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Volume-outcome effects for children undergoing resection of renal malignancies

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Abstract

Introduction—Adults undergoing oncologic resections at low-volume centers experience increased perioperative morbidity and mortality. The volume-outcome effect has not been extensively studied in pediatric oncologic resections.

Methods—To clarify volume-outcome effects in pediatric oncologic resections, we analyzed resection of renal malignancies in children less than 15 y of age. We conducted a cross-sectional analysis of hospital discharges included in the health care utilization project kids' inpatient database from 1997 to 2009, examining in-hospital operative complications, length of stay (LOS), and inflation-adjusted hospital charges. Hospital volume was expressed as low ($n = 1-2$), medium ($n = 3-4$), and high ($n > 4$) annual volume of resections.

Results—One thousand five hundred thirty-eight patients underwent renal malignancy resection. Of these, 527 patients had resection in low-, 422 in medium-, and 589 in high-volume hospitals. Relative to low-volume hospitals, those resected in medium-volume hospitals had an odds ratio of 0.62 (95% confidence interval 0.39–0.99, $P = 0.046$) for operative complication and those in high-volume hospitals had an odds ratio of 1.02 (95% confidence interval 0.63–1.65, $P = 0.95$). There was no detectable association with LOS ($P = 0.113$) or inflation-adjusted charges ($P = 0.331$).

Conclusions—The number of complications, total charges, and LOS attributable to resection of a childhood renal malignancy did not differ among high-, medium-, or low-operative volume hospitals, although oncologic outcomes could not be determined because of the limited nature of this administrative database.

Keywords

Wilms' tumor; Volume-outcome effects

1. Introduction

Adult patients undergoing complex cancer operations in low-volume hospitals tend to have increased perioperative and long-term morbidity and mortality [1]. This phenomenon has been documented in malignancies of the colon [2], pancreas [3], esophagus [4], lung [5], stomach, breast, soft tissues, and rectum [6]. Known as the volume-outcome effect, these findings have fueled much of the current effort to establish centers of excellence for technically demanding operations in hopes of achieving improved outcomes associated with reduced cost and length of stay (LOS). Although the volume-outcome effect has been well described for adult cancers, this relationship remains relatively unexamined in pediatric cancer operations. Specifically, no nationwide database has been examined for immediate postoperative outcomes in pediatric solid tumor resections.

There is no standard definition for volume strata in volume-outcome effect research. In a surgical volume study in adults, Birkmeyer *et al.* evaluated operative volume as a continuous variable and in five groups of nearly equal size using whole number cutoff points. In that study, the lowest volume procedure varied from <2 to >11 [1]. Another population-based study examined open descending thoracic aneurysm repairs as a continuous variable and in tertiles with a range of one to four total procedures [7].

Previous studies in children have shown a link between institution procedure volume and outcome in cardiac transplantation [8], pyloric stenosis [9], corrections for scoliosis [10], and ventriculoperitoneal shunt placement [11]. Unlike adult cancer care, pediatric oncology is already localized primarily to children's hospitals with the support of specialist pediatric oncologists. A 2009 study reviewed long-term survival outcomes for children undergoing oncologic resections in Florida hospitals contained within the state tumor registry. In that regional study, hospital operative volume was unrelated to 5- or 10-y survival [12]. The authors hypothesized that this equity in outcome may be related to adherence to consensus treatment regimens, such as those recommended by the children's oncology group (COG). No regional or national study exists to examine the volume effect on outcomes in the first 30 d of pediatric cancer treatment.

In adult operations, the volume-outcome effect is related to increased complications, LOS, and cost when complex procedures are performed at low-volume centers. These findings have driven the development of centers of excellence. The same concerns exist about pediatric oncologic operations, although no large population database has been examined for operative volume-associated outcomes for procedures treating pediatric renal malignancies. We used the health care cost and utilization project (HCUP) kids' inpatient database (KID) to evaluate the volume-outcome effect on coded complications, LOS, and dollars charged.

