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Research Paper

The contemporary management of perforated appendicitis in adults: To operate or wait?

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ARTICLE INFO	A B S T R A C T	
<i>Keywords:</i> Perforated appendicitis Emergency general surgery Antibiotics	<i>Objectives:</i> The optimal management of perforated appendicitis remains controversial. Many studies advocate for antibiotics and an interval appendectomy whereas others suggest that performing an appendectomy at the time of presentation decreases post-operative morbidity. Confounding this argument further are the patients who fail non-operative management and end up requiring surgery during their initial hospitalization. This study aims to determine if early operative intervention should be considered for perforated appendicitis. <i>Methods:</i> This was a retrospective review of all patients who underwent an appendectomy (both laparoscopic or open) for perforated appendicitis between 2015 and 2020 at our institution. <i>Results:</i> A total of 271 patients met inclusion criteria for this study. Of this group, 250 patients underwent an immediate appendectomy whereas the remaining 21 patients underwent a trial of non-operative management and eventually required an appendectomy during their initial admission. When comparing the immediate versus delayed operative groups, there were no differences in demographic data including age and gender, and no differences in various imaging findings including AAST Grade IV or V appendicitis. Operatively, patients in the delayed group had a longer operative time (83.1 \pm 32.9 vs. 64.1 \pm 26.2, $p = 0.01$), were more likely to require an open operation (23.8 % vs. 2.8 %, $p < 0.0001$), and were more likely to have a drain placed intra-operatively (42.9 % vs 14.4 %, $p = 0.004$). While there were no differences in 30-day readmission rates, patients in the delayed group had a significantly longer hospital length of stay than patients in the immediate group (9.4 \pm 7.4 vs. 3.1 \pm 3.3, $p = 0.008$). <i>Conclusions:</i> Patients undergoing an immediate appendectomy for perforated appendicitis can discharge from the hospital sooner and demonstrate no increase in post-operative morbidity suggesting that surgeons can initially manage this disease process in an operative fashion.	
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Introduction

Appendicitis remains one of the most common diagnoses that requires emergent surgery [1]. Historically, early surgery was performed in order to prevent progression to perforated appendicitis which is known to be associated with an increased risk of morbidity and mortality [2–4]. However, this historical perspective has been challenged by more recent literature suggesting that acute appendicitis can be managed successfully with antibiotics alone [5–8].

When focusing specifically on perforated appendicitis, the data are even less clear. It is estimated that perforation occurs in upwards of 20-30 % of all cases of acute appendicitis, and is oftentimes accompa-

Traditionally, operating on perforated appendicitis in the acute setting is deferred as it is thought to be associated with a higher leak rate

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nied by a peri-appendiceal abscess [9–11]. Thus, many studies advocate for the initial non-operative management of perforated appendicitis which can range from treatment with intravenous (IV) antibiotics to radiologic drainage of an associated abscess, or a combination of both strategies [12–14]. In the non-operative management paradigm, while the appendix is not removed in the acute setting, many patients undergo an interval appendectomy approximately 6–8 weeks after their initial presentation. [13]

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from the appendiceal stump, a more technically challenging operation due to inflammation and distorted anatomy, and a higher rate of conversion to an open operation [12,15–18]. However, nonoperative management in the setting of perforated appendicitis is not without its own set of risks and patient morbidity including increased hospital lengths of stay, prolonged courses of antibiotics, and recurrent hospitalizations [15,17,19,20]. Confounding this argument further are the patients who fail initial non-operative management and end up requiring operative intervention during their index hospitalization. Currently, there are no clear recommendations on how best to manage this patient population. Thus, this study aims to determine if early operative intervention should be considered for perforated appendicitis. We hypothesize that early operative intervention results in decreased patient morbidity.

Materials and methods

This was a single center retrospective review of all patients >18 years of age who underwent an appendectomy for perforated appendicitis at Parkland Memorial Hospital between January 1, 2015 and December 31, 2020. Based on the retrospective nature of this study, informed consent was waived. There was also no formal patient recruitment or follow-up performed.

Data Collection

Following approval from the University of Texas Southwestern Medical Center Institutional Review Board (STU 2022-0259), patients were identified using the electronic medical record at Parkland Memorial Hospital. Various data points were then taken from each individual medical record, operative reports, and imaging reports. Patients were excluded from this study if they presented with acute, non-perforated appendicitis, or if they did not undergo an appendectomy. Patients were diagnosed with perforated appendicitis based on initial imaging that was obtained at the time of their arrival to the hospital. In the imaging report, the radiologist either noted that the appendix was perforated or defined the degree of appendicitis as AAST (American Association for the Surgery of Trauma) grade III-V. After patients meeting the inclusion criteria were identified, they were separated based on whether they underwent an immediate appendectomy at the time of admission of if they underwent a trial of non-operative management and then required an appendectomy later in their admission. Management decisions regarding whether a patient underwent an immediate appendectomy or an initial trial of non-operative management were made at the time of initial presentation by the attending surgeon.

