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Association between Hospital Volume and Within-Hospital Intensive Care Unit Transfer for Sickle Cell Disease in Children's Hospitals

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Abstract

Objective—To assess the relationship between hospital volume and intensive care unit (ICU) transfer among hospitalized children with sickle cell disease (SCD).

Study design—We conducted a retrospective cohort study of 83477 SCD-related hospitalizations at children's hospitals (2009–2012) using the Pediatric Health Information System database. Hospital-level all-cause and SCD-specific volumes were dichotomized (low versus high). Outcomes were within-hospital ICU transfer (primary) and length of stay (LOS) total (secondary). Multivariable logistic/linear regressions assessed the association of hospital volumes with ICU transfer and LOS.

Results—Of 83477 eligible hospitalizations, 1741 (2.1%) involving 1432 unique children were complicated by ICU transfer. High SCD-specific volume (OR 0.77, 95% CI 0.64–0.91) was associated with lower odds of ICU transfer while high all-cause hospital volume was not (OR 0.87, 95% CI 0.73–1.04). A statistically significant interaction was found between all-cause and SCD-specific volumes. When results were stratified according to all-cause volume, high SCD-

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specific volume was associated with lower odds of ICU transfer at low all-cause volume (OR 0.46, 95% CI 0.38–0.55). High hospital volumes, both all-cause (OR 0.94, 95% CI 0.92–0.97) and SCD-specific (OR 0.86, 95% CI 0.84–0.88), were associated with shorter LOS.

Conclusions—Children’s hospitals vary substantially in their transfer of children with SCD to the ICU according to hospital volumes. Understanding the practices utilized by different institutions may help explain the variability in ICU transfer among hospitals caring for children with SCD.

Keywords

anemia; sickle cell; quality of health care; hospital medicine

Sickle cell disease (SCD) is a chronic, genetic condition that affects approximately 1 in 375 African-American children born in the U.S.¹ SCD is characterized by hemolysis, unpredictable pain episodes, and invasive infections.² Despite clinical advances,³ the care of children with SCD continues to be marked by significant morbidity and substantial medical expenditures.^{4, 5} Many children with SCD rely heavily on acute care services, particularly hospitalization.^{6–9} Among pediatric chronic conditions, SCD-related hospitalizations have longer lengths of stay (LOS) and higher rates of re-hospitalization.^{10–13} Although disease burden may partially explain high resource utilization among hospitalized children with SCD, variations in care may also influence such outcomes.^{14, 15}

Despite the abundance of studies assessing the influence of hospital volume in adult care,^{16–19} few studies have examined the impact of hospital volume on resource utilization for pediatric conditions.^{20–25} Studies examining the effect of hospital volume on pediatric SCD outcomes may be particularly useful given the multi-faceted care required to manage complications during hospitalization.^{14, 26, 27} Prior studies of individuals with SCD have assessed the hospital volume-outcome relationship for LOS and readmission.^{14, 15, 28} The impact of hospital volume on intensive care unit (ICU) transfer has not been previously studied. As a clinical measure, transfer to the ICU may provide another meaningful outcome variable for the impact of hospital volume on resource utilization among hospitalized children with SCD.²⁹

The primary objective of this study was to determine the association between hospital volume (all-cause volume, SCD-specific volume) and within-hospital ICU transfer. A secondary objective was to examine the association between hospital volumes and LOS. We hypothesized that higher hospital volumes, particularly SCD-specific volume, would be associated with lower rates of ICU transfer and shorter LOS.

METHODS

For this retrospective cohort analysis, we used the Pediatric Health Information System (PHIS) database, maintained by the Children’s Hospital Association (Overland Park, Kansas). PHIS contains discharge data (demographics, diagnosis codes, procedure codes) and billing data (clinical charges) from 47 tertiary care, pediatric hospitals in the United States. Data are maintained by the Children’s Hospital Association, participating hospitals,

and Truven Health Analytics (Ann Arbor, MI). Data are de-identified. However, all children in the database have unique patient identifiers so that they can be followed across multiple encounters. In accordance with the Common Rule 46 CFR 46.102(f) and the policies at the Baylor College of Medicine Institutional Review Board, this study using de-identified data was not considered human subjects research.

