Factors associated with a prolonged hospital stay during induction chemotherapy in newly diagnosed high risk pediatric acute lymphoblastic leukemia

Short title: Prolonged length of stay in pediatric leukemia

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Highlights:

- High risk ALL patients experience significant adverse events during induction
- Factors predictive of prolonged hospital stay during induction were identified
- Outpatient management of new ALL patients is often not feasible or safe
- An aggressive and close outpatient follow up of these patients is indicated

Abstract

Background:

High Risk (HR) or Very High Risk (VHR) acute lymphoblastic leukemia (ALL) treated with 4 drug induction chemotherapy is often associated with adverse events. The aim of this study was to identify risk factors associated with a prolonged inpatient length of stay LOS during induction chemotherapy.

Procedure:

Data from patients (N=73) (age<21 years) was collected through a retrospective chart review. Univariable and multivariable logistic regression was used to test for statistical significance. The overall survival and disease (leukemia)-free survival were analyzed

using the Kaplan–Meier method and log-rank test.

Results:

Of the 73 patients, 42 (57%) patients were discharged on day 4 of induction (short LOS, group A), while 31 (43%) patients (group B) experienced a prolonged LOS or an ICU stay (16 ± 27.7 days, median hospital stay=8 days vs 4 days (group A), p=0.02) due to organ dysfunction, infectious or metabolic complications. Group B patients were more likely to have a lower platelet count, serum bicarbonate, and a higher blood urea nitrogen (BUN) on day 4 of treatment (OR=4.52, 8.21, and 3.02, respectively, p<0.05). Multivariable analysis identified low serum bicarbonate (p=0.002) and a platelet count<20,000/µL (p=0.02) on day 4 of induction to be predictive of a prolonged LOS. Twenty six (group A (n=16, 36%) and B (n=11, 35%), p =0.8) patients experienced unplanned admissions, within 30 days of discharge.

Conclusions:

A significant proportion of newly diagnosed HR or VHR pediatric ALL patients experience a prolonged LOS and unplanned re-admissions. Aggressive discharge planning and close follow up is indicated in this cohort of patients.

Abbreviations used:

WBC	White Blood Cell
ANC	Absolute Neutrophil Count
BUN	Blood Urea Nitrogen

AST	Aspartate Aminotransferase
AST	Alanine Aminotransferase
PT	Prothrombin Time
INR	International Normalized Ratio
OS	Overall Survival
LFS	Leukemia-Free Survival
ESR	Erythrocyte sedimentation rate
AM	Ante meridiem (morning)
SVT	Supra ventricular tachycardia
APC	Absolute phagocytic count
HR	High-risk
VHR	Very high-risk
PICU	Pediatric intensive care unit
LOS	Hospital length-of-stay
OR	Odds-ratio
ALL	Acute lymphoblastic leukemia

T-ALL	T- Acute lymphoblastic leukemia
B-ALL	B-Acute lymphoblastic leukemia
MRD	Minimal residual disease
NCI	National Cancer Institute
COG	Childrens Oncology Group
AML	Acute myeloid leukemia
MLL	Mixed lineage leukemia gene
PEG	Pegylated
iAMP21	Intra-chromosomal amplification of chromosome 21
ph+	Philadelphia chromosome positive
ph-like	Philadelphia chromosome like
NA	Not available
N/E	Not estimable
µL	Micro-litre
F/N	Febrile neutropenia
SIADH	Syndrome of inappropriate ADH secretion

SD	Standard deviation
C.I.	Confidence Interval

Keywords: leukemia; pediatric; length-of-stay

Introduction

Induction chemotherapy results in high remission rate in high risk (HR) and very high risk (VHR) childhood acute lymphoblastic leukemia (ALL), but is associated with significant morbidity.[1,2] HR B-ALL is defined as: white blood cell count (WBC) ≥50,000/μL or age ≥10 years (National Cancer Institute (NCI) criteria) at presentation, or/and central nervous system (CNS) positive leukemia, or testicular leukemia[3-5]. Patients who are >13 years or experience induction failures; and/or if the leukemia blasts harbor mixed-lineage leukemia gene (MLL) rearrangements or intrachromosomal amplification of chromosome 21 (iAMP21), *BCR-ABL* translocation, are stratified as very high risk (VHR) B-ALL [3,6,7]. Pediatric and young adults with HR, VHR ALL, and T-lymphoblastic leukemia (T-ALL), are initially treated with a standard 4 drug induction regimen[2], aimed at achieving a MRD negativity by day 29[8]. Induction therapy is often associated with a high burden of care due to increased therapy-related adverse events that require pediatric intensive care unit (PICU) care or a prolonged inpatient length of stay (LOS) [9-12]. However, despite standard induction regimens, there is a high variability amongst institutions with regards to timing of discharge for patients who appear clinically well [13]. We conducted a retrospective, single institutional study with the objective to identify risk factors that are associated with a complicated or prolonged LOS during induction chemotherapy for pediatric patients (age <21 years) with HR and VHR ALL, and to analyze the impact of prolonged length of stay (LOS), on unplanned re-admission rates and long term outcomes, in newly diagnosed patients with HR or VHR ALL. Our hypothesis was that patients who have shorter LOS have, less frequent or severe lab abnormalities, and are less likely to have an unplanned admission during induction therapy and a superior survival. Conversely, patients who experienced

