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Abstract

Introduction—Surgical treatment of congenital heart disease represents a major cause of pediatric hospitalization and healthcare resource use. Larger centers may provide more efficient care with resulting shorter length of postoperative hospitalization (LOH).

Materials and Methods—Data from 46 centers over 25 years was used to evaluate whether surgical volume was an important determinant of LOH using a competing risk regression strategy that concurrently accounted for deaths, transfers, and discharges with some time interactions.

Results—Earlier discharge was more likely for infants and older children compared to neonates (subhazard ratios at post-operative day 6 of 1.64 [99% confidence interval (CI): 1.57, 1.72] and 2.67 [99% CI: 2.53, 2.80], respectively), but less likely for patients undergoing operations in Risk Adjustment for Congenital Heart Surgery categories 2, 3, 4, and 5&6 compared to category 1 (subhazard ratios at post-operative day 6 of 0.66 [99% CI: 0.64, 0.68], 0.34 [95% CI: 0.33, 0.35], 0.28 [99% CI:0.27, 0.30], and 0.10 [99% CI: 0.09, 0.11], respectively). There was no difference by sex (non-time dependent subhazard ratio 1.019 [99%CI: 0.995, 1.040]). For every 100-unit increase in center annual surgical volume, the non-time dependent subhazard for discharge was

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1.035 (99% CI: 1.006, 1.064) times greater and center-specific exponentiated random effects ranged from 0.70 to 1.42 with a variance of 0.023.

Discussion—The conditional discharge rate increased with increasing age and later era. No sex-specific difference was found. Centers performing more operations discharged patients sooner than lower volume centers but this difference appears to be too small to be of clinical significance. Interestingly, unmeasured institutional characteristics estimated by the center random effects were variable suggesting that these played an important role in LOH and merit further investigation.

Keywords
Length of Hospitalization; Congenital Heart Disease; Competing Risk Regression; Pediatric Cardiac Care Consortium

Introduction

One percent of all children born in the United States have congenital heart disease (CHD), which makes this the most common type of birth defect [1–3]. CHD is a leading cause of infant mortality and morbidity and a significant societal and financial burden [4, 5]. The mortality risk, while significant, has greatly improved over the last 25 years [6]. Compared to infants undergoing surgery in the mid 1980s, infants undergoing surgery in the mid 2000s had 6.5 times lower odds of death after controlling for center surgical volume, risk category, age group, and sex [6]. In 2004, the costs for hospitalizations for individuals with CHD in the U.S. was $1.4 billion [7] with estimated costs for a privately insured infant of almost $100,000 [5, 8]. These costs reflect the high level of resource intensity needed for the care and procedures for these children. Cardiac surgery and the associated period of critical illness are fundamentally expensive, but both costs and outcomes could potentially be improved with a better understanding of the differences in care from center to center.

Post-operative length of hospitalization (LOH), after adjustment for disease severity, is a widely used, yet inexact, indicator of hospital performance. For example, LOH is viewed as an indicator of quality of care, hospital efficiency, a surrogate measure for significant complications, and resource utilization [9]. This is particularly true within the context of CHD. LOH has been used as an indicator for significant morbidity linked to poor neurodevelopmental outcomes [10]. Furthermore, post-operative LOH has also been shown to be an important metric for comparison of institutional efficiency [11].

Previous work has examined the effects of patient and institutional characteristics on mortality outcomes. However, despite the significance of the LOH, there is little information on the effect of these characteristics on LOH. Among the institutional characteristics previously studied, there has been a focus on center surgical volume as a predictor of outcomes. It has been suggested that if higher-volume pediatric cardiac surgery centers have better outcomes, overall care may be improved by regionalization of some or all pediatric cardiac operations. Vinocur et al found that while surgical volume was a contributing factor, volume-independent center-specific effects were more important for predicting post-operative mortality [6]. This finding suggests that institutional excellence in surgical
management is not entirely mediated through surgical volume, but also through other unmeasured center characteristics.

In this study we use the Pediatric Cardiac Care Consortium (PCCC) database to study the effects of patient and center characteristics on post-operative LOH from 1982 to 2007. We were particularly interested in determining whether surgical volume was an important predictor of post-operative LOH.

**Materials and Methods**

**Data**

The PCCC is a multi-center registry that collects patient-level data to improve quality of care for congenital cardiac procedures [12]. Between 1982 and 2007, 112,030 admissions and 118,084 operations for CHD were reported in the PCCC from 90,124 patients in 57 centers located in North America. Information collected included data on invasive cardiac procedures as well as cardiac and non-cardiac diagnoses [12]. All cardiac operations with the exception of isolated ductal ligation in preterm infants under 2.5 kg were reported prospectively by the centers and classified according to their complexity by using the Risk Adjustment for Congenital Heart Surgery system version 1 (RACHS1) [6, 12, 13]. This rubric is a widely used, validated system for classifying congenital cardiac operations into six categories by expected early mortality rates [14].

