Association of postoperative organ space infection after intraoperative irrigation in appendicitis

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BACKGROUND: The benefit of intraoperative irrigation on postoperative abscess rates compared to suction alone is unclear. The American Association for the Surgery of Trauma grading system provides distinct disease severity stratification to determine if prior analyses were biased by anatomic severity. We hypothesized that for increasing appendicitis severity, patients receiving (high, ≥2 L) intraoperative irrigation would have increased postoperative organ space infection (OSI) rate compared to (low, <2 L) irrigation.

METHODS: Single-institution review of adults (>18 years) undergoing appendectomy for appendicitis during 2010-2016. Demographics, operative details, irrigation volumes, duration of stay, and complications (Clavien-Dindo classification) were collected. American Association for the Surgery of Trauma grades were assigned by two independent reviewers based on operative findings. Summary, univariate, and area under the receiver operating curve analyses were performed.

RESULTS: Patients (n = 1187) were identified with a mean (SD) age of 41.6(18.4) years (45% female). Operative approach included laparoscopy (n = 1122 [94.5%]), McBurney incision (n = 10 [0.8%]), midline laparotomy (n = 16 [1.3 %]), and laparoscopy converted to laparotomy (n = 39 [3.4%)]. The mean (SD) volume of intraoperative irrigation was 410(1200) mL. Complication rate was 26.1%. Median volume of intraoperative irrigation in patients who developed postoperative OSI was 3 [0–4] compared to 0 [0–0] in those without infection ($p < 0.0001$). Area under the receiver operating curve analysis determined that 2 or more liters of irrigation was associated with postoperative OSI (c statistic: 0.83, 95% confidence interval, 0.76–0.89; $p < 0.001$).

CONCLUSION: Irrigation is used for increasingly severe appendicitis with wide variation. Irrigation volumes of 2 L or greater are associated with postoperative OSI. Improving standardization of irrigation volume (<2 L) may prevent morbidity associated with this high-volume disease. (*J Trauma Acute Care Surg.* 2018;84: 628–635. Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved.)

LEVEL OF EVIDENCE: Therapeutic, level IV.

KEY WORDS: Appendicitis; irrigation; AAST; grade; surgical site infection.

Appendicitis is a common surgical problem. Surgical site infection and postoperative abscess are complications associated with increasing anatomic injury.[1–4] In perforated appendicitis, the optimal management of this contamination is unclear.[5,6] In the era of open surgery, management of peritoneal contamination followed a common surgical tenet "dilution is the solution to pollution" that encouraged surgeons to use large-volume irrigation in an attempt to reduce intra-abdominal contamination and subsequent infection.[7] This tenet persisted into the current laparoscopic era of contaminated perforated viscus treatment.[8–10]

Optimal methods and precise volumes of irrigation are debated.[11] The literature describes intraoperative irrigation as a risk factor for postoperative intra-abdominal infection.[12,13] In both pediatric and adult populations, prospective randomized studies demonstrated equivalence in reducing postoperative abscess rates when comparing suction alone to irrigation in the setting of complicated appendicitis.[11,14] These studies, however, used a broad and inclusive definition of complicated appendicitis, which limits comparison and generalizability. Classification of appendicitis in a binary manner (simple versus complex) may oversimplify disease severity.[2] Insufficient stratification of disease severity potentially limits the ability to identify differences for several important clinical outcomes such as duration of stay, operative management, a unplanned laparotomy, or complications.[4] To address variation in diagnosis and prognosis for emergency general surgery (EGS) conditions, the American Association for the Surgery of Trauma (AAST) developed a grading system to uniformly assign severity to several EGS diseases, including appendicitis.[15–18] The system is based on the Organ Injury Scale, which is well validated for describing anatomic injury and outcomes in trauma.[19]

Currently, there is a paucity of data evaluating the impact of increasing anatomic injury severity with intraoperative management of peritoneal contamination. Using the AAST EGS grading system, we aimed to determine whether the use of intraoperative peritoneal irrigation was associated with higher rates of postoperative organ space infection for each AAST EGS appendicitis grade. We hypothesized that in the setting of increasing disease severity, patients who received high-volume intraoperative peritoneal irrigation (≥2 L) would be associated with increased rates of postoperative organ space infection.

METHODS

This was a retrospective review undertaken by the authors. Institutional review board approval was obtained before conducting the study.