prolonged LOS or PICU stay were more likely to have more severe cytopenias, increased severity or frequency of lab abnormalities and worse overall survival.

Materials & Methods

All patients diagnosed, in 2009-2016 with de novo HR or VHR ALL or T-ALL, and treated with a standard 4-drug induction [2] (Vincristine, dexamethasone or prednisone, PEG-asparaginase, and duanorubicin) at Riley Children's Hospital, Indiana University, Indianapolis, were included in this, institutional review board approved, retrospective study. Ph+ALL patients received tyrosine kinase inhibitors either in induction or in consolidation chemotherapy phase. Data was collected on 73 patients from day = 0 (one day prior to starting induction chemotherapy) through day = 4, by chart review, and included both clinical and lab values (normal ranges were established using institutional guidelines). Absolute neutrophil count (ANC) was calculated as 0.01 x (% bands +% neutrophils) x total leukocyte count [14]. An ANC was determined as 'rising' if the mean ANC on days 3 and 4 was higher than mean ANC on admission, days 1 and 2.

Statistical Analysis

Available demographic data was compared across groups using t-tests for continuous variables and Chi-Square tests for categorical variables. The patients who had readmission within 30 days of discharge were summed and averaged on the number of outpatient days and were compared between groups using the Wilcoxon Rank Sum test. Rising ANC was compared using the Chi-Square test. Univariable logistic analyses

were used to test the lab values on days 0-4 for group B admissions. Additionally, on day 4, variables with p-value<0.05 were considered for inclusion in multivariable stepwise logistic regression models. Variables with p-values<0.05 were considered significant and remained in the model. Step-wise multivariable was used due to small numbers of patients and making sure not to over parameterize the model.

Kaplan-Meier methods were used for overall survival (OS) and disease (leukemia)-free survival (LFS). Overall survival calculated the time from date of diagnosis until date of death. If a patient did not die, their values were censored and were calculated from the date of diagnosis until the last follow-up date. LFS was calculated as date of diagnosis until first relapse date. If a patient did not relapse, their values were censored and calculated as the time from date of diagnosis until the last follow-up date. Comparisons were made using the log-rank test. Cox proportional models were used to evaluate the significance of each lab value for OS and LFS from day 4 to determine if any variable was deemed significant.

Similar analyses were performed for a subset of lab values for patients on day 4 for patients who were admitted to or transferred to the PICU during their hospital stays and those patients who were not admitted to or transferred to the PICU.

SAS version 9.4 (SAS Institute, Cary, NC) was used for analysis.

Results

Data obtained from clinically well appearing patients, n=42 (group A), who had an initial short LOS (4±0 days, discharged after day 4 PEG-asparaginase), was compared to data from patients who had a LOS >4 days due to persistent fevers, or lab abnormalities, or admission to or transfer to the PICU (n=31, group B, Table 1). N=42 (57%) patients (group A) were discharged on day 4 of induction (short LOS), while n=31 (43%) patients (group B) experienced a prolonged LOS (median hospital stay=8 days vs 4 days (group A), P=0.02) or an ICU stay (n=13, (18%), (Table 1), due to organ dysfunction, infectious or metabolic complications. Only 2 patients (3%) died during induction chemotherapy. There were no differences in age, race, or ethnicity found between the two groups (Table 1). Fifteen (36%) of group A patients had adverse cytogenetics [15] (ph+ ALL =10, hypodipolid = 3, iAMP21 =2, compared to four (13%) in group B (ph+=3, hypodiploid =1) (Table 1, p=0.03). The higher number of ph+ patients (n=13) in our cohort could be due to higher median age and/or due to random variation. Eight patients were excluded as they received a 3 drug induction (n=6), had Downs Syndrome (N=1) ALL and Munchausen Syndrome (N=1). Three patients in each group had T-ALL and five from each group were transplanted at relapse. Social variables (other than race and ethnicity), such as distance from center, affecting LOS and physician level factors (e.g bias towards keeping patients for a shorter or longer LOS), were not studied in detail due to the retrospective nature of the study. While there were no significant differences in this small sample size, and low number of Black (total three, group A had one black patient and group B had two) and Asian (only one patient was Asian (groupB) patients, non-white patients appeared to be more likely to have a delayed discharge and to be admitted to the ICU based on effect size alone. In the

subset of patients on whom blood cultures were obtained, no positive blood cultures (0/22=0%) were detected during the initial 4 days of admission in group A, while 4/15 (27%) had positive cultures in group B (p=0.04, TABLE 1). Nineteen (45%) of group A patients had a rising ANC, while eleven (35%) of group B patients had a rising ANC by days 3 and 4 (p=0.4).

