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Outcomes and Resource Utilization Associated with Use of Routine Pre-Discharge White Blood Cell Count for Clinical Decision-Making in Children with Complicated Appendicitis: A Multicenter Hospital-Level Analysis[☆]

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ABSTRACT

Background: The objective was to explore the hospital-level relationship between routine pre-discharge WBC utilization (RPD-WBC) and outcomes in children with complicated appendicitis.
Methods: Multicenter analysis of NSQIP-Pediatric data from 14 consortium hospitals augmented with RPD-WBC data. WBC were considered routine if obtained within one day of discharge in children who did not develop an organ space infection (OSI) or fever during the index admission. Hospital-level

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observed-to-expected ratios (O/E) for 30-day outcomes (antibiotic days, imaging utilization, healthcare days, and OSI) were calculated after adjusting for appendicitis severity and patient characteristics. Spearman correlation was used to explore the relationship between hospital-level RPD-WBC utilization and O/E's for each outcome.
Results: 1528 children were included. Significant variation was found across hospitals in RPD-WBC use (range: 0.7–100%; $p < 0.01$) and all outcomes (mean antibiotic days: 9.9 [O/E range: 0.56–1.44, $p < 0.01$]; imaging: 21.9% [O/E range: 0.40–2.75, $p < 0.01$]; mean healthcare visit days: 5.7 [O/E 0.74–1.27, $p < 0.01$]); OSI: 14.1% [O/E range: 0.43–3.64, $p < 0.01$]). No correlation was found between RPD-WBC use and antibiotic days ($r = +0.14$, $p = 0.64$), imaging ($r = -0.07$, $p = 0.82$), healthcare days ($r = +0.35$, $p = 0.23$) or OSI ($r = -0.13$, $p = 0.65$).
Conclusions: Increased RPD-WBC utilization in pediatric complicated appendicitis did not correlate with improved outcomes or resource utilization at the hospital level.
Level of Evidence: III.
Type of Study: Clinical Research

1. Introduction

Appendicitis is the most common abdominal surgical emergency of childhood, and approximately 30% of children present with complicated disease [1–3]. Complicated appendicitis is associated with relatively high rates of organ space infection (OSI) and increased resource utilization, including prolonged length of stay and extended antibiotic treatment [1,4,5]. Approximately one-third of postoperative OSI's are diagnosed after discharge from the index admission and can result in unplanned revisits and significant morbidity [6–8]. Identification of children at risk for OSI at time of discharge can be challenging, particularly in patients who are otherwise clinically ready for discharge.

Use of a routine pre-discharge white blood cell count (RPD-WBC) has been proposed as a diagnostic adjunct to identify children who may be at increased risk for OSI following discharge [6–11]. Proponents of the practice use RPD-WBC as a means to optimize resource utilization by minimizing antibiotics, imaging, and length of stay in children at low risk of OSI, while selectively targeting further diagnostic evaluation and treatment to those at high risk [9,10]. However, these assertions are anecdotal as the effect of RPD-WBC utilization on patient outcomes or resource utilization has never been systematically evaluated. When considering that pre-discharge WBC are routinely obtained at 35–50% of children's hospitals, data providing further insight surrounding the potential benefits (or lack thereof) of RPD-WBC may address the current equipoise surrounding this practice in children with complicated appendicitis [9,10,12].

With the above considerations, the objective of this multicenter correlation analysis was to explore whether hospitals with higher utilization of RPD-WBC had improved outcomes and decreased resource utilization compared to those with lower rates, measured in four areas: (1) antibiotic utilization, (2) imaging use, (3) healthcare days, and (4) OSI rates. We hypothesized that no correlation exists between RPD-WBC utilization and the four outcomes.

