Predictive Value of Routine WBC Count Obtained Before Discharge for Organ Space Infection in Children with Complicated Appendicitis: Results from the Eastern Pediatric Surgery Network

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BACKGROUND: The objective of this study was to evaluate the clinical utility of a routine predischarge WBC count (RPD-WBC) for predicting postdischarge organ space infection (OSI) in children with complicated appendicitis.

STUDY DESIGN: This was a multicenter study using NSQIP-Pediatric data from 14 hospitals augmented with RPD-WBC data obtained through supplemental chart review. Children with fever or surgical site infection diagnosed during the index admission were excluded. The positive predictive value (PPV) for postdischarge OSI was calculated for RPD-WBC values of persistent leukocytosis ($\geq 9.0 \times 10^3$ cells/μL), increasing leukocytosis (RPD-WBC > preoperative WBC), quartiles of absolute RPD-WBC, and quartiles of relative proportional change from preoperative WBC. Logistic regression was used to calculate predictive values adjusted for patient age, appendicitis severity, and use of postdischarge antibiotics.

RESULTS: A total of 1,264 children were included, of which 348 (27.5%) had a RPD-WBC obtained (hospital range: 0.8 to 100%, $p < 0.01$). The median RPD-WBC was similar between children who did and did not develop a postdischarge OSI (9.0 vs 8.9; $p = 0.57$), and leukocytosis was absent in 50% of children who developed a postdischarge OSI. The PPV of RPD-WBC was poor for both persistent and increasing leukocytosis (3.9% and 9.8%, respectively) and for thresholds based on the quartiles of highest RPD-WBC values (>11.1, PPV: 6.4%) and greatest proportional change (<32% decrease from preoperative WBC; PPV: 7.8%).

CONCLUSIONS: Routine predischarge WBC data have poor predictive value for identifying children at risk for postdischarge OSI after appendectomy for complicated appendicitis. (J Am Coll Surg 2023;236:1181–1187. © 2023 by the American College of Surgeons. Published by Wolters Kluwer Health, Inc. All rights reserved.)

Appendicitis is the most common abdominal surgical emergency in childhood, with an annual incidence of 80,000 cases in the US alone.[1-4] Approximately 25% of children are found to have complicated disease at exploration, and of these, 10% to 15% will develop a postoperative organ space infection (OSI).[2,5-7] One-third of OSIs are

Members of the Eastern Pediatric Surgery Network are listed in the Appendix.

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Abbreviations and Acronyms

IQR = interquartile range
OSI = organ space infection
RPD-WBC = routine predischarge WBC count

diagnosed after discharge from the index admission and are associated with unplanned hospital revisits, prolonged length of stay, and increased resource utilization.[3,8-11]

Identification of patients at risk of OSI at time of discharge may lead to improved outcomes through targeted surveillance imaging and refining treatment endpoints such as antibiotic duration and discharge criteria. The use of a routine predischarge WBC count (RPD-WBC) has been reported as a strategy for stratifying postdischarge OSI risk and informing clinical decision-making.[12-14] However, existing studies remain conflicting as to the clinical utility of RPD-WBC data for this purpose and how RPD-WBC thresholds should best be used to discriminate postdischarge OSI risk in children otherwise clinically ready for discharge.[9,10,13] Considering that approximately 95% of children with complicated disease will not develop an OSI after discharge (irrespective of WBC testing), WBC thresholds with relatively high positive predictive value for OSI may potentially provide the best clinical utility for informing treatment decisions.

With the above considerations, the goal of this multicenter analysis was to evaluate the predictive value of RPD-WBC data to identify children at risk of postdischarge OSI after appendectomy for complicated appendicitis. More specifically, we aimed to characterize predictive values associated with RPD-WBC data in the context of different thresholds based on absolute value and relative change from WBC data obtained preoperatively, adjusting for patient age, disease severity, and postdischarge antibiotic use.

