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Early versus late surgical management of complicated appendicitis in children: A statewide database analysis with one-year follow-up[☆]

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ABSTRACT

Background: Complicated appendicitis is common in children, yet the timing of surgical management remains controversial. Some support initial antibiotics with delayed operation whereas others support immediate operation. While a few randomized trials have evaluated this question, they have been small, single-center trials with limited follow-up. We present a database analysis of outcomes in early versus late surgical management of complicated appendicitis with one-year follow-up.

Methods: We conducted a retrospective review of children with complicated appendicitis presenting between 2000 and 2013, utilizing a New York State database. We compare children undergoing later versus early appendectomy with a primary outcome measure of any complication within one year as determined from ICD-9 codes.

Results: 8840 children were included in the analysis, 7708 of whom underwent early appendectomy. Patients with late appendectomy were significantly more likely to have at least one complication when compared to those undergoing early appendectomy (34.6% vs 26.7%, $p < 0.01$).

Conclusions: We present the first population-level study evaluating early versus late appendectomy in children with complicated appendicitis with a one-year follow-up period. Children undergoing late appendectomy were more likely to have a complication than those undergoing early appendectomy. These data corroborated previous studies supporting early operative management.

Level of evidence: This study provides level III evidence of a treatment study.

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Appendicitis is the most common disease requiring surgical treatment in children [1,2] and up to 30% of children with appendicitis present with appendiceal rupture [3]. Yet, the treatment of such complicated appendicitis – i.e. appendicitis resulting in abscess or generalized peritonitis – is varied. Traditionally it is managed with immediate surgery. However, in the 1980s treatment with initial antibiotics followed by “interval appendectomy” after a period of four to sixteen weeks was described [4] and this approach in management became increasingly popular. In this time period, several retrospective studies, including a meta-analysis, suggested reduced morbidity with late appendectomy [5–7].

In recent years, however, new data have questioned this practice. One study found that a substantial percentage of patients with suspected acute perforated appendicitis and a plan for interval

appendectomy require unplanned readmission [8]. Additionally, a randomized control trial demonstrated that patients undergoing immediate appendectomy had quicker return to normal activity, fewer adverse events, and lower cost to the system when compared to those with late appendectomy [9,10]. A separate randomized trial looking only at children with an appendiceal abscess had mixed findings in terms of clinical parameters when comparing early to late appendectomy [11], but demonstrated that children experienced better quality of life and parents suffered less stress when undergoing early appendectomy [12].

1. Purpose

Despite the emerging data favoring early appendectomy, no consensus exists on the optimal management of complicated appendicitis in children, and practice patterns continue to vary dramatically. This may in part be because of the fact that the majority of studies on the topic – both in favor of and against early appendectomy – were

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single-center studies, with small sample sizes, and limited follow-up periods. Thus, the purpose of our study was to compare surgical outcomes for early versus late surgical management of complicated appendicitis using a large state-level all payer database.

2. Material and methods

2.1. Data source

We utilized the New York State Department of Health Statewide Planning and Research Cooperative (SPARCS) database for analysis. This database, established in 1979, collects patient, treatment, and provider information for every hospital discharge, ambulatory surgery, emergency department visit, and outpatient service. The database includes demographic information including race and ethnicity as classified and defined by SPARCS, ICD-9 codes pertaining to primary and secondary diagnoses, procedure, length of stay, and charges. A unique identifier is assigned to every patient allowing for longitudinal analysis.

2.2. Study population

We included all children less than age 18 admitted between 2000 and 2013 with a primary diagnosis of appendicitis with generalized peritonitis (ICD-9-CM 540.0) or any diagnosis of acute appendicitis with peritoneal abscess (ICD-9-CM 540.1). Procedure codes of open and laparoscopic appendectomy (ICD-9-CM 47.01, 47.09) were used to determine the timing of surgery. Patients were excluded if they never underwent an appendectomy as we were unable to distinguish between patients being treated without surgery, patients lost to follow-up, or patients receiving further care outside of New York State. We additionally excluded children who had prior hospitalization for uncomplicated appendicitis. A detailed patient selection process is described in Fig. 1.

