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ORIGINAL ARTICLE

CT Scan Findings Can Predict the Safety of Delayed Appendectomy for Acute Appendicitis

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Abstract

Background The relationship between duration of in-hospital waiting time and outcomes from appendectomy in patients with suspected appendicitis remains equivocal. The aim of this study was to investigate the influence of in-hospital waiting time on perforation rates and clinical outcomes in patients with suspected appendicitis who underwent appendectomy.

Methods A retrospective review of 5956 patients who underwent appendectomy at a single institution from January 2008 to December 2016 was performed. Patients were separated into two groups based on the duration from hospital arrival to surgery: patients with an in-hospital waiting time ≤ 12 h (no-delay group; $n = 5287$) and those with an in-hospital waiting time > 12 h (delayed group; $n = 669$). One-to-one propensity score matching ($n = 421$ per group) was performed to compare perforation rates and postoperative outcomes between the groups.

Results After propensity score matching, an in-hospital waiting time > 12 h was not associated with increased rates of perforation and significant complications, such as wound infection and abscess. However, in the matched cohorts and in the patients whose initial CT scans suggested perforated appendicitis, the delayed group had a higher risk of developing postoperative ileus (OR 9.18, 95% CI 1.16–72.74, $p = 0.021$; OR 2.17, 95% CI 1.03–4.59, $p = 0.048$, respectively) and longer postoperative length of hospital stay (87.38 vs. 79.07 h, $p = 0.008$; 161.61 vs. 130.87 h, $p < 0.001$, respectively) than the no-delay group.

Conclusions Our results indicate that a > 12-h in-hospital waiting time to surgery for appendicitis presents very little risk to the patient. However, the surgeon needs to carefully weigh the "safety" of a delay to surgery for appendicitis in patients whose initial CT scans suggested perforated appendicitis.

Keywords Appendectomy · In-hospital waiting time · Perforation · Outcomes

Introduction

Appendectomy for acute appendicitis is the most frequent emergency surgery procedure performed by general surgeons. In general, appendectomy must be performed within several hours of diagnosis, and delaying surgery can increase the rate of perforated appendicitis.[1–3] However, a new opinion has emerged regarding the natural history of acute appendicitis and the association between in-hospital waiting time and perforation has been extensively studied. Numerous studies have reported that a correlation exists between pre-hospital waiting time and perforation, but in-hospital waiting time and perforation were not correlated.[4–8] These results suggest that most perforations occur early, often before patients' arrival to a hospital, and that perforation can rarely be prevented even if in-hospital waiting time is reduced, because spontaneous resolution of appendicitis is common.[9,10] Despite numerous studies, conflicting outcomes still draw an unclear link between in-hospital waiting time and perforation, which has resulted in many controversies regarding prompt appendectomy for acute appendicitis.

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Investigations on the association between in-hospital waiting time and complication rates have also shown contradicting results. Several publications have indicated that in-hospital waiting time increases complication rates[4,11–14]; however, other publications have reported that in-hospital waiting time does not increase complication rates.[5,6,15,16] These studies have several limitations. For example, the previous studies did not distinguish between patients who were perforated at presentation from patients who experienced perforation while awaiting operation in the hospital. Moreover, a potential selection bias existed in which the groups with a shorter waiting time had a greater proportion of patients with perforation and low morbidity. Though a multivariate analysis was performed to minimize the bias, the issue of such a bias remains. To address this issue, a randomized trial is required; however, to the best of our knowledge, no such study has been conducted.

Therefore, the aim of this study was to investigate the influence of in-hospital waiting time on perforation rates and clinical outcomes in patients with suspected appendicitis who underwent appendectomy using propensity score matching to reduce bias caused by imbalanced covariates.

Materials and Methods

Patient Selection

We identified 6103 consecutive patients with acute appendicitis who underwent appendectomy between January 2008 and December 2016, at our hospital. After excluding 83 patients who underwent interval appendectomy and 64 patients who underwent incidental appendectomy, 5956 patients were finally included, and their medical records were used for a retrospective study. The organization's institutional review board approved this retrospective, observational, single-center study and waived the informed consent requirement.

Our hospital is a 640-bed secondary care center without residents and all procedures were performed by seven surgeons. The surgical approach used was based on the surgeon's preference. Although the frequency of open appendectomy was high, the frequency of laparoscopic appendectomies increased as of 2010, which was when all surgeons started performing laparoscopic surgery (Fig. 1). Patients were initially evaluated by an emergency department physician. There was no established clinical protocol at our institution; therefore, imaging studies (abdominal ultrasound and/or computed tomography [CT] scan) were obtained at the discretion of the emergency department physician. Intravenous hydration and intravenous antibiotics were administered as soon as a diagnosis of appendicitis was confirmed.