Data points collected from the electronic medical record included demographic information, co-morbidities, length of stay data, various emergency department (ED) vital signs and laboratory values, time from symptom onset to presentation to the ED, time of antibiotic administration, and time to the operating room, various imaging findings such as The American Association for the Surgery of Trauma (AAST) grade of appendicitis, the size of the appendix, the presence of an appendicolith, phlegmon, or fluid collection, intra-operative findings including the AAST intra-operative grade of appendicitis, the presence of purulent peritonitis, and level of contamination, and post-operative complications including surgical site infections, leaks, and readmission within 30days after discharge.

Statistical analysis

Statistical analysis was performed using both Microsoft Excel and SPSS version 29.0.1.0 (SPSS Software, IBM Corp, Armonk, NY). Descriptive statistics are reported as the mean +/- standard deviation for continuous normally distributed. Medians with interquartile ranges [IQR] were used for skewed data. Categorical variables were compared using Chi-squared tests whereas continuous variables were compared using both student's *t*-tests and the Mann Whitney *U* Test. Categorical variables are reported as frequencies. Statistical significance was set at *p*

< 0.05.

Results

Between January 1, 2015 and December 31, 2020 a total of 2242 patients underwent an appendectomy at Parkland Memorial Hospital. Of these patients, 1971 were excluded as they had non-perforated appendicitis. Of the 271 remaining patients with perforated appendicitis, 250 (92.3 %) were taken to the operating room and underwent an appendectomy at the time of admission (immediate group). The remaining 21 (7.7 %) patients were initially managed non-operatively but subsequently failed non-operative management (delayed group) and were taken to the operating room for an appendectomy during their index hospitalization (Fig. 1).

Of the 271 patients included in this study, the majority were male (66.4 %) and the average age of the population was 38.1 ± 13.6 years old. The median body mass index (BMI) of the study population was 28 [26–31] and the most common co-morbidities noted include alcohol use (38.4 %), tobacco use (29.0 %), and hypertension (14.8 %). Patients spent on average 2 [1–4] days in the hospital. There were no mortalities within the study population. Additional patient characteristics are summarized in Table 1.

When comparing patients in the immediate versus the delayed groups, there were no differences in demographic data including age $(37.9 \pm 13.7 \text{ vs. } 40.5 \pm 13.3, p = 0.4)$, BMI (29 [25–31] vs. 29 [26–30], p = 0.1), initial heart rate (93.4 ± 18.9 vs. 86.5 ± 18.6, p = 0.1), or initial systolic blood pressure (124.6 ± 17.1 vs. 129.7 ± 21.0, p = 0.3). There were also no differences in the rates of various co-morbidities between groups. When evaluating the initial white blood cell (WBC) count, patients who were taken immediately to the operating room (OR) had a higher WBC count when compare with patients who failed nonoperative management (15.4 ± 8.1 vs. 11.7 ± 5.5, p = 0.008). Hospital length of stay was found to be statistically longer it the patients who failed non-operative management (3.1 ± 3.3 vs. 9.4 ± 7.4, p = 0.0009) (Table 2).

In regards to imaging, patients in the delayed group were more likely to have the American Association for the Surgery of Trauma (AAST) Grade III appendicitis (13/21, 61.9 % vs. 69/250, 27.6 %, p = 0.005) defined as imaging findings of appendiceal wall necrosis with local periappendiceal fluid or contrast extravasation [21]. The delayed group was also more likely to have computed tomography (CT) findings of a drainable fluid collection (8/21, 38.1 % vs. 33/250, 13.2 %, p = 0.005). There were no differences in the rates of AAST Grade IV and V appendicitis, the presence of an appendicolith, the presence of a phlegmon, or in the size of the appendix as measured in millimeters (Table 3).