The independent variable was early versus late appendectomy. Early appendectomy was defined as surgery within 2 days of admission during index hospitalization as it has previously been shown that there are minimal differences in outcome between 12, 24 and 48-h delay from diagnosis to surgery [13]. Late appendectomy was defined as having

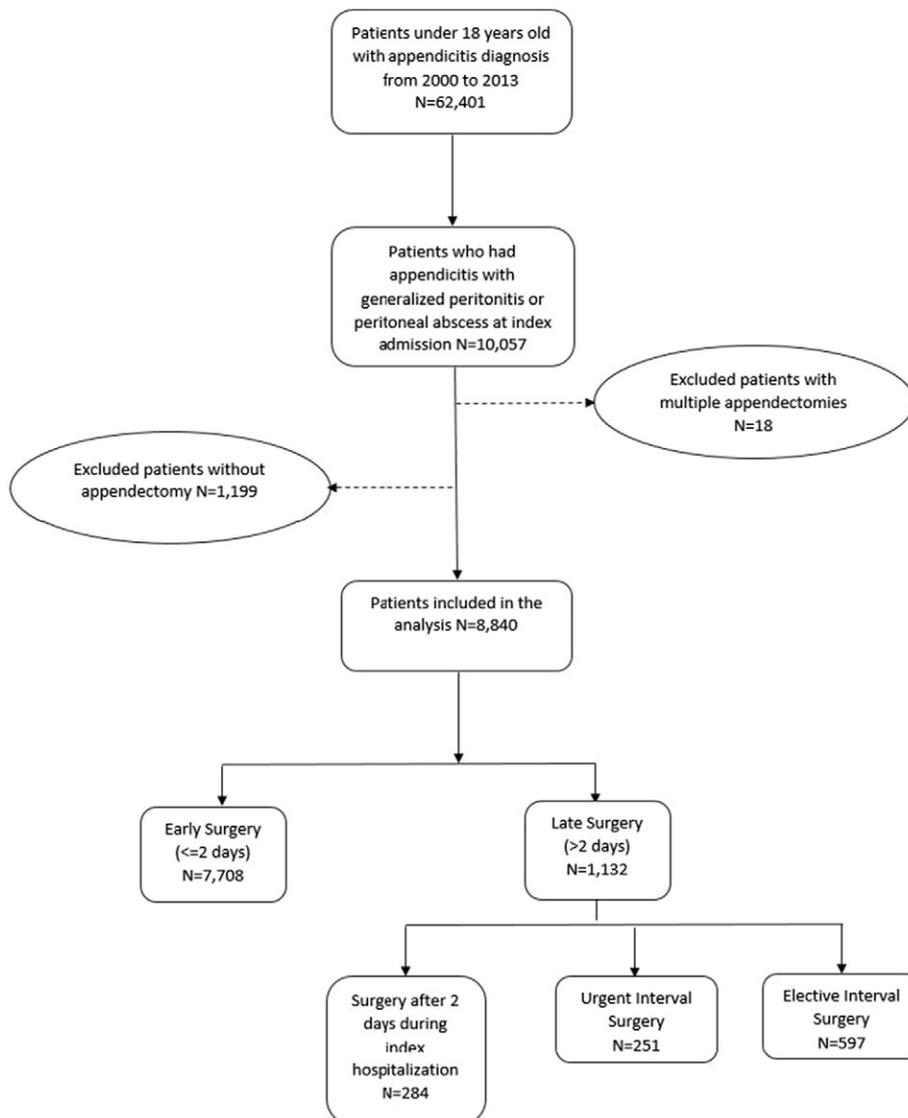


Fig. 1. Patient selection process.

surgery greater than two days after admission, whether during index hospitalization or at subsequent admission. We subdivided the late appendectomy group into subgroups on the basis of those who had appendectomy late but during index admission, those who had appendectomy during an urgent subsequent admission, and those who had appendectomy during an elective subsequent admission.

Patient characteristics included age, race, insurance status, initial diagnosis and surgical approach (open or laparoscopic). Pediatric comorbidities or associated symptoms were adapted from a previously described comorbidity model and were included if they applied to more than 10 patients in the study population; [14] a diagnosis of obesity (ICD-9 codes of 27,800, 27,801, 27,802) was also included as a comorbidity [15]. Hospital volume was determined based on average annual numbers of pediatric appendectomy procedures and categorized into tertiles.