METHODS

Study design and data source

This was a retrospective, multicenter cohort study using data from the American College of Surgeon's NSQIP-Pediatric augmented with operative report and RPD-WBC data obtained through supplemental chart review at 14 centers participating in the Eastern Pediatric Surgery Network. Data in NSQIP-Pediatric are collected through a standardized chart review process by dedicated surgical clinical reviewers. The accuracy of NSQIP-Pediatric data is facilitated by periodic auditing, mandatory recertification for reviewers, and availability of American College of Surgeons clinical support for questions regarding data definitions and abstraction.[15,16] Supplemental chart review was facilitated through creation of a manual of operations and training videos, which were reviewed by each site prior to supplemental data collection. Standardized 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 (approval IRB-P00042228).

Study cohort

Children (ages 3 to 18 years) undergoing appendectomy were identified from the NSQIP-Pediatric database from July 2015 to June 2020. Patients with complicated appendicitis based on validated NSQIP-Pediatric intraoperative criteria (visible hole, extraluminal fecalith, abscess, or diffuse fibrinopurulent exudate outside the pelvis or right lower quadrant) were considered for inclusion.[2,5] Patients were excluded if they were diagnosed with a surgical site infection (including incisional or organ space infection), underwent percutaneous drainage, or had a postoperative fever prior to discharge from the index hospitalization.

Classification of exposures and outcomes

A WBC obtained in the postoperative period was categorized as a RPD-WBC if it was obtained within 1 calendar day of discharge in patients meeting inclusion criteria. The goal of these criteria was to minimize inclusion of WBC data obtained in response to clinical deterioration rather than for routine predischarge prognostication. WBC values are reported in units of 10^3 cells/μL.

Test characteristics associated with RPD-WBC data were evaluated in the context of the absolute value of the RPD-WBC and of the relative proportional change from preoperative WBC to provide a comprehensive assessment of predictive value using clinically meaningful thresholds that could be used at the point of care. These included the presence of persistent leukocytosis (RPD-WBC ≥ 9.0), increased leukocytosis relative to preoperative WBC (RPD-WBC > preoperative WBC), and both quartiles and deciles of RPD-WBC value and RPD-WBC proportional change relative to preoperative WBC.

The primary outcome of the study was organ space infection or need for percutaneous drainage after discharge from the index admission. We evaluated the rate of postoperative abdominal imaging (ultrasound, CT, or MRI) during the index admission by the RPD-WBC group and across different RPD-WBC values. The goal of this secondary analysis was to evaluate for possible selection bias within the cohort. If a large proportion of children with an elevated RPD-WBC value were to have imaging obtained prior to discharge, this might bias the sample by preferentially excluding children with elevated RPD-WBC resulting in diagnosis of OSI during the index admission.

Statistical analysis

Chi-square and Wilcoxon rank sum tests were used for univariate comparisons. Multivariate logistic regression was used to model postdischarge OSI as a function of RPD-WBC threshold test positivity, adjusting for patient age, appendicitis severity, and use of antibiotics after discharge. Least squares means estimates of the adjusted rates of postdischarge OSI in patients above and below the RPD-WBC thresholds were used to derive positive and negative predictive values. Similarly, logistic regression models with the RPD-WBC threshold positivity as the outcome and postdischarge OSI as a covariate were used to estimate sensitivity and specificity, adjusting for the same covariates. Appendicitis severity was categorized as 1 vs multiple intraoperative findings of complicated disease based on previously validated risk stratification criteria.[2,5] The analyses were performed with SAS statistical software (version 9.4; SAS Institute, Inc.). Statistical significance threshold was considered with a 2-sided p < 0.05.

RESULTS

Study population

A total of 1,264 children with complicated appendicitis were included. RPD-WBC were obtained in 27.5% (348) of all patients, and rates varied 125-fold among hospitals (0.8% to 100%; p < 0.01). Children who had a RPD-WBC obtained were older (median: 10 years [interquartile range (IQR) 7 to 13] vs 9 years [IQR 7 to 12]; p = 0.01) and had similar rate of female sex (40.5% vs 37.5%; p = 0.32) compared to those who did not have a RPD-WBC obtained.

Postoperative abdominal imaging was obtained during the index hospitalization in 4.8% of patients and was similar among those who did and did not have RPD-WBC obtained (4.3% vs 5.0%; p = 0.60). In children with the highest quartile of absolute RPD-WBC values (>11.1), postoperative abdominal imaging was obtained in 8.0% of cases compared to 3.1% in the lower 3 quartiles of RPD-WBC values (≤11.1; p = 0.05). The postdischarge OSI rate overall was 4.4% and was similar among patients who did and did not have a RPD-WBC obtained (4.0% vs 4.6%; p = 0.66).