Patients' Characteristics

The following variables were abstracted from the electronic medical record baseline patients' demographics, duration of prehospital abdominal pain, admission physiologic and laboratory values, and operative approach (laparoscopy, McBurney incision, or laparotomy). The operative report was queried for intraoperative irrigation volume. This was secondarily confirmed using hospital billing data specific to intraoperative supplies and not related to administered resuscitative or maintenance fluids.

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Patients were selected using *the International Classification for Diseases* (*ICD*) codes 9th and 10th revision. These codes included *ICD-9* 540.0, 540.1, and 540.9. For the *ICD-10*, we used the codes K35.2 and K35.3. These codes were input into our search tool that queried our electronic medical record during the years 2010 to 2016. We excluded patients with inflammatory bowel disease, appendiceal malignancies, pregnant patients, and patients younger than 18 years.

AAST Grade Assignment for Appendicitis

The AAST EGS grade is a clinical, imaging, operative, and pathologic disease severity classification system. Defined criteria exist for several EGS diseases. For this study, we used the operative criteria. The AAST grades were independently assigned from patients' operative report findings by two authors (M.C.H. and E.F.). The final AAST grade was used for all analyses.

Primary Outcome

The primary outcome was development of postoperative organ space infection as defined by (abscess, anastomotic dehiscence, or fistula) for 90 days postoperatively. Abscess was defined as a fluid collection visualized postoperatively on cross-sectional imaging confirmed by a radiologist interpretation. If a patient required operative resection and anastomosis of bowel, anastomotic leak was defined as staple/suture dehiscence resulting in free fluid/air requiring reoperation. Enterocutaneous fistula was defined as the leakage of enteric content from any gastrointestinal lumen (except for an ostomy) that communicates through an externalized opening via (1) an epithelialized tract or (2) into the open abdominal wound.

Secondary Outcomes

Secondary outcomes included development of any complication, which were defined according to the National Surgical Quality Improvement Program (NSQIP) definitions,[20] hospital duration of stay, re-laparotomy, temporary abdominal closure rate, surgical site infection (superficial and deep and organ space), 30-day mortality, and 30-day readmission rate. Complication severity was assigned using the Clavien-Dindo index.[21] Thirty-day mortality was defined from the date of patient dismissal, and in-patient mortality was defined as from the time of admission to in-patient expiration.

Statistical Analyses

Univariate analyses were used to evaluate the relationship of the AAST grade and primary/secondary outcomes using the Fisher exact test, nonparametric (Wilcoxon each pair), and analysis of variance tests when appropriate. To determine associations of the grade, the Cochran-Armitage test for trend was used for categorical/nominal outcomes and the Spearman correlation was used for continuous variables. To determine the cutoff of intraoperative irrigation volume that was considered (high versus low), the receiver operating characteristic (ROC) analysis was performed. The Youden index was used to determine the maximal sensitivity and specificity that associated high versus low intraoperative irrigation volume with developing a postoperative organ space infection. Continuous variables were described using mean values with standard deviations (SD) if normally distributed and medians with interquartile ranges [IQRs] if gross skewness was present. Categorical variables were summarized as proportions. Variables on univariate analyses with $p < 0.05$ were included in a multivariable logistic regression analysis to determine risk factors predictive for the development of postoperative complication. The measures of discrimination for this model were reported using the Hosmer-Lemeshow, Pearson χ^2, and McFadden r^2 goodness-of-fit tests as well as the AUROC (area under the ROC) with its 95% confidence intervals (CIs). All data analyses were performed using JMP (SAS Institute, Inc, Cary, NC). GraphPad Prism (GraphPad Software, Inc, La Jolla, CA) was used for all visual graphics.

RESULTS

Baseline Demographics and Initial Presentation

During 2010-2016, there were 1187 patients with acute appendicitis who underwent appendectomy. The mean (SD) age was 41.6(18.4) years; 45% were female. At initial presentation, patients displayed a median [IQR] of 1 [1–2] days of prehospital abdominal pain. Patients frequently reported generalized abdominal pain (n = 682 [57%]). At admission, the mean (SD) white blood cell count was 13.2 (4.6), heart rate was 84(16) beats per minute, and temperature was 36.9°C(0.5°C).

The AAST EGS grade and associations with patients' characteristics are reported in Table 1. The AAST EGS grades included Grade I (n = 747 [62.9%]), Grade II (n = 219 [18.5%]), Grade III (n = 126 [10.6%]), Grade IV (n = 50 [4.2%]), Grade V (n = 45 [3.8%]). There was no association with sex or age for increasing AAST EGS grade. Relative to AAST EGS Grade I, patients demonstrated a statistically significant trend for increasing AAST EGS grade and duration of prehospital symptoms, with the highest in AAST EGS Grade V (3 [1–4] days). For admission temperature, heart rate, and degree of leukocytosis, statistically significant differences were not associated with increasing AAST grade.