2.3. Outcomes of interest

The primary outcome of interest was all complications within one year of follow-up (with end of study December 2014). Complications were defined by ICD-9 codes previously utilized in studies evaluating pediatric appendicitis [15–17]. Secondary outcomes included index hospital length of stay (LOS), total days of hospitalization within a one-year follow-up period, readmission rates, and cumulative hospital charges within one-year of index hospitalization. The rehospitalization during which patients underwent late appendectomy was not counted as a readmission. Prolonged total LOS and high total charges were defined as greater than 75th percentile.

2.4. Statistical analysis

For patients who had early or late appendectomy, events and percentages were presented for baseline patient demographics, initial diagnosis, surgery type, comorbidities and hospital volume. Chi-Square tests for categorical variables and Student's t-tests for continuous variables were used to assess differences in baseline characteristics. Significance was determined at $p < 0.05$.

Events and percentages were also presented for one-year in-hospital outcomes including complications and readmission and were compared between groups using Chi-Square test. Median and interquartile range of length of stay (LOS) at index admission, total LOS and total charges within 1 year were obtained and compared using Wilcoxon rank sum tests. Generalized linear mixed models, accounting for hospital clustering were used to adjust for baseline patient demographics, primary diagnosis and comorbidities. Adjusted odds ratios and 95% confidence intervals were obtained for major events, readmission, prolonged total LOS and excessive total charges.

Subgroup analyses were conducted to compare specific approaches in the late surgery group to the early surgery group. Similar statistical methods were implemented. Sensitivity analyses were performed evaluating patients with a diagnosis of appendicitis with generalized peritonitis and appendicitis with abscess separately as well as evaluating a cutoff of one day for defining patients with early appendectomy. All analyses were performed using SAS v9.3 (SAS Institute Inc., Cary, NC).

2.5. Conflict of interest and sources of funding

The authors have no conflicts of interest to declare. The study is funded by the Center for Effectiveness and Surgical Outcomes Research in the Department of Surgery at Weill Cornell Medicine.

3. Results

A total of 10,057 children were admitted for complicated appendicitis between 2000 and 2013 in New York State. 1217 children were excluded owing to having never underwent appendectomy or owing to

having multiple procedure codes for appendectomy (Fig. 1). Of the remaining 8840 children, 59.5% were male, 60.0% were White, 11.5% were Black, and 37% were on Medicaid. 48.7% presented with an initial diagnosis of generalized peritonitis and the remainder presented with an initial diagnosis of peritoneal abscess. 7708 children (87%) underwent immediate appendectomy.

Children undergoing late appendectomy were younger (Late vs. Early: average age 9.6 vs. 10.6 years, $p < 0.01$) and less likely to be male (54.9% vs. 60.2%, $p < 0.01$) (Table 1). Patients with Medicaid (41.0% vs. 36.6%, $p < 0.01$) and Black patients (13.9% vs. 11.2%, $p = 0.02$) comprised a larger percentage of the late appendectomy group when compared to the immediate appendectomy group. Patients with an initial diagnosis of appendicitis with abscess were significantly more likely to have a late appendectomy (74.0% vs. 48.0%, $p < 0.01$). When compared to early surgeries, late surgeries were more likely to be performed with laparoscopic approach (60.9% vs. 39.2%, $p < 0.01$). Children with a comorbidity of anemia, dehydration, gastroenteritis, and pleural effusion were more likely to undergo late appendectomy. Of note, the diagnosis of gastroenteritis could be viewed as a misdiagnosis contributing to the delay in appendectomy, rather than a consequence of that decision.

On univariate analysis, patients with late appendectomy were significantly more likely to have at least one complication when compared to those undergoing early appendectomy (26.1% vs. 22.9%, $p < 0.01$) (Table 2); specifically, they were more likely to have urinary (4.5% vs. 2.7%, $p < 0.01$), pulmonary (7.4% vs. 5.1%, $p < 0.01$), or iatrogenic complications (2.7% vs. 0.8%, $p < 0.01$) than those undergoing immediate appendectomy. Conversely, patients undergoing late appendectomy were less likely to have wound complications (6.1% vs. 8.1%, $p = 0.02$). Both the initial hospitalization (median 8 vs. 5 days, $p < 0.01$) and the total one-year hospitalization time (10 vs. 6 days, $p < 0.01$) were longer in the late surgery group than the early surgery group. Readmission rates (18.5% vs. 10.1%, $p < 0.01$) and total charges (Median \$47,125 vs. \$20,877, $p < 0.01$) were similarly higher in the late surgery group.