Absolute values of WBC

The median RPD-WBC value was 8.9 (IQR 7.0 to 11.1) and was similar in those that did and did not develop a postdischarge OSI (9.0 vs 8.9; p = 0.57; Figs. 1, 2). Persistent leukocytosis (RPD-WBC ≥ 9.0) was present in 48.9% of RPD-WBC cases and did not differ between those that did and did not develop a postdischarge OSI (OSI 50.0% and no OSI 48.8%; p = 0.93). Positive predictive values for RPD-WBC thresholds ranged between 3.9% and 10.7% and were marginally better than the baseline postdischarge OSI probability of 4.6% in patients without any RPD-WBC data (Table 1). Negative predictive values associated with RPD-WBC thresholds ranged from 96.2% and 97.5% and were marginally better than the 95.4% probability of not developing a postdischarge OSI in patients without any RPD-WBC data (Table 1).

Relative change in WBC value from preoperative to predischarge

The median admission WBC value was 17.2 (IQR 13.4 to 20.6) for patients who had RPD-WBC obtained and was similar in those that did and did not develop a postdischarge OSI (15.3 [IQR 11.1 to 18.3] vs 17.3 [IQR 13.4 to 20.6]; p = 0.22; Fig. 1). Increasing leukocytosis (RPD-WBC greater than preoperative WBC) was present in 21.4% of patients who developed a postdischarge OSI compared to 7.8% of patients who did not (p = 0.07; Fig. 2). The median change in WBC value from preoperative WBC to RPD-WBC was a 48% decrease (IQR -59% to -32%) and was similar between those that did and did not develop a postdischarge OSI (33% decrease [IQR -55% to 0%] vs 48% decrease [IQR -59% to -33%]; p = 0.13; Figs. 1, 3). Positive predictive values for RPD-WBC thresholds based on relative change from preoperative values ranged from 4.0% to 10.7% and only marginally improved upon the baseline postdischarge OSI probability of 4.6% in patients without RPD-WBC data (Table 1). Negative predictive values ranged between 96.6% and 97.5% and were only marginally better than the 95.6% probability of not developing a postdischarge OSI in patients without RPD-WBC data (Table 1).

DISCUSSION

In this multicenter analysis of 1,264 children with complicated appendicitis, substantial practice variation was found in the use of routine predischarge WBC data across hospitals. Among children who had a RPD-WBC obtained, all thresholds based on RPD-WBC values and relative change from preoperative WBC values had poor ability to predict postdischarge OSI. It is noteworthy that

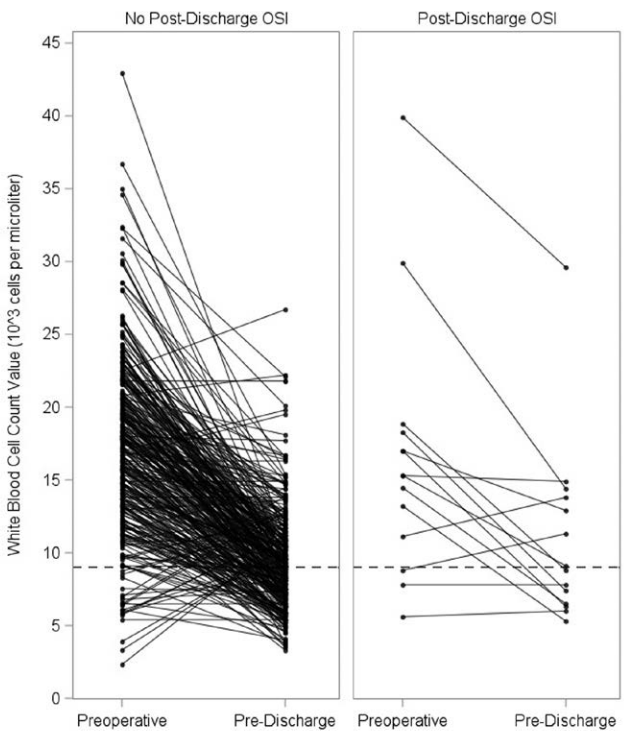

Figure 1. Relationship between preoperative and predischarge WBC count values in children with complicated appendicitis who did and did not develop a postdischarge organ space infection (OSI). The leukocytosis threshold of 9×10^3 cells/μL is marked by the dashed line.

the predictive value of RPD-WBC data was poor even at the extremes of leukocytosis thresholds, at which positive predictive values associated with the highest deciles of absolute WBC and proportional change were only as high as 10.7%. The practical implications of these findings are that even at the highest PPV performance threshold identified, nearly 90% of children who test "positive" will not develop a postdischarge OSI.