2. Methods

2.1. Data source

This was a retrospective, multicenter correlation study utilizing data from the American College of Surgeon's National Surgical Quality Improvement Program-Pediatric (NSQIP-Pediatric) augmented with data obtained through supplemental chart review at 14 centers participating in the Eastern Pediatric Surgery Network (EPSN). The NSQIP-Pediatric database includes appendicitis-specific clinical data used to compare risk-adjusted adverse event and resource utilization data among its 152 member hospitals [13]. Data are collected by dedicated surgical clinical reviewers through a rigorous chart review process using standardized criteria and definitions. Accuracy of NSQIP-Pediatric data is ensured by periodic auditing, mandatory recertification for clinical reviewers, and availability of American College of Surgeons clinical support to address questions regarding definitions and data abstraction protocols [14].

All sites performed supplemental chart review to collect WBC and operative report data for patients identified from the NSQIP-Pediatric database. To facilitate standardized chart review, a manual of operations and standardized training videos were developed and reviewed by each site prior to supplemental data collection. Study data were uploaded directly to the data coordinating center using a secure transfer process. The American College of Surgeons was not involved in the management or transfer of any study data. This study was approved by the institutional review board of Boston Children's Hospital (IRB-P00042228).

2.2. Study cohort

Children (ages 3–18) undergoing appendectomy were identified from the NSQIP-Pediatric database at 14 EPSN hospitals from July 2015 to June 2020. Patients with complicated appendicitis based on validated NSQIP-Pediatric intraoperative criteria were considered for inclusion [2,15]. Patients with missing data, lacking antibiotic treatment on postoperative day one, and treated with antibiotics without full colorectal coverage were excluded.

2.3. Classification of exposures and outcomes

A routine pre-discharge white blood cell count (RPD-WBC) was defined as a postoperative WBC count obtained within one day of discharge in a child who did not have a postoperative fever or OSI during their index hospitalization. Children with fevers or OSI were excluded from the calculation of hospital-level RPD-WBC utilization rates to minimize inclusion of patients whose pre-discharge WBC was obtained in response to clinical deterioration (rather than routine assessment).

Study outcomes included hospital-level rates of postoperative antibiotic days, postoperative abdominal imaging (including CT scan, ultrasound, or MRI), revisit rate (any emergency room or inpatient encounters), postoperative healthcare days (inpatient hospitalization, emergency room visits, and surgical clinic encounters), and OSI. Outcomes were assessed both during the index admission and cumulative 30-day postoperative period to provide a comprehensive assessment of how outcomes and resource utilization could be influenced by RPD-WBC use. All patients meeting the study's inclusion criteria (including those with and without a RPD-WBC and those with index hospitalization fevers and/or OSI) were included in the assessment of hospital-level outcomes.

2.4. Statistical analysis

Chi square and Wilcoxon rank sum tests were used for univariate comparisons. Generalized linear mixed effects models were used to estimate hospital-level observed-to-expected ratios (O/E) for each outcome, adjusting for patient demographics and appendicitis severity. Model covariates were selected a priori. Patient demographics included in the model were age at time of operation, sex, race, and insurance status (public, private, other, unknown). Appendicitis severity was categorized as one versus more than one intraoperative finding of severe disease based on previously validated NSQIP-Pediatric criteria [2,15]. A logistic link was used for binary outcomes and a gamma link was used for continuous outcomes. Hospital-level O/E's were estimated by exponentiating the shrinkage estimate of each hospital's random effect [16]. Hospitals were considered statistical outliers if the 95% confidence interval of the O/E did not include 1. The Spearman correlation coefficient (r) was used to examine the hospital-level relationship between rate of RPD-WBC use and outcomes. Analyses were performed with SAS statistical software (version 9.4; SAS Institute, Inc). Statistical significance threshold was considered with a two-sided $P < 0.05$.