Data Collection and Variables

Medical records were reviewed to identify the following factors: age, sex, body mass index (BMI), comorbidities, abdominal operation history, initial vital signs, preoperative laboratory findings, time of symptoms onset, time of admission, time of surgery, surgical techniques (open vs. laparoscopic), CT findings, presence of perforation, postoperative complications, readmission, operating duration, and postoperative length of hospital stay (LOS). Comorbidities were classified according to the study by Charlson et al.[17] Blood samples, including white blood cell count, neutrophil count, and C-reactive protein (CRP) level, were collected from all patients after admission into the emergency department. The time of admission was separated into either regular (between 08:00 and 17:59) or overtime (between 18:00 and 07:59) hours to evaluate whether the time of admission affected in-hospital waiting time or outcomes.

The time of symptoms' onset was recorded using the emergency room admission notes, and the time of hospital arrival was defined as the time of patient registration in the

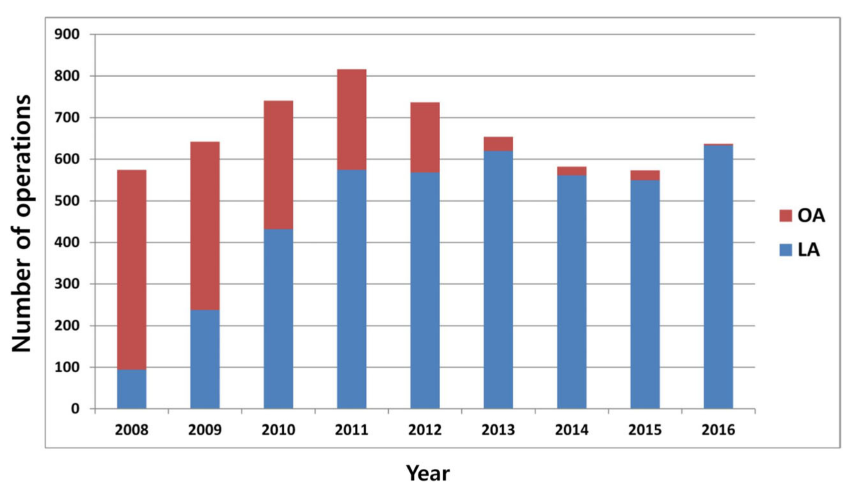

Fig. 1 Types of operation, laparoscopic appendectomy (LA) vs. open appendectomy (OA) over time

emergency room. The time of surgery was defined as the time of incision according to the anesthesia records. Pre-hospital waiting time was calculated as the time interval between onset of symptoms and hospital arrival, and in-hospital waiting time was calculated as the time interval between hospital arrival and surgery.

Outcome Measures

To investigate the association of in-hospital waiting time with perforation rates and clinical outcomes, the study population was separated into two groups based on the duration of in-hospital waiting time: patients with an in-hospital waiting time ≤ 12 h (no-delay group) and those with an in-hospital waiting time > 12 h (delayed group). The cutoff of 12 h was used as it was believed to be helpful for outcome comparison, as indicated in many previous studies.[5] We compared perforation rates, postoperative complications, readmission incidence, operating duration, and postoperative LOS between groups, using a propensity score-based matching method in order to minimize bias. Additional analysis was performed to assess risk factors of postoperative ileus in the matched groups. In addition, patients were further divided into two groups based on the existence of perforated or non-perforated appendicitis that was determined via the initial CT scan findings. Then, we compared the postoperative outcomes between the no-delay group and the delayed group.

Perforated appendicitis was diagnosed based on spillage of appendiceal contents, peritonitis, or abscess observed at the beginning of the surgery, or was pathologically confirmed as an appendiceal wall defect caused by transmural necrosis. Postoperative complications included wound infections, intra-abdominal abscesses, postoperative ileus, incisional hernias, internal organ injuries, bleeding, cardiovascular diseases, and pulmonary diseases. Definitions of wound infections were based on the guidelines from the Centers for Disease Control and Prevention.[18] A postoperative intra-abdominal abscess was diagnosed based on the presence of fever, abdominal pain, and/or gastrointestinal dysfunction, and was confirmed via radiological evidence of intra-abdominal fluid collection.[19] Postoperative ileus was diagnosed if two or more of the following five criteria were met on or after postoperative day 4: nausea or vomiting, inability to tolerate an oral diet over the preceding 24 h, the absence of flatus over the preceding 24 h, abdominal distension, and/or radiologic confirmation.[20] Operating duration was calculated from the initiation of skin incision to the completion of skin closure, according to anesthesia records. Postoperative LOS was defined as the time from the completion of skin closure to discharge from the ward.

Statistical Analysis

Statistical analyses were performed using SPSS version 22 (IBM Corp., Armonk, NY, USA). All calculated p values were two-sided, and $p < 0.05$ was considered statistically significant. The odds ratios (OR) and 95% confidence intervals (CI) are reported. Categorical variables are presented as numbers (percentages), whereas continuous variables are reported as mean ± standard deviation or median (interquartile range (IQR)). The chi-squared test or Fisher's exact test were used to compare groups for categorical variables. Student's t test was used to compare the continuous variables. Univariate and multivariate logistic regression analyses were performed to determine the influence of the following variables on postoperative ileus: age, sex, BMI, abdominal operation history, comorbidity, pre-hospital waiting time, in-hospital waiting time, surgical technique, and CT findings.