To our knowledge, this is the first multicenter study to evaluate predictive value of routine WBC data obtained prior to discharge for postdischarge OSI in children with appendicitis. In a single-center retrospective analysis of RPD-WBC data in 450 children with gangrenous and complicated appendicitis, a threshold of WBC > 12.0 (45.3% of all patients) was associated with a 27% increased risk of OSI.[9] While existing literature suggests that leukocytosis of varying thresholds identified from a RPD-WBC is associated with increased OSI risk, data from the present analysis would suggest that any increased risk (and therefore potential clinical utility) associated with this finding is likely to be negligible given the poor positive predictive value and low prevalence of OSI's after discharge.[9,10] It is worth noting that although the observed negative predictive values associated with RPD-WBC thresholds examined in this analysis were all relatively high (95.5 to 97.5%), the clinical utility of these NPV data over not testing at all are negligible considering that 96.0% of all patients will not develop a postdischarge OSI.

These data may have important implications for reducing resource utilization in children who are otherwise clinically ready for discharge. For example, abandoning the practice of obtaining a RPD-WBC that might influence decisions to delay discharge or obtain abdominal imaging may greatly reduce resource utilization and days absent from school and work for patients and caregivers, respectively. Furthermore, omission of RPD-WBC testing would have obvious benefits in avoiding the discomfort and cost associated with unnecessary laboratory testing. The potential impact of this practice change could be substantial when considering the current magnitude of practice variation observed in this analysis. Survey data and review of clinical practice guidelines estimate that between 35% and 40% of hospitals utilize laboratory data prior to discharge to guide clinical decisions including antibiotic treatment duration and imaging use.[12,14]

The results of this analysis must be interpreted in the context of its limitations. Although NSQIP utilizes a rigorous chart review process and standardized definitions for both exposures and outcomes, the data collected in NSQIP-Pediatric are retrospective, and errors in misclassification and identification of outcomes are possible. The clinical indications for obtaining a WBC in the postoperative period were not known, and assumptions were made that WBC collected within 1 day of discharge in children who did not have a preceding fever or surgical site infection were "routine" and not in response to clinical deterioration. This assumption is supported by the observations that postdischarge OSI rates were similar between patients who did and did not have an RPD-WBC obtained and that the practice of obtaining RPD-WBC was exceedingly rare at some hospitals while routine at others. However, it is possible that such misclassification could occur that would bias our results to overestimate the predictive value of RPD-WBC data. In contrast, predischarge WBC data may have resulted in a decision to delay discharge or obtain imaging, leading to an OSI diagnosis during the index admission. These children would have been excluded from the analysis, effectively biasing the results toward underestimation of PPV of RPD-WBC data. However, given that index abdominal imaging rates were low and similar regardless of whether a RPD-WBC was obtained, we believe these misclassified cases are likely to be infrequent and would not appreciably impact the conclusions of this analysis surrounding the limited utility of RPD-WBC data for clinical decision-making.