3. Results

1528 (hospital median: 108.5, IQR 70.5–148.8) children with complicated appendicitis were included. The median age was 10 (IQR 7–13) and 37.6% were female. Overall, 50.3% of patients had

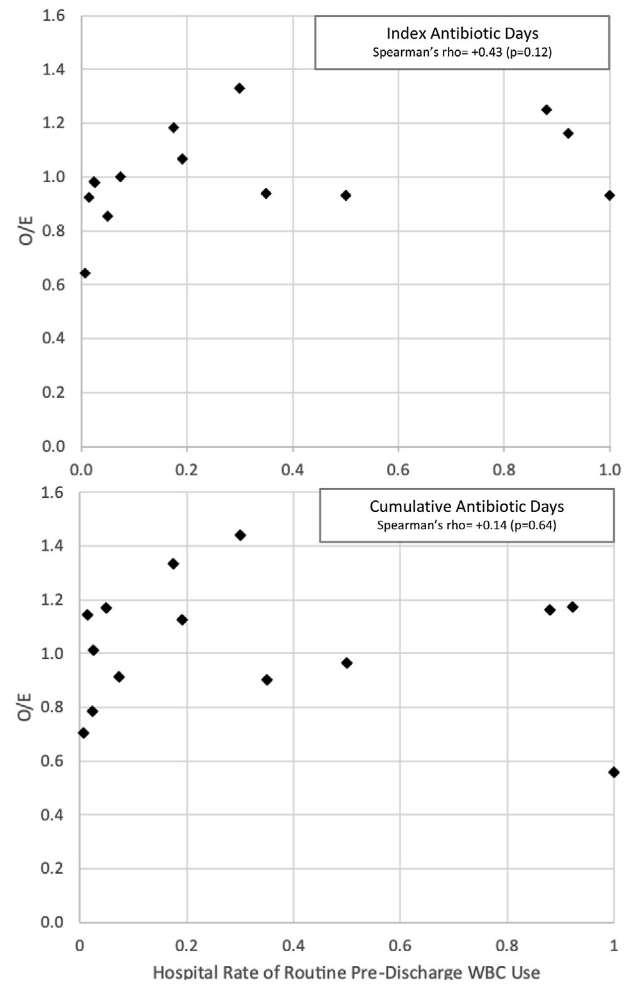

Fig. 1. Correlation of Antibiotic Days and Routine Pre-Discharge WBC Utilization: Correlation of 14 children's hospitals' adjusted observed-to-expected (O/E) antibiotic days (during index admission and cumulative 30-day postoperative period) and use of routine pre-discharge white blood cell count.

Table 1
Unadjusted means/rates and adjusted observed-to-expected ratios (O/Es) for antibiotic utilization outcomes by hospital, ranked by routine pre-discharge white blood cell count (RPD-WBC) use. Outliers are highlighted with light grey representing lower than expected O/Es and dark grey representing higher than expected O/Es.

Hospital	RPD-WBC Use	Postoperative Antibiotic Utilization Outcomes							
		Index Antibiotic Days		Discharge Antibiotic Days		Any Discharge Antibiotics		Total Antibiotic Days	
	% (N)	Mean	O/E	Mean	O/E	Rate	O/E	Mean	O/E
1	100% (34/34)	4.19	0.93	0.44	0.71	13.9%	0.06	5.11	0.56
2	92.2% (130/141)	5.37	1.16	5.76	1.24	86.8%	1.36	11.22	1.17
3	88.0% (73/83)	5.82	1.25	4.38	1.11	73.2%	0.64	11.14	1.16
4	50.0% (21/42)	4.33	0.93	5.05	1.16	79.1%	1.14	10.07	0.97
5	35.0% (36/103)	4.05	0.94	3.73	0.87	79.5%	0.87	8.37	0.90
6	30.0% (12/40)	6.00	1.33	6.19	1.17	98.4%	5.37	13.94	1.44
7	19.2% (18/94)	5.11	1.07	5.02	1.17	79.8%	0.97	10.93	1.13
8	17.5% (11/63)	5.33	1.18	6.32	1.44	81.3%	0.84	12.57	1.33
9	7.4% (7/95)	4.63	1.00	2.90	0.75	72.4%	0.67	8.66	0.91
10	5.0% (3/60)	3.83	0.85	6.29	1.28	91.3%	2.18	11.01	1.17
11	2.5% (2/79)	4.33	0.98	3.96	0.98	74.4%	0.67	9.59	1.01
12	2.3% (3/128)	4.40	0.98	2.96	0.63	84.0%	1.68	7.99	0.78
13	1.5% (3/201)	4.38	0.92	6.45	1.30	93.4%	2.67	11.27	1.14
14	0.69% (1/145)	2.87	0.64	2.77	0.65	80.1%	0.80	6.80	0.70

complicated appendicitis with multiple intraoperative findings of severe disease, which varied significantly across hospitals (range: 26.7%–75.0%, $p < 0.01$).

