

# Effects of Timing of Appendectomy on the Risks of Perforation and Postoperative Complications of Acute Appendicitis

Jong Wan Kim<sup>1</sup> · Dong Woo Shin<sup>1</sup> · Doo Jin Kim<sup>2</sup> · Jeong Yeon Kim<sup>1</sup> ·  
Sung Gil Park<sup>1</sup> · Jun Ho Park<sup>2</sup>

Published online: 12 October 2017  
© Société Internationale de Chirurgie 2017

## Abstract

**Background** It is generally believed that appendectomy should be performed immediately to prevent perforation and complications. Therefore, our objectives were to investigate the effect of timing of appendectomy on the incidence of perforation and complications.

**Methods** We retrospectively reviewed the medical records of patients who underwent laparoscopic appendectomy between January 2014 and June 2015. The time from symptom onset to appendectomy was categorized into three periods: time from symptom onset to hospital admission (symptomatic time), time from admission to appendectomy (hospitalization time), and time from symptom onset to appendectomy [symptomatic period + hospitalization period (overall time)]. Multivariable analyses were performed to identify independent factors associated with perforation and complications.

**Results** A total of 1753 patients were included in the present study. Perforation occurred in 28.2% of patients, and postoperative complications occurred in 10.0% of patients. Multivariable analysis showed that BT > 38 °C ( $P = 0.006$ ), WBC count >13,000 cells/ $\mu$ l ( $P = 0.02$ ), neutrophil ratio >80% ( $P < 0.001$ ), and symptomatic time >24 h ( $P < 0.001$ ) were independent factors of appendiceal perforation, while the neutrophil ratio >80% ( $P < 0.001$ ) and symptomatic time >48 h ( $P = 0.003$ ) were independently associated with complications.

**Conclusions** The present study showed that the symptomatic time and overall time were significantly associated with perforation and complications, whereas hospitalization time was not associated with either perforation or complications.

## Introduction

Appendicitis is one of the most common diseases requiring emergent surgery after the onset of symptoms [1]. It is generally accepted that prompt surgery is necessary to

prevent disease progression, which is associated with an increased risk of morbidity and mortality [2–4]. However, this concept has been challenged by recent studies showing that appendicitis can be managed by semi-elective surgery after initial use of antibiotics [5–7]. In addition, several studies have reported that the administration of antibiotics alone enabled surgeons to perform interval appendectomy at up to 6–8 weeks after the diagnosis of appendicitis [8, 9]. These studies suggested the possibility of elective surgery for appendicitis, rather than emergent surgery. An excessive overnight caseload might increase fatigue among hospital staff, and a number of studies have emphasized that sleep deprivation has negative effects on the cognitive abilities and clinical performance of residents [10–12] and

✉ Jun Ho Park  
zoono@hanmail.net

<sup>1</sup> Department of Surgery, Dongtan Sacred Heart Hospital, Hallym University College of Medicine, 40, Sukwoo-Dong, Hwaseong-Si, Gyeonggi-Do 445-170, Republic of Korea

<sup>2</sup> Department of Surgery, Kangdong Sacred Heart Hospital, Hallym University College of Medicine, 150 Seongan-ro, Gangdong-gu, Seoul 05355, Republic of Korea

might ultimately affect the patient's safety. Therefore, it might be prudent to delay some surgical procedures. We hypothesized that appendectomy could be delayed in a semi-elective manner to alleviate the surgical caseload and avoid the negative effects of fatigue and sleep deprivation. However, some studies have shown that delayed appendectomy is unsafe because the risks of perforation and complications increase with time [13, 14]. Therefore, the present study was designed to evaluate the effect of time from symptom onset to appendectomy on the risks of perforation and postoperative complications.

## Methods

We retrospectively reviewed the medical records of all patients who were diagnosed with acute appendicitis and underwent appendectomy at two hospitals affiliated to Hallym University, Korea (Dong Tan Sacred Heart Hospital and Kang Dong Sacred Heart Hospital) between January 2014 and June 2015. Patients underwent either laparoscopic or open surgery.

We included patients of all ages in this study.

We excluded patients who underwent incidental appendectomy, interval appendectomy, and negative appendectomy. We excluded patients who were treated with antibiotics or percutaneous procedures (e.g., percutaneous drainage). We also excluded patients if the time of symptom onset was not recorded in their medical chart.

