 72.84 ± 18.70 | 0.878 | 46 | 67.21 ± 18.18 | 0.464 | 51 | 62.89 ± 16.52 | 0.263 |
| | No | 5 | 79.34 ± 19.73 | | 11 | 66.30 ± 18.46 | | 6 | 74.13 ± 19.79 | | 11 | 62.50 ± 22.53 | | 13 | 69.49 ± 22.08 | |
| PF | Yes | 8 | 77.62 ± 13.14 | 0.496 | 10 | 75.01 ± 7.97 | 0.813 | 8 | 75.24 ± 16.64 | 0.713 | 10 | 62.92 ± 21.79 | 0.540 | 11 | 52.08 ± 11.17 | **0.013** |
| | No | 32 | 82.89 ± 20.58 | | 47 | 76.47 ± 18.89 | | 33 | 72.49 ± 19.21 | | 47 | 67.02 ± 18.50 | | 53 | 66.71 ± 18.30 | |

Value in bold indicate significant P value.
Abbreviation: HRQoL: Health-related Quality of Life; PedsQL™: pediatric quality of life inventory™; CM: cancer module; FIM: family impact module; LR: low risk; IR: intermediate risk; HR: high risk; E/O, Emaciation/Overweight; WBC: white blood cell; HB: hemoglobin; PLT: platelet count; SD: standard deviation; PF: past medical history and family medical history.
$P \leq 0.05$: significant.
$P \leq 0.01$: highly significant.

age was positively correlated with parent proxy report scores (β = 0.27, $p = 0.040$). In the family influence module model, PF is a favorable factor (β = 0.29, $p = 0.025$).

### 3.5. Correlation analysis of HRQoL impairment

The cutoff values for each dimension are shown in Table 1 of the supplementary material. As shown in Table 5, within PedsQL™ 4.0 child self-report, the impairment of the total scale score was related to residence ($p = 0.046$). Furthermore, impaired physical function demonstrated connections with both residence ($p = 0.046$) and caregivers' occupation ($p = 0.014$). Emotional functioning ($p = 0.043$) and school functioning ($p = 0.029$) were found to be linked with caregivers' occupation, while impaired social functioning was solely associated with residence. In contrast, within PedsQL™ 4.0 parent-proxy report, disease severity ($p = 0.024$) was identified as a factor influencing physical function. Additionally, being the only child was found to impact emotional ($p = 0.038$) and social function ($p = 0.029$).

The findings in Table 6 reveal significant associations. Impaired social functioning demonstrates a connection with PF ($p = 0.040$), indicating its pivotal role in this dimension. Moreover, caregivers' occupation exhibits notable relationships, influencing cognitive functioning ($p = 0.033$), worry ($p = 0.005$), and family relationship ($p = 0.037$) dimensions. Additionally, the impairment of family relationship is linked to the domain of Medical & Health ($p = 0.023$).

### 3.6. Prognosis analyses

Among these patients, there were 9 deaths (14.7 %) and 7 relapses (11.5 %) to follow-up cases were recorded. As Table 3 shows, in PedsQL™ 4.0 parent proxy-report, the total score was an independent prognostic variable for AML ($p = 0.010$, Fig. 1A), and school functioning score also had a negative impact on prognosis ($p = 0.050$, Fig. 1B). Additionally, impaired daily activities, as indicated in FIM 2.0, exhibited a negatively impact on prognosis ($p = 0.005$, Fig. 1C).

In addition, as shown in Table 7, the inclusion of patient disease typing, disease risk, and efficacy of induction therapy in multivariate analyses showed that total score reported by PedsQL™ 4.0 parental proxy ($p = 0.020$) and daily activity on FIM 2.0 ($p = 0.026$) emerged as independent prognostic variables for acute myeloid leukemia, highlighting their importance in predicting prognosis. The scores of the other dimensions were not significantly correlated with patients' prognosis.

## 4. Discussion

Many studies emphasize that patients with AML experience a significant deterioration in their quality of life primarily after diagnosis and during treatment [5,18,19]. Most studies have focused on the impact of treatment on the quality of life of children or adults with the disease, however, limited research has been conducted on the factors affecting HRQoL of children after completing treatment. In addition to focusing on treatment-related factors, our study aimed to investigate whether impaired quality of life predicted long-term survival outcomes in children with AML.