The unit of analysis was each unique hospitalization. Hospitalizations were identified using International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis codes for all SCD-related diagnoses listed as the primary or any secondary discharge codes. Based on previous studies,^{14, 15, 30} the ICD-9 codes consisted of 282.41 (sickle cell thalassemia without crisis), 282.42 (sickle cell thalassemia with crisis), 282.6× (sickle cell disease), and 517.3 (acute chest syndrome). We selected all the hospitalizations of children ages 0–18 years meeting the above ICD-9-CM criteria discharged from 42 PHIS hospitals contributing ICU data between January 1, 2009 and December 31st, 2012.

The primary outcome was transfer to the within-hospital ICU. This outcome was transfer of a child with SCD from the emergency department or inpatient service of a hospital to its ICU (hereafter ICU transfer). ICU care was identified in PHIS using clinical transaction classification (CTC), a proprietary system used to categorize hospital billing services that has been used in previous PHIS studies.^{31, 32} We excluded ICU consultations or other types of intensive care units (e.g., neonatal intensive care unit) using CTC codes. External direct admissions to the ICU, defined as transfers from outside hospitals or the field, were excluded by removing hospitalizations where only ICU charges occurred on the first day of service. The secondary outcome was overall LOS (in days).

All-cause volume was defined as the frequency counts of all discharges by hospital during the 4-year study period. SCD-specific volume was defined as the frequency counts of all SCD-related discharges (primary or secondary diagnosis) by hospital during the 4-year study period. All-cause and SCD-specific hospital volume cut-points were determined using piecewise logistic regression models. Initial parameter estimates were obtained by running a logistic regression model with ICU transfer designated as the primary outcome, and either total all-cause volume or total SCD-specific volume across the entire study period as the independent variable. Utilizing the initial parameter estimates and non-linear least squares estimation, we obtained piece-wise slope estimates and estimates of the breakpoint. The cut-point for low versus high all-cause or SCD-specific volume was taken to be the estimated breakpoint (Figure 1). Hospitals with total volumes during the study period less than or equal to these cut-points were designated as low volume hospitals and hospitals with volumes greater than these cut-points were designated as high volume hospitals. Although the natural cut-points for hospital volume varied depending on the outcome of interest, for ease of presentation, we used a single set of cut-points based on our primary outcome of ICU transfer.

Patient-level variables included age, sex, primary payer (public, private, other), and median household income for the patient's home zip code. Median household income was categorized into quartile groups with the 4th quartile being the highest.^{33, 34} Hospitalization-level variables consisted of designation of SCD-related diagnosis (primary versus

secondary), number of co-diagnoses, day of admission (weekday or weekend), overall hospital transfer volume (minus SCD), case mix index (CMI), hospital identification code, and hospitalization year. Weekend admissions were defined as admissions on Saturday and Sunday, which have been correlated with reduced hospital staffing.³⁵ CMI is a widely used surrogate for illness severity and risk of mortality used in prior PHIS-based studies.³⁶ CMI in PHIS is based on All Patient-Refined Diagnosis-Related Group (APR-DRG) categories and severity levels. It is calculated by Truven as the ratio of the average charge for patients in a particular APR-DRG category/severity level combination to the average charge for all patients who comprise their national pediatric database. Higher CMI is indicative of a hospital that may provide more advanced care to a generally sicker population. Hospitalization year was included to account for temporal factors in the study outcomes.

Statistical Analyses

Differences in demographic information and hospital utilization characteristics between patients with SCD who were and were not transferred to ICU were assessed. We used a chi-square test for association for categorical variables and the Wilcoxon rank sum test for continuous variables. Because outcomes from distinct hospitalizations for the same patient are likely correlated, the univariate hospital characterization analysis consisted of a comparison of all hospitalizations among the transfer to ICU cohort with all hospitalizations among the cohort of patients who were never transferred to the ICU during the study period. Univariate comparisons of demographic information were performed at the patient-level.