Table 1

Characteristics of children undergoing early appendectomy and late appendectomy for complicated appendicitis.

	Early Surgery	Late Surgery	p value
Total Patients	7708	1132	
Age(Mean (sd))	10.6 (4.2)	9.6 (4.5)	<0.01
Sex			<0.01
Male	4637 (60.2%)	621 (54.9%)	
Race			0.02
White	4660 (60.5%)	648 (57.2%)	
Black	864 (11.2%)	157 (13.9%)	
Other	2184 (28.3%)	327 (28.9%)	
Insurance			<0.01
Medicaid	2821 (36.6%)	464 (41.0%)	
Commercial	4250 (55.1%)	603 (53.3%)	
Medicare and Other	637 (8.3%)	65 (5.7%)	
Initial Diagnosis			<0.01
Generalized Peritonitis	4009 (52.0%)	294 (26.0%)	
Peritoneal Abscess	3699 (48.0%)	838 (74.0%)	
Surgery type			<0.01
Laparoscopic	3022 (39.2%)	689 (60.9%)	
Comorbidity on first admission			
Pulmonary disease	652 (8.5%)	91 (8.0%)	0.63
Anemia	105 (1.4%)	26 (2.3%)	0.02
Obesity	143 (1.9%)	17 (1.5%)	0.40
Dehydration	571 (7.4%)	127 (11.2%)	<0.01
Asthma	528 (6.9%)	71 (6.3%)	0.47
Gastroenteritis	108 (1.4%)	41 (3.6%)	<0.01
Pleural Effusion	111 (1.4%)	28 (2.5%)	<0.01
Hospital Volume			<0.01
Low	2782 (36.1%)	148 (13.1%)	
Medium	2638 (34.2%)	336 (29.7%)	
High	2288 (29.7%)	648 (57.2%)	

Table 2
Outcomes among patients who underwent early and late surgery for complicated appendicitis.

	Early Surgery (N = 7708)	Late Surgery (N = 1132)	p-value
Outcome during index admission			
Median LOS in days (IQR)	5 (4–8)	8 (5–12)	<0.01
Outcome during 1 year follow up			
Gastrointestinal	753 (9.8%)	125 (11.0%)	0.18
Wound	626 (8.1%)	69 (6.1%)	0.02
Other Infectious	737 (9.6%)	90 (8.0%)	0.08
Urinary	205 (2.7%)	51 (4.5%)	<0.01
Pulmonary	396 (5.1%)	84 (7.4%)	<0.01
Iatrogenic	61 (0.8%)	30 (2.7%)	<0.01
Cardiovascular	33 (0.4%)	NR	0.95
Any Complication	1763 (22.9%)	296 (26.1%)	0.01
Number of Complications			<0.01
0	5945 (77.1%)	836 (73.9%)	
1	988 (12.8%)	188 (16.6%)	
2+	775 (10.1%)	108 (9.5%)	
Readmission ^a	781 (10.1%)	210 (18.5%)	<0.01
Total LOS (days)			
Median (IQR)	6 (4–8)	10 (7–15)	<0.01
Prolonged (>75%)	1490 (19.3%)	637 (56.3%)	<0.01
Total Charges (\$) (IQR)			
Median (IQR)	20,877 (12955–35,804)	47,125 (29528–76,068)	<0.01
Excessive (>75%)	1556 (20.2%)	654 (57.8%)	<0.01

NR = Not Reportable (for events of ≤10), LOS = Length of Stay, IQR = Interquartile Range.

^a Readmission for the late surgery group did not include the admission for any interval appendectomy.

After adjusting for patient characteristics and hospital volume (Table 3), we found that patients undergoing a late appendectomy were significantly more likely to have urinary (OR 1.48, 95% CI 1.06–2.09) or iatrogenic complications (OR 2.65, 95% CI 1.62–4.31) and were more likely to be readmitted (OR 1.81, 95% CI 1.51–2.17). This group of patients was also more likely to have prolonged total LOS (OR 4.70, 95% CI 4.04–5.48) and excessive total charges (OR 4.29, 95% CI 3.60–5.12).