Patients' characteristics included age, gender, American Society of Anesthesiologists (ASA) score, white blood cell (WBC) count, neutrophil count, neutrophil-to-WBC ratio (neutrophil ratio), and body temperature (BT) at initial diagnosis. Perioperative data included the operation time, time to flatus, time to soft food intake, postoperative hospital stay, and postoperative complications.

The time from symptom onset to appendectomy was categorized into three periods: time from symptom onset to hospital admission (symptomatic time), time from admission to appendectomy (hospitalization time), and time from symptom onset to appendectomy [i.e., symptomatic period + hospitalization period (overall time)]. The times from admission to the start of surgery were recorded in the patients' electronic medical records at both hospitals. The timing of symptom onset was based on the patient's medical history at the first examination. If the time at symptom onset was precisely recorded (i.e., date and time), we used the recorded value in the calculation. If the approximate time at symptom onset was recorded (e.g., morning or evening), we estimated the time using 6-h strata as follows: if the first symptom occurred in the morning, the onset of symptoms was recorded as 6 a.m.; if the first symptom occurred in the evening, the onset of symptoms

was recorded as 6 p.m. Even though some patients were transferred from other hospitals, we defined the start of hospitalization as the time of admission to our hospitals. The continuous variables, including symptomatic time and hospitalization time, were categorized according to their mean values.

Perforation was assessed based on the intraoperative findings. In equivocal cases, perforation was assessed using the patient's pathologic report. Postoperative complications were defined as wound infection, intra-abdominal abscess, ileus, or acute gastroenteritis (AGE) occurring up to 30 days after the patient was first discharged.

The primary outcomes of this study were to identify independent factors associated with perforation or postoperative complications. The secondary outcome was the length of postoperative hospital stay.

## Statistical analysis

All analyses were performed using IBM SPSS Statistics for Windows version 23 (IBM Corp., Armonk, NY, USA). Continuous variables were analyzed using Student's *t* test or the Mann–Whitney U test. Categorical variables were analyzed using the  $\chi^2$  test or Fisher's exact test. The continuous variables, including symptomatic time and hospitalization time, were categorized according to their mean values for inclusion in the regression models. The likelihood ratio test was performed to determine the trends in perforation and complications over time. Multivariable logistic regression was performed to identify independent factors associated with perforation or postoperative complications. Confounding factors selected for multivariable logistic regression included those factors that were found to be statistically associated with perforation and complication in univariate analyses as well as factors previously reported to be associated with perforation and complications. *P* values of <0.05 were considered statistically significant.

## Results

A total of 1765 patients with acute appendicitis underwent appendectomy at Dong Tan Sacred Heart Hospital or Kang Dong Sacred Heart Hospital between January 2014 and June 2015. Overall, 1753 (99.3%) patients underwent laparoscopic appendectomy and 12 (0.7%) patients underwent open appendectomy. Because so few patients underwent open surgery, these cases were excluded from further analysis. Of the 1753 patients, 1258 (71.8%) had simple appendicitis and 495 (28.2%) had perforated appendicitis.

Table 1 shows the patients' characteristics according to the presence of perforation. Patients with perforated appendicitis were significantly older than those with simple appendicitis (mean: 34.4 vs. 30.0 years,  $P < 0.001$ ). In terms of laboratory/clinical findings, the WBC count, neutrophil ratio, and BT were higher in patients with perforated appendicitis than in patients with simple appendicitis. Additionally, the operation time, time to flatus, the time to soft food intake, and the postoperative hospital stay (4.4 vs 2.6 days,  $P < 0.001$ ) were longer in patients with perforated appendicitis than in patients with simple appendicitis. Complications occurred in a total of 176 patients (10.0%). The most common complication was wound infection, followed by intra-abdominal abscess, AGE, and ileus. The complication rate was similar between patients with simple appendicitis and patients with perforated appendicitis (9.8 vs 10.7%;  $P = 0.56$ ). The rates of individual complications, including wound infection, intra-abdominal abscess, and AGE were also similar in both groups, but the rate of ileus tended to be higher in patients with perforated appendicitis (1.2 vs 0.5%,  $P = 0.09$ ).