To minimize the effect of selection bias and potential confounding factors in this retrospective cohort study, estimated propensity scores were used to match the no-delay group to the delayed group. This model was used to obtain a one-to-one match using the optimal matching method, and matching was performed without replacement and used a caliper width of 0.1 standard deviations of the logit of the estimated propensity score. The following covariates were matched: age, sex, BMI, comorbidity, abdominal operation history, body temperature, pulse rate, white blood cell count, neutrophil shift, CRP, time of admission, pre-hospital waiting time, surgical technique, and CT findings. The 14 variables were selected because they could affect the group allocation and postoperative outcomes. Brookhart et al. suggested that variables that are unrelated to the exposure, but related to the outcome, should always be included in a propensity score model.[21] The inclusion of these variables likely decreased the variance of estimated exposure effect without increasing bias; we also considered this when selecting the variables.

Results

Baseline Characteristics of Unmatched and Propensity Score-Matched Patients

This study analyzed data from 5956 consecutive patients with acute appendicitis who underwent appendectomy, comprising the no-delay group ($n = 5287$) and the delayed group ($n = 669$). The mean age of the patients was 34.6 ± 18.3 years, consisting of 3298 (55.4%) men and 2658 (44.6%) women. The median pre-hospital waiting time was 20.5 h (IQR 8.0–40.8 h), and the median in-hospital waiting time was 5.1 h (IQR 3.6–7.7 h) (Table 1). Before propensity score matching, older age (≥ 65 years), female sex, comorbidities, elevated CRP levels, admission during overtime hours, and shorter

Table 1 Demographic characteristics of patients with suspected appendicitis who underwent appendectomy ($n = 5956$)

Age, mean ± SD, years	34.6 ± 18.3
Gender (male)	3298 (55.4)
Time interval, median (25–75% IQR), h	
Pre-hospital waiting time	20.5 (8.0–40.8)
In-hospital waiting time	5.1 (3.6–7.7)
Radiological tools	
CT	5086 (85.4)
Sonography	870 (14.6)
CT and sonography	72 (1.2)
Surgical technique	
Open appendectomy	1687 (28.3)
Laparoscopic appendectomy	4269 (71.7)
Conversion	53 (0.9)
Histological finding	
Non-perforated appendicitis	3957 (66.4)
Perforated appendicitis	1702 (28.6)
Tumor	67 (1.2)
Normal appendix	228 (3.8)
Overall morbidity	356 (6.0)
Complications	
Wound infection	220 (3.7)
Intra-abdominal abscess	37 (0.6)
Postoperative ileus	79 (1.3)
Incisional hernia	7 (0.1)
Internal organ injury	2 (0)
Bleeding	4 (0)
Cardiovascular	3 (0)
Pulmonary	4 (0)
Readmissions	68 (1.1)
Total operating duration, median (25–75% IQR), m	49.8 (40.2–64.8)
Postoperative LOS, median (25–75% IQR), h	77.7 (55.5–107.2)

All data are presented as number (percentage) of patients unless otherwise noted

SD standard deviation, *IQR* interquartile range, *CT* computed tomography, *LOS* length of hospital stay

pre-hospital waiting time were significantly more frequent in the delayed group than they were in the no-delay group. Laparoscopic appendectomy and CT findings of perforated appendicitis were significantly more frequent in the no-delay group (Table 2). To overcome biases due to the different distributions of covariates between the no-delay group and the delayed group, one-to-one propensity score analysis was conducted. The propensity score-matched cohort comprised 842 patients: the no-delay group ($n = 421$) and the delayed group ($n = 421$) (Fig. 2). After propensity score matching was performed, the initially observed differences between the groups became closely balanced; thus, no significant differences were observed for any baseline characteristics (Table 2).

Postoperative Outcomes in Unmatched and Propensity Score-Matched Patients

Before propensity score matching, we compared postoperative outcomes between the no-delay group and the delayed group (Table 3). Perforation rates were significantly higher in the no-delay group compared to the delayed group (OR 0.78, 95% CI 0.65–0.94, $p = 0.009$). The delayed group was more likely to experience postoperative ileus compared to the no-delay group (OR 1.87, 95% CI 1.06–3.30, $p = 0.028$). Postoperative LOS was also significantly longer in the delayed group compared to the no-delay group (101.43 vs. 91.10 h, respectively, $p = 0.006$). After propensity score matching, perforation rates, overall morbidity, and wound infection were not significantly different between the groups. Additionally, readmission incidence and total operating duration did not differ between the groups. The delayed group was more likely to experience postoperative ileus compared to the no-delay group (OR 9.18, 95% CI 1.16–72.74, $p = 0.021$). Postoperative LOS was also significantly longer in the delayed group compared to the no-delay group (87.38 vs. 79.07 h, respectively, $p = 0.008$) (Table 4).