Group A had higher mean platelet counts ($x10^9$/L) on days 0 (day of admission) through day 4, higher mean hemoglobin levels on day 4, higher serum bicarbonate on day 4, and lower BUN on day 4, compared to group B (Figure 1). Group B patients had higher serum calcium on day 0 and lower serum phosphorus levels on day 1, compared to group A (Figure 1). Data is presented graphically only (Figure 1), however, no statistical analysis was performed on these raw values due to missing data points (Supplemental Table 2S). No difference in serum lactic dehydrogenase (LDH), liver chemistries (AST, ALT), PT, INR, serum albumin and bilirubin), d-dimer, erythrocyte sedimentation rate (ESR), absolute blast count, serum sodium and potassium (supplemental data not provided for review) or ANC (TABLE 2S) was detected between the two groups.

On univariable analysis, patients in group B had a higher incidence of fever≥38^0C on day 1 (p= 0.047), were more likely to have a pre-transfusion (AM) hemoglobin <8g/dL on days 2 and 3 (p=0.037 and 0.005, respectively), a lower serum bicarbonate values on days 2, 3 (p= 0.001, 0.039 respectively), an abnormal serum calcium on days 2 and 3 (p= 0.006 and 0.017 respectively), and an abnormal serum phosphate on day 3 (p=0.038)(TABLE 2). On day 4 of induction chemotherapy (discharge day for all group A patients), patients with a pre-transfusion platelet count<20,000 /µL (p=0.037), lower

serum bicarbonate (p=0.002), and a higher BUN (p=0.033) were more likely to have a prolonged LOS (OR=4.52, 8.21, and 3.02, respectively) (TABLE 2 and TABLE 3).

Multivariable stepwise logistic regression identified a low serum bicarbonate (p=0.002) and a platelet count<20,000/mm3 (p=0.021) on day 4 of admission to be predictive of a prolonged hospital stay (TABLE 3).

Data from patients who were admitted or transferred to the PICU (n=13) were compared to patients who experienced no PICU stay (n=60). This analysis yielded no significant difference in blood counts or laboratory values, LFS and OS between the two groups (supplemental data, TABLE S1).

Sixteen (36%) from group A were readmitted within 30 days of discharge for varied indications such as fever, neutropenia, hypotension, fatigue, dehydration, and SVT (TABLE 4). Six of these 16 patients were re-admitted to the PICU (15%). Eleven patients (35%) from group B were readmitted within 30 days of discharge (p=0.8, TABLE 1.), of which 3 (10%) were re-admitted to the PICU or transferred to the PICU during their re-admission. The sum of outpatient days eligible for readmission (after discharge) were lower in group B compared to group A, but this difference was not statistically different (group A had a sum of 170 days (mean±SD, 10.6± 8.3) and group B had a sum of 124 days (mean±SD of 11.3± (7.5), (p=0.8)). Furthermore, at day 35 of induction (arbitrary fixed time point), the proportion of “eligible for readmission” sum of days in readmitted patients versus patients who did not experience a readmission was also not different in the two groups (group A (170/780=0.22) and group B (107/450=0.24), (p=0.8)). LFS was significantly worse in group B compared to group A

(5 year LFS=58% (group B) vs 89% (group A), p=0.03) (Figure 2). No difference in the OS was observed in the two groups (5 year OS=67% (group B) vs 83% (group A), p=0.9) (Figure 3).

Discussion

Pediatric patients with newly diagnosed ALL often have a high symptom burden and significant morbidity during the initial (induction) phase of chemotherapy requiring a prolonged hospital stay [9,13].

Pediatric Oncologists are frequently faced with the challenge of assessing if a newly diagnosed HR/VHR ALL patient can be safely discharged home early in their hospital stay for induction chemotherapy (usually by day 4). Due to a lack of published data on factors associated with or predictive of a complicated course during induction, the timing of discharge is often arbitrary and varies amongst different providers and institutions [13]. At Riley Hospital for Children, Indianapolis, Indiana, we routinely discharge HR and VHR ALL patients on Day 4 of induction chemotherapy, after they receive PEG-Asp, if they are afebrile, tolerating oral medications, have completed teaching, deemed clinically stable (not toxic appearing) and follow up visit is arranged. However, other institutions have adopted a policy of keeping all newly diagnosed HR and VHR ALL patients inpatient for the entire duration of induction chemotherapy [13] or until ANC and/or APC is rising[16 17] . Current supportive care guidelines from the Children's Oncology Group (COG) recommend hospitalization for the duration of chemotherapy and associated marrow aplasia for patients on phase III AML trial[18] but no specific guidelines exist for non-Downs syndrome ALL patients.