Operative Outcomes

Operative approaches included laparoscopy (n = 1122 [94.5%]), McBurney incision (n = 10 [0.8%]), midline laparotomy (n = 16 [1.3%]), and laparoscopy converted to laparotomy (n = 39 [3.4%]). Table 1 demonstrates that as the AAST EGS grade increased, there was an association with surgical approach. For increasing AAST EGS grade, there was an increased frequency of midline laparotomy and conversion from laparoscopy to laparotomy. This coincided with a decreased frequency of laparoscopy and McBurney incision for increasing AAST EGS grade. The rate of open abdomen therapy was (0.9%, n = 6). There was a 26.1% overall complication rate (n = 310). Overall complication severity (Clavien-Dindo index) included no complication (n = 912 [77%]), Grade I (n = 119 [10%]), Grade II (n = 55 [4.6%]), Grade III (n = 71 [6%]), Grade IV (n = 25 [2.1%]), and Grade V (n = 5 [0.4%]). For increased disease severity, there were elevated median [IQR] Clavien-Dindo grades. This indicated that severe disease was associated with higher rates and severity of complications. The frequency of various surgical site infections included superficial (n = 76 [6.4%]), deep incisional (n = 24 [2%]), and organ space (n = 62 [5.2%]). Twenty-two patients (1.8%) required a unplanned laparotomy. The 30-day mortality rate was 0.4% (n = 5). The 30-day readmission rate was 6.6% (n = 79). Complication data

TABLE 1. AAST Grade and Clinical Outcomes

	AAST Grade					
Characteristics	I	II	III	IV	V	*p*
n (%)	747 (63%)	219 (18.4%)	126 (10.6%)	50 (4.2%)	45 (3.8%)	-
Male, %	50.3	59.8	64.3	54	66.7	0.3000
Age, years	59 [38–72]	55 [39–65]	55 [36–66]	42 [27–55]	33 [25–47]	0.0020
Clinical presentation						
Duration of illness, days	1 [1–2]	1 [1–2]	2 [1–3]	2 [1–3]	3 [1–4]	0.0010
Temperature, °C	36.8 [36–37]	36.8 [36–37.1]	36.8 [36–37.3]	36.9 [36–37.2]	37 [36–37.4]	0.0100
Heart rate, bpm	82 [72–93]	82 [74–94]	89 [77–100]	90 [75–102]	89 [78–99]	0.0010
White blood cell count, $\times 10^9$/L	12.8 [10–15.6]	13 [10.3–15.3]	14 [10.6–16.9]	12.6 [10–17]	15 [10.3–18]	0.0060
Surgical method						
Local incision, n (%)	3 (0.4)	2 (0.9)	2/126	2 (4)	0 (0)	0.0300
Laparoscopy, n (%)	739 (98.9)	207 (94.5)	110/126	38 (76)	26 (57.8)	<0.0001
Midline laparotomy, n (%)	1 (0.1)	1 (0.5)	2/126	3 (6)	8 (17.8)	<0.0001
Conversion, n (%)	4 (0.5)	9 (4.1)	12/126	7 (14)	11 (24.4)	<0.0001
Liters of irrigation	0 [0–0]	0 [0–0]	0 [0–2]	2 [1–3]	2 [1–4]	<0.0001
Postoperative outcomes						
Duration of stay	1 [0–1]	1 [0–2]	2 [1–5]	[2–5]	5 [3–9]	<0.0001
Clavien-Dindo grade	0 [0–0]	0 [0–0]	0 [0–0]	1 [0–3]	2 [1–3]	<0.0001

Values are reported as median [IQR] unless otherwise noted.

according to NSQIP are reported in Appendix 1 (Appendix, Supplemental Digital Content 1, http://links.lww.com/TA/B63).[22]

AAST Grade and Irrigation Outcomes

The mean (SD) volume of intraoperative saline irrigation was 0.41 (1.2) L. Table 1 reflects that for increasing AAST grade, there were increased median [IQR] liters of irrigation used. When the volume of irrigant was categorized into high (≥2 L) versus low (<2 L), the rates of postoperative organ space infections were increased in patients receiving high- compared to low-volume irrigation (Table 2). Repeat analysis with only patients receiving laparoscopy demonstrated similar rates of postoperative organ space infection between high and low irrigation groups (Table 2). Figure 1 demonstrates the rates of postoperative organ space infection. Increased median volumes of irrigation were demonstrated in patients who developed postoperative organ space infection in increasingly severe appendicitis, grade for grade ($p < 0.05$). The Youden index (sensitivity +,specificity −1) was maximized at 0.66 and determined that the volume of irrigation associated with postoperative organ space infection was 2.00 L. The ROC c-statistic for this cutoff was 0.83 (95% CI, 0.76–0.89; $p < 0.001$). Figure 2 represents that for increasing volume of irrigation, there was an association of increased rates of postoperative organ space infection.