3.1. Routine pre-discharge WBC utilization

RPD-WBC was obtained in 27.1% of all patients and utilization rates varied 145-fold among hospitals (0.69%–100%, $p < 0.01$; Table 1, Figs. 1–4). Median value of RPD-WBC was 8.9 (IQR 7.0–11.0).

3.2. Antibiotic utilization

The mean duration of antibiotic treatment during the index admission was 4.6 ± 3.5 days, mean duration of antibiotics prescribed at discharge was 4.6 ± 3.3 days, and mean cumulative 30-day antibiotic treatment days was 9.9 ± 5.7 days. Overall, 81.3% of children were prescribed antibiotics at discharge. Both unadjusted and adjusted O/E measures of antibiotic utilization varied widely across centers (all $p < 0.01$; Table 1). No correlation was found between hospital-level RPD-WBC utilization rates and antibiotic days during index admission ($r = +0.43$ [95% CI -0.12 to +0.78], $p = 0.12$), at discharge ($r = +0.08$ [95% CI -0.47, +0.58], $p = 0.80$), or the cumulative 30-day postoperative period ($r = +0.14$ [95% CI -0.42 to +0.62], $p = 0.64$; Fig. 1). There was no correlation between hospital-level RPD-WBC utilization rates and rate of children prescribed antibiotics at discharge ($r = -0.27$ [95% CI -.70, +0.31], $p = 0.37$).

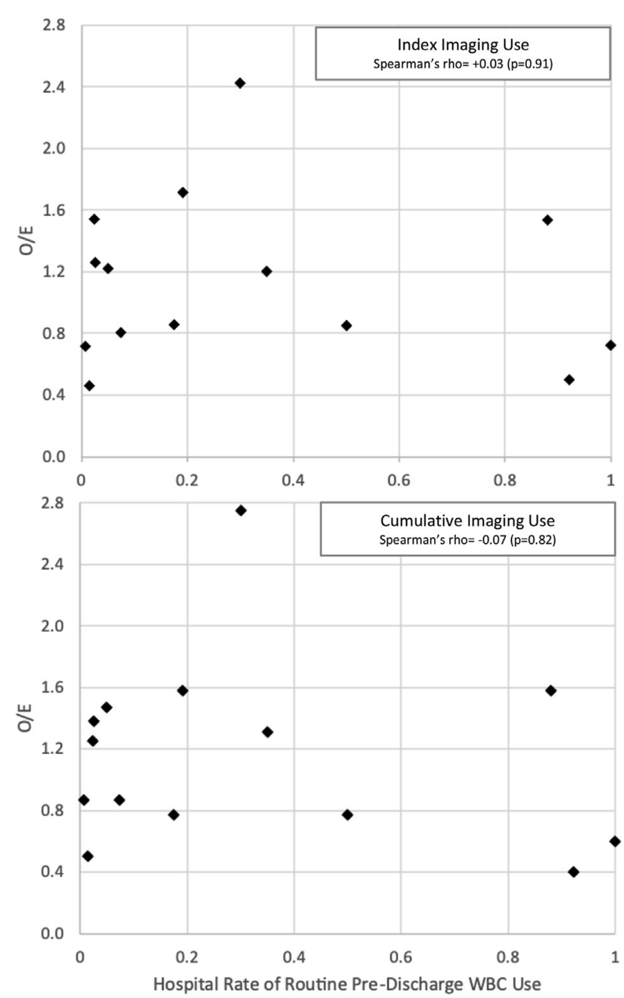

Fig. 2. Correlation of Postoperative Imaging and Routine Pre-Discharge WBC Utilization: Correlation of 14 children's hospitals' adjusted observed-to-expected ratios (O/E) for postoperative abdominal imaging use (during index admission and cumulative 30-day postoperative period) and use of routine pre-discharge white blood cell count.