Intraoperative findings including the rates of AAST Grade IV and V appendicitis [21], the presence of purulent peritonitis, and the level of intraperitoneal contamination were similar between groups. Patients in the delayed group were more likely to have a drain placed intraoperatively (9/21, 42.9 % vs. 36/250, 14.4 %). Delayed patients were also more likely to undergo a conversion from a laparoscopic to an open appendectomy (9/21, 42.9 % vs. 7/250, 0.4 %, p < 0.0001). Patients in the delayed group also had longer operative times (minutes) when compared with the immediate group (83.1 ± 32.9 vs. 64.1 ± 26.2, p = 0.01) (Table 4).

Finally, when considering post-operative outcomes, there were no differences in rates of superficial surgical site infections (5/250, 2.0 % vs. 0, p = 0.8), deep surgical site infections (2/250, 0.80 % vs. 0, p = 0.9), or organ space infections (35/250, 14.0 % vs. 5/21, 23.8 %, p = 0.5) between the immediate and delayed groups. There were no instances of an appendiceal stump leak in either group. Furthermore, there were no differences in the rates of an unexpected return to the OR (4/250, 1.6 % vs. 1/21, 4.8 %, p = 0.5) or in 30-day readmissions (28/250, 11.2 % vs. 2/21, 9.5 %, p = 0.9). There were no mortalities noted in either group (Table 5).

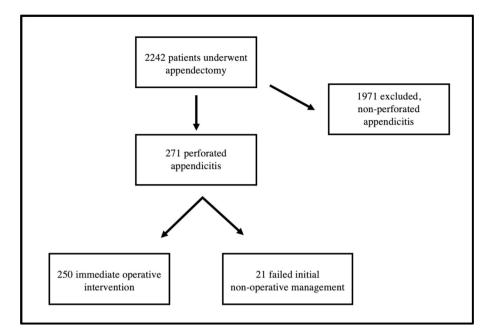


Fig. 1. Study population.

Table 1

Demographic data and clinical characteristics of all patients presenting with perforated appendicitis.

	Total (<i>N</i> = 271)
Age	38.1 ± 13.6
Male	180 (66.4 %)
BMI, median (kg/m2)	28.8 [26-31]
ED HR	92.9 ± 18.9
ED SBP	124.9 ± 17.4
ED WBC	15.1 ± 8.0
Hospital LOS	2 [1-4]
Co-Morbidities	12 (10 %)
HTN	40 (14.8)
DM	29 (10.7)
Chronic Steroids	8 (3.0 %)
Tobacco Use	81 (30.0 %)
OSA	5 (1.8 %)
EtOH Use	104 (38.4 %)
Symptom onset to ED (hrs)	33.2 ± 28.6

BMI: body mass index; ED: emergency department; HR: heart rate; SBP: systolic blood pressure; WBC: white blood cell; LOS: length of stay; HTN: hypertension; DM: diabetes mellitus; OSA: obstructive sleep apnea.

Discussion

When considering the management of acute appendicitis, traditional management has been centered around surgical removal with an appendectomy [22]. More recently, studies have also supported managing acute, non-perforated appendicitis with antibiotics alone [8]. Unlike acute, non-perforated appendicitis, the management of perforated appendicitis is a much more nuanced discussion and has historically involved a combination of intravenous and oral antibiotics, imageguided drainage, bowel rest, and an eventual appendectomy in the outpatient setting [15,23]. Operating on perforated appendicitis in the acute setting during the index hospitalization has been shown to be associated with a high rate of post-operative complications and increased patient morbidity that has been quoted at upwards of 30 % in some studies [24–27]. Increased inflammation and contamination distorts the anatomical field making a safe dissection more technically challenging, is known to lead to a higher rate of conversion to an open

Table 2

Comparison of demographic data for patients undergoing immediate surgery versus those who failed an initial trial of non-operative management.

	Immediate (N = 250)	Delayed (<i>N</i> = 21)	<i>p</i> -value
Age	$\textbf{37.9} \pm \textbf{13.7}$	40.5 ± 13.3	0.4
Male	168 (67.2 %)	12 (57.1 %)	0.6
BMI	29 [<mark>25–31</mark>]	29 [26–30]	0.1
ED HR	93.4 ± 18.9	$\textbf{86.5} \pm \textbf{18.6}$	0.1
ED SBP	124.6 ± 17.1	129.7 ± 21.0	0.3
Initial WBC	15.4 ± 8.1	11.7 ± 5.5	0.008
Hospital LOS	3.1 ± 3.3	$\textbf{9.4} \pm \textbf{7.4}$	0.0009
Symptom onset to ED			
(hrs)	32.1 ± 26.7	$\textbf{46.6} \pm \textbf{44.5}$	0.2
Co-Morbidities			
HTN	36 (14.4 %)	4 (19.0 %)	0.8
DM	25 (10.0 %)	4 (19.0 %)	0.4
Chronic Steroids	8 (3.2 %)	0	0.7
Tobacco Use	73 (29.2 %)	8 (38.1 %)	0.7
OSA	4 (1.6 %)	1 (4.8 %)	0.6
EtOH Use	99 (39.6 %)	5 (23.8 %)	0.4

BMI: body mass index; ED: emergency department; HR: heart rate; SBP: systolic blood pressure; WBC: white blood cell; LOS: length of stay; HTN: hypertension; DM: diabetes mellitus; OSA: obstructive sleep apnea.