Multivariable logistic regression was used to assess the relationship between ICU transfer and all-cause volume, SCD-specific volume, and the interaction between the two. We fit a generalized estimating equation (GEE) assuming a first-order autoregressive variance/covariance structure to account for potential correlation in outcomes between repeated hospitalizations with an individual patient. The multivariable logistic regression model consisted of all previously listed covariates and selected two-way interactions. We also fit a hospital-level effect to account for any clustering of discharges seen in the same institution, and a year within study period effect to account for changes over time. Given collinearity between SCD-specific volume and overall hospital ICU transfer volume, we omitted overall ICU transfer volume from the final model. For model effects determined to be statistically significant, odds ratios (OR) and 95% confidence intervals (CI) were constructed to compare the different levels of each factor.

Associations between hospital volume and LOS were modeled using a generalized linear mixed model (GLMM) assuming an underlying exponential distribution to account for the considerable degree of skewness present in the LOS data. We fit LOS data using the natural log link function, and, as in the logistic regression model, we assumed a first-order autoregressive variance/co-variance structure to account for potential correlation in outcomes between repeated hospitalizations for an individual patient. Covariates included in the GLMM were the same as those considered in the logistic regression GEE model. Overall hospital ICU transfer volume was omitted from the final model due to collinearity with SCD-specific volume. All analyses were performed using SAS, Version 9.3 (SAS Institute, Cary, NC), and p-values < 0.05 were considered statistically significant.

RESULTS

Results in Table I describe both patient-level and hospital-level characteristics of the 16,092 patients accounting for 83,477 hospitalizations for SCD-related diagnoses among the 42 hospitals that met our entry criteria. Of the 83,477 hospitalizations, nearly all were identified by a SCD diagnosis with only 9 identified by ACS. There were 1,741 transfers to the ICU (2.1%) among 1,432 individual patients with a median number of hospitalizations per patient of 6 (interquartile range 3–12) during the 48-month study period. Of all ICU transfers, 33% originated from the emergency department and 67% originated from the inpatient floor. HbS disease with crisis accounted for 38% of ICU transfers with a SCD-related primary diagnosis (data not shown). No other SCD-related primary diagnosis accounted for greater than 5% of ICU transfers. Figure 2 shows the variations in SCD ICU transfer volumes transposed over the overall ICU transfer volumes among the 42 hospitals.

Association between Hospital Volumes and Within-hospital ICU Transfer

High SCD-specific hospital volume was associated with a lower odds of ICU transfer (OR 0.77, 95% CI 0.64–0.91) in multivariable models (Table II). However high all-cause volume was not associated with ICU transfer. There was a statistically significant interaction effect between SCD-specific hospital volume and all-cause volume ($p < 0.001$). When stratified by all-cause volume, high SCD-specific volume was associated with lower odds of ICU transfer (OR 0.46, 95% CI 0.38–0.55) only when there was low all-cause volume.

Association between Hospital Volumes and Overall LOS

The median overall LOS for the study sample was 1 (interquartile range 1,3) day. The median ICU-specific LOS was 2 (interquartile range 1,3). Both all-cause hospital volume and SCD-specific volume were associated with overall LOS such that higher volumes were associated with shorter LOS (Table II). An interaction effect was found between all-cause hospital volume and SCD-specific hospital volume ($p < 0.001$). When stratified according to all-cause hospital volume, high SCD-specific hospital volume was associated with shorter LOS regardless of all-cause volume.

DISCUSSION

Given the clinical and financial burden of pediatric SCD, there is significant interest in improving outcomes and reducing variability in care among hospitalized children. Consistent with our hypothesis, we found that SCD-specific hospital volumes were individually associated with a lower rate of ICU transfer and shorter LOS. Most interestingly, the influence of SCD-specific volume on ICU transfer was persistent only when hospital all-cause volume was low. SCD-specific volume also influenced LOS regardless of level of all-cause hospital volume. Our findings suggest that hospital volume-outcome relationships, observed previously in primarily procedure-based conditions among adults, also exist for pediatric SCD.