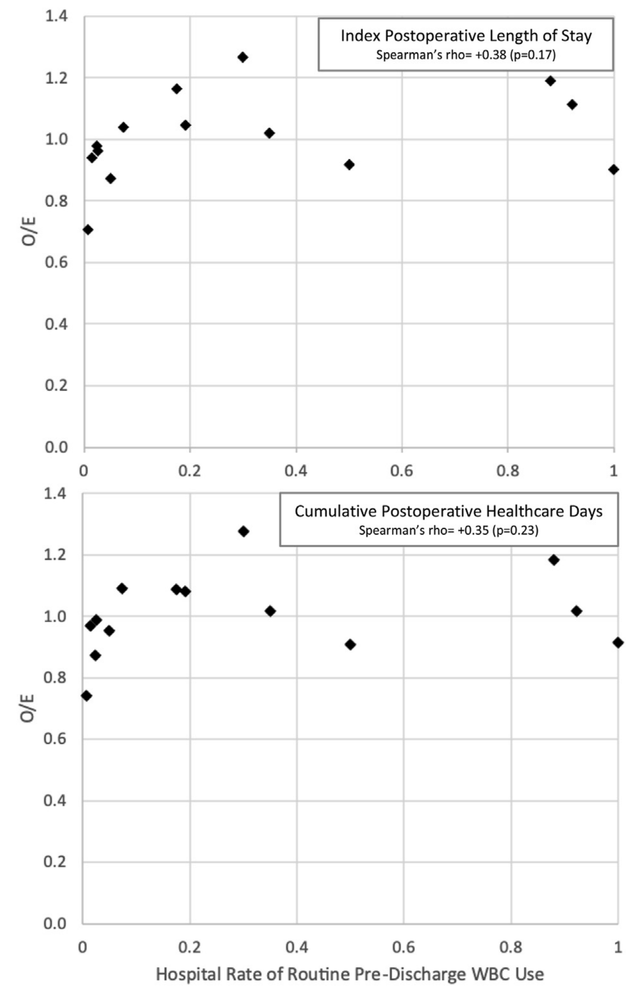

Fig. 3. Correlation of Healthcare Days and Routine Pre-Discharge WBC Utilization: Correlation of 14 children's hospitals' adjusted observed-to-expected (O/E) healthcare days (index length of stay and cumulative 30-day postoperative days) and use of routine pre-discharge white blood cell count.

3.3. Imaging utilization

The overall rate of postoperative abdominal imaging use during the index admission was 14.5%. Postoperative imaging rates during the index admission ranged from 6.0 to 33.9% across hospitals and adjusted hospital-level O/E's for index imaging rates ranged from 0.46 to 2.42 ($p < 0.01$). Four of 14 hospitals were statistical outliers for index imaging based on O/Es, with 2 hospitals having higher and 2 having lower O/E's. The overall rate of postoperative abdominal imaging during the 30-day postoperative period was 21.9%. 30-day postoperative imaging rates ranged from 7.8 to 48.4% across hospitals and adjusted hospital-level O/E's ranged from 0.40 to 2.75 ($p < 0.01$). Three of 14 hospitals were statistical outliers for 30-day postoperative imaging based on O/Es, with 1 hospital having higher and 2 having lower O/E's (Table 2).

No correlation was found between hospital-level RPD-WBC utilization rates and imaging use during the index admission ($r = +0.03$ [95% CI -0.51 to +0.55], $p = 0.91$) or 30-day postoperative period ($r = -0.07$ [95% CI -0.58 to +0.48], $p = 0.82$; Fig. 2).