Table 3 Imaging findings across both cohorts.

000			
	Immediate (N = 250)	Delayed (N $= 21$)	p-value
Size of Appendix (mm)	13.8 ± 3.8	13.6 ± 3.5	0.8
AAST Grade III	69 (27.6 %)	13 (61.9 %)	0.005
AAST Grade IV	36 (14.4 %)	5 (23.8 %)	0.5
AAST Grade V	7 (2.8 %)	2 (9.5 %)	0.3
Appendicolith	167 (66.8 %)	15 (721.5 %)	0.9
Phlegmon	111 (44.4 %)	14 (66.7^)	0.1
IR Drainable Collection	33 (13.2 %)	8 (38.1 %)	0.009

AAST: American Association for the Surgery of Trauma; IR: interventional radiology.

operation, and may mean performing a larger resection including a partial colectomy [25]. However, more recent literature is suggesting a trend towards more immediate operative intervention in the setting of

Table 4

Intraoperative findings.

	Immediate (N = 250)	Delayed (N = 21)	p-value
AAST Grade III	124 (49.6 %)	9 (42.9 %)	0.8
AAST Grade IV	71 (28.4 %)	6 (28.6 %)	0.9
AAST Grade V	53 (21.2 %)	6 (28.6 %)	0.7
Purulent Peritonitis	219 (87.6 %)	20 (95.2 %)	0.6
Left Operative Drain	36 (14.4 %)	9 (42.9 %)	0.004
Conversion to Open	7 (0.4 %)	9 (42.9 %)	< 0.0001
Level of Contamination			
Clean Contaminated	16 (6.4 %)	0	0.5
Contaminated	141 (56.4 %)	11 (52.4 %)	0.9
Dirty	93 (37.2 %)	10 (47.6 %)	0.6
Operative Time (min.)	64.1 ± 26.2	83.1 ± 32.9	0.01

AAST: American Association for the Surgery of Trauma.

Table 5

Post-operative outcomes.

	Immediate (N = 250)	Delayed (N $=$ 21)	p- value
Surgical Site Infection			
Superficial	5 (2.0 %)	0	0.8
Deep	2 (0.80 %)	0	0.9
Organ Space	35 (14.0 %)	5 (23.8 %)	0.5
Appendiceal Stump Leak	0	0	-
Unanticipated Return to			
OR	4 (1.6 %)	1 (4.8 %)	0.5
30-Day Readmission	28 (11.2 %)	2 (9.5 %)	0.9
Mortality	0	0	-

OR: operating room.

perforated appendicitis [16,17,23,28].

The current study identified that over a five-year time period, approximately 12 % of patients who underwent an appendectomy presented with perforated appendicitis, this is consistent with findings published by Wu et al. who quoted an approximate 14 % rate of perforated appendicitis. Furthermore, despite the presence of perforation, only 11 patients required conversion from a laparoscopic to an open approach. Of these 11 patients, five patients required a partial colectomy. Despite the presence of increased inflammation within the operative field, our study population did not demonstrate any postoperative leak from the appendiceal stump or from an anastomosis.

To our knowledge, this study is the first to compare patients who underwent an immediate appendectomy versus those patients who failed an initial trial of non-operative management and who ultimately required an appendectomy during their index hospitalization. When comparing both groups, no significant differences in co-morbidities across the two populations were noted. Though one may hypothesize that patients undergoing a trial of non-operative management may be medically more complex and thus worse operative candidates overall, this was not the case in this series. When considering the white blood cell count in particular, patients taken to the operating room immediately had a higher initial white blood cell count in the emergency department. A lower initial white blood cell count, despite the presence of perforation, may represent an inability to mount an appropriate response to an infection and in many instances, may suggest that these patients should be managed operatively sooner. This lower white blood cell count may also explain why these patients failed non-operative management.