Our study aimed to identify specific criteria that are associated with a complicated course during induction in this cohort of patients, by comparing clinical and laboratory characteristics during the first four days of induction chemotherapy, between patients who were discharged after a brief LOS (discharged on day four of induction chemotherapy) (group A) versus patients who experienced a prolonged LOS (>4 days) or intensive care unit stay (group B) during induction chemotherapy, to help determine a safe discharge plan in these patients. We also compared readmission (within 30 days) rates for both groups.

On univariable analysis (Table 2), more patients with a prolonged LOS (group B) were more likely to be febrile, have lower hemoglobin platelet counts, and serum bicarbonate; and increased BUN and calcium/phosphate abnormalities. These findings are indicative of an extended need for supportive measures, transfusion requirements for anemia and thrombocytopenia, higher likelihood of electrolyte abnormalities, acidosis and organ dysfunction, in patients who experience a prolonged LOS.

Approximately, one third of patients in both groups experienced unplanned readmissions within 30 days due to varied reasons. Despite this high readmission rate, we noted a low overall induction mortality of 2.7% (n=2), similar to previously reported studies [11,19].

Patients who were discharged on day 4 of induction treatment (group A) had a higher 5 year disease (leukemia) free survival (Figure 2, p=0.03), but no difference was noted in overall survival. However, various factors that were not analyzed in this study, such as, a higher number of ph+ALL patients in group A necessitating a tyrosine kinase inhibitor

during induction and consolidation [20] (ten versus three in group B), an unknown ph-like ALL signature [21], timing of transplant, and MRD [15], may have skewed these results. In addition, while treatment delays during the intensive phase of treatment has not be shown to impact an increase of relapse [22], nonadherence to treatment during maintenance therapy is associated with a significant risk of relapse . It is plausible that the inferior LFS in group B was a result of treatment delays [23]. Treatment response and post-transplant salvage therapies per se, should not have affected early discharge or LOS, as they would not even have occurred yet. These findings underscore the need for future large cooperative and prospective studies aimed at studying the impact of longer LOS, during induction on LFS in this cohort of patients.

Recent studies have shown that LOS is longer in newly diagnosed ALL patients (not risk stratified) if they are either admitted over the weekend [24,25] and that LOS >7 days is ultimately associated with fewer readmissions to the PICU [13]. However, while we did not analyze timing of admission (weekend or not), our analysis suggests that LOS does not impacts the frequency of unplanned admissions in HR/VHR ALL patients. Patients with a longer LOS were as likely to be readmitted, within 30 days, as those with a shorter LOS (TABLE 4). This may be explained by the fact that higher intensity of treatment (4 drug induction) is potentially associated with an overall increased incidence of complications in this group of patients, often necessitating a readmission, regardless of initial short LOS.

Neutropenia usually results from leukemic infiltration into the bone marrow or from bone marrow suppression secondary to ongoing infection at the time of leukemia diagnosis.

ANC <200/mm3 has been identified as a risk factor for readmission and infection during induction chemotherapy [11,14,26]. However, these studies included both low risk (receiving 3-drug induction) and HR/VHR patients in their analysis [14]. While degree of neutropenia, and/or presence of a rising ANC is often taken into consideration when determining a safe discharge, our data suggests that this may not be predictive of readmission or LOS in this cohort of HR/VHR ALL patients, as we found no difference in ANC and unplanned re-admission within 30 days in the 2 groups.

Limitations of this study include its retrospective nature and small cohort of patients representing a subgroup of newly diagnosed pediatric ALL. This relatively small sample of patients may not have allowed adequate power to uncover other laboratory abnormalities, performance status, or comorbidities as predictors associated with a complicated hospital admission for induction chemotherapy, and needs to be validated prospectively and in an independent cohort of similar cases. Additionally, validation is required of the variables examined here, however such as platelets, bicarbonate, fever, etc. A randomized trial to examine these would be ideal, but difficult to accomplish.

Future directions include prospectively collecting data, during HR/VHR ALL induction therapy, to establish discharge criteria based on a scoring algorithm.

While outpatient management during induction chemotherapy in HR or VHR ALL patients is attractive due to reduced costs and improved patient comfort [18], our study supports the notion that this may not be the safest option in this group of patients.