**Exclusion Criteria**

Centers were excluded if they were outside of the United States or performed less than 10 cases per year. Center records were excluded from years with partial participation, or with missing or conflicting data. Patients who were 18 years old or older and those with diagnosed syndromes were excluded. We also excluded operations not categorized by the RACHS1 methodology, and admissions during which more than one operation was performed. These exclusions were designed to increase internal study validity and to meet the assumptions of our methods, but do limit the generalizability of our study results. We included multiple admissions per patient and used a clustered bootstrap to estimate confidence intervals.

**Variable construction**

The RACHS1 rubric was used for risk adjustment. In this system, the lowest mortality risk procedures are placed in category 1, while the highest risk procedures are in category 6 [14]. This graded system facilitates analysis, but also may obscure variability within a given categories. Because of the rarity of category 5 operations (0.16%), we combined categories 5 and 6. Other variables included patient sex, age at operation as a categorical variable (neonates - less than 28 days, infants - 28 days or greater and less than 1 year, and children - greater than 1 year and less than 18 years), 5 year period (between 1982 and 2007), time between admission and surgery, and center annualized surgical volume as a continuous variable. The surgical volume was calculated for each five-year period as the total number of operations at a given center divided by the number of participating years during that time.
period, and analyzed in terms of a 100-unit change. The outcome of interest was the time from surgery to discharge.

**Statistical Modeling**

Descriptive statistics and unadjusted cumulative incidence plots were computed for the variables of primary interest. Our primary aim was to evaluate the impact of volume and of volume-independent center effects on risk-adjusted length of hospitalization (LOH) using a competing risks approach with a random effect or frailty for center [15]. The integrated likelihood ratio test (ILRT) was used to test the null hypothesis: the variance of the center effects is equal to zero. In this modeling strategy, discharge, death, and transfer were treated as competing risks because the occurrence of one prevents the occurrence of the other [16]. This methodology is necessary because without taking the relationship between LOH and deaths into account, centers with shorter lengths of stay due to early deaths may appear to outperform centers with longer length of stay and fewer deaths. Furthermore, excluding deaths may add bias to the analysis by removing poor outcomes.

Using a competing risks approach, an individual in the risk set that experiences the competing event is maintained in the risk set for the event of interest [17]. An excellent discussion of these methods can be found in Lau et al 2009 and Fine et al [16, 17]. The method for estimating and testing for center random effects in competing risks can be found in Katsahian et al [15]. The assumption of proportional hazards for each variable was evaluated using plots of the scaled Schoenfeld residuals and tested using the weighted residuals using the method of Grambsch and Therneau [18]. Relevant time interactions (log scale) were added to the model for variables violating the assumption of proportional hazards, specifically age group, time period, and RACHS1 category. Time interactions were not included for sex, time from admission to surgery, and volume based on the plots of the scaled Schoenfeld residuals. Volume was modeled linearly on the log-subhazard scale. The final model, after the addition of time interactions, included age group, sex, RACHS1 category, time between admission and surgery, surgical volume, and five year time period in a competing risk model with discharge as the primary outcome and death and transfers to other centers treated as competing risks. Confidence intervals (99%) were computed using a clustered bootstrap that sampled all patient admissions for a given patient if selected to account for potential correlation within patient due to multiple admissions for a patient. The confidence interval was adjusted for 33 comparisons using a Bonferroni type correction (1-0.05/33 ~ 99.8%). For variables that interacted with time, subhazard ratios and confidence intervals were computed at the 25th, 50th, and 75th-percentile of length of hospitalization for patients who were discharged (four, six, and ten days, respectively). SAS version 9.3 and R version 3.2.1 were used for modeling and graphics generation [19, 20].

**Results**

We used the PCCC data from 1982 to 2007. This data has been described previously [6], and included 53 centers, 86,801 patients, 107,830 admissions, and 113,494 operations (Figure 1). After exclusions, we used 46 centers with 58,682 patients who underwent 70,449 operations. There were 4,541 (5.7%) instances where an operation was one of multiple that
occurred during a single admission; all of these operations in the corresponding 2,160 admissions were excluded. The bootstrap estimates of the fixed effects and their interactions with time were used to compute results for four, six, and ten days after surgery in Table 1. Unadjusted cumulative incidence plots for discharge for age group, sex, RACHS group, five-year time period, and surgical volume quartile are found in Figures 2 – 6, respectively.