Risk Factor Analysis of Postoperative Ileus in the Propensity Score-Matched Cohort

The results of the univariate and multivariate analyses of risk factors for postoperative ileus are presented in Table 5. In the univariate analysis, pre-hospital waiting times (1–2 days), in-hospital waiting times (> 12 h), and perforated appendicitis on CT were significantly related to the occurrence of a postoperative ileus. The multivariate analysis revealed that in-hospital waiting times (OR 10.60, 95% CI 1.31–85.61, $p = 0.027$) and perforated appendicitis on CT (OR 5.73, 95% CI 1.79–22.08, $p = 0.011$) were significant independent risk factors of postoperative ileus.

Postoperative Outcomes of Patients Whose Initial CT Scans Suggested Non-perforated and Perforated Appendicitis

Patients were further divided into two groups based on the existence of non-perforated ($n = 3793$) and perforated ($n = 1295$) appendicitis on initial CT scan findings. We compared postoperative outcomes between the no-delay group and the delayed group (Table 6). In patients whose initial CT scans suggested non-perforated appendicitis, an in-hospital waiting time > 12 h was not associated with higher perforation rate. Additionally, overall morbidity, wound infection, abscess, postoperative ileus, readmission incidence, total operating duration, and postoperative LOS did not differ between the no-delay and delayed groups. In patients whose initial CT scans suggested perforated appendicitis, perforation rates, overall

Table 2 Analysis of unmatched and matched patients stratified according in-hospital waiting time

Covariates	Unmatched patients			Propensity-matched patients		
	No-delay group (*n* = 5287)	Delayed group (*n* = 669)	*p* value	No-delay group (*n* = 421)	Delayed group (*n* = 421)	*p* value
Age (years)			0.001			0.563
≤ 65	4972 (94.0)	606 (90.6)		420 (99.8)	419 (99.5)	
> 65	315 (6.0)	63 (9.4)		1 (0.2)	2 (0.5)	
Sex (male:female)	2953:2334 (55.9:44.1)	345:324 (51.6:48.4)	0.036	201:220 (47.7:52.3)	192:229 (45.6:54.4)	0.534
BMI (> 25 kg/m^2)	1221 (24.0)	157 (23.9)	0.949	77 (18.3)	75 (17.8)	0.858
Comorbidity (Charlsonindex > 0)	511 (9.7)	98 (14.6)	< 0.001	18 (4.3)	17 (4.0)	0.863
Abdominal operation history (yes)	551 (10.5)	86 (12.9)	0.055	30 (7.1)	30 (7.1)	1.000
Fever (> 37.8 °C)	447 (8.5)	58 (8.7)	0.851	11 (2.6)	13 (3.1)	0.679
Tachycardia (> 100 bpm)	442 (8.4)	70 (10.5)	0.067	24 (5.7)	22 (5.2)	0.762
Leukocytosis (> 10,000/mm^3)	3925 (74.2)	486 (72.6)	0.376	323 (76.7)	325 (77.2)	0.870
Neutrophil shift (yes)	2109 (39.9)	272 (40.7)	0.711	172 (40.9)	172 (40.9)	1.000
C-reactive protein (> 0.8 mg/dl)	3200 (60.6)	321 (48.1)	< 0.001	171 (40.6)	175 (41.6)	0.779
Time of admission			< 0.001			1.000
Regular hours (08:00–17:59)	3719 (70.3)	221 (33.0)		135 (32.1)	135 (32.1)	
Overtime hours (18:00–07:59)	1568 (29.7)	448 (67.0)		286 (67.9)	286 (67.9)	
Pre-hospital waiting time, days			< 0.001			0.892
≤ 1	2908 (55.0)	436 (65.2)		302 (71.7)	301 (71.5)	
1–2	1196 (22.6)	107 (16.0)		57 (13.5)	53 (12.6)	
2–3	590 (11.2)	47 (7.0)		25 (5.9)	24 (5.7)	
> 3	593 (11.2)	79 (11.8)		37 (8.8)	43 (10.2)	
Laparoscopic appendectomy	3821 (72.3)	448 (67.0)	0.004	313 (74.3)	306 (72.7)	0.585
Perforated appendicitis on CT	1169 (26.1)	126 (20.6)	0.003	63 (15.0)	59 (14.0)	0.695

All data are presented as number (percentage) of patients unless otherwise noted

BMI body mass index, *SD* standard deviation, *bpm* beats per minute, *CT*, computed tomography

morbidity, wound infection, readmission incidence, and total operating duration were not significantly different between the no-delay and delayed groups. However, the delayed group was more likely to experience postoperative ileus than the no-delay group (OR 2.17, 95% CI 1.03–4.59, $p = 0.048$). Postoperative LOS was also significantly longer in the delayed group compared to the no-delay group (161.61 vs. 130.87 h, respectively, $p < 0.001$).