Conversely, an early discharge is safe in a subgroup of patients. Treating physicians could opt for a discharge only after normalization of electrolyte abnormalities and renal functions, and when no transfusion support is needed (stable hematocrit and platelet count). Nevertheless, after discharge, an aggressive and close outpatient follow up of these patients is indicated in these patients, as they remain prone to complications and readmissions.

Conclusions

A significant proportion of HR and VHR pediatric ALL patients experience a prolonged or complicated inpatient hospital stay and readmission during induction chemotherapy. We have identified clinical factors and laboratory abnormalities that are associated with and may be predictive of a complicated or prolonged hospitalization for induction chemotherapy in this population of patients. Our study supports aggressive discharge planning and close follow up, during induction, in this cohort of patients.

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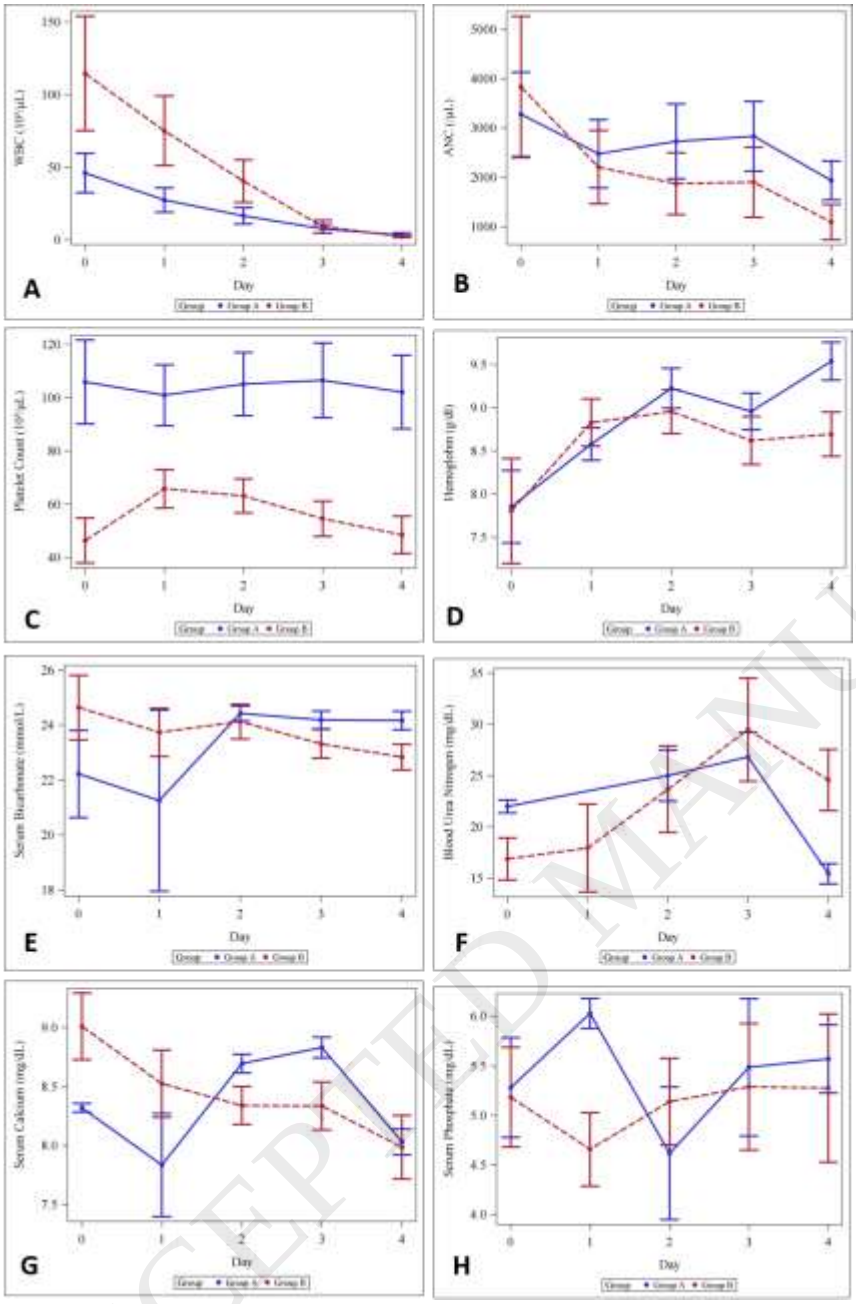

FIGURE 1. Graphs representing laboratory Values on day 0 (one day prior to starting treatment) through day 4 of induction therapy. The A) white blood cell count (WBC, (10^3/µL), B) absolute neutrophil count (ANC, 10^3/µL), C) platelet count 10^3/µL, D) hemoglobin (grams/dl), E) serum bicarbonate, F) blood urea nitrogen (BUN), G) serum

calcium and H) phosphate are depicted in line graphs for each group (blue for group A and red for group B). Mean±SD are depicted by circles and error bars, respectively. See table 2S for raw values.