Our model produces subhazard ratios, presented as ratios of discharge rates between two groups or a per unit-change for continuous measures, on a given post-operative day conditioned on a person remaining in the hospital up until that day. Compared to neonates, infants had a subhazard ratio of 1.81 (99% CI: 1.72 – 1.92) and children had a subhazard ratio of 3.25 (99% CI: 3.06 – 3.44) on the fourth day after surgery, respectively. For variables with time interactions, subhazard ratios were computed at four, six, and ten days after surgery (Table 1), representing the 25th, 50th, and 75th percentiles for LOH. Comparing females to males, the subhazard ratio was 1.019 (99% CI: 0.995 – 1.040). The subhazards for sex were relatively proportional over time, so no time interaction was included in the model with sex (that is, the ratio is the same four, six, and ten days after surgery).

Relative to the most recent time period (2003–07), the subhazard ratio increased from 0.58 (99% CI: 0.55 – 0.61) in 1982–87, to 1.16 (99% CI: 1.12 – 1.20) in 1998 to 2002, respectively, on the fourth day after surgery. In other words, the conditional rate of discharge on the fourth day after surgery in 1982–87 was 0.58 times the conditional rate of discharge in 2003–07. By six days after surgery, the conditional rate of discharge for a patient in 1982–87, conditioned on a patient still remaining in the hospital up to that time, increased to 0.63 (95% CI: 0.64 – 0.68) times the rate in 2003–07. Comparing risk categories, the subhazard for RACHS1 category 2, 3, 4, and 5&6 versus category 1 were 0.51 (99% CI: 0.49 – 0.53), 0.23 (99% CI: 0.22 – 0.24), 0.19 (99% CI: 0.18 – 0.21), and 0.06 (99% CI: 0.05 – 0.07), respectively, four days after surgery. Time from admission to surgery, a proxy for pre-operative clinical instability, was associated with a 0.981 (99% CI: 0.977, 0.986) subhazard ratio for each additional day between admission and surgery.

A 100-unit difference in annualized surgical volume was associated with a 1.035 (99% CI: 1.006 – 1.064) subhazard ratio. Last, the random effect for center had an estimated variance of 0.023 (99% CI: 0.021 – 0.029). The p-value from the ILRT was <0.001.

**Discussion**

As expected, the subhazard for discharge (or cause-specific conditional rate of discharge) increased with older age groups, lower surgical risk categories, and generally more recent era. The trend for improved subhazard ratios for each subsequent 5 year period was disrupted only for the 1997 to 2002 time period which estimated a higher subhazard than the 2002 to 2007 time period. There could be several explanations for this finding including changes in discharge criteria and clinical practices (such as the introduction of new procedures for higher risk patients or a shift from simple procedures to transcatheter approaches). For example, in this last period the widespread adoption of transcatheter closure of atrial septal defects substantially displaced a common low-risk operation with typically short postoperative LOH. In addition, over time there has been a change in the
membership of the consortium that may partially account for this finding. We did not find a significant difference by sex, unlike other studies suggesting girls had shorter LOH by 0.8 days [21].

Our principal question was whether institutional surgical volume or center-specific volume-independent effects made significant contributions to the conditional discharge rates after pediatric cardiac operations. We found that for every increase by 100 operations at a given center, the associated subhazard ratio is 1.035 (99% CI: 1.006 – 1.064). This result is marginally statistically significant, but is of dubious clinical relevance (for example, it is much smaller than the subhazard ratio between the two most recent 5-year time periods).

In a previous analysis focused on postoperative mortality among the same patients, Vinocur et al. found that center-specific variation exists but is only partially explained by operative volume, particularly for the moderate- and high-risk operations. Instead, unmeasured volume-independent center-specific characteristics accounted for more of the variability in mortality [6]. In our analysis, the variance of center-specific random effects was 0.023, indicating that institutional characteristics not captured by the data were important contributors to the conditional discharge rates. The adjusted center-specific exponentiated random effects varied widely (after controlling for surgical volume and other factors) with a magnitude that suggests that center-specific factors not captured by surgical volume may have a larger influence on LOH than operation volume. Future studies should attempt to better characterize these apparently important, but as yet obscure, factors. One approach would be to assess the relative contributions to LOH of potentially modifiable factors previously reported in focused studies, such as presence of dedicated cardiac intensive care unit [22], use of fast-track protocols to extubation [23] or intensive care discharge [24], and specific approaches to central line care [25], sternal closure [26], and various aspects of blood transfusion management [27].