To clarify volume-outcome effects in childhood oncologic operations, we chose to study renal malignancies. These procedures, although potentially complex, are likely to be performed at low-, medium-, and high-volume pediatric cancer centers and are also performed using standard nephroureterectomy techniques. This is in contrast to other pediatric solid malignancies, such as hepatoblastoma, which may require varying hepatectomy techniques or even liver transplantation. This variation in operative treatment

would confuse comparison of surgical outcomes, and some procedures, such as liver transplantation, are likely to only be performed at high-volume specialty centers. Additionally, neuroblastomas also are highly protean and may be amenable to simple adrenalectomy or may require complex thoracoabdominal approaches, which likely affect referral patterns. We believe that analyzing resection for renal tumors may overcome some of these confounding factors. This study has undergone review by the Vanderbilt University Institutional Review Board and has received exempted approval (IRB# 111048) determining that the study does not qualify as "human subject" research.

2. Methods

2.1. Database and cohort

The HCUP KID is a prospectively collected administrative database and is the only data set of hospital use, outcomes, and charges specifically designed to study utilization of pediatric hospital services in the United States [13]. The KID has been published every 3 y starting in 1997. Each edition contains individual-level discharge data containing approximately 100 variables collected in the previous calendar year. The KID performs an 80% sampling of complicated in-hospital births and pediatric cases from each hospital contained within its sampling frame, enabling national estimates, using provided discharge weights [13]. We obtained the HCUP KID for the individual years 1997, 2000, 2003, 2006, and 2009. Patients undergoing resections for renal tumors were identified using diagnosis and procedure codes from the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM). All patients with ICD-9-CM code 189.0 (malignant neoplasm of the kidney) and one of the two codes, 55.51 (nephroureterectomy) or 55.40 (partial nephrectomy) were included for analysis. We excluded all patients aged more than 14 y. By restricting age, we excluded cancers with onsets at older ages, such as renal cell carcinoma, which overlap with adult malignancies.

Averaged yearly hospital volume was first evaluated as a continuous variable and then divided into tertiles using the whole number of operations that most closely divided the cohort into thirds. The primary outcomes examined were number of complications, LOS, and hospital charges. Data were stratified by age, gender, race, hospital teaching status, location, year, and payer type with adjustment for physician clustering. Adjustment for physician clustering is useful to account for the effect of multiple operations by a single physician. HCUP provides a blinded but individual physician identification number enabling this analysis. Some states do not release physician identification information for reasons of confidentiality, thus this analysis excluded data from some states. Overall data were evaluated in its unweighted form because national estimates were not required for the analysis. We analyzed each hospital in relation to its own number of recorded operations (Table 1).

2.2. Outcomes

Surgical complications can be identified by ICD-9-CM code. Several authors have classified these complications into specific categories of operative wound infections, urinary complications, pulmonary complications, gastrointestinal complications, systemic

complications, and procedural complications [14]. The adult complication list that we used has been used in a number of national inpatient sample-related studies. It is comprehensive and includes cardiovascular and cerebrovascular complications that seldom occur in children but were included in the analysis for completeness. Safford *et al.*, in a study of outcomes after pyloromyotomy, used a list of ICD-9-CM codes completely contained within this other more comprehensive adult list [9]. Utilizing these codes, we analyzed complications in aggregate and performed subset analysis for operative wound, urinary, pulmonary, cardiovascular, systemic, or procedural complications. The study was not powered to detect significant associations with complication subsets. Table 2 lists the included codes.

LOS was evaluated using the entire LOS variable reported in the HCUP database and included time from patient admission until discharge. It is possible that hospitals vary in the speed of diagnosis and operative scheduling. To test institutional variation in the time to establish a diagnosis and in the true postoperative LOS, we also performed a secondary analysis in which we subtracted the time until primary procedure from the LOS, to generate a new variable capturing the LOS after operation. Because the initiation of chemotherapy may prolong LOS, we attempted to exclude these patients (ICD-9-CM V58.11 or V07.39) from analysis. However, no child in this cohort had ICD-9-CM codes for administration of chemotherapy. We did not exclude those receiving initial radiation therapy, as LOS is not increased substantially by a single radiation treatment.

We adjusted inpatient charges to the cost in 2009 in US dollars (the most recent year in this study) using the consumer price index (CPI) published by the United States Department of Labor, Bureau of Labor Statistics [15]. Charges were compared among high-, medium-, and low-volume hospitals using the same volume criteria. The CPI used for 2009 was 214.537; 2006, 201.6; 2003, 184.0; 2000, 172.2; and 1997, 160.5. The formula used to adjust cost was $(214.513 - [\text{CPI for year being adjusted}]/100 + 1) \times \text{charges} = \text{charges adjusted to the cost in 2009 in dollars}$.