Abbreviations:

Pediatric intensive care unit (PICU)

White blood count (WBC)

Standard deviation (SD)

Absolute neutrophil count (ANC)

Blood urea nitrogen (BUN)

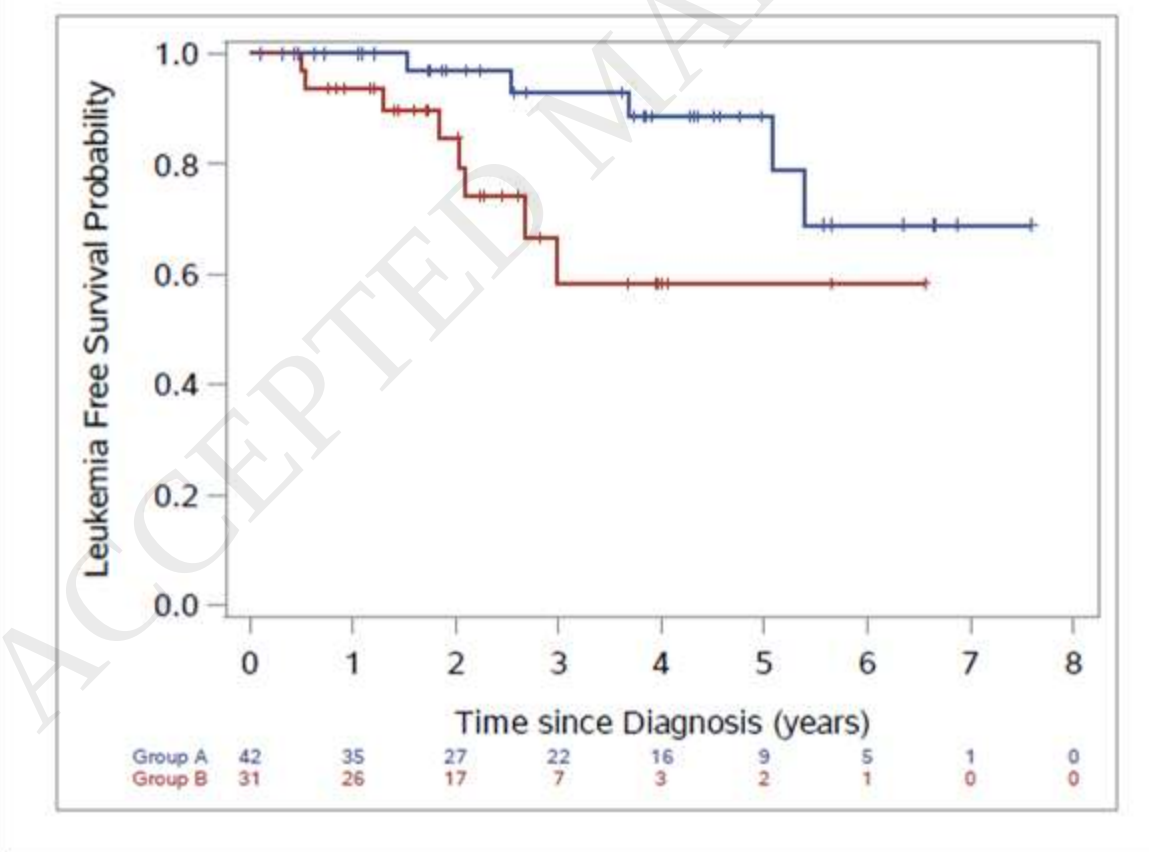

FIGURE 2. Leukemia-Free Survival in patients discharged on day 4 (group A, short length of stay = 4 days, depicted in blue graph) versus patients who experienced a prolonged hospital stay or PICU admission during after diagnosis (group B, red).