Limitations

The first set of limitations relates to the retrospective nature of the study and limited availability of certain data that may better explain the observed LOH. Among patient factors, we were not able to control for critical illness severity, race, insurance status, and distance from surgical center. We were also unable to control for type of center (e.g., academic, children’s, or general hospital), availability of rehabilitation services in the same center (where this phase of hospitalization would contribute to our measured LOH, vs transfer to a separate facility), individual surgeon training and experience, and other center-specific practices such as those mentioned previously. The second limitation relates to the use of the RACHS1 risk categorization. While using this system permits validated case-mix comparisons across centers, we are not able to examine whether our results differed between operations within each risk category. Other systems exist, but O’Brian et al. examined results by different risk stratification systems and have found discrimination differences to be small [28, 29]. The last limitation relates to the approach to surgical volume. In this study, volume was calculated over discrete intervals starting before and ending after each case. Theoretically, if volume functions as a proxy for experience, it would best be calculated on a rolling basis in the window preceding each operation. However, this is unlikely to affect our
results, as centers in our dataset rarely changed volume substantially over time [6]. Because participation in the PCCC is voluntary with few centers performing over 350 operations per year, this study cannot address the volume-LOH relationship at very large centers. Conversely, very few centers perform more than 350 procedures nationally per year, making our data representative of the majority of centers’ practices [30].

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Bibliography


Figure 1.
Center, patient, admission and operation exclusions illustrated

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Figure 2.
Unadjusted cumulative incidence of discharge by age group. LOH is shorter with increasing age.
Figure 3.
Unadjusted cumulative incidence of discharge by sex. LOH may be slightly shorter for females.
Figure 4.
Unadjusted cumulative incidence of discharge by RACHS group. LOH is longer with increasing surgical complexity.
Figure 5.
Unadjusted cumulative incidence of discharge by 5-year interval. LOH is shorter in more recent eras with an exception for the period of 1998 to 2002.
Figure 6.
Unadjusted cumulative incidence of discharge by institutional surgical volume quartile. LOH varies little by surgical volume.
Figure 7.
Plot of relationship between institutional surgical volume rank and exponentiated center random effect. There is substantial center-specific heterogeneity (after controlling for other variables) presumably related to unmeasured center characteristics.
### Table 1

Subhazard ratios and 99% confidence intervals for 0, 1, and 2 days after surgery.

<table>
<thead>
<tr>
<th>Days after surgery</th>
<th>0 days</th>
<th>1 days</th>
<th>2 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
<td>SHR</td>
<td>99% CI</td>
<td>SHR</td>
</tr>
<tr>
<td>Parameters with time interactions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age Group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infants vs. Neonates</td>
<td>1.812</td>
<td>(1.718, 1.922)</td>
<td>1.643</td>
</tr>
<tr>
<td>Children vs. Neonates</td>
<td>3.250</td>
<td>(3.056, 3.437)</td>
<td>2.665</td>
</tr>
<tr>
<td>Quinquennium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1982–1987 vs. 2003–2007</td>
<td>0.578</td>
<td>(0.548, 0.611)</td>
<td>0.625</td>
</tr>
<tr>
<td>1988–1992 vs. 2003–2007</td>
<td>0.636</td>
<td>(0.609, 0.668)</td>
<td>0.681</td>
</tr>
<tr>
<td>1993–1997 vs. 2003–2007</td>
<td>0.922</td>
<td>(0.876, 0.965)</td>
<td>0.889</td>
</tr>
<tr>
<td>1998–2002 vs. 2003–2007</td>
<td>1.157</td>
<td>(1.115, 1.203)</td>
<td>1.067</td>
</tr>
<tr>
<td>Risk Category RACHS -1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 vs. 1</td>
<td>0.512</td>
<td>(0.494, 0.527)</td>
<td>0.658</td>
</tr>
<tr>
<td>3 vs. 1</td>
<td>0.227</td>
<td>(0.218, 0.236)</td>
<td>0.341</td>
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<td>4 vs. 1</td>
<td>0.194</td>
<td>(0.179, 0.210)</td>
<td>0.282</td>
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<tr>
<td>5 &amp; 6 vs. 1</td>
<td>0.060</td>
<td>(0.051, 0.068)</td>
<td>0.101</td>
</tr>
<tr>
<td>Parameters without time interactions</td>
<td>SHR</td>
<td>99% CI</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female vs. Male$^d$</td>
<td>1.019</td>
<td>(0.995, 1.040)</td>
<td></td>
</tr>
<tr>
<td>Time from admission to surgery, days$^d$</td>
<td>0.981</td>
<td>(0.977, 0.986)</td>
<td></td>
</tr>
<tr>
<td>Volume, 100 unit change$^d$</td>
<td>1.035</td>
<td>(1.006, 1.064)</td>
<td></td>
</tr>
</tbody>
</table>

$a$ Defined as <28 days old

$b$ Defined as 28 days to 365 days old

$c$ Defined as 1 to 18 years old

$^d$ Subhazard ratio estimates did not include an interaction with time. The ratio is assumed constant over the LOH.