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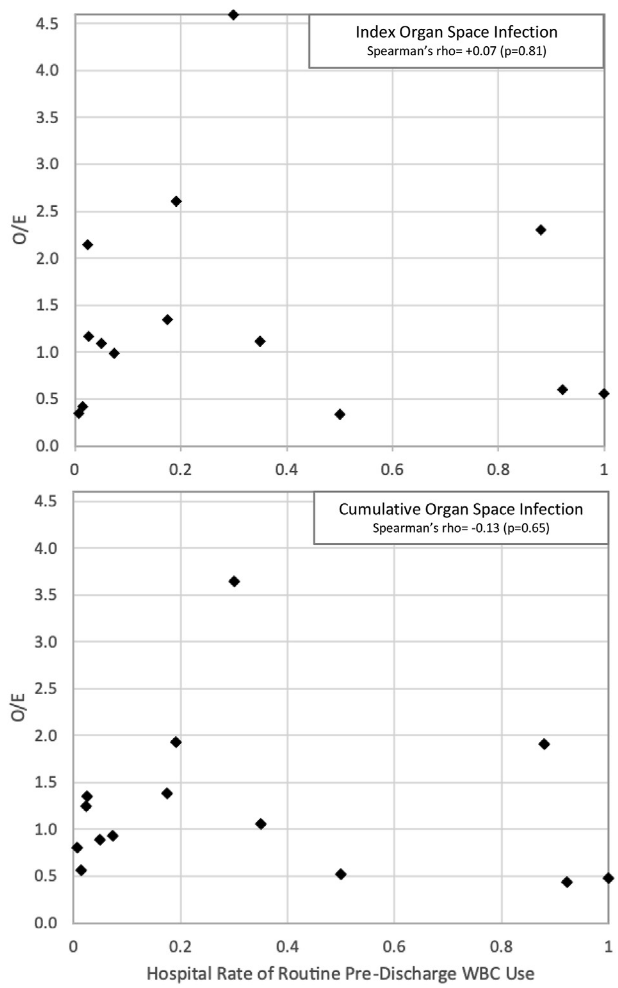

Fig. 4. Correlation of Organ Space Infections and Routine Pre-Discharge WBC Utilization: Correlation of 14 children's hospitals' adjusted observed-to-expected ratios (O/E) for organ space infection rate (diagnosed during index admission and cumulative 30-day postoperative period) and use of routine pre-discharge white blood cell count.

3.4. Health care visit days

The mean PLOS during index admission was 4.8 ± 4.0 days. The mean index PLOS ranged from 3.3 to 6.1 days across hospitals and adjusted hospital-level O/E for index PLOS ranged from 0.71 to 1.26 ($p < 0.01$). Three of 14 hospitals were statistical outliers for index PLOS based on O/Es, with 2 hospitals having higher and 1 having lower O/E's. The mean cumulative 30-day postoperative healthcare days was 5.7 ± 4.4 days. Mean cumulative healthcare days ranged from 4.1 to 7.6 days across hospitals and adjusted hospital-level O/E's ranged from 0.74 to 1.27 ($p < 0.01$). Three of 14 hospitals were statistical outliers for cumulative healthcare days based on O/Es, with 2 hospitals having higher and 1 having lower O/E's (Table 2). The overall revisit rate was 13.0%. Revisit rate ranged from 5.6 to 21.0% across hospitals and adjusted-hospital level O/E for revisits ranged from 0.73 to 1.37 ($p = 0.04$). Zero of the 15 hospitals were statistical outliers for revisit rates.

No correlation was found between hospital-level RPD-WBC utilization rates and healthcare days during index admission ($r = +0.38$ [95% CI -0.18 to +0.76], $p = 0.18$) or cumulative during the 30-day postoperative period ($r = +0.35$ [95% CI -0.23 to +0.74], $p = 0.23$; Fig. 3) or revisit rates ($r = -0.20$ [95% CI -0.66 to +0.37], $p = 0.51$).

3.5. Organ space infections

The overall rate of OSI diagnosed during the index admission was 9.8%. Index admission OSI rates ranged from 0.0 to 30.6% across hospitals and adjusted hospital-level O/E's for index OSI rates ranged from 0.34 to 4.59 ($p < 0.01$). Five of 14 hospitals were statistical outliers for index OSI based on O/Es, with 3 hospitals having higher and 2 having lower O/E's. The overall rate of OSI diagnosed during the 30-day postoperative period was 14.1%. 30-day postoperative OSI rates ranged from 2.8% to 40.3% across hospitals and adjusted hospital-level O/E's ranged from 0.43 to 3.64 ($p < 0.01$). Four of 14 hospitals were statistical outliers for 30-day postoperative OSI based on O/Es, with 3 hospitals having higher and 1 having lower O/E's (Table 2).