Table 3 demonstrates the multivariable analysis for several risk factors for increased postoperative organ space infection, which demonstrated that increasing AAST grade (in reference to AAST Grade I), use of more than 2.00 L of intraoperative irrigation, and temporary abdominal closure as variables independently associated with the development of a postoperative organ space infection. This model demonstrated good discrimination capability (AUROC, 0.85; 95% CI, 0.81–0.87) but poor calibration (Hosmer-Lemeshow χ^2 test, $p = 0.001$). Other measures of calibration included the Pearson χ^2 goodness-of-fit test, which demonstrated a $p = 0.15$ and the McFadden r^2 was 0.33. Table 4 outlines potential confounders between low and high irrigation groups. The greater irrigation group demonstrated greater durations of prehospital symptoms, increased median AAST EGS grade, and a reduced rate of laparoscopy compared to the lesser irrigation group (Table 4).

DISCUSSION

Several studies have been performed that compare laparoscopic versus open surgical approaches, operative versus nonoperative management, type of intraoperative irrigation, or methods to better improve postoperative care for this voluminous surgical

TABLE 2. A. Comparison of Organ Site Infection Rates by High (≥2 L) Versus Low (<2 L) Irrigation for Each AAST Grade Including All Patients. B. Comparison of Organ Site Infection Rates by High (≥2 L) Versus Low (<2 L) Irrigation for Each AAST Grade Excluding Patients who Underwent Open or Laparoscopic Converted to Open Appendectomy

A			
	Low Irrigation (%)	High Irrigation (%)	*p*
AAST I	83	17	0.01
AAST II	0	100	0.001
AAST III	42	58	0.001
AAST IV	18	82	0.004
AAST V	35	65	0.02
B			
	Low Irrigation (%)	High Irrigation (%)	*p*
AAST I	83	17	0.01
AAST II	0	100	0.001
AAST III	43	57	0.04
AAST IV	25	75	0.001
AAST V	22	78	0.0001

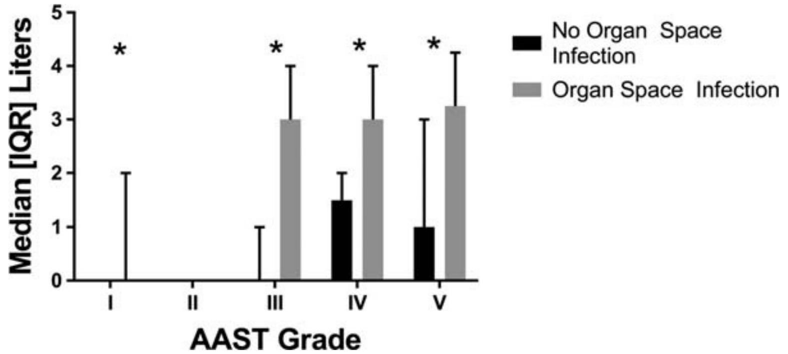

Figure 1. Increased irrigation volume is associated with postoperative organ space infection in each AAST grade. *Asterisk* denotes significance ($p < 0.05$).

disease.[11,23–28] Previous work used existing appendicitis diagnosis systems, which demonstrated a limited nature to describe disease severity, and these methods are not necessarily generalizable.[29–31] Whether the use of a granular stratification such as the AAST EGS system would lead to differing conclusions for prior work remains unknown. Certainly, any future EGS study must incorporate disease severity stratification to reduce disease severity bias. Our analysis is a first of its kind wherein application of the AAST EGS grade afforded detailed information regarding the impact of intraoperative irrigation and subsequent postoperative organ space infection rates. We demonstrated that as appendicitis disease severity increased, large volumes of irrigation were associated with increasing postoperative organ space infection. This validates the works by St. Peter et al. and Moore et al. and suggests the judicious use of intraoperative irrigation for all types of appendicitis.