Survival rates for AML are rising, yet costly novel treatments, prolonged therapy durations, specialist consultations, and centralized care contribute to high healthcare expenses [20]. Financial strain is known to diminish quality of life [21,22], particularly affecting hematological malignancy patients. In the United States, AML imposes a yearly burden exceeding $300,000 per patient on commercial insurers [23]. In China, health insurance significantly eases this burden for about 70 % of patients. Our study shows that insured patients report higher HRQoL scores than those paying out-of-pocket. Additionally, urban/rural residence affects HRQoL, reflecting economic impact. Reduced financial stress correlates with better quality of life. Ensuring comprehensive medical coverage and minimizing out-of-pocket expenses can improve the well-being of children with AML.

Previous studies have highlighted the importance of family-related variables to quality of life [24–26], and this holds true for

**Table 4**
Multiple regression analyses examining the effects of variables on HRQoL.

| Dependent Variable and Predictors | | | B | SE B | β | t | F | $R^2$ |
|---|---|---|---|---|---|---|---|---|
| PedsQL™4.0 | Child self-report | Only child | 6.64 | 5.75 | 0.19 | 1.16 | 2.09 | 0.16 |
| | | Caregivers' occupation | −3.35 | 6.84 | −0.09 | −0.49 | | |
| | Parent proxy report | Disease severity | −7.16 | 4.44 | −0.20 | −1.61 | 5.43 | 0.23 |
| | | Only child | 10.49 | 4.40 | **0.30**** | **2.38**** | | |
| | | Medical & Health | −15.40 | 5.41 | **−0.35***** | **−2.84***** | | |
| CM 3.0 | Child self-report | Divorced family | −16.26 | 8.00 | **−0.31**** | **−2.03**** | 4.78 | 0.22 |
| | | Chronic history | −20.81 | 10.02 | **−0.32**** | **−2.08**** | | |
| | Parent proxy report | Child age | 10.27 | 4.87 | **0.27**** | **2.11**** | 4.86 | 0.23 |
| | | HB | −6.08 | 5.23 | −0.16 | −1.16 | | |
| FIM 2.0 | | Caregivers' occupation | 4.70 | 5.34 | 0.12 | 0.88 | 4.17 | 0.17 |
| | | PF | 13.71 | 5.61 | **0.29**** | **2.45**** | | |

Abbreviation: HRQoL: Health-related Quality of Life; PedsQL™: pediatric quality of life inventory™; CM: cancer module; FIM: family impact module; HB: hemoglobin; PF: past medical history and family medical history.
Note. Italicized variables are dependent variables.
*$P < 0.10$, **$P < 0.05$, ***$P < 0.01$, ****$P < 0.001$.

**Table 5**
Factors associated with HRQoL impairment in PedsQL™ 4.0

| | Child self-report | | | | | Parent-proxy report | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Total score | Physical functioning | Emotional functioning | Social functioning | School functioning | Total score | Physical functioning | Emotional functioning | Social functioning | School functioning |
| Child age | 0.320 | 0.320 | 0.211 | 0.257 | 0.660 | 0.847 | 0.118 | 0.885 | 0.577 | 0.486 |
| Child gender | 1 | 0.695 | 0.301 | 1 | 0.723 | 0.506 | 0.369 | 0.752 | 0.697 | 0.752 |
| Disease typing | 0.211 | 0.677 | 1 | 0.627 | 0.704 | 0.517 | 0.735 | 0.555 | 0.735 | 0.477 |
| Disease severity | 0.439 | 0.439 | 0.121 | 0.373 | 0.247 | 0.358 | **0.024**** | 0.614 | 0.070* | 0.103 |
| Body type | 0.650 | 1 | **0.039**** | 0.257 | 0.182 | 0.713 | 0.144 | 0.750 | 0.463 | 0.361 |
| Only child | 1 | 1 | 0.301 | 1 | 0.480 | 0.410 | 0.589 | **0.038**** | **0.029**** | 0.325 |
| Residence | **0.046**** | **0.046**** | 0.736 | **0.049**** | 0.873 | 0.266 | 0.392 | 0.958 | 0.217 | 0.572 |
| WBC (10^9/L) | 1 | 1 | 1 | 1 | 0.696 | 0.358 | 0.728 | 0.799 | 0.728 | 0.313 |
| HB (g/L) | 0.400 | 1 | 0.122 | 1 | 0.281 | 0.626 | 0.799 | 0.776 | 0.356 | 0.161 |
| PLT (10^9/L) | 0.702 | 1 | 1 | 0.634 | 0.730 | 0.358 | 0.591 | 0.614 | 0.920 | 0.235 |
| Caregivers' occupation | 0.102 | **0.014**** | **0.043**** | 0.322 | **0.029**** | 0.753 | 0.702 | 0.975 | 1 | 0.230 |
| Divorced family | 1 | 1 | 0.944 | 0.338 | 0.178 | 1 | 1 | 1 | 0.089* | 1 |
| Medical & Health | 0.257 | 0.257 | 0.627 | 1 | 0.117 | 0.136 | 0.115 | 0.603 | 0.436 | 0.226 |
| PF | 0.650 | 0.650 | 0.677 | 1 | 0.660 | 0.420 | 0.427 | 0.286 | 1 | 0.075* |

Abbreviation: HRQoL: Health-related Quality of Life; PedsQL™: pediatric quality of life inventory™; WBC: white blood cell; HB: hemoglobin; PLT: platelet count; PF: past medical history and family medical history.
*$P < 0.10$, **$P < 0.05$, ***$P < 0.01$, ****$P < 0.001$.