2.3. Statistical analysis

The unit of analysis was the patient rather than the hospital system. The association between complications and volume was assessed using logistic regression. For LOS and cost, linear regression was used, in which LOS and cost were log transformed to account for skewness, and the regression models accounted for clustering by physician as well as adjusted for patient age, gender, race, quartile of household income, year of inclusion in HCUP KID, hospital identification, hospital teaching status, hospital location (urban *versus* rural), geographic region of hospital, and the expected primary payer. These variables were considered to have the greatest clinical plausibility to cause variation in patient outcome and were readily available within the database. Each multivariable analysis was first performed as a univariate logistic regression. Statistical analysis was performed using Stata version 11.2 (Stat Corp., College Station, Texas).

3. Results

The combined HCUP database contained 13,941,435 hospitalizations, of which 1538 met inclusion criteria and contained the appropriate ICD-9-CM codes for malignant renal tumor and nephroureterectomy or partial nephrectomy (Figure).

3.1. Complications

When hospital volume was expressed in tertiles, regression analyses showed a reduction in risk for complication for children in middle-volume tertile relative to the lowest volume tertile (odds ratio [OR] 0.62, 95% confidence interval [CI] 0.39–0.99, $P = 0.046$, $n = 974$). The high-volume hospitals and low-volume hospitals, respectively showed no effect (OR 1.01, 95% CI 0.63–1.65, $P = 0.946$) relative to the lowest volume hospitals. Individual physician identification numbers were not available for all patient records because some states mandate blinding to physician for confidentiality purposes. We applied the same regression model without adjusting for physician clustering, and the ORs did not significantly change, but the relative benefit to the middle tertile now showed only marginal statistical significance ($P = 0.053$). When volume was expressed as a categorical measure, 17.7% of children in the lowest tertile of operative volume experienced complications, 13.7% in the middle tertile, and 16.3% in the highest volume tertile ($P = 0.261$). When hospital volume was expressed as a continuous variable, there was no appreciable volume-outcome effect ($P = 0.429$).

3.2. Charges

The mean charge for the entire hospitalization including a resection for a kidney malignancy was US \$68,427 (95% CI \$64,310–72,554) in 2009 ($n = 1490$). By low, medium, and highest volume tertiles, mean costs were \$66,875, \$65,447, and \$71,943, respectively. Linear regression analysis showed no relative difference between the volume groups ($P = 0.156$). Inflation-adjusted charges did of course increase substantially, with 1997 inflation-adjusted charges averaging \$46,223.24 and 2009 charges averaging \$88,643.97, an increase of 91.8% above inflation for the study period or an average of 6.1% greater than inflation each year through the study period.

3.3. Length of stay

LOS did not significantly differ between volume groups. The total mean LOS was 9.34 d, ranging from 9.07 d in the lowest tertile of operative volume to 9.54 d in the highest tertile. Postoperative LOS varied from 6.93 to 7.84 d and was not statistically different between tertiles ($P = 0.274$). The number of days from admission until the primary procedure averaged 1.91 d with very little variation between volume groups. Linear regression analysis showed no detectable association of hospital volume with LOS ($P = 0.1103$).

3.4. Mortalities and transfers

Only one death occurred in the entire cohort, and it occurred in a higher volume center. Insufficient data were available to perform additional mortality analysis. Hospital transfer data (available in 2009 edition of HCUP only) showed that 10% of the low-volume hospitals

received renal malignancy resection patients as transfers, whereas the middle and high-volume centers received 8.0% and 9.3%, respectively.

4. Discussion

For resection of childhood renal malignancies, the number of complications, total charges, and LOS do not differ significantly among high-, medium-, or low-operative volume hospitals. Slightly decreased odds of operative complications were observed for resections performed at medium-volume hospitals. In addition to the volume effect, these differences in outcome may reflect a referral bias. The most complex patients may be disproportionately resected at the high-volume hospitals and the least complex at the low-volume hospitals. Hospital volume has minimal effect on the variables of interest, and we think that the volume-outcome effect is not of substantial clinical importance in resections for childhood renal malignancies.