This study extends prior work on the hospital volume-outcome relationship in SCD. In a study by McCavit et al, lower SCD-specific hospital volume was associated with decreased LOS.¹⁴ Our finding of an inverse relationship between hospital volume and LOS contradicts

those findings. The difference in results may be due to underlying differences in the study populations. Our study sample consisted solely of children in children's hospitals whereas the sample in the study by McCavit et al included adults and children in diverse hospital settings. Underlying differences in disease severity and patterns in specialty care utilization according to age may have also contributed to the discordant findings between the two studies. However, our findings are consistent with the literature on the hospital volume-outcome relationship that generally demonstrates an inverse relationship between hospital volume and LOS.³⁷ Other studies exploring the hospital volume-outcome relationship among hospitalized children with SCD have found no statistically significant associations between SCD-specific hospital volume and outcomes including 30-day readmission, intubation, LOS, and cost of care.^{15, 28} Building upon these previous studies,^{14, 15, 28} we assessed both all-cause volume and SCD-specific volume which facilitated a more robust analysis.

In addition to providing novel data on ICU transfer among hospitalization children with SCD, this work also contributes to the general literature on the hospital volume-outcome relationship in pediatrics. Most studies on hospital volume in pediatrics have focused on neonatal intensive care units (NICUs) and pediatric trauma centers, with mortality as the most frequently assessed primary outcome.^{20–22, 24} Few studies have explored other outcomes that may be relevant to a broader set of pediatric medical conditions. The clinical management of children in ICU settings will likely increase over time, with longer survival of children with chronic conditions and advancements in medical technologies.²⁹ Therefore, this study demonstrates that other outcomes, such as ICU transfer, merit further study in order to address potentially escalating resource utilization in pediatric inpatient care.

Our finding that high SCD-specific volume was associated with ICU transfer and LOS among hospitalized children with SCD has important implications for health policy and equity of care across all populations of children with SCD. It could be reasoned that children with SCD should be cared for in hospitals with high SCD-specific volumes (i.e., regionalization of care) given that significant experience with caring for SCD may reduce ICU transfer and LOS which may in turn reduce medical expenditures. However, some individuals, especially racial/ethnic minorities may not have access to high volume hospitals due to geography or referral pattern.³⁸ Therefore, efforts should more appropriately focus on reducing variability in care between institutions rather than redirecting care to high volume hospitals. Policy efforts may be directed towards initiatives, if indicated, that may be more actively incorporated at low volume hospitals. Specific strategies may include decision aids and clinical practice guidelines related to the management of fever, pain, and acute chest syndrome as detailed in the recently published expert panel report about the management of SCD.³⁹ More data on patient experience in low and high volume hospitals may be beneficial given previous research documenting how discrimination impacts SCD care.^{40, 41} Lastly, low volume and high volume hospitals may develop more cooperative agreements to facilitate consultation and transfer of care when needed. Potential barriers to these strategies include adequacy of resources and competing financial incentives.

Among our findings, the result of SCD as a secondary diagnosis predisposing to ICU transfer but being associated with shorter LOS was unexpected. We postulate that conditions

that may have been listed as primary diagnoses were likely protocol-driven ICU stays with rapid turnaround resulting in overall short hospital stays. For example, a primary diagnosis of pneumonia may have required respiratory support and exchange transfusion for concern of ACS. Once the patient received such care, they may have rapidly improved such that overall hospital stay was relatively shorter. In contrast, SCD-related primary diagnoses such as crisis could have a potentially overall longer hospital stay because severe pain can take a long time to successfully manage despite the use of pain management protocols. Therefore, a hospitalization with SCD pain complicated by an ICU stay may have a very long LOS.

Our study had several limitations. Outpatient data were unavailable, including pre-hospitalization management, disease severity, access to SCD centers, and medication use. It is possible that hospital factors such as provider care ratios, census, admission order sets, specialty units, and discharge planning, may partially explain the differences observed between low volume and high volume hospitals.¹⁶ It may be more efficient at smaller volume hospitals to use an ICU for rarer/higher risk procedures or patient groups than to establish a separate SCD unit which functions at that higher level. PHIS does not have the data necessary to test this hypothesis or whether specific procedures precipitate transfer. The generalizability of the results is limited to children's hospitals. Data were subject to misclassification or coding errors. Lastly, it is possible that better outcomes led to higher volume and therefore the hospital volume-outcome relationship acts in the opposite direction.