**Table 6**
Factors associated with HRQoL impairment in FIM 2.0

| | Total score | Parent HRQoL summary | Physical functioning | Emotional functioning | Social functioning | Cognitive functioning | Communi -cation | Worry | Family summary | Daily activities | Family relationships |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Child age | 0.250 | 0.914 | 0.667 | 0.531 | 0.078* | 0.078* | 0.492 | 0.942 | 0.468 | 0.504 | 0.656 |
| Child gender | 1 | 0.082* | 1 | 1 | 0.474 | 0.315 | 1 | 0.193 | 0.708 | 0.302 | 0.509 |
| Disease typing | 1 | 1 | 1 | 0.490 | 0.689 | 0.124 | 1 | 0.513 | 0.670 | 0.267 | 0.463 |
| Disease severity | 0.406 | 1 | 0.150 | 0.742 | 0.140 | 0.073* | 1 | 0.690 | 0.443 | 1 | 1 |
| Body type | 0.171 | 1 | 1 | 0.438 | 0.397 | 0.414 | 1 | 0.546 | 0.062* | 0.677 | 0.052* |
| Only child | 0.109 | 0.313 | 1 | 0.351 | 0.723 | 0.423 | 0.460 | 0.525 | 1 | 0.738 | 0.322 |
| Residence | 0.454 | 0.090* | 1 | 0.628 | 0.278 | 0.728 | 0.444 | 0.974 | 1 | 1 | 0.900 |
| WBC (10^9/L) | 0.353 | 0.701 | 1 | 0.139 | 0.097* | 0.111 | 1 | 0.880 | 0.401 | 0.252 | 1 |
| HB (g/L) | 0.225 | 0.312 | 0.646 | 0.108 | 0.163 | 0.094* | 0.444 | 0.309 | 0.124 | 0.090* | 0.188 |
| PLT (10^9/L) | 0.220 | 0.144 | 0.329 | 1 | 0.254 | 0.609 | 1 | 0.959 | 0.704 | 0.726 | 1 |
| Caregivers' occupation | 1 | 0.257 | 0.652 | 1 | 1 | **0.033**** | 1 | **0.005***** | 0.111 | 0.080 | **0.037**** |
| Divorced family | 1 | 0.118 | 1 | 1 | 1 | 1 | 1 | 0.341 | 0.499 | 1 | 1 |
| Medical & Health | 0.623 | 0.192 | 0.266 | 0.243 | 1 | 0.188 | 0.206 | 0.390 | 0.343 | 0.411 | **0.023**** |
| PF | 0.091* | 1 | 0.201 | 0.196 | **0.040**** | 0.992 | 1 | 1 | 0.617 | 0.356 | 0.384 |

Abbreviation: HRQoL: Health-related Quality of Life; FIM: family impact module; WBC: white blood cell; HB: hemoglobin; PLT: platelet count; PF: past medical history and family medical history.
*$P < 0.10$, **$P < 0.05$, ***$P < 0.01$, ****$P < 0.001$.