Moore et al.[6] recently highlighted the probable lack of use of irrigation for appendicitis. The authors demonstrated that for similar patients undergoing laparoscopic or open appendectomy, the addition of copious irrigation did not result in a reduction of postoperative organ space infection.[6] Most of the patients who developed postoperative abscesses, however, displayed appendiceal perforation.[6] Our data highlight that for increasingly severe appendicitis (Grades III, IV, and V), the addition of irrigation was associated with development of postoperative organ space infection. Conversely, in a recent prospective trial by Sun et al., patients were randomized to receiving 2 L or more intraoperative irrigation, or suction alone.[32] Between the two groups, the patients who received high-volume intraoperative irrigation demonstrated a prolonged operative duration but diminished postoperative organ space infection rate compared to suctions alone (3.1% versus 9.2%).[32] While direct comparison of disease severity is not possible, patients in our cohort with AAST EGS Grade I who received high-volume irrigation demonstrated a reduction in organ space infection rates compared to those who received low-volume irrigation. In the future, application of rigorous study inclusion criteria, ideally based on uniform classifications, may improve comparison of cohort study findings and improve outcome reporting.

Too often, the spectrum of disease is dismissed in favor for simple binary definitions, especially to estimate appendicitis severity.[33] In this series, it is apparent that surgeons were biased toward using increased irrigation volume as disease severity increased. Presumably, surgeons are assessing variation in the degree of contamination or inflammation and using intraoperative irrigation as a method to reduce potential complications. The AAST grading revealed differences in operator's

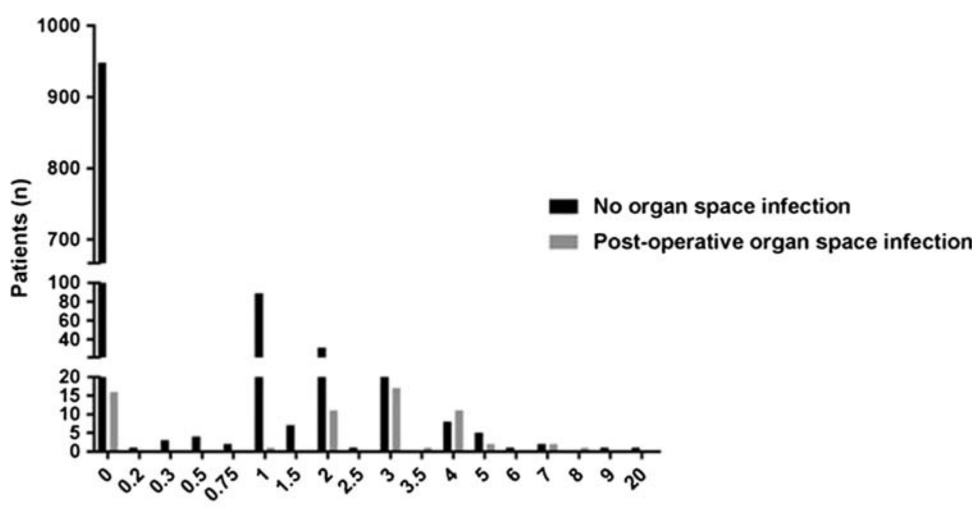

Figure 2. Frequency of patients who developed organ space infection and the amount of irrigation received.

TABLE 3. Multivariable Analysis for Predictors of Organ Space Infection

AAST Grade	Odds Ratio	95% Confidence interval	p
I	(Reference)	(Reference)	–
II	1.1	1.08–1.2	0.02
III	1.3	1.2–2.3	0.01
IV	1.8	1.6–2.1	0.002
V	2.2	2–2.6	0.03
>2 L of irrigation	8.5	4.3–17.1	0.0001
Temporary abdominal closure	1.2	1.1–1.4	0.04

decision making, reflecting that (1) despite similar anatomic severity, high variations in practice exist and (2) use of greater than 2 L of irrigation was associated with increased rates of postoperative organ space infection.[10,34]

St. Peter et al. and Snow et al. demonstrated that increasing volumes of intraoperative irrigation were associated with postoperative organ space infection using binary definitions of complicated appendicitis.[11,14] Conversely, several studies have compared the use of intraoperative lavage compared to suction alone and demonstrated either no differences in outcomes or increased rates of complications.[8,13,35,36] A significant minority of patients, however, developed postoperative organ space infection despite less than 2 L of intraoperative irrigation. This is likely due to the surgeons recognizing appendicitis severity and/or patients demonstrating critical physiology and using temporary abdominal closure therapy. This underscores the need to be aware of patients who are at an increased risk for postoperative organ space infection with potential areas for abscess formation before fascial closure.

