Global Heterogeneity of Pediatric Acute Lymphoblastic Leukemia Central Nervous System Diagnostics

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Introduction

- Central nervous system (CNS) involvement in pediatric acute lymphoblastic leukemia (pALL) is assessed via cell-counting and cell-morphology methods from cerebrospinal fluid (CSF).
- Based on the number of blasts detected, patients are stratified into three (or more) CNS stages (1-2-3) and treated accordingly.
- International guidelines ensure comparable disease assessment from bone marrow, but CNS staging guides lack detail.
- CNS2 status varies widely in clinical trials, ranging from 3% to 40%, with unclear prognostic significance.[1]

Aim

- **To assess current CNS diagnostic practices in pALL.**
- **To identify factors needing clarification or standardization.**

Methods

- **Survey**: **1.** Center information. **2.** Methods: frequency of use, timeframes, dyes, volumes, thresholds, technical details, stabilizing solutions, definitions of CNS2 and traumatic lumbar puncture (LP). **3.** LP: contraindications, strategy (systemic therapy before/after staging), technical details. **4.** Others: ophthalmology, MRI scans **5.** Number of new pALL cases in two years.
- **Distribution**: via email; 1. international study coordinators within their reach 2. PubMed search for non-international study participants.
- **Data analysis**: IBM SPSS Statistics was used for Pearson correlation, Mann-Whitney U, and Fisher's exact tests. Significance level set at $p < 0.05$.

Results

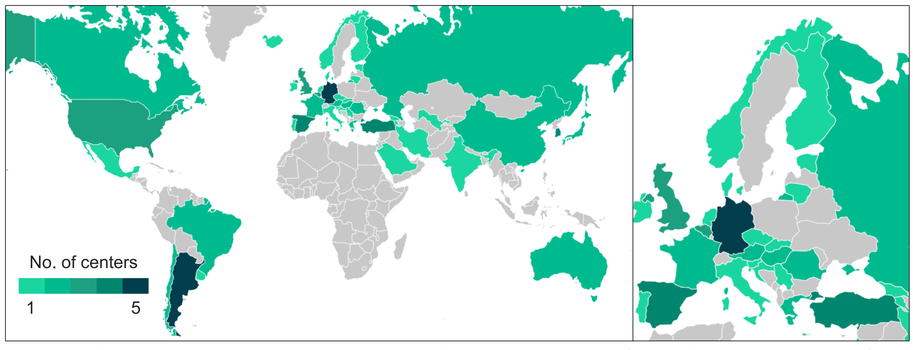


Figure 1. Participants: 5 continents, 47 countries, 82 centers responded (avg. 1.7 centers per country).

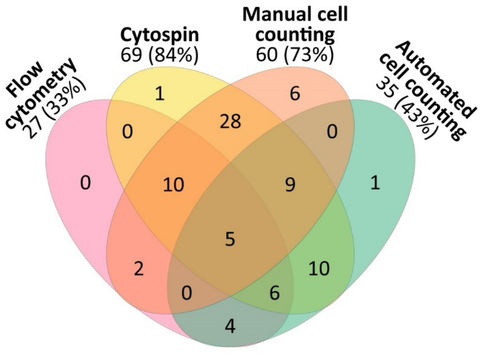


Figure 2. The number of centers using different combinations of analytics to detect white blood cells in CSF. 16% do not use cytospin, 9% do not use either flow cytometry or cytospin routinely.

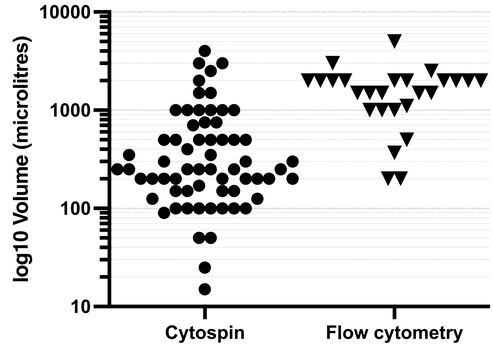


Figure 4. Volumes of CSF used: Cytospin: 15-3000 µL (mean 607.7, median 300, SD 830); Flow cytometry: 200-4000 µL (mean 1604.4, median 1500, SD 1006.2)

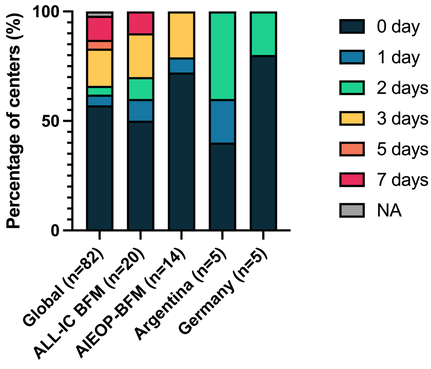


Figure 3. Permitted days of systemic therapy before the staging LP on a global scale, within study groups, and countries.

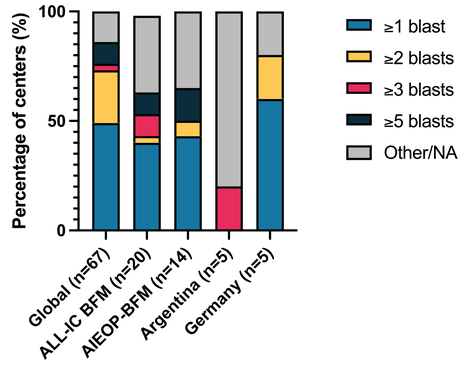


Figure 5. The definition of CNS2 by cytospin on a global scale, within study groups, and countries.

Statistical results: More centers use cytospin for every CNS assessment in high-income countries than in middle-income countries (92% vs. 65%, p= 0.006). A similar trend was noted for flow cytometry (39% vs. 17%, p= 0.07). No significant differences were observed in the use of manual and automated cell counting between income groups.[2] Centers using cytospin for every CNS assessment identified a median of 8% CNS2 cases, compared to 1% in centers that do not use it in every case (p= 0.007).

Summary

- The **first global survey** on CNS staging of pALL highlights the **wide heterogeneity** in choosing and employing analytic methods.
- The results **might resolve conflicting evidence about the prognostic value of CNS stages**.
- **Standardization is urgently needed.**

References

[1] Thastrup et. al - Central nervous system involvement in childhood acute lymphoblastic leukemia: challenges and solutions. Leukemia

[2] https://blogs.worldbank.org/opendata/new-world-bank-country-classifications-income-level-2022-2023

Footnotes

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