Discussion

In the present study, we investigated the influence of in-hospital waiting time on perforation rates and clinical outcomes of patients who underwent appendectomy. To our knowledge, this study is the first to identify outcomes of prolonged in-hospital waiting time for appendectomy, using a propensity score-based matching method in order to minimize bias. Our results showed that propensity score-matched patients with an in-hospital waiting time > 12 h did not increase the risk of perforation and significant complications, such as wound infection and abscess, but had a higher risk of developing postoperative ileus and had longer postoperative LOS than patients with an in-hospital waiting time ≤ 12 h. Moreover, in 3793 patients whose initial CT scans suggested non-perforated appendicitis, an in-hospital waiting time > 12 h was not associated with higher perforation rate. Conversely, in 1295 patients whose initial CT scans suggested perforated appendicitis, patients with an in-hospital waiting time > 12 h had a higher risk of developing postoperative ileus and had longer postoperative LOS than patients with an in-hospital waiting time ≤ 12 h.

In general, appendectomy must be performed within several hours of diagnosis, and delaying surgery can increase the rate of perforated appendicitis.[1–3] However, numerous studies have reported that a correlation exists between pre-hospital waiting time and perforation, but in-hospital waiting time and perforation were not correlated.[4–8] A meta-analysis of 11 non-randomized studies showed that short in-hospital waiting times of 12–24 h were not associated with an increased risk of complex appendicitis.[5] Our findings are consistent with the aforementioned studies that

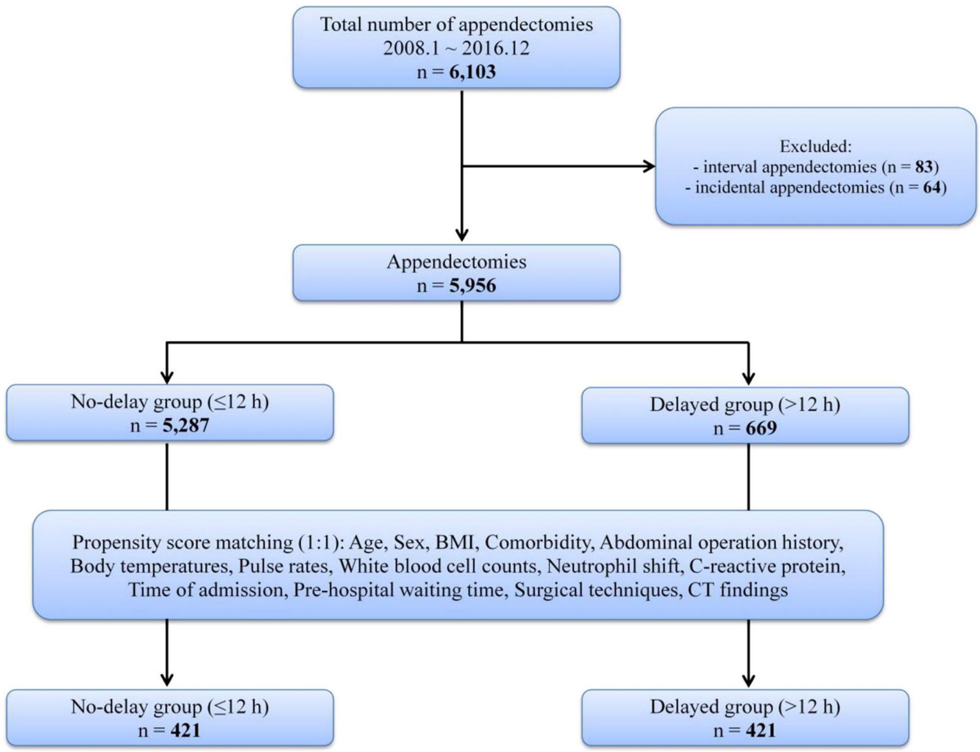

Fig. 2 Study flow chart

found no increased rates of perforation among patients who had delayed appendectomy.