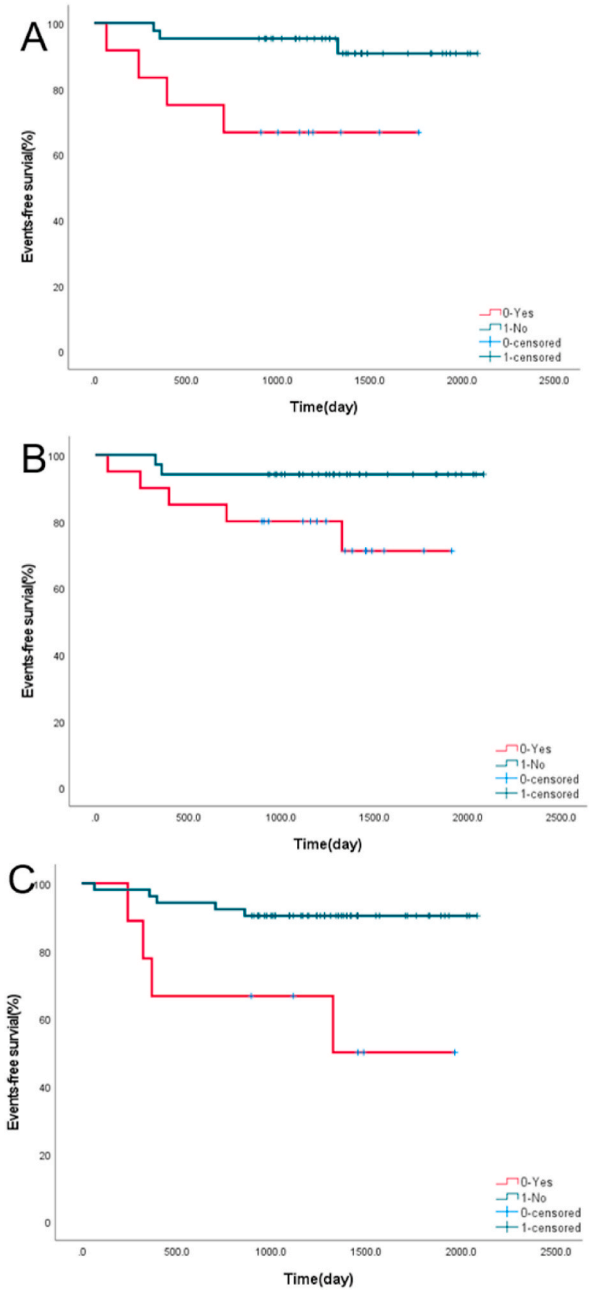


**Fig. 1.** Kaplan-Meier Survival Curves by PedsQL™ score. A Patients with high PedsQL™ 4.0 parent proxy-report total scores survived significantly better than those with low scores ($p = 0.010$). **B** Patients with high School functioning scores in PedsQL™ 4.0 parent proxy-report survived significantly better than those with low scores ($p = 0.050$). **C** Patients with high Daily activities scores in FIM 2.0 survived significantly better than those with low scores ($p = 0.005$).
Abbreviation: HRQoL: Health-related Quality of Life; PedsQL™: pediatric quality of life inventory™; FIM: family impact module.

patients with AML. AML not only threatens lives but also disrupts family dynamics, impacting patients and their caregivers [27,28]. However, our study revealed that families with a history of leukemia experienced a higher quality of life, possibly due to enhanced psychological resilience. Children from dysfunctional families tend to have compromised HRQoL, particularly in social and emotional domains [24]. Divorce was significantly associated with lower survival rates in adults with AML [19], and its impact on children is substantial [29]. The family environment significantly impacts a child's growth, and divorce represents a life event with a high level of stress for the entire family. Our data of CM 3.0 children self-report revealed that parental divorce correlated with reduced quality of life. Physicians evaluating children with AML can pay attention to signs of parental separation issues, and referral to professionals specializing in separation-related matters may be beneficial for conflicting parents [30].

**Table 7**
Multiple regression analysis of the effect of impaired HRQoL on survival prognosis.

| | B | SE | Ward | P | Exp(B) |
|---|---|---|---|---|---|
| Disease severity | −0.066 | 0.897 | 0.005 | 0.942 | 0.936 |
| Induction therapy efficacy | −0.175 | 0.880 | 0.040 | 0.842 | 0.839 |
| Disease typing | −12.476 | 341.440 | 0.001 | 0.971 | 0 |
| the total score in PedsQL™ 4.0 parent proxy-report | 2.387 | 1.027 | 5.400 | 0.020 | 10.883 |
| school functioning in PedsQL™ 4.0 parent proxy-report | 0.237 | 0.936 | 0.064 | 0.800 | 1.268 |
| impaired daily activities in FIM2.0 | 2.349 | 1.054 | 4.966 | 0.026 | 10.475 |

Abbreviation: PedsQL™: pediatric quality of life inventory™; FIM: family impact module.

Our research indicated that a caregiver's full-time care significantly influenced a child's physical, psychological, and academic functioning. Additionally, having only one child correlated with higher quality of life scores and less impairment in emotional and social functioning. This finding aligns with research on acute lymphoblastic leukemia (ALL), where larger families are associated with impaired emotional and social functioning [31]. Older children were perceived by parents to have better HRQoL and less program anxiety, while children themselves noted age primarily influenced pain and physical appearance. This is consistent with Cheng et al.'s findings [32].Lee et al. also highlighted the increased risk of mental illnesses in pediatric cancer patients [33]. Though challenging to address directly, family-based psychosocial interventions and age-appropriate support can improve HRQoL outcomes for these children and their families [34,35].

