

Volume—Outcome Relationships in Pediatric Acute Lymphoblastic Leukemia: Association Between Hospital Pediatric and Pediatric Oncology Volume With Mortality and Intensive Care Resources During Initial Therapy

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Abstract

A volume—outcome relationship has been shown in adult oncology. We investigated if an inverse association of volume and death exists in pediatric acute lymphoblastic leukemia (ALL) care. In assessing the association of volume and outcomes in a cohort of hospitalized pediatric ALL patients, we did not show an inverse relationship between volume and mortality or need for intensive care.

Background: There are few contemporary studies of volume—outcome relationships in pediatric oncology. Children with acute lymphoblastic leukemia (ALL) are treated at a wide variety of hospitals. We investigated if inpatient hospital volume influences outcomes. The objective of this study was to evaluate the relationship between inpatient pediatric and pediatric oncology volume and mortality and intensive care resources (ICU care). We hypothesized an inverse relationship between volume and these outcomes. **Patients and Methods:** This was a retrospective cohort study. Patients 0 to 18 years of age in the Pediatric Health Information System or Perspective Premier Database from 2009 to 2011 with ALL were included. Exposures were considered as the average inpatient pediatric and pediatric oncology volume. The primary outcome was inpatient mortality; secondary outcome was need for ICU care. **Results:** The included population comprised 3350 patients from 75 hospitals. The inpatient mortality rate was 0.86% (95% confidence interval, 0.58%-1.2%). In the unadjusted analysis, mortality increased as pediatric oncology volume increased from low (0%) to high volume (1.3%) ($P = .009$). The small number of deaths precluded multivariable analysis of this outcome. Pediatric and pediatric oncology volume was not associated with ICU care when we controlled for potential confounders. **Conclusion:** Induction mortality was low. We did not observe an inverse relationship between volume and mortality or ICU care. This suggests that in a modern treatment era, treatment at a low-volume center might not be associated with increased mortality or ICU care in the first portion of

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Outcomes of Induction Therapy in ALL and Patient Volume

therapy. This relationship should be evaluated in other oncology populations with higher mortality rates and with longer-term outcomes.

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Introduction

Volume–outcome relationships associate the amount of care provided at a hospital level to the quality of care received by an individual patient.¹ These relationships have been studied extensively in procedural fields, and an inverse relationship between volume and patient mortality found.^{2,3} Studies in adult oncology have suggested that higher-volume centers have better outcomes for surgical and nonsurgical management.⁴⁻⁶ In pediatric oncology, a volume–outcome relationship has been less well examined. A systematic review undertaken to evaluate volume in pediatric oncology concluded that higher volumes are related to better survival.⁷ However, the generalizability of this finding might be limited by the heterogeneity of the cancer populations included and of the definitions of the volume exposures.⁷ More recent studies focused on specific pediatric tumors including Wilms tumor and neuroblastoma did not find a relationship between volume and outcome.^{8,9} The potential effect of a volume–outcome association across different types of pediatric malignancy is needed because the findings might help either optimize the provision of care for these patients, or help to reinforce current practice.

Acute lymphoblastic leukemia (ALL) is the most common pediatric malignancy and, therefore, represents an important group in which to investigate the volume–outcome paradigm. It is estimated that thirty-five hundred pediatric patients will be diagnosed with ALL in the United States in 2016.¹⁰ Fortunately, remarkable improvements in survival have occurred in recent decades, resulting in a 90% survival rate.¹¹ The improvement in survival has been achieved via optimization of risk classification and intensification of chemotherapy. This has led to well established, but complex, treatment protocols that require comprehensive hospital services. Previous studies of the volume–outcome relationship among children with ALL did suggest an association, but this represented an earlier era of therapy.¹² Currently, there are a number of established protocols for the management of ALL that might reduce variation in outcomes. However, recent data suggest that mortality among children with ALL continues to vary according to institution.¹³ It is possible that this variation in mortality might be related to hospital volume. A better understanding of the volume–outcome association across different types of pediatric malignancy is needed. We hypothesized that mortality and need for intensive care resources (ICU care) during the period of ALL induction chemotherapy would be inversely related to a hospital's volume of inpatient pediatric and pediatric oncology patients.

Patients and Methods

Overview and Study Design

A retrospective cohort study of patients with new-onset ALL was performed with 2009 to 2011 data from the Pediatric Health

Information System (PHIS) and Perspective Data Warehouse (Premier Inc, Charlotte, NC). Forty-one hospitals from PHIS, and 34 hospitals from Premier were included. The institutional review board of the Children's Hospital of Philadelphia reviewed the study and determined exempt status.

Data Sources

The PHIS database has previously been described in detail.^{14,15} Briefly, PHIS includes administrative and billing data from 46 freestanding, noncompeting, not for profit tertiary children's hospitals across the United States. PHIS data include demographic characteristics, dates of service, discharge disposition, International Classification of Diseases, Ninth Revision (ICD-9) discharge diagnosis and procedure codes, and detailed billed resource utilization information. Data are deidentified at the time of submission and subjected to reliability and validity checks. Data quality is assured through a combined effort between the Children's Hospital Association (Overland Park, KS), Truven Health Analytics, and participating hospitals.

Perspective Data Warehouse, maintained by Premier, Inc (Charlotte, NC) is a large administrative database representative of a distinct consortium of US not for profit hospitals. Hospitals contributing to the Premier database include academic and community hospitals. These institutions represent one-sixth of all hospitalizations in the United States. Importantly, although PHIS hospitals are dedicated children's hospitals, hospitals in Premier admit children and adults. Data elements in Premier are similar to those found in PHIS and include demographic and hospitalization data, ICD-9 discharge diagnoses and procedures codes, pharmacy billing data, and charges.¹⁶

Study Cohort

A previously established and validated inpatient cohort of pediatric ALL patients from PHIS was extended to include the years under study.¹⁴ A parallel cohort was constructed from Premier using the same steps applied to assemble the PHIS cohort. In brief, all patients younger than 19 years of age with a discharge ICD-9 code for ALL (204.xx) were identified. Pharmacy billing records were reviewed for medications and timing consistent with known ALL induction chemotherapeutic regimens. We restricted the study population to 2009 to 2011 to use parallel years from each data source. Patients with an ICD-9 code for trisomy 21 (758.0) were excluded because of potential for differential morbidity, mortality, and clinical practice in this population. There were 2 hospitals that contribute to Premier and PHIS. Data for these hospitals from Premier were omitted to avoid duplicate patients (see [Supplemental Figure 1](#) in the online version). Of note, only 1 patient had a discharge status that was unknown.

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