On subset analyses evaluating peritoneal abscess and generalized peritonitis separately, we found that patients with peritoneal abscess were significantly more likely to have iatrogenic complications (OR 2.22, 95% CI 1.23–4.04), be readmitted (OR 1.88, 1.51–2.34), have prolonged length of stay (OR 4.45 95% CI 3.70–5.34), and have excessive total charges (OR 4.08, 95% CI 3.29–5.05) if undergoing late surgery as compared to early surgery (Table 4). Similarly, patients with a diagnosis

Table 3
Adjusted odds ratio (95% CI) for 1-year outcomes among patients who underwent early and late surgery for complicated appendicitis.

	Early Surgery (N = 7708)	Late Surgery (N = 1132)	p-value
Outcome during 1 year follow up			
Gastrointestinal	Ref	0.97 (0.78–1.22)	0.81
Wound	Ref	0.70 (0.53–0.92)	0.01
Other Infectious	Ref	0.72 (0.56–0.92)	0.01
Urinary	Ref	1.48 (1.06–2.09)	0.02
Pulmonary	Ref	1.32 (0.95–1.84)	0.10
Iatrogenic	Ref	2.65 (1.62–4.31)	<0.01
Cardiovascular	Ref	0.83 (0.30–2.27)	0.71
Any Complication	Ref	1.01 (0.86–1.19)	0.91
Readmission ^a	Ref	1.81 (1.51–2.17)	<0.01
Prolonged Total LOS	Ref	4.70 (4.04–5.48)	<0.01
Excessive Total Charges	Ref	4.29 (3.60–5.12)	<0.01

^a Readmission for the late surgery group did not include the admission for any interval appendectomy.

Table 4
Adjusted odds ratio (95% CI) for 1-year outcomes among patients who underwent early and late surgery and had peritoneal abscess diagnosis.

	Crude numbers of cases		Adjusted Odds Ratios	
	Early Surgery (N = 3699)	Late Surgery (N = 838)	Late Surgery vs Early Surgery	p-value
Outcome during 1 year follow up				
Gastrointestinal	400 (10.8%)	95 (11.3%)	0.94 (0.72–1.23)	0.65
Wound	316 (8.5%)	46 (5.5%)	0.65 (0.46–0.93)	0.02
Other Infectious	386 (10.4%)	62 (7.4%)	0.66 (0.49–0.90)	<0.01
Urinary	94 (2.5%)	33 (3.9%)	1.36 (0.88–2.11)	0.17
Pulmonary	219 (5.9%)	62 (7.4%)	1.20 (0.80–1.80)	0.36
Iatrogenic	38 (1.0%)	21 (2.5%)	2.22 (1.23–4.04)	<0.01
Cardiovascular	17 (0.5%)	NR	1.29 (0.37–4.50)	0.69
Any Complication	910 (24.6%)	219 (26.1%)	1.00 (0.82–1.23)	0.96
Readmission ^a	388 (10.5%)	162 (19.3%)	1.88 (1.51–2.34)	<0.01
Prolonged Total LOS	878 (23.7%)	489 (58.4%)	4.45 (3.70–5.34)	<0.01
Excessive Total Charges	831 (22.5%)	484 (57.8%)	4.08 (3.29–5.05)	<0.01

^a Readmission for the late surgery group did not include the admission for appendectomy.

of generalized peritonitis were significantly more likely to have an intraabdominal abscess (OR 2.09, 95% CI 1.37–3.20), have a urinary complication (OR 1.75, 95% CI 1.00–3.03), have an iatrogenic complication (OR 4.24, 95% CI 1.81–9.96), require readmission (OR 1.66, 95% CI 1.17–2.34), have a prolonged length of stay (OR 5.79, 95% CI 4.36–7.69), and have excessive total charges (OR 5.61, 95% CI 4.04–7.78) if undergoing late surgery instead of early surgery (Table 5).

On sensitivity analysis in which the cutoff between early and late appendectomy was reduced to one day from two days, the number of patients in the early appendectomy group decreased by 235 to 7473. When evaluating adjusted odds ratio for having complications, there were no differences from our primary results with the exception that pulmonary complications, which were more likely in the late group, achieved significance (OR 1.43 95% CI 1.06–1.93).