Our study findings indicated that higher PedsQL™ 4.0 parent proxy-report scores and daily activity in FIM 2.0 might predict longer survival in children with AML, consistent with previous research [36]. Simultaneously, our investigation found that impaired school functioning negatively impacted prognosis. Given the potential impact of treatment modalities on the integration of daily life, returning to school after a cancer diagnosis may raise concerns of social stigmatization and lead to decreased self-esteem in the learning environment [37]. Encouraging children with cancer to develop supportive relationships with peers and teachers may promote improved functioning in school.

It is paramount to note that our study relied on parent-proxy assessments due to the young age of approximately 50 % of the participants aged below 7 years, preventing autonomous self-reporting. Intriguingly, we found significant correlations between parents' and children's perspectives. Parents' expectations and perceptions of their child's pain not only influence the child's pain experience but also affect their psychosocial functioning, potentially impacting long-term prognosis [38]. Moreover, our findings from FIM 2.0 revealed that 46.9 % of caregivers of AML patients experienced compromised quality of life, surpassing the 26.3 % reported by their children. This suggests that AML has a greater impact on parental well-being, possibly due to various factors such as age, social status, and personal experiences. This underscores the importance of prioritizing parental well-being, which could lead to improved quality of life for both patients and their families.

Some limitations of the study should be addressed. Firstly, our research was conducted at a single-site academic center with a relatively small sample size. Therefore, replication of our findings with larger and more diverse samples is necessary to strengthen the generalizability of the results. Secondly, this study focused on 5-year survival, and more events such as recurrence rates and event-free survival can be included in future studies. The study included a small number of relapse cases in the sample, resulting in limited depth of analysis due to potential statistical variability. Finally, specific treatments such as hematopoietic stem cell transplantation (HSCT) can have a significant impact on 5-year survival. Future research should take these limitations into account. However, this study still gives us a valuable insight into some of the influencing factors that are important regarding HRQoL for those with AML.

## 5. Conclusion

Our research underscores the substantial impact of age, financial constraints, and family circumstances on the HRQoL of pediatric AML patients. Moreover, we have established that HRQoL is not only a reflection of the patient's well-being but also a crucial factor in predicting the 5-year survival of children with AML. The early impairment in the quality of life serves as a predictor for long-term outcomes in children with AML. This work provides a foundation from which additional research can continue to identify specific demographic measures such as financial and familial status of caregivers, readily obtainable during interviews. These factors could potentially improve our predictive capabilities and facilitate timely interventions.

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## Data availability statement

The datasets generated and/or analyzed during the current study are not publicly available to preserve the privacy of the

participants but are available from the corresponding author on reasonable request.

## Ethics approval and consent to participate

The research protocol followed the Declaration of Helsinki and was approved by the Medical Ethics Committee of Children's Hospital of Nanjing Medical University (the ethical approval referenced number: 201806179-1). All study participants have obtained written informed consent from their parents (or legal guardians) at the time of enrollment in this study and have signed to authorize us to use all of their data.

## Consent for publication

Not applicable.

## CRediT authorship contribution statement

**Tianhao Wu:** Writing – original draft, Formal analysis, Data curation, Conceptualization. **Wenfeng Fu:** Investigation, Formal analysis, Data curation, Conceptualization. **Yao Xue:** Writing – review & editing, Writing – original draft, Conceptualization. **Liwen Zhu:** Writing – original draft, Validation, Data curation. **Xiaopeng Ma:** Visualization, Validation, Funding acquisition, Formal analysis. **Yuting Wei:** Writing – original draft, Visualization. **Huimin Li:** Visualization, Validation. **Yaping Wang:** Software, Resources. **Meiyun Kang:** Investigation, Funding acquisition. **Yongjun Fang:** Writing – review & editing, Visualization, Validation, Resources. **Heng Zhang:** Writing – review & editing, Resources, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Abbreviations

| | |
|---|---|
| AML: | acute myelocytic leukemia |
| HRQoL: | Health-related Quality of Life |
| PedsQL™ | pediatric quality of life inventory™ |
| CM | cancer module |
| FIM 2.0 | family impact module 2.0 |
| SPSS | Statistical Package for Social Science |
| WBC | white blood cell |
| HB | hemoglobin; PLT: platelet count |
| ICU | Intensive Care Unit |
| SD | Standard Deviation |
| ICC | intraclass correlation coefficient |
| LR | low risk |
| IR | intermediate risk |
| HR | high risk |
| E/O | Emaciation/Overweight |
| PF | past medical history and family medical history |

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e31948.

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