Although there have been a number of studies that examined the association between in-hospital waiting time and outcomes in patients with acute appendicitis who underwent appendectomy, the results are contradictory. Several studies have confirmed that delaying appendectomy significantly increased the rate of complications.[4,11–14] For example, in a study of 1081 cases of appendicitis, Ditilo et al. concluded that the risk of developing advanced pathology and postoperative complications increased with time; therefore, delayed appendectomy was unsafe.[11] Moreover, Teixeira's review of over 4000 patients with acute appendicitis who underwent appendectomy demonstrated that appendectomy delays were associated with

Table 3 Postoperative outcomes before matching

Outcome	No-delay group (n = 5287)	Delayed group (n = 669)	OR (95% CI)	p value
Perforated appendicitis, n (%)	1601 (30.3)	170 (25.4)	0.78 (0.65–0.94)	0.009
Overall morbidity, n (%)	310 (5.9)	39 (5.8)	0.99 (0.71–1.40)	0.972
Complications, n (%)				
Wound infection	199 (3.8)	21 (3.1)	0.83 (0.53–1.31)	0.419
Abscess	36(0.7)	1 (0.1)	0.22 (0.03–1.60)	0.118
Postoperative ileus	64 (1.2)	15 (2.2)	1.87 (1.06–3.30)	0.028
Readmissions, n (%)	58 (1.1)	10 (1.5)	1.37 (0.70–2.69)	0.335
	Mean ± SD	Mean ± SD	Mean Difference (95% CI)	
Total operating duration, h	1.00 ± 1.28	1.00 ± 0.56	–0.01 (–0.11 to 0.87)	0.826
Postoperative LOS, h	91.10 ± 75.15	101.43 ± 92.49	–10.33 (–14.40 to –2.22)	0.006

LOS length of hospital stay, *OR* odds ratio, *CI* confidence interval, *SD* standard deviation

Table 4 Postoperative outcomes after matching

Outcome	No-delay group (n = 421)	Delayed group (n = 421)	OR (95% CI)	p value
Perforated appendicitis, n (%)	85 (20.2)	91 (21.6)	1.09 (0.78–1.52)	0.611
Overall morbidity, n (%)	21 (5.0)	20 (4.8)	0.95 (0.51–1.78)	0.873
Complications, n (%)				
Wound infection	19 (4.5)	11 (2.6)	0.57 (0.27–1.21)	0.192
Postoperative ileus	1 (0.2)	9 (2.1)	9.18 (1.16–72.74)	0.021
Readmissions, n (%)	1 (0.2)	5 (1.3)	5.05 (0.59–43.39)	0.217
	Mean ± SD	Mean ± SD	Mean Difference (95% CI)	
Total operating duration, h	1.04 ± 2.36	0.97 ± 0.56	0.07 (–0.16 to 0.30)	0.554
Postoperative LOS, h	79.07 ± 39.57	87.38 ± 49.87	–8.31 (–14.40 to –2.22)	0.008

LOS length of hospital stay, *OR* odds ratio, *CI* confidence interval, *SD* standard deviation

a significantly increased risk of surgical site infection.[4] Similarly, our study showed that in-hospital waiting times were associated with an increased risk of developing postoperative ileus in a matched cohort. We found that postoperative LOS was also significantly longer in the delayed group compared to the no-delay group. In particular, in patients whose initial CT scans suggested perforated appendicitis, the delayed group had a higher risk of developing postoperative ileus and had longer postoperative LOS than the no-delay group. Therefore, the results of our study do not support an in-hospital waiting time of > 12 h for surgical treatment of appendicitis in patients whose initial CT scans suggested perforated appendicitis. Carr argued that perforated appendicitis has a greater rate of morbidity.[22] Additionally, although non-ruptured appendicitis sometimes resolves spontaneously, it can also progress to perforation over time. Moreover, Carr indicated that there was no longer a need for studies seeking evidence in support of a delay for the care of appendicitis. The author added that he also performs appendectomy at night, because delaying surgical care results in prolonged pain and suffering on the patient's part. Considering our results, we partially agree with Carr's viewpoint.

Conversely, multiple studies have shown that delayed appendectomy was not associated with an increased risk of postoperative complications.[5,6,15,16] A study comprising more than 30,000 patients did not find an association between hospital waiting time and 30-day outcomes.[6] Further, in a study by Shin et al., no significant difference in

Table 5 Risk factors of postoperative ileus in the propensity score-matched cohort

Variable	Univariate analysis OR (95% CI)	p value	Multivariate analysis OR (95% CI)	p value
Age (> 65 years)		1.000	NA	
Gender (male)	1.32 (0.37–4.70)	0.670	NA	
BMI (> 25 kg/m^2)	0.83 (0.18–3.86)	0.821	NA	
Abdominal operation history (yes)		1.000	NA	
Comorbidity (Charlsonindex > 0)		1.000	NA	
Pre-hospital waiting time, days				
≤ 1	Reference		Reference	
1–2	5.65 (1.39–22.94)	0.015	4.29 (0.99–18.55)	0.051
2–3	3.12 (0.34–28.47)	0.313	2.24 (0.23–21.87)	0.488
> 3	1.90 (0.21–17.17)	0.570	0.81 (0.08–8.22)	0.856
In-hospital waiting time (> 12 h)	9.18 (1.16–72.74	0.021	10.60 (1.31–85.61)	0.027
Laparoscopic appendectomy	0.54 (0.15–1.92)	0.304	NA	
Perforated appendicitis on CT	6.11 (1.74–21.44)	0.008	5.73 (1.79–22.08)	0.011