SCD-specific hospital volume was associated with lower odds of within-hospital ICU transfer and shorter LOS among hospitalized children with SCD. In settings where all-cause volume was low, SCD-specific volume was an especially important influence on ICU transfer. SCD-specific volume was also significantly associated with shorter LOS regardless of level of all-cause hospital volume. Although future prospective studies are warranted, our findings suggest that the hospital volume-outcome relationship extends beyond surgical procedures and outcomes typically measured in pediatric studies (e.g., mortality). Our results support the need for further exploration of how care is organized for pediatric SCD and investment in strategies to improve care and standardize processes when appropriate across institutions as a matter of ensuring equitable care for all children with SCD.

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Abbreviations

ACS	acute chest syndrome
CI	confidence interval
ICU	intensive care unit
LOS	length of stay
OR	odds ratio

PHIS Pediatric Health Information System
SCD sickle cell disease

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Figure 1.

Piecewise logistic regression results for (i) All-cause hospital volume and (ii) SCD-specific hospital volume. The top panel displays the mathematically derived cut-point for all-cause hospital volume (494,927) and the bottom panel displays the mathematically derived cut-point for SCD-specific volume (2,659).

Figure 2.
SCD ICU transfer volumes (line) transposed over the overall ICU transfer volumes (bars) among the 42 hospitals.

Table I

Characteristics of SCD-Related Hospitalizations and SCD Patients with Transfer to ICU vs. No Transfer to ICU

Level of Analysis	Discharge Level		Patient Level	
Variable	All SCD Hospitalizations	No Transfer to ICU	Transfer to ICU	p-value
Child characteristic^a	N=83,477	N=14,660	N=1,432	
Age in years, Median (Q1,Q3)	8 (3,14)	7(2,13)	7(2,12)	0.8280
Age Group, N(%)				<.001*
0–4	26,820 (32.1)	5,660 (38.6)	524 (36.6)	
5–9	19,122 (22.9)	3,373 (23.0)	375 (26.2)	
10–14	19,102 (22.9)	3,159 (21.5)	332 (23.2)	
15–18	18,433 (22.1)	2,468 (16.8)	201 (14.0)	
Race, N(%)				0.1276
White	1,643 (2.0)	328 (2.2)	26 (1.8)	
Black	74634 (89.4)	11,998 (81.8)	1,161 (81.1)	
Hispanic	2,755 (3.3)	429 (2.9)	40 (2.8)	
Other	4,445 (5.3)	805 (5.5)	72 (5.0)	
Mixed	----- ^b	1,100(7.5)	133(9.3)	
Sex, N(%)				<.001*
Male	42,999 (51.5)	7,422 (50.6)	840 (58.7)	
Female	40,478 (48.5)	7,238 (49.4)	592 (41.3)	
Expected Payer, N(%)				<.001*
Public	59,218 (70.9)	8,935 (60.9)	865 (60.4)	
Commercial	20,375 (24.4)	3,188 (21.7)	236 (16.5)	
Other	3,884 (4.7)	442 (3.0)	24 (1.7)	
Mixed	----- ^b	2,095 (14.3)	307 (21.4)	
Household Income, N(%)				0.2051
1 st Quartile	31,104 (37.3)	5,289 (36.1)	533 (37.2)	
2 nd Quartile	19,729 (23.6)	3,362 (22.9)	309 (21.6)	
3 rd Quartile	17,301 (20.7)	3,095 (21.2)	315 (22.0)	
4 th Quartile	14,263 (17.1)	2,674 (18.2)	243 (17)	
Missing/Not Available	1,080 (1.3)	240 (1.6)	32 (2.2)	
Hospitalization characteristics	N=83,477	N=71,397	N=12,080 ^c	
Designation of SCD diagnosis, N(%)				0.9179
Primary	52,615 (63.0)	44,996 (63.0)	7,619 (63.1)	
Secondary	30,862 (37.0))	26,401 (37.0)	4,461 (36.9)	
Number of Co-Dx, Median (Q1,Q3)	2 (1,4)	2 (1,4)	3 (1,6)	<.001*
Day of Admission				<.001*