Recent work evaluating aggregate and single-institution experiences with appendicitis demonstrate morbidity in the10% to 12% and mortality at 0.5% to 1%.[37,38] One author demonstrated the ability to increasingly use laparoscopy for more complex disease, which our analysis echoes.[39] However, as our data are stratified in more detail, we demonstrate increasing rates of laparoscopy converted to open procedures and diminishing rates of overall use of laparoscopy for increasingly severe disease. We submit that this finding would be demonstrated if other institutions assigned AAST EGS grade to their cohorts. With respect to mortality, we demonstrated a similar mortality rate, even compared to nationally aggregated data.[40] Finally, our cohort reports on complications granularly as defined by NSQIP variables. It further classifies the complication severity according to the Clavien-Dindo classification system that is a well-validated method that illuminates subsequent therapy.

Appendicitis is a disease that displays variable treatment.[41,42] To estimate the practices and management of appendicitis, a survey of North American pediatric surgeons from 2004 demonstrated that only 7% of respondents reported using no irrigation for perforated appendicitis.[34] In our cohort, 78% of surgeons used no irrigation. Despite this, for increasingly severe disease, surgeons in this cohort used irrigation with high variation. We conclude that for increasingly severe disease, routine high-volume irrigation may be detrimental. Given nonstandard methods for irrigation, our data demonstrate that for increasing appendicitis severity (AAST Grades I–V), minimal to no irrigation may be a better practice, even in the setting of increasingly severe appendicitis.

There are several limitations to this paper, specifically its retrospective nature. The ability to uncouple increasing disease severity and the amount of irrigation used is difficult to address in a retrospective nature. It is possible that the amount of irrigation used was not captured in the operative dictation; however, we confirmed the volume irrigated using billing data and the resident operative note. Furthermore, we are undertaking efforts to prospectively validate this work. Nevertheless, there are likely other confounders unaccounted for, but this work represents a first step to account for disease severity, which has been previously not considered. The AAST grade was assigned based on operative report data, which may not sufficiently describe the true degree of disease severity present, thereby underestimating the AAST score. Furthermore, this study was undertaken in a population that may not be generalizable to other environments such as low and middle income countries, where laparoscopy is less common or where demographics are different. Finally, we demonstrate that our multivariable model demonstrates the ability to discriminate organ space infection risk, however poor the ability to calibrate using the Hosmer-Lemeshow test. This is a cause for concern given the large sample size. Other measures of goodness of fit (Pearson χ^2 and McFadden r^2) addressed this poor calibration and suggest that additional variables may not be necessary to describe this model.

CONCLUSION

The AAST grading provides a robust framework for the analysis of important technical aspects in the surgical treatment of appendicitis that permitted the insightful analysis suggesting that high-volume intraoperative irrigation is associated with

TABLE 4. Patients Characteristics of High Versus Low Irrigation

Characteristic	Low Irrigation (n = 1117)	High Irrigation (n = 70)	p
Age	46 [36–54]	52 [38–66]	0.2
% Male	54	62	0.1
Duration of prehospital symptoms, days	1 [1–2]	2 [1–3]	0.0001
Temperature, °C	36.8 [36.7–37.1]	36.9 [36.7–37.2]	0.1
White blood cell count, $\times 10^9$/L	13 [10.1–15.7]	14.3 [10.5–17.2]	0.07
AAST EGS grade	2 [1–3]	3 [3–5]	0.001
Open abdomen therapy, %	1	3	0.3
Laparoscopy, %	96	70	0.001

postoperative organ space infection. We have demonstrated, retrospectively, that greater irrigation volumes are associated with increased risk of postoperative organ space infection. The AAST grading, although retrospective, adds more granularity for understanding different disease states related to appendicitis. The use of AAST grading is potentially a variable that may provide better surgical outcome benchmarking so that future research is more readily translatable and generalizable. Standardization of care processes in appendicitis may benefit from simple changes to improve postoperative outcomes and minimize morbidity. Future application of the AAST grade in national data sets may provide improved surgical benchmarking so that standard practices can be studied and applied better.

AUTHORSHIP

M.C.H., J.M.A., E.J.F., and M.D.Z. contributed to the design, analysis, and interpretation of this work. The remaining authors contributed to the conceptual design, analysis, interpretation, drafting, and final version of the work.

DISCLOSURE

The authors declare no conflicts of interest.

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