Among patients in the late surgery group, 284 (25.1%) children underwent an appendectomy greater than two days after admission during index hospitalization, 251 (22.2%) at an urgent subsequent admission, and 597 (52.7%) at an elective subsequent admission (see Table A.1 in the Appendix for characteristics of children undergoing late surgery by subgroup). Compared to the early surgery group, patients having late surgery during the index hospitalization were more

Table 5
Adjusted odds ratio (95% CI) for 1-year outcomes among patients who underwent early and late surgery and had generalized peritonitis diagnosis.

	Crude numbers of cases		Adjusted Odds Ratios	
	Early Surgery (N = 4009)	Late Surgery (N = 294)	Late Surgery vs Early Surgery	p-value
Outcome during 1 year follow up				
Intra-abdominal abscess	202 (5.0%)	33 (11.2%)	2.09 (1.37–3.20)	<0.01
Gastrointestinal	353 (8.8%)	30 (10.2%)	1.08 (0.71–1.65)	0.71
Wound	310 (7.7%)	23 (7.8%)	0.92 (0.57–1.47)	0.71
Other Infectious	351 (8.8%)	28 (9.5%)	0.92 (0.59–1.42)	0.7
Urinary	111 (2.8%)	18 (6.1%)	1.75 (1.00–3.03)	0.05
Pulmonary	177 (4.4%)	22 (7.5%)	1.59 (0.88–2.88)	0.12
Iatrogenic	23 (0.6%)	NR	4.24 (1.81–9.96)	<0.01
Cardiovascular	16 (0.4%)	NR	0.41 (0.04–3.83)	0.43
Any Complication	853 (21.3%)	77 (26.2%)	1.11 (0.82–1.51)	0.49
Readmission ^a	393 (9.8%)	48 (16.3%)	1.66 (1.17–2.34)	<0.01
Prolonged Total LOS	612 (15.3%)	148 (50.3%)	5.79 (4.36–7.69)	<0.01
Excessive Total Charges	725 (18.1%)	170 (57.8%)	5.61 (4.04–7.78)	<0.01

^a Readmission for the late surgery group did not include the admission for appendectomy.

likely to experience any complication (OR 2.10, 95% CI 1.60–2.74) (see Table A.2 in the Appendix for adjusted outcomes of children undergoing late appendectomy by subgroup). These patients had the highest complication rate in nearly all measured complications, the longest total length of stay, and the highest costs. Patients who underwent elective interval appendectomy did not have a higher risk of experiencing complications compared to patients undergoing early surgery. However, this group of patients was more likely to have longer total length of stay and higher total charges.

4. Discussion

This is the first population level study evaluating outcomes following early and late appendectomy for pediatric patients with complicated appendicitis over a one-year follow-up period. Our data showed that children undergoing late appendectomy were more likely to suffer complications, have longer total length of stay, and incur greater charges when compared to those undergoing early appendectomy.

These findings were consistent with a previous randomized controlled trial in which patients with suspected perforated appendicitis but no abscess had lower costs, shorter length of stay and lower complication rates when treated with early rather than late appendectomy [9,10]. A separate randomized trial which evaluated early versus delayed surgical management of appendiceal abscess also found more healthcare visits in the late management group [11]. That trial differed from our findings in that they found significantly longer operating times and longer time to goal intake in the early operation group — parameters we were unable to measure. Additionally, they did not find differences in recurrence of abscess or hospital charges; however, that trial was limited to 40 patients and may not have detected subtler differences.

Our late management group includes children who had their appendectomy during index hospitalization but greater than two days from hospitalization. While it is not uncommon for children planned for immediate appendectomy to experience some delay owing to resuscitation and OR availability, it is unlikely that this delay would exceed two days. Thus, we believe that these patients likely represented children in which the surgeon initially planned for interval appendectomy but the child failed to clinically improve. Our subgroup analysis revealed that the complication rate and cost were highest among this group. While these patients may represent children with more severe cases of peritonitis, the question remains whether earlier operation could have prevented some of the complications and cost that these children incurred.