BMI body mass index, *CT* computed tomography, *OR* odds ratio, *CI* confidence interval, *NA* not applicable

Table 6 Postoperative outcomes after stratification by presence of perforation on CT

Non-perforated appendicitis on CT				
Outcome	No-delay group (n = 3306)	Delayed group (n = 487)	OR (95% CI)	p value
Perforated appendicitis, n (%)	550 (16.6)	79 (16.2)	0.97 (0.75–1.26)	0.818
Overall morbidity, n (%)	140 (4.2)	17 (3.5)	0.82 (0.49–1.37)	0.442
Complications, n (%)				
Wound infection	104 (3.1)	12 (2.5)	0.78 (0.43–1.43)	0.415
Abscess	11(0.3)	0 (0.0)		0.379
Postoperative ileus	18 (0.5)	5 (1.0)	1.90 (0.70–5.13)	0.201
Readmissions, n (%)	25 (0.8)	3 (0.6)	0.81 (0.25–2.70)	0.736
	Mean ± SD	Mean ± SD	Mean Difference (95% CI)	
Total operating duration, h	0.90 ± 1.15	0.92 ± 0.47	–0.02 (–0.12 to 0.09)	0.876
Postoperative LOS, h	79.85 ± 79.71	84.98 ± 48.21	–5.13 (–12.40 to 2.14)	0.301
Perforated appendicitis on CT				
Outcome	No-delay group (n = 1169)	Delayed group (n = 126)	OR (95% CI)	p value
Perforated appendicitis, n (%)	1030 (88.1)	107 (84.9)	0.76 (0.45–1.28)	0.299
Overall morbidity, n (%)	134 (11.5)	18 (14.3)	1.29 (0.76–2.19)	0.350
Complications, n (%)				
Wound infection	73 (6.2)	6 (4.8)	0.75 (0.32–1.76)	0.509
Abscess	20(1.7)	1 (0.8)	0.46 (0.06–3.45)	0.713
Postoperative ileus	40 (3.4)	9 (7.1)	2.17 (1.03–4.59)	0.048
Readmissions, n (%)	27 (2.3)	6 (4.8)	0.81 (0.25–2.70)	0.126
	Mean ± SD	Mean ± SD	Mean Difference (95% CI)	
Total operating duration, h	1.34± 1.55	1.36 ± 0.74	–0.02 (–0.30 to 0.25)	0.960
Postoperative LOS, h	130.87 ± 66.85	161.61 ± 141.93	–30.73 (–56.04 to –5.42)	<0.001

LOS length of hospital stay, *OR* odds ratio, *CI* confidence interval, *SD* standard deviation

outcomes was noted between subgroups waiting for operation for < 8 vs. > 8 h.[16] However, we must use caution in interpreting these studies and remember not to generalize the findings.

Previous studies concerning delayed appendectomy and outcomes may have contained potential selection bias in the comparisons between patients with in-hospital delay and patients without in-hospital delay. Typically, patients who are younger and healthier are more likely to receive surgical treatment early. On the other hand, for patients who are older, and who have significant comorbidities, the waiting time to surgery may be longer. Young et al. showed that the clinical presentation of acute appendicitis in older patients was atypical, and the duration between emergency department registration and operation was significantly longer in older patients.[23] Furthermore, surgeons tend to prioritize patients with perforation or those who have serious inflammation approximating perforation. In these cases, surgical intervention is provided sooner rather than later, as the potential for diagnostic confusion is minimal, and the patients' condition can quickly deteriorate.[24] In addition, Eldar et al. noted that males had shorter intervals from surgical admission to induction of anesthesia than females.[25] Busch et al. found that the size of the institution, time of admission, and surgical technique were independent predictors of in-hospital waiting times > 12 h.[3] In our analysis of the baseline characteristics of the unmatched cases, longer waiting times was more likely to occur in patients who were aged > 65 years, were female, had several comorbidities, had experienced shorter pre-hospital waiting times, were without elevated CRP levels, were admitted during overtime hours, had undergone open surgery, and were without perforated appendicitis on CT. Many of the factors were also interrelated with the risk for confounding effects. Despite the use of multivariate logistic regression analysis, there is always concern for bias.

In observational studies, the selection of treatment method is influenced by the patient's baseline characteristics. As such, differences in baseline characteristics must be taken into account when evaluating treatment outcomes, which necessitates randomized controlled trials to evaluate potential correlations between treatment methods and outcomes. However, it is not realistic to perform a randomized controlled trial for the purpose of verifying the outcomes of a prolonged hospital waiting time in patients with suspected appendicitis who are undergoing appendectomy. Given the previous research, it would be unethical to delay surgical treatment due to the potential of perforation. To minimize differences in baseline characteristics, propensity score matching has been increasingly used in recent years.[26] In our study, propensity score matching was used to minimize the differences in covariates in each group that could potentially affect the outcomes, thereby attempting a more reliable result in our non-randomized retrospective study.