The overall time from symptom onset to appendectomy was significantly longer, by about 12 h, in patients with perforated appendicitis than in patients with simple appendicitis (44.4 vs 33.9 h;  $P < 0.001$ ) (Table 2). The mean symptomatic time was 34.7 and 24.8 h in patients with perforated appendicitis and patients with simple appendicitis, respectively, and this difference was statistically significant ( $P < 0.001$ ). However, the mean

hospitalization time was not significantly different between the two groups (perforated appendix vs simple appendicitis: 8.4 vs. 8.3 h;  $P = 0.76$ ). We also categorized time variables into several categories based on the mean value, such as 24 h for symptomatic time and 8 h for hospitalization time. For symptomatic time, because the category  $<24$  h included the majority of patients in this study (70.6%: 1238/1753), we subdivided this category into two groups ( $<12$  h and 12–24 h). As indicated in Fig. 1, the rate of perforation increased with increases in overall time ( $P < 0.001$ ) and symptomatic time ( $P < 0.001$ ), but not hospitalization time ( $P = 0.41$ ).

Multivariable analysis showed that BT  $> 38$  °C ( $P = 0.006$ ), WBC count  $>12,000$  cells/ $\mu$ l ( $P = 0.02$ ), neutrophil ratio  $>80\%$  ( $P < 0.001$ ), and symptomatic time were independently associated appendiceal perforation. The odds ratio for appendiceal perforation was 2.7 among patients with symptomatic time  $>24$  h in multivariable regression ( $P < 0.001$ ). Hospitalization time was not significantly associated with perforation (Table 3).

Table 4 shows the patients' characteristics according to the presence and absence of postoperative complications. The mean ages of patients with complications and patients without complications were 29.5 and 31.4 years, respectively ( $P = 0.15$ ). There were no differences between the two groups in terms of gender, ASA, laboratory variables (WBC count and neutrophil ratio), or BT. However, operation time and time to soft food intake were significantly longer in patients with complications. Accordingly,

**Table 1** Characteristics of patients according to the presence of perforation

Characteristics	Simple ( $n = 1258$ )	Perforation ( $n = 495$ )	$P$
Age	30.0 (15.8)	34.4 (18.0)	$<0.001$
Male	707 (56.2)	274 (55.4)	0.74
ASA $\geq 2$	160 (12.7)	98 (19.8)	$<0.001$
BT (°C)	36.9 (0.6)	37.0 (0.7)	$<0.001$
WBC ( $\times 10^3/\mu$ l)	12.1 (4.2)	13.8 (4.7)	$<0.001$
Neutrophil ratio (%)	74.8 (13.0)	80.5 (9.6)	$<0.001$
Operation time (min)	43.5 (20.4)	55.8 (24.0)	$<0.001$
Time to flatus (days)	1.0 (0.7)	1.2 (0.8)	$<0.001$
Time to soft diet (days)	1.3 (0.7)	2.2 (1.2)	$<0.001$
Duration of postoperative hospital stay (days)	2.6 (1.2)	4.4 (2.2)	$<0.001$
Complication	123 (9.8)	53 (10.7)	0.56
Wound infection	90 (7.2)	32 (6.5)	0.60
Intra-abdominal abscess	20 (1.6)	9 (1.8)	0.74
AGE	13 (1.0)	8 (1.6)	0.31
Ileus	6 (0.5)	6 (1.2)	0.09

Data presented are numbers of patients (percentage) or means (standard deviations)

ASA American Society of Anesthesiologists, WBC white blood cell count, BT body temperature, AGE acute gastroenteritis

**Table 2** Relationship between perforation and time intervals

	Simple	Perforation	<i>P</i>
Symptomatic time	24.8 (38.1)	34.7 (41.7)	<0.001
Hospitalization time	8.3 (5.1)	8.4 (5.0)	0.76
Overall time	33.9 (38.5)	44.4 (41.4)	<0.001

Data are presented as mean ± standard deviation

Symptomatic time was defined as the time from onset of first symptom to admission. Hospitalization time was defined as the time from admission to operation. Overall time was defined as the time from onset of first symptom to operation, which was calculated by adding the patient time and hospitalization time

postoperative hospital stay was significantly longer in patients with complications than in patients without complications (3.8 vs. 3.0 days;  $P = 0.001$ ).