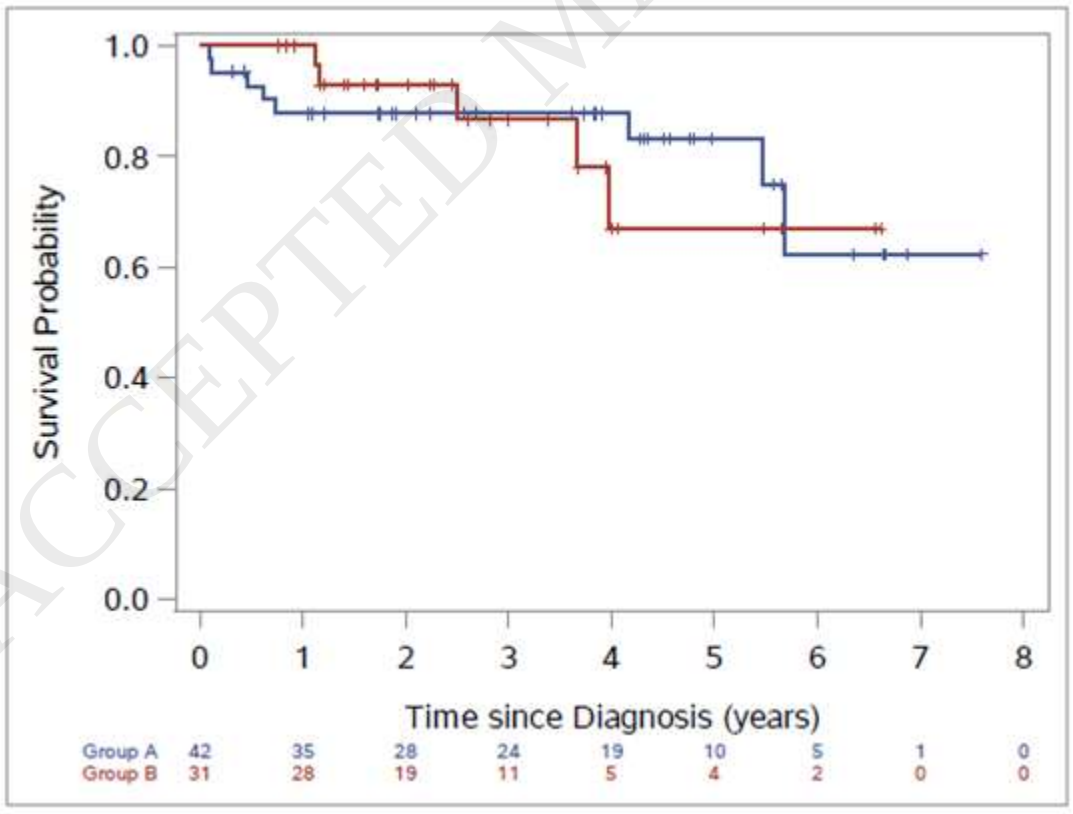

FIGURE 3. Overall Survival in patients discharged on day 4 (group A, short length of stay = 4 days, depicted in blue graph) versus patients who experienced a prolonged hospital stay or PICU admission during after diagnosis (group B, red).

Legend:

TABLE 1. Patient characteristics of Group A (short LOS=4 days) compared to patients with a prolonged LOS or PICU admission) (Group B). *p-value from Chi-square test for categorical variables and from t-test for continuous variables

Abbreviations:

Length-of-stay (LOS)

Pediatric intensive care unit (PICU)

White blood count (WBC)

Standard deviation (SD)

TABLE 1.

Variable Mean±SD (% or median)	Group A (N=42)	Group B (N=31)	p-value
Sex			
Female	10 (24%)	10 (32%)	0.4
Male	32 (76%)	21 (68%)	
Race and ethnicity			
Non-White	1 (2%)	3(9.6%)	0.3
White	41 (98%)	28 (90.3%)	
Hispanic or Latino	8 (19%)	4 (13%)	0.5
Not Hispanic or Latino	34 (81%)	27 (87%)	
Age at Diagnosis	12.1±4.9 (13.5)	14.1±4.2 (15)	0.08
Length of Stay (LOS) (days)	4±0 (4)	16±27.7 (8)	0.02
Readmission within 30 days	16 (38%)	11 (35%)	0.8
WBC at presentation	46.0±75.3 (19.5)	114.6±197.0 (37.2)	0.1
Positive Blood Culture	0/22 (0%)	4/15 (26%)	0.04
High Risk Cytogenetics	15 (36%)	4 (13%)	0.03

TABLE 2. Univariable analysis of clinical and lab data for Days 0-4. **N/E = value is not estimable, due to either all, or almost all values being within one category.

Abbreviations:

White blood count (WBC)

Absolute neutrophil count (ANC)

Blood urea nitrogen (BUN)

Not estimable (N/E)

TABLE 2.