Moreover, we found that 29.6% of patients discharged without appendectomy required urgent readmissions — a number consistent with findings seen by other authors who reported unplanned readmission rates of 35% [8,9]. Finally, it is worth noting that of patients who are relegated to late surgery, only about half have an elective operation, suggesting a high rate of failure of the initial plan for interval appendectomy. Collectively, these findings suggest that the initial decision to not operate immediately results in the planned interval operation in only select cases and overall the decision to wait is associated with greater morbidity and cost.

It is worth noting, that at high volume centers, a greater proportion of children undergoing late operation had their procedure as an elective, interval procedure when compared to medium and low volume centers. The reasons for this are unclear. One likely explanation is that parents may select for high-volume centers after their initial hospitalization, provided they do not need to return on an urgent basis. This would have the effect of seemingly increasing the number of children who make it to elective interval appendectomy. Alternatively, high volume centers may be more skilled at selecting which children can be effectively relegated to late surgery. Regardless, the difference between hospital volume and practice pattern warrants further investigation.

In our study, patients with peritoneal abscess comprised a much larger percentage of the late surgery group than the early surgery group. This may present a confounder — i.e. patients undergoing late surgery do worse because they are more likely to be patients with abscess. However, our findings of increased complications in the late surgery group persisted when examining patients with generalized peritonitis and patients with peritoneal abscess separately.

Among complications we evaluated, wound infection and other infection were the only outcomes with a higher complication rate in the early appendectomy group. A similar finding of greater wound complications was also seen in a meta-analysis which included adult patients [7]. In our study, children undergoing early appendectomy were significantly more likely to have an open operation. Given the lower risk of wound infection for laparoscopic appendectomy [18] and the increasing uptake of laparoscopic surgery in pediatric cases [19], we believe that this finding will not persist as laparoscopy continues to displace open surgical approaches.

In addition to our primary outcome, we identified sociodemographic factors that were associated with significant differences in care. We note, for example, that Black children and children on Medicaid were more likely to be treated with late appendectomy and, within the late group, more likely to require urgent operation — i.e. the groups with worst outcomes. We believe that these findings warrant further studies on issues surrounding health care access and delivery that may drive these disparities.

Our study was limited by its reliance on administrative data. By using ICD-9 codes for “acute appendicitis with generalized peritonitis” and “acute appendicitis with peritoneal abscess” we were selecting for patients in which the surgeon deemed the patient to have a more complicated course of appendicitis. These codes are subject to bias by the coding physician and do not allow for further differentiation between degree of disease severity — e.g. the extent of or number of abscessed visualized on the CT scan. Nevertheless, while reliance on administrative data is limiting, these codes have previously been used to categorize patients with complicated appendicitis in population level studies [20,21]. The retrospective nature of our study was additionally limiting, namely it introduces a substantial possibility of selection bias. There remained the possibility that patients treated with late appendectomy were systematically different — i.e. sicker — than those treated with early appendectomy and there might be a residual confounding after adjusting for identified conditions and comorbidities. Additionally, the database did not have information on interventional radiology procedures for all years and omitted certain patient-specific variables such as operating time and time to feeding, as mentioned earlier. To overcome these limitations, we utilize subgroup analysis to determine which specific groups of late operation were driving the correlation with worse outcomes. Finally, our choice of two days to define early appendectomy is arbitrary and other studies have used 12 or 24 h [22,23]. However, a sensitivity analysis in which the cutoff for early appendectomy was one day showed broadly the same results as those presented in our main analysis.

5. Conclusion

This study is the first population-based, longitudinal analysis comparing early appendectomy to delayed surgery. We found continued evidence to support immediate operation in children with complicated appendicitis, whether they present with or without abscess. While we found a higher rate of wound infections in the group undergoing early surgery, patients undergoing early surgery had lower overall complications, hospital days and costs of care at one year of follow-up. While debate about the gold standard for management of complicated appendicitis is likely to continue, we believe that this study demonstrates continued evidence favoring early management.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jpedsurg.2017.09.012>.