No correlation was found between hospital-level RPD-WBC utilization rates and OSI during the index admission period

Table 2
Unadjusted means/rates and adjusted observed-to-expected (O/Es) for cumulative 30-day postoperative outcomes by hospital, ranked by routine pre-discharge white blood cell count (RPD-WBC) use. Outliers are highlighted with light grey representing lower than expected O/Es and dark grey representing higher than expected O/Es.

Hospital	RPD-WBC Use	Cumulative 30-day Postoperative Outcomes					
		Postoperative Imaging		Healthcare Days		Organ Space Infection	
	% (N)	Rate	O/E	Mean	O/E	Rate	O/E
1	100% (34/34)	11.1%	0.60	5.25	0.91	2.8%	0.48
2	92.2% (130/141)	7.8%	0.40	5.75	1.02	4.8%	0.43
3	88.0% (73/83)	32.1%	1.58	6.98	1.18	23.2%	1.91
4	50.0% (21/42)	18.6%	0.77	5.49	0.91	7.0%	0.53
5	35.0% (36/103)	26.0%	1.31	5.58	1.02	11.8%	1.06
6	30.0% (12/40)	48.4%	2.75	7.60	1.27	40.3%	3.64
7	19.2% (18/94)	31.9%	1.58	6.48	1.08	21.8%	1.93
8	17.5% (11/63)	14.7%	0.77	5.97	1.09	16.0%	1.38
9	7.4% (7/95)	19.0%	0.87	6.40	1.09	11.4%	0.93
10	5.0% (3/60)	29.0%	1.47	5.30	0.95	8.7%	0.89
11	2.5% (2/79)	27.8%	1.38	5.59	0.99	16.7%	1.35
12	2.3% (3/128)	28.2%	1.25	4.99	0.87	21.2%	1.25
13	1.5% (3/201)	11.4%	0.50	5.72	0.97	8.1%	0.57
14	0.69% (1/145)	18.6%	0.87	4.10	0.74	10.9%	0.80

(r = +0.07 [95% CI -0.48 to +0.58], p = 0.81) or 30-day postoperative period (r = −0.13 [95% CI -0.62 to +0.43], p = 0.65; Fig. 4).

4. Discussion

In this analysis of 1528 children with complicated appendicitis at 14 NSQIP-Pediatric hospitals, marked practice variation was found in the utilization of routine WBC obtained prior to discharge. The magnitude of equipoise surrounding this practice was substantial, with some hospitals obtaining a RPD-WBC in every patient while others rarely, if ever, obtaining a RPD-WBC. Marked variation in outcomes was also observed across hospitals for OSI and measures of resource utilization, however, increasing use of RPD-WBC at the hospital-level did not correlate with reduced OSI's or resource utilization for any study measure.

To our knowledge, this is the first multicenter analysis to examine the relationship between RPD-WBC and outcomes in children with complicated appendicitis and the most comprehensive to date in terms of evaluating the spectrum of outcomes that may plausibly be influenced. Previous analyses have been limited to single center studies evaluating the effects of WBC utilization on OSI and discharge antibiotic use. In a retrospective single center analysis of 450 children with complicated appendicitis who had RPD-WBC obtained, WBC >12,000 was associated with a 27% increased OSI risk [7]. The existing literature is limited and conflicting as to whether RPD-WBC data can be used to affect meaningful change in care or outcomes on children with complicated appendicitis. In a single center analysis, post-discharge antibiotic utilization was compared between 152 children who received post-discharge antibiotics if RPD-WBC was elevated to 136 patients without RPD-WBC data treated with mandatory post-discharge antibiotics. Discharge antibiotic use was significantly lower in the RPD-WBC group (100% vs. 11.2%) and no differences were found in post-discharge OSI (7.9% vs. 4.4%), though the analysis may have been underpowered [6]. In contrast, a single center study of 313 children demonstrated that implementation of a clinical practice guideline that (among numerous other important changes) eliminated RPD-WBC use, reduced RPD-WBC utilization (44.4% vs. 4.1%) and OSI's (24.1% vs. 9.8%) while improving resource utilization (postoperative CT use 29.3% vs. 13.1%; PLOS 5.1 vs. 4.6 days) [17]. The present multicenter analysis found no correlation between RPC-WBC utilization and outcomes at the hospital-level.