The literature provides no consensus of what constitutes a high-operative volume institution. Operative volumes have been divided into halves, tertiles, quartiles, and quintiles and evaluated as a continuous variable. Within these delineations, often the top cohort is compared with the lowest. The highest quality studies tend to evaluate volume as a continuous variable and then divide the total volume into categories for more clinically meaningful results. In a 2002 study, Birkmeyer *et al.* examined surgical volume for 14 types of procedures, first evaluating volume as a continuous variable and then in quintiles based on volume. The lowest volume procedure, cystectomy, varied in volume from < 2 to >11, whereas the highest volume procedure, coronary artery bypass grafting, ranged from < 230 to >849 procedures per year [1]. In an analysis of the national inpatient sample, a database similar to the HCUP KID, the authors divided operative repairs for descending thoracic aortic aneurysms into tertiles with a median of one procedure in lowest volume strata (range 1–1), two in medium-volume hospitals (range 2–3), and four (range 3–25) in high-volume hospitals [7]. These studies show that though limited by variation in total number of procedures, important conclusions can still be considered. The highest volume center in our study performed 18 resections for renal malignancy in 1 y (data not shown).

Pediatric hospitals now almost universally participate in standardized COG protocol regimens for children with cancer. It may be that this protocol-driven treatment environment leads to greater standardization of care regardless of regional location or respective institutional volume. This could account for how these results contrast with many of the results in the adult literature. Although not coded within this database, it is likely that most of the surgeons operating on these children are pediatric fellowship trained. The lengthy and rigorous training that these physicians complete may result in less variation between pediatric surgeons. It may be also that renal malignancies represent an index pediatric surgery in which all fellowship-trained pediatric surgeons are well versed. Even though a surgeon may work at a lower volume hospital, he or she may have had more extensive exposure to these operations during fellowship training.

Surgical factors besides volume may have a large impact on morbidity and survival. It is not possible from an administrative database, such as the HCUP KID, to determine adherence to a

surgical standard. The national Wilms' tumor study has used nodal sampling and surgical spill as indicators of compliance with COG operative guidelines [16]. This database does not provide information on surgical margin status. An analysis of surgical technique may show that clear marginal resections and adherence to COG surgical guidelines have a great impact on survival, recurrence, and complications. A targeted evaluation of a tumor registry could provide this sort of analysis.

The primary objective of this study was to clarify whether hospital operative volume affects short-term outcomes. It can be questioned whether it is valid to try to find associations or differences between volume and outcome when five annual operations are defined as "high volume." Pediatric renal resections for malignancy are not performed frequently, given the relative rarity of such tumors nationally, so creating groups with larger yearly volumes is not possible. One could entertain the idea of combining similar solid tumor operations performed by pediatric general surgeons. Although this combination would compare somewhat dissimilar operations, it would be able to compare differences in outcome with greater power in a future study. We are unable to say that a hospital performing a high volume of oncologic nephrectomies necessarily also performs a higher volume of other oncologic surgeries. These results may not be applicable to different pediatric malignancies.

The HCUP KID contains only hospital discharge information and does not permit tracking of multiple admissions (i.e., readmissions) for a single patient. It is impossible to capture complications occurring after hospital discharge. Thus, we are unable to determine 30-d complications or 5- and 10-y outcomes for these patients. We can only answer questions regarding inpatient complications occurring at the time of definitive tumor resection.

Reverse causality can be a concern in cross-sectional type analyses when outcome and disease data are determined simultaneously. It is possible that public reporting of positive results can cause an increase in surgical volume over time. We are unable to detect this type of bias, but because we did not find large differences in outcome, it is not likely that volume is affected by referral bias related to outcome. An additional primary concern about cross-sectional style data is that the exposure can impact the postdisease survival, eliminating patients from the cohort. In this case, the outcomes are being measured in such close proximity to the exposure that mortality is not much affected by the exposure. In fact our cohort has a single mortality in patients resected for renal malignancy.

5. Conclusion

The volume-outcome effect does not substantially affect in-hospital complications, LOS, or charges for resections of renal malignancies in children. The long-term relationship of hospital operative volume to morbidity and mortality cannot be determined through this study. Parents may take children diagnosed with a renal malignancy to the nearest children's hospital without fear of increased in-hospital complications or costs.

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The study examined inpatient admissions for pediatric renal resections in 1997, 2000, 2003, 2006, and 2009 using the Kids' Inpatient Database (KID), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality.

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Figure.
Study cohort.

Table 1

Demographics and tertile characteristics.