Level of Analysis	Discharge Level		Patient Level	
Variable	All SCD Hospitalizations	No Transfer to ICU	Transfer to ICU	p-value
Weekday	63,703(76.3)	54,336 (76.1)	9,367 (77.5)	
Weekend	19,774(23.7)	17,061 (23.9)	2,713 (22.5)	
Case Mix Index, Mean (SE)	1.20 (0.01)	1.11 (0.005)	1.70 (0.030)	<.001*
Hospitalization admission year, N(%)				<.001*
2009	22,124 (26.5)	19,070 (26.7)	3,054 (25.3)	
2010	20,438 (24.5)	17,327 (24.3)	3,111 (25.8)	
2011	20,409 (24.5)	17,345 (24.3)	3,064 (25.4)	
2012	20,506 (24.5)	17,655 (24.7)	2,851 (23.6)	

Q1: 1st Quartile/25th percentile; Q3: 3rd Quartile/75th percentile

^a For Transfer patients, child characteristic data represent values at first transfer to ICU. For non-transfer patients, child characteristic data represent values at initial hospitalization.

^b Only a single payer or a single race may be coded in PHIS per hospitalization; a patient with multiple hospitalizations can have a mixture of payers or race codes.

^c Represents all hospitalizations for 1,432 patients with a transfer to ICU. Of 12,080 hospitalizations, 1,741 resulted in a transfer to ICU.

* Statistically significant at P<0.05 for patient-level results.

Table II

Multivariable Analysis of ICU Transfer and Hospital Length of Stay (LOS) among SCD-Related Hospitalizations

Variable	Transfer OR (95% CI)*	LOS, Ratio of Means (95% CI)*
Age Group (years)		
0–4	Reference	Reference
5–9	1.24 (1.06–1.45)	1.03 (1.00–1.05)
10–14	1.04 (0.88–1.23)	1.18 (1.15–1.21)
15–18	0.84 (0.7–1.01)	1.36 (1.33–1.44)
Sex		
Female	Reference	Reference
Male	1.22 (1.08–1.38)	0.98 (0.96–1.00)
Payer		
Commercial	Reference	Reference
Public	0.99 (0.85–1.14)	1.01 (1.00–1.03)
Other	0.59 (0.43–0.81)	0.89 (0.85–0.93)
Household Income		
1 st Quartile	Reference	Reference
2 nd Quartile	0.85 (0.73–0.99)	1.00 (0.98,1.02)
3 rd Quartile	0.86 (0.73–1.01)	1.00 (0.98,1.03)
4 th Quartile	0.92 (0.75–1.11)	1.02 (0.99,1.05)
Designation of SCD Diagnosis		
Primary	Reference	Reference
Secondary	1.46 (1.29–1.64)	0.77 (0.76–0.79)
SCD Volume		
Low	Reference	Reference
High	0.77 (0.64–0.91)	0.86 (0.84–0.88)
All-cause Volume		
Low	Reference	Reference
High	0.87 (0.73–1.04)	0.94 (0.92–0.97)
All-cause/SCD volume interaction		
All-cause volume = Low		
SCD volume Low	Reference	Reference
SCD volume High	0.46 (0.38–0.55)	0.76 (0.74–0.78)
All-cause volume = High		
SCD volume Low	Reference	Reference
SCD volume High	1.28 (0.95–1.73)	0.96 (0.93–1.00)
Number of Co-diagnoses (continuous)	1.25 (1.23–1.28)	1.07 (1.06–1.08)
Day of Admission		
Weekend	Reference	Reference
Weekday	1.09 (0.96–1.24)	0.99 (0.97–1.01)

Variable	Transfer OR (95% CI)*	LOS, Ratio of Means (95% CI)*
Case Mix Index (continuous)	1.11 (1.08–1.15)	1.18 (1.17–1.19)
Hospital Admission Year (continuous)	0.91 (0.86–0.95)	0.98 (0.97–0.99)

* Statistically significant results are bolded.