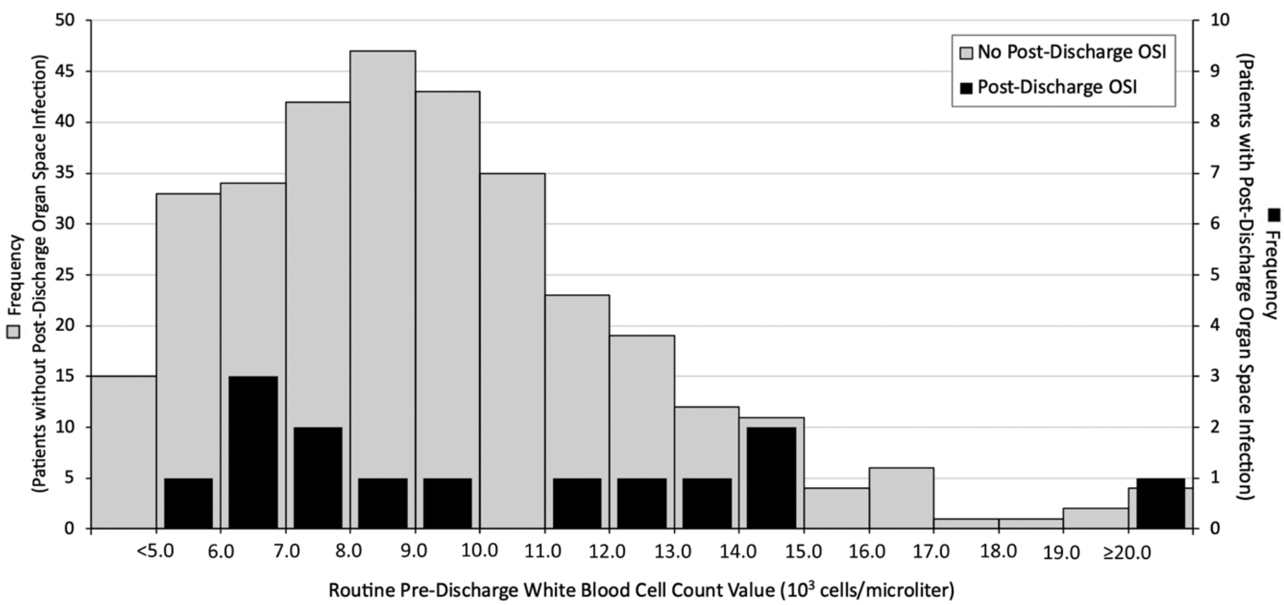

Figure 2. Relative distribution of routine predischarge WBC count in children with complicated appendicitis who did and did not develop a postdischarge organ space infection (OSI).

CONCLUSIONS

Despite these limitations, the results of this analysis suggest that postdischarge organ space infections are not reliably predicted by routine WBC data obtained prior to discharge in children otherwise clinically ready for discharge. Whether or not clinical utility exists for WBC data in patients with clinical evidence of persistent or recurrent OSI remains uncertain. Future efforts should therefore explore the predictive value of postoperative WBC data in the context of clinically relevant

Table 1. Test Performance of Routine Predischarge WBC Data for Postdischarge Organ Space Infection based on Thresholds of Absolute Values and Proportional Change from Preoperative WBC, Positive Predictive Value

Positive test threshold	PPV (95% CI)	NPV (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Absolute value of routine predischarge WBC count, %				
Persistent leukocytosis (≥9.0)	3.9 (1.8 to 8.2)	96.2 (92.2 to 98.2)	50.0 (25.9 to 74.2)	51.2 (45.8 to 56.6)
WBC value, by quartile				
Quartile 2: ≥7.0	3.6 (1.9 to 6.8)	95.5 (88.4 to 98.3)	71.1 (43.4 to 88.8)	24.4 (20.1 to 29.3)
Quartile 3: ≥8.9	3.8 (1.8 to 7.9)	96.1 (91.8 to 98.2)	50.4 (26.2 to 74.5)	48.8 (43.5 to 54.2)
Quartile 4: >11.1	6.4 (2.8 to 14.0)	97.0 (94.0 to 98.5)	41.4 (19.5 to 67.3)	76.0 (71.1 to 80.3)
Highest decile of WBC value (≥14.0)	8.3 (2.6 to 23.4)	96.6 (93.9 to 98.2)	20.6 (6.7 to 48.7)	90.9 (87.3 to 93.6)
Relative change from preoperative to predischarge WBC counts, %				
Increasing leukocytosis (RPD-WBC > preoperative)	9.8 (3.1 to 27.0)	96.7 (94.0 to 98.2)	20.8 (6.7 to 48.9)	92.4 (89.0 to 94.9)
Percent change from preoperative, by quartile				
Quartile 2: <59% decrease from preoperative	4.0 (2.2 to 7.3)	96.6 (89.9 to 98.9)	78.2 (49.8 to 92.8)	25.0 (20.6 to 29.9)
Quartile 3: <48% decrease from preoperative	4.3 (2.1 to 8.6)	96.6 (92.6 to 98.5)	55.8 (30.3 to 78.6)	50.3 (44.9 to 55.6)
Quartile 4: <32% decrease from preoperative	7.8 (3.7 to 15.7)	97.5 (94.6 to 98.8)	50.2 (26.0 to 74.3)	76.1 (71.2 to 80.4)
Highest decile of % change (no decrease or increase from preoperative)	10.7 (4.0 to 25.8)	96.9 (94.3 to 98.4)	28.4 (10.9 to 56.2)	90.6 (86.9 to 93.3)