In regards to imaging findings, patients taken to the operating room initially had higher rates of more severe appendicitis as defined by the AAST grading system [21]. We suspect that while there was a significantly higher amount of AAST Grade III appendicitis in the patients in the delayed group, many of these patients were initially trialed with non-operative management as their imaging was also more likely to note a higher rate of drainable abscesses. The presence of an appendicolith has been previously demonstrated as a risk factor for a failure of nonoperative management [8], however, there were no differences in the rates of appendicoliths between groups.

Intraoperatively, there was no difference in the rates of AAST Grades III-V appendicitis between both groups. Also, there was no difference in the level of contamination between both groups and no difference in the rates of irrigation that was performed at the conclusion of the case. Notably, when looking at post-operative infectious complications, there were no differences in the rates of superficial, deep, or organ space infections between the immediate and delayed groups despite the fact that the patients in the delayed group had a higher likelihood of requiring an open operation. These findings differ from previously published data by Ingraham et al. that noted that patients undergoing a laparoscopic appendectomy for perforated appendicitis had a higher rate of postoperative abscess development when compared with patients undergoing an open operation [29]. The lack of difference in abscess formation across the immediate and delayed groups could be due to a few reasons. First, the vast majority of patients were able to be successfully managed with a laparoscopic operation and there were no significant differences in contamination levels across both groups suggesting that the level of inflammation and purulence that were encountered intraoperatively was less extensive than expected. Furthermore, while peritoneal irrigation is a controversial technique [30,31] that is oftentimes performed based on surgeon preference, the vast majority of patients did undergo peritoneal irrigation which may have successfully diluted the amount of contamination present.

Previous literature has promoted performing an appendectomy at the initial time of presentation for perforated appendicitis due to the increased patient morbidity that is demonstrated after failure of nonoperative management. This patient morbidity is mainly centered on readmissions and the need for additional interventions [16]. In the current study, the rate of failure of non-operative management was 7.7 % which is lower than the rate quoted in the literature of around 25 % [16]. Patients who failed non-operative management had a significantly longer hospital length of stay at an average of 9 days versus patients who underwent immediate operative intervention who stayed in the hospital for an average of 3 days. Despite undergoing an immediate appendectomy in the setting of perforation, patients in this group demonstrated no increased post-operative morbidity and did not demonstrate an increased rate of 30-day readmissions.

This study has several limitations. First, it was a retrospective review and thus inherent to the conduct of the study, there are likely gaps in the data of the medical record. Second, given the retrospective nature, the decision regarding which patients underwent immediate operative intervention versus a trial of non-operative management was oftentimes not clearly documented in the medical record. Furthermore, in patients who failed an initial trial of non-operative management, it was oftentimes difficult to discern what variable was used to decide to pursue surgical intervention unless this was well documented in the medical record. Furthermore, This study only included patients who underwent an operation and did not evaluate patients who were successfully managed non-operatively during their index hospitalization. Due to the small sample size of our population, we did not perform a regression analysis and there were no adjustments for potential confounding variables in the data. Ultimately, this study was exploratory in nature and thus causation cannot be implied.

Conclusions

The current study compares data on patients undergoing an immediate appendectomy for perforated appendicitis versus patients who failed an initial trial of non-operative management and who required an appendectomy during their index hospitalization. Patients who were managed with an immediate operation were discharged from the hospital sooner and do not demonstrate an increase in post-operative morbidity. These data suggest that surgeons can initially manage perforated appendicitis in an operative fashion. Ultimately, further research including a multicenter study is needed to compare immediate surgical intervention, failed non-operative management necessitating operative intervention, and successful non-operative management in order to make conclusions regarding the most effective way to manage this disease process.

CRediT authorship contribution statement

Caitlin A. Fitzgerald: Writing – review & editing, Writing – original draft, Methodology, Data curation, Conceptualization. Caroline Kernell: Data curation. Valeria Mejia-Martinez: Data curation. Giselle Peng: Data curation. Heba Zakaria: Data curation. Michelle Zhu: Data curation. Dale Butler: Writing – review & editing, Writing – original draft, Conceptualization. Brandon Bruns: Writing – review & editing, Writing – original draft, Formal analysis, Conceptualization.

Declaration of competing interest

The authors have no conflicts of interest to disclose.

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Author contributions

CAF designed the study, assisted with data collection, performed the statistical analysis and wrote the manuscript. CK, VMM, GP HZ, and MZ assisted with data collection. DB and BB designed the study and edited the manuscript.

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Ethics approval

Approval was obtained from the University of Texas Southwestern Medical Center Institutional Review Board (STU 2022–0259).

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