Category	Overall	Tertile			P
		Lowest	Middle	Top	
Number	1538	527	422	589	
Age (y) (SD)	3.54 (3.04)	3.51 (2.97)	3.66 (3.01)	3.48 (3.12)	0.641
Female gender (%)	51.86	52.48	49.29	53.14	0.453
Race (%)					0.017
White	57.18	56.02	53.03	61.46	
Black	16.19	19.21	18.79	11.24	
Hispanic	17.86	16.20	20.00	17.89	
Asian	1.59	2.55	1.52	0.69	
Native American	0.92	0.69	0.91	1.15	
Other	6.26	5.32	5.76	7.57	
Quartile of income (%)					<0.001
Lowest	20.40	22.61	22.25	17.13	
Second	23.73	25.73	28.36	18.69	
Third	23.60	21.25	21.52	27.16	
Highest	32.27	30.41	27.87	37.02	
Year of inclusion (%)					0.001
1997	13.85	43.66	25.35	30.99	
2000	16.97	38.70	19.92	41.38	
2003	20.87	31.15	32.71	36.14	
2006	22.76	29.71	31.71	38.57	
2009	25.55	32.82	25.45	41.73	
Region (%)					<0.001
Northeast	20.48	40.63	25.40	33.97	
Midwest	20.74	27.27	30.09	42.63	
South	32.90	38.74	28.85	32.41	
West	25.88	29.15	25.13	45.73	
Teaching hospital (%)	91.92	86.50	93.33	96.07	<0.001

Category	Overall	Tertile		P
		Lowest	Middle	
Urban (%)	99.03	97.85	99.23	100.00
Deaths (%)	0.07	0.00	0.00	0.17
Payer (%)				0.447
Medicare	0.13	0.19	0.24	0.214
Medicaid	34.94	37.19	36.84	
Private insurance	58.80	58.06	55.74	
Self-pay	1.69	1.33	1.44	
Other	4.43	3.23	5.74	
Any complication (%)	15.99	17.65	13.51	16.30
Procedural	0.39	0.38	0.47	0.34
Infection	0.59	0.38	0.47	0.85
Urinary	0.59	0.38	0.95	0.51
Pulmonary	4.62	5.88	3.08	4.58
Gastric	7.54	8.54	5.92	7.81
Cardiac	2.02	2.66	1.42	1.87
Systemic	0.07	0.00	0.24	0.00
LOS (d) (SD)	9.34 (11.72)	9.07 (9.16)	9.42 (12.31)	9.54 (13.24)
Net LOS (d) (SD)	7.43 (8.80)	6.93 (7.05)	7.84 (11.12)	7.63 (8.31)
Charges (\$) (SD)	68,427 (81,203)	66,875 (73,799)	65,447 (69,620)	71,943 (94,154)
Procedure volume (#) (SD)	4.29 (2.86)	1.54 (0.50)	3.5 (0.50)	7.32 (2.30)
				<0.001

SD = standard deviation.

Table 2

Surgical complications—ICD-9-CM codes [14].

Operative wound complications	
Postoperative hematoma	998.12
Postoperative seroma (noninfected)	998.13
Disruption of operative wound	998.3
Postoperative infection	998.5
Postoperative infected seroma	998.51
Postoperative skin abscess, skin infection, septic wound complications, intraabdominal abscess, and subdiaphragmatic abscess	998.59
Persistent postoperative fistula	998.6
Delayed wound healing	998.83
Urinary complications	
Postoperative urinary retention and urinary tract infection	997.5
Pulmonary complications	
Postoperative acute pneumothorax	512.1
Postoperative pulmonary edema	518.4
Adult respiratory distress syndrome and postoperative acute respiratory insufficiency	518.5
Postoperative atelectasis, pneumonia, and Mendelson syndrome	997.3
Gastrointestinal complications	
Peritoneal adhesions with obstruction	560.81
Postoperative: small bowel obstruction, ileus, ileus requiring nasogastric tube, nausea, vomiting, pancreatitis, and complication of anastomosis of gastrointestinal tract	997.4
Persistent postoperative fistula	998.6
Cardiovascular complications	
Postoperative deep venous thrombosis	997.79
Postoperative pulmonary embolism	415.11
Postoperative stroke	997.02
Phlebitis or thrombophlebitis from procedure	997.2
Cardiac arrest/insufficiency during or resulting from a procedure	997.1
Systemic complications	
Postoperative shock (septic and hypovolemic)	998.0
Postoperative fever	998.89
Complications during procedure	
Accidental puncture or laceration, complicating surgery	998.2
Foreign body accidentally left during procedure	998.4
Bleeding complicating procedure	998.11