Variable	Day=0		Day=1		Day=2		Day=3		Day=4	
Group	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**
WBC	46.0±75.3 [31]	114.6±197.0 [25]	27.4±45.4 [29]	75.1±127.0 [28]	16.5±31.0 [30]	40.5±72.9 [25]	7.6±16.3 [30]	9.1±23.7 [30]	3.3±8.5 [32]	2.3±3.4 [30]
ANC	3277±5525 [42]	3831±7968 [31]	2355±4180 [40]	2134±3947 [30]	2660±4634) [39]	1813±3383 [31]	2833±4417 [39]	1841±3827 [31]	1939 ±2533 [41]	1094±1989 [31]
Platelet count	103±99 [41]	46.4±47.3 [31]	101±71 [39]	65.8±39.9 [30]	105.2±75 [40]	63.1±35.4 [31]	106.6±88.5 [40]	54.6±36.9 [31]	102.2±89.5 [38]	48.5±39.2 [31]
Hemoglobin	7.9±2.4 [32]	7.8±3.2 [27]	8.6±1.1 [34]	8.8±1.5 [28]	9.2±1.4 [35]	9.0±1.4 [29]	9.0±1.3 [36]	8.6±1.5 [31]	9.5±1.4 [41]	8.7±1.4 [31]
Bicarbonate	22.2±4.8 [9]	24.6±4.4 [14]	21.3±6.6 [4]	23.7± 3.8 [19]	24.4±1.8 [42]	24.1±3.5 [31]	24.2±2.1 [42]	23.3±2.9 [31]	24.2±2.2 [42]	22.8±2.6 [[31]
BUN	22.0±1.4 [5]	16.9± 8.0 [15]	NA	17.9± 16.1 [14]	25.0±5.0 [4]	23.7±16.3 [15]	26.8±5.8 [6]	29.5±20.2 [16]	15.4±6.4 [42]	24.6±16.6 [31]
Calcium	8.3±0.1 [5]	9.0±1.2 [19]	7.8±1.5 [12]	8.5±1.3 [20]	8.7±0.5 [42]	8.3±0.9 [31]	8.8±0.6 [42]	8.3±1.1 [31]	8.0±0.4 [10]	8.0±1.2 [20]
Phosphate	5.3±1.1 [5]	4.1±2.4 [16]	6.0±0.6 [17]	4.7±1.7 [21]	4.6±2.3 [12]	5.1± (2.0 [20]	5.5±1.8 [7]	5.3±2.7 [18]	5.6±1.1 [10]	5.3± 3.1 [17]

TABLE 3. Results of the univariable and multivariable logistic regression. 30 variables were analyzed as potential predictors of prolonged hospital stay, and step-wise multivariable analysis was performed using the univariable results with $p<0.05$ (using at most 4 variables due to the small sample size). Age, sex, fever, and other lab values had $p \geq 0.05$ and were not included in the step-wise multivariable model.

Abbreviations:

Blood urea nitrogen

Confidence interval (C.I.)

TABLE 3.

Variable	Comparison	Univariate1		Multivariate	
		Odds Ratio (95% C.I.)	**p-value**	**Odds Ratio (95% C.I.)**	**p-value**
Bicarbonate	Abnormal vs Normal	8.21 (2.07, 32.6)	0.002	9.71 (2.35, 40.12)	0.0017
BUN	Abnormal vs Normal	3.02 (1.09, 8.39)	0.033		
Calcium	Abnormal vs Normal	2.64 (0.97, 7.18)	0.058		
Platelets	<20,000 vs >=20,000	4.52 (1.09, 18.76)	0.037	5.86 (1.31, 26.18)	0.0205

TABLE 4: Blood counts (Absolute neutrophil count (ANC) (103/µL), pre-transfusion hemoglobin (grams/dl) and platelet count (103/µL)) on Day 4 of induction chemotherapy

for group A and B patients who had an unplanned re-admission within 30 days of discharge. *p-value from t-test for continuous variables.

Abbreviations:

Absolute neutrophil count (ANC)

Fever and neutropenia (F/N)

Syndrome of inappropriate ADH secretion (SIADH)

Standard deviation (SD)

TABLE 4.

Group	Reason for Unplanned admission	ANC	Hemoglobin	Platelet count
A (n=16 = 36%)	Diarrhea	192	9.6	73
	F/N	155	9.7	42
	F/N	11880	9.3	61
	F/N	88	NA	124
	F/N	150	8	32
	Fatigue, decreased appetite	820	9.2	26
	Diarrhea, dehydration	4545	8.6	67
	Pain control	1403	11.6	242
	Septic shock	NA	7.8	302
	Dehydration	160	8.4	10
	F/N	1197	9.6	49
	Septic shock	852	9.7	44
	Dehydration	2697	12	185
	Abscesses	0	7.6	78
	Abdominal pain, transaminitis	945	11	101
	Sinus venous thrombosis	17	9.8	248
Mean±SD		1673±3081	9.5±1.2	105.3±89.9
B (n=11 = 35%)	SIADH	496	9.7	146
	Coagulopathy	1530	8.4	38
	F/N	108	11.1	24
	F/N	28	10.2	49
	F/N	336	8.4	53

	F/N	40	6.8	61
	Abdominal pain	220	8.7	107
	Cachexia	1280	9.4	45
	Septic Shock	1420	8.5	69
	Bleeding	3922	8.6	16
	Increasing blast count	715	7.9	91
Mean±SD		917.7±1142	8.9±1.2	63.5±38.2
p-value*		0.4	0.3	0.1