Postoperative ileus is generally defined as a transient impairment of bowel motility after abdominal surgery, and is a major contributor to postoperative discomfort. Postoperative ileus delays the start of a regular diet, and therefore, postoperative hospital stay is prolonged.[27] Kim et al. reported that delaying appendectomy > 36 h after increased symptom onset was associated with an increased risk of postoperative ileus.[28] Similarly, our study showed that in-hospital waiting times > 12 h were associated with an increased risk for developing postoperative ileus in a matched cohort. Furthermore, our data confirmed that in-hospital waiting times > 12 h and perforated appendicitis based on CT findings were a significant independent risk factor of postoperative ileus in univariate and multivariate analyses after propensity score matching. Therefore, in order to avoid postoperative ileus in patients with perforated appendicitis on CT, we should attempt to reduce in-hospital waiting times ≤ 12 h. In experimental and clinical studies, postoperative ileus was related to the degree of surgical manipulation and the magnitude of the inflammatory response.[29] The longer the duration of illness, the more serious the inflammation or the length of exposure becomes; thus, it is possible that a more technically difficult operation, which requires more mobilization and more tissue trauma, may have induced increased ileus. Artinyan et al. found two factors that were correlated with postoperative ileus in multivariate analysis: total opiate dose and estimated blood loss.[30] Though our study did not evaluate pre- or postoperative opiate use, it is possible that opiate use in patients with prolonged in-hospital waiting times influenced the incidence of postoperative ileus.

Overall, in our study, the number of patients who experienced a postoperative ileus was quite low ($n = 79$, 1.3%), which is what might be expected for a series of patients undergoing appendectomy. Though statistically significant, the difference in the rates of postoperative ileus between the no-delay and delayed groups in the matched cohort was remarkably small (2.1 vs. 0.2%) and of questionable clinical significance. Furthermore, though statistically significant, the difference in postoperative LOS between the no-delay and delayed groups was only about 8 h, and this is too questionable to have clinical significance. As such, one might easily conclude that an in-hospital waiting time of > 12 h is of limited risk to the patient, as there is no difference in the perforation rate or in the rates of significant complications, such as wound infection and abscess. However, in patients whose initial CT scans suggested perforated appendicitis, the difference in the rates of postoperative ileus between the no-delay and delayed groups was remarkable (7.1 vs. 3.4%), and the difference in postoperative LOS between the groups was about 31 h. Therefore, the surgeon needs to carefully weigh the "safety" of a delay to surgery for appendicitis in patients whose initial CT scans suggested perforated appendicitis.

This study had several limitations. First, this was a non-randomized retrospective study. Although the analyses were performed after propensity score matching, there could have been residual confounding factors, because the historical background of the two groups differed. Second, with a relatively small sample size, especially in the delayed group, the study may be underpowered. As a secondary care center, our hospital tends to perform appendectomies during both daytime and evening hours. For this reason, compared to previous studies, the proportion of patients with a > 12-h in-hospital waiting time was relatively small (11%). Third, the study was performed at a single center; thus, the results may not be generalizable. Fourth, the timing of antibiotic administration and imaging studies might have important effects on in-hospital waiting times or outcomes; however, we were unable to collect data about these occurrences before surgery. There may be a possibility that patients with severe appendicitis may have been administered antibiotics earlier or had the CT scan conducted early. Finally, we did not include data on narcotics or prokinetic drugs that affected bowel motility. These drugs may be important factors due to their potentially positive or negative influence on postoperative ileus, but we were unable to include them in our analysis. Despite these limitations, our study used propensity score matching to reduce the bias from imbalanced covariates, which previous observational studies contained, and yielded important findings.

Conclusions

In summary, we performed a propensity score-matched analysis to identify outcomes of a prolonged in-hospital waiting time in patients with suspected appendicitis who underwent appendectomy. In-hospital waiting time > 12 h was not associated with increased rates of perforation and significant complications, such as wound infection and abscess. However, in the matched cohorts and in patients whose initial CT scans suggested perforated appendicitis, patients with an in-hospital waiting time > 12 h had a higher risk of developing postoperative ileus and had longer postoperative LOS than patients with an in-hospital waiting time ≤ 12 h. Furthermore, in-hospital waiting time > 12 h and perforated appendicitis on CT were significant independent risk factors of postoperative ileus. Although this single-center, retrospective study cannot sufficiently state that in-hospital waiting time affects postoperative outcomes of patients undergoing appendectomy, our results support that an in-hospital waiting time to surgery for appendicitis of > 12 h presents very little risk to the patient. However, the surgeon needs to carefully weigh the "safety" of a delay to surgery for appendicitis in patients whose initial CT scans suggested perforated appendicitis.

Authors' Contributions All the above authors meet the following conditions for authorship: (a) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; (b) drafting the article or revising it critically for important intellectual content; (c) final approval of the version to be published; and (d) agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interests.

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