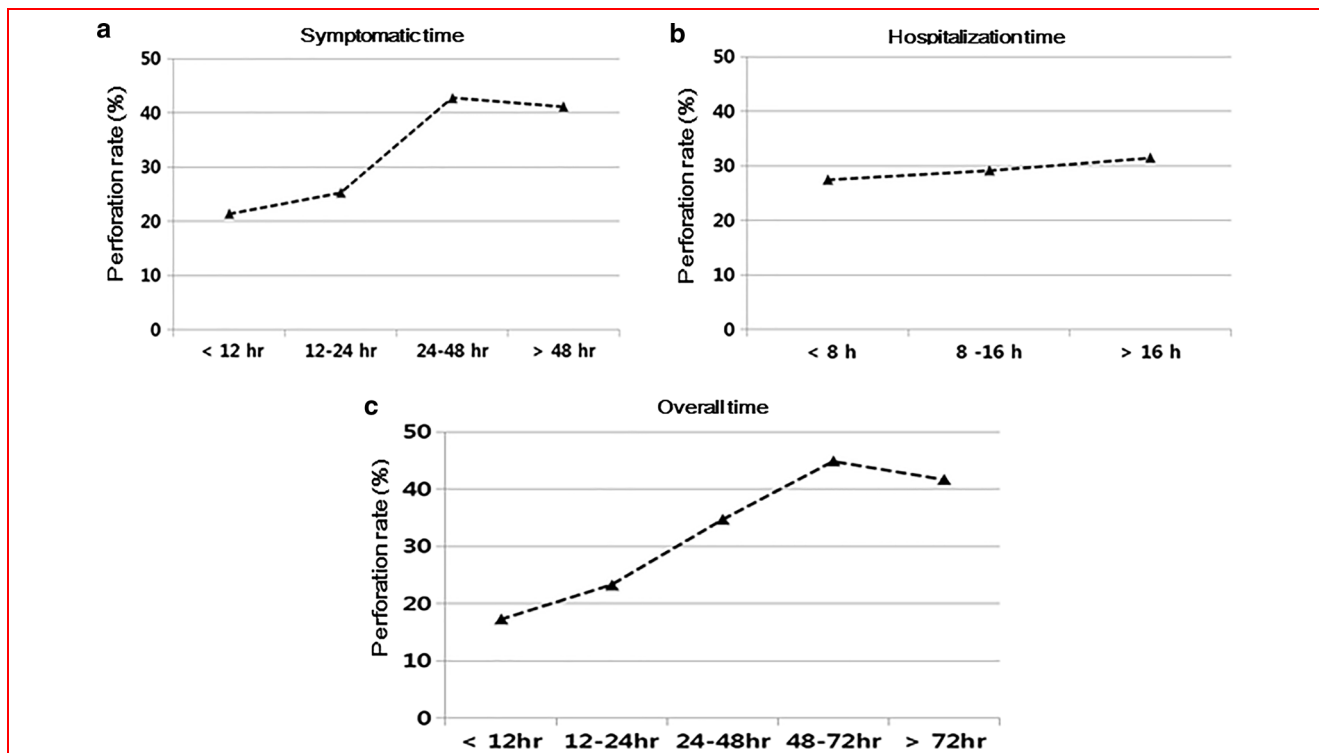
The overall time from symptom onset to appendectomy (44.4 vs 36.0 h;  $P = 0.03$ ) (Table 5) and the symptomatic time (35.9 vs 26.7 h;  $P = 0.018$ ) were significantly longer in patients with complications than in patients without complications. However, the mean hospital time was similar between patients with complications and patients without complications (9.0 vs 8.3 h;  $P = 0.43$ ). As described above, we categorized symptomatic time into 24-h groups and hospitalization time into 8-h groups. And the category <24 h in the symptomatic time was

subdivided into two groups (<12 h and 12–24 h). As shown in Fig. 2, the rate of complications increased significantly with increasing symptomatic time ( $P = 0.046$ ) and overall time ( $P = 0.042$ ). However, the rate of complications did not increase with increasing hospitalization time ( $P = 0.20$ ).

Multivariable analysis showed that neutrophil ratio >80% ( $P < 0.001$ ) and symptomatic time were independently associated with postoperative complication. The odds ratio for appendiceal perforation was 2.0 among patients with symptomatic time >48 h ( $P = 0.003$ ). Hospitalization time was not significantly associated with perforation (Table 6).