In aggregate the results of this analysis would suggest that the practice of obtaining RPD-WBC may not adequately discriminate children that would and would not benefit from further diagnostic imaging or ongoing treatment in a manner that improves a hospital's outcomes. Increased use of RPD-WBC did not correlate with reduced revisit rates or cumulative 30-day healthcare visit days, suggesting RPD-WBC use does not facilitate early recognition and treatment of clinically relevant OSI's during the index admission. Furthermore, increased use of RPD-WBC was not correlated with lower antibiotic utilization during the index admission or cumulative 30-day period, suggesting the practice does not improve antibiotic stewardship. Similar lack of correlation was found between RPD-WBC use and imaging utilization, suggesting selective imaging based on RPD-WBC did not improve radiation stewardship or imaging-associated resource utilization. Hospitals routinely obtaining RPD-WBC may therefore want to critically examine their outcomes to examine whether the practice had led to improved patient care or value over time. Limiting RPD-WBC utilization could also reduce discomfort and distress associated with unnecessary venipuncture and reduce resource utilization by avoiding laboratory charges.

The results of this study must be viewed in the context of its limitations. While data collection methods for NSQIP-Pediatric and the supplemental chart review process were robust and standardized, misclassification of exposures and outcomes is possible due to their retrospective nature. Data regarding the clinical decision to obtain a pre-discharge WBC were not available and assumptions were made that WBC collected within a day of discharge in children was done so routinely. It is probable that some of these patients had laboratory data obtained due to clinical deterioration, resulting in misclassification of some exposures. However, the exclusion of patients with postoperative fevers and OSI's diagnosed during the index admission from the calculation of RPD-WBC utilization rates should serve to limit this potential misclassification. The observation that hospitals' utilization of pre-discharge WBC ranged from virtually never to always using this definition suggests face validity of the assumption of a “routine” laboratory assessment, particularly in the context of the relatively low pre-discharge OSI rate of 9.8%. Hospitals included in this analysis may have utilized RPD-WBC data differently for clinical decision-making (e.g., establish discharge readiness, antibiotic duration, need for surveillance imaging), which we were unable to account for in this analysis. Individual centers may have identified specific clinical scenarios or pathways in which RPD-WBC provide benefit that may not be apparent in this hospital-level correlation analysis. Further work directed at the specific clinical decisions informed by a RPD-WBC may be warranted. The results of this study were derived from a consortium of academic teaching hospitals and may not be generalizable to other healthcare settings. Finally, despite the relatively large number of patients, with 14 centers this analysis is only powered to detect strong correlations (alpha: 0.05, Power: 0.80, effect size: rho >|0.70|) [18]. While the limited sample size may prevent detection of statistical significance of weaker correlations, it is noteworthy that the strength of the correlations between RPD-WBC utilization and 30-day cumulative outcomes were negligible to weak at best. Furthermore, there was a positive correlation with increased RPD-WBC and cumulative healthcare and antibiotic days, arguably the two most important measures of resource utilization, which suggest that RPD-WBC is unlikely to be associated with reduced resource utilization.

Despite the limitations above, the results of this analysis suggest that hospitals' utilization of RPD-WBC does not correlate with improved outcomes or lower resource utilization. These results challenge the clinical utility of routinely obtaining WBC counts prior to discharge to guide clinical decision-making and may have important implications for management of children with complicated appendicitis given the tremendous equipoise surrounding this practice among hospitals.

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