NPV, negative predictive value; PPV, positive predictive value; RPD-WBC, routine predischarge WBC count.

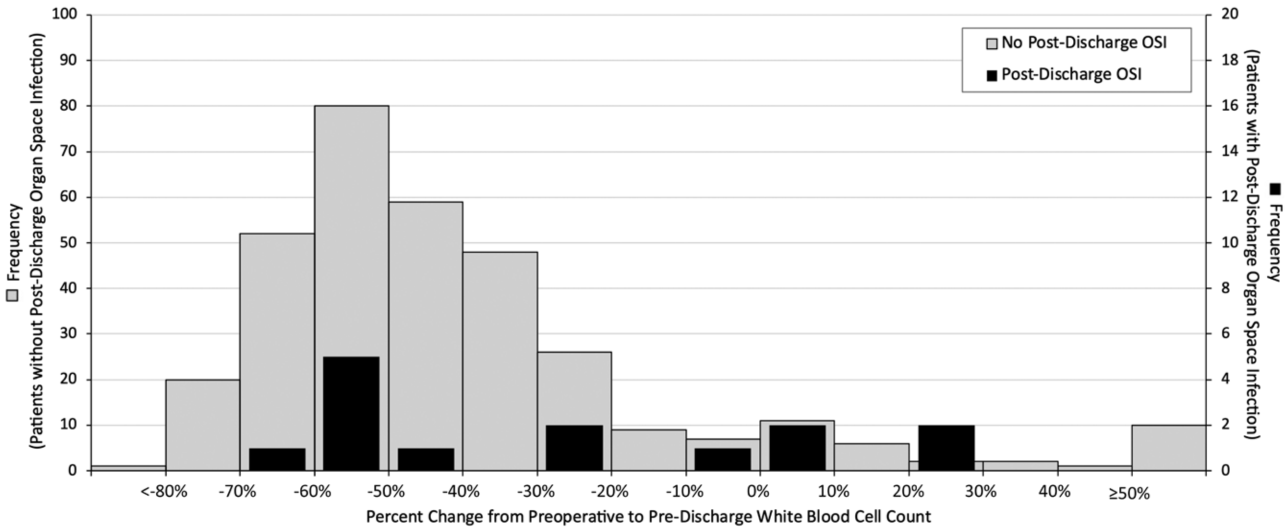

Figure 3. Relative distribution of proportional change between preoperative and routine predischarge WBC counts in children with complicated appendicitis who did and did not develop a postdischarge organ space infection (OSI).

symptoms, such as fever, recurrent abdominal pain, and diarrhea.

APPENDIX

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Invited Commentary

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Acute appendicitis represents one of the most common indications for emergent surgery, with more than 70,000 pediatric appendectomies performed each year in the US.[1] Approximately 25% of children with acute appendicitis in the US are found to have complicated disease at exploration.[2] Postoperative organ space infection (OSI) occurs in 15% to 20% of these children and is associated with prolonged length of hospital stay, hospital revisits, and increased resource use.[3] There is little consensus about postdischarge antibiotics after appendectomy for complicated appendicitis.[4] Use of clinical pathways with predischarge WBC count and if elevated, using a longer duration of postoperative antibiotics either in the hospital or after discharge demonstrated a trend towards diminishing readmission rate and decreased use of CT imaging but did not affect OSI rate.[5]

The authors of this multicenter study evaluated the predictive value of routine WBC data obtained before discharge for postdischarge OSI in children between the ages of 3 and 18 years with appendicitis.[6] This was a retrospective study of the Eastern Pediatric Surgery Network of 1,264 children treated for complicated appendicitis from July 2015 to June 2020. They used NSQIP Pediatric data