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References

- [1] Addiss DG, Shaffer N, Fowler BS, et al. The epidemiology of appendicitis and appendectomy in the United States. *Am J Epidemiol* 1990;132(5):910–25.
- [2] Lund DP, Murphy EU. Management of perforated appendicitis in children: A decade of aggressive treatment. *J Pediatr Surg* 1994;29(8):1130–4.
- [3] Ponsky TA, Huang ZJ, Kittle K, et al. Hospital- and patient-level characteristics and the risk of appendiceal rupture and negative appendectomy in children. *JAMA* 2004;292(16):1977–82.
- [4] Janik JS, Ein SH, Shandling B, et al. Nonsurgical management of appendiceal mass in late presenting children. *J Pediatr Surg* 1980;15(4):574–6.
- [5] Ho CM, Chen Y, Lai HS, et al. Comparison of critical conservative treatment versus emergency operation in children with ruptured appendicitis with tumor formation. *J Formos Med Assoc* 2004;103(5):359–63.
- [6] Henry MCW, Gollin G, Islam S, et al. Matched analysis of nonoperative management vs immediate appendectomy for perforated appendicitis. *J Pediatr Surg* 2007;42(1):19–24.
- [7] Simillis C, Symeonides P, Shorthouse AJ, et al. A meta-analysis comparing conservative treatment versus acute appendectomy for complicated appendicitis (abscess or phlegmon). *Surgery* 2010;147(6):818–29.
- [8] Nazarey PP, Stylianos S, Velis E, et al. Treatment of suspected acute perforated appendicitis with antibiotics and interval appendectomy. *J Pediatr Surg* 2014;49(3):447–50.
- [9] Blakely ML, Williams R, Dassinger MS, et al. Early vs interval appendectomy for children with perforated appendicitis. *Arch Surg* 2011;146(6):660–5.
- [10] Myers AL, Williams RF, Giles K, et al. Hospital cost analysis of a prospective, randomized trial of early vs interval appendectomy for perforated appendicitis in children. *J Am Coll Surg* 2012;214(4):427–34.
- [11] Peter SD, Aguayo P, Fraser JD, et al. Initial laparoscopic appendectomy versus initial nonoperative management and interval appendectomy for perforated appendicitis with abscess: a prospective, randomized trial. *J Pediatr Surg* 2010;45(1):236–40.
- [12] Schurman JV, Cushing CC, Garey CL, et al. Quality of life assessment between laparoscopic appendectomy at presentation and interval appendectomy for perforated appendicitis with abscess: analysis of a prospective randomized trial. *J Pediatr Surg* 2011;46(6):1121–5.
- [13] Fair BA, Kubasiak JC, Janssen I, et al. The impact of operative timing on outcomes of appendicitis: a National Surgical Quality Improvement Project analysis. *Am J Surg* 2015;209(3):498–502.
- [14] Tai D, Dick P, To T, et al. Development of pediatric comorbidity prediction model. *Arch Pediatr Adolesc Med* 2006;160(3):293–9.
- [15] Tian Y, Sweeney JF, Wulkan ML, et al. The necessity of sociodemographic status adjustment in hospital value rankings for perforated appendicitis in children. *Surgery* 2016;159(6):1572–82.
- [16] Guller U, Hervey S, Purves H, et al. Laparoscopic versus open appendectomy. *Ann Surg* 2004;239(1):43–52.
- [17] Jen HC, Shew SB. Laparoscopic versus open appendectomy in children: outcomes comparison based on a statewide analysis. *J Surg Res* 2010;161(1):13–7.
- [18] Aziz O, Athanasiou T, Tekkis PP, et al. Laparoscopic versus open appendectomy in children: a meta-analysis. *Ann Surg* 2006;243(1):17–27.
- [19] Lee SL, Yaghoubian A, Kaji A. Laparoscopic vs open appendectomy in children: outcomes comparison based on age, sex, and perforation status. *Arch Surg* 2011;146(10):1118–21.
- [20] Wei P-L, Liu S-P, Keller JJ, et al. Volume–outcome relation for acute appendicitis: evidence from a nationwide population-based study. *PLoS One* 2012;7(12):e52539.
- [21] Sutton TL, Pracht EE, Ciesla DJ. Acute appendicitis: variation in outcomes by insurance status. *J Surg Res* 2016;201(1):118–25.
- [22] Caruso AM, Pane A, Garau R, et al. Acute appendicitis in children: not only surgical treatment. *J Pediatr Surg* 2017;52(3):444–8.
- [23] Tsai HY, Chao HC, Yu WJ. Early appendectomy shortens antibiotic course and hospital stay in children with early perforated appendicitis. *Pediatr Neonatol* 2017;58(5):406–14.