## Discussion

The present study revealed that the overall time from onset of symptoms to appendectomy was significantly longer in patients with perforated appendicitis versus patients with simple appendicitis (44.4 vs. 33.9 h;  $P < 0.001$ ) and in patients with complications than in patients without complications (44.4 vs 36.0 h;  $P = 0.03$ ). When the duration of symptoms was divided into the symptomatic period before admission and the hospitalization period, the symptomatic



**Fig. 1** Relationship between perforation and time in terms of the proportion of affected patients in each time period. Likelihood ratio tests revealed trends toward an increase in perforation rate according to symptomatic time (a;  $P < 0.001$ ) and overall time (c;  $P < 0.001$ ) but not hospitalization time (b;  $P = 0.41$ )

**Table 3** Logistic regression analysis of predictors associated with perforation

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
Age >55 years	1.772 (1.246–2.520)	0.001	1.242 (0.824–1.870)	0.30
Male	0.964 (0.782–1.189)	0.74	1.005 (0.808–1.250)	0.98
ASA ≥ 2	1.689 (1.281–2.227)	<0.001	1.348 (0.979–1.857)	0.07
BT > 38 °C	2.488 (1.656–3.738)	<0.001	1.828 (1.192–2.804)	0.006
WBC > 1.3 × 10 <sup>3</sup> /μl	1.282 (1.041–1.580)	0.02	1.295 (1.043–1.607)	0.02
Neutrophil ratio >80%	1.606 (1.274–2.024)	<0.001	1.674 (1.311–2.137)	<0.001
Symptomatic time ≤12 h	Reference		Reference	
12–24 h	1.255 (0.957–1.644)	0.10	1.296 (0.984–1.709)	0.07
24–48 h	2.674 (2.000–3.575)	<0.001	2.670 (1.980–3.600)	<0.001
>48 h	2.410 (1.756–3.307)	<0.001	2.462 (1.769–3.426)	<0.001
Hospitalization time ≤8 h	Reference		Reference	
8–16 h	1.099 (0.873 – 1.385)	0.422	1.180 (0.928–1.501)	0.18
>16 h	1.226 (0.891 –1.688)	0.211	1.228 (0.881–1.710)	0.23

ASA American Society of Anesthesiologists, BT body temperature, WBC white blood cell count, h hour

**Table 4** Characteristics of patients according to the presence of complication

Characteristics	Non-complication ( <i>n</i> = 1577)	Complication ( <i>n</i> = 176)	<i>P</i>
Age	31.4 (16.7)	29.5 (15.4)	0.15
Male	881 (55.9)	100 (56.8)	0.82
ASA ≥ 2	233 (14.8)	25 (14.2)	0.83
BT (°C)	36.9 (0.6)	36.9 (0.6)	0.87
WBC (× 10 <sup>3</sup> /μl)	12.6 (4.4)	12.7 (4.6)	0.70
Neutrophil ratio (%)	76.3 (12.5)	77.4 (11.4)	0.27
Operation time (min)	46.5 (21.3)	51.3 (28.3)	0.03
Time to flatus (days)	1.1 (0.8)	1.2 (0.8)	0.08
Time to soft diet (days)	1.5 (0.9)	1.7 (1.4)	0.04
Duration of postoperative hospital stay (days)	3.0 (1.5)	3.8 (2.9)	0.001
Perforation	442 (28.0)	53 (30.1)	0.56

Data presented are numbers of patients (percentage) or means (standard deviations)

ASA American Society of Anesthesiologists, BT body temperature WBC white blood cell count

time was significantly associated with the rates of perforation and complications. The neutrophil ratio was also significantly and independently associated with perforation and complications in the multivariable analyses.

Acute appendicitis was initially described in terms of its natural history and progression in 1886 by Reginald H. Fitz [15]. Since then, it has become widely accepted that untreated appendicitis progresses to perforation, which is associated with significant increases in morbidity, mortality, hospital stay, and resource usage [2–4, 16, 17].

A high overnight caseload might cause excessive fatigue and sleep deprivation among hospital and surgical staff,

and several studies have reported negative effects of sleep deprivation on cognitive abilities [10–12]. Accordingly, sleep deprivation could adversely affect surgical performance and patient safety. And some surgical procedures, such as appendectomy, could be delayed on a semi-elective manner to reduce the overnight caseload and avoid the negative effects of sleep deprivation. Recent studies in pediatric patients suggest that hydration and administration of antibiotics allowed surgeons to delay surgery without detrimental effects on patient outcome [5, 18]. Furthermore, randomized controlled trials have suggested that

**Table 5** Relationship between complications and time intervals

	Non-complication	Complication	<i>P</i>
Symptomatic time	26.7 (38.0)	35.9 (49.8)	0.018
Hospitalization time	8.3 (5.1)	9.0 (5.0)	0.43
Overall time	36.0 (38.3)	44.4 (49.6)	0.03

Data are presented as mean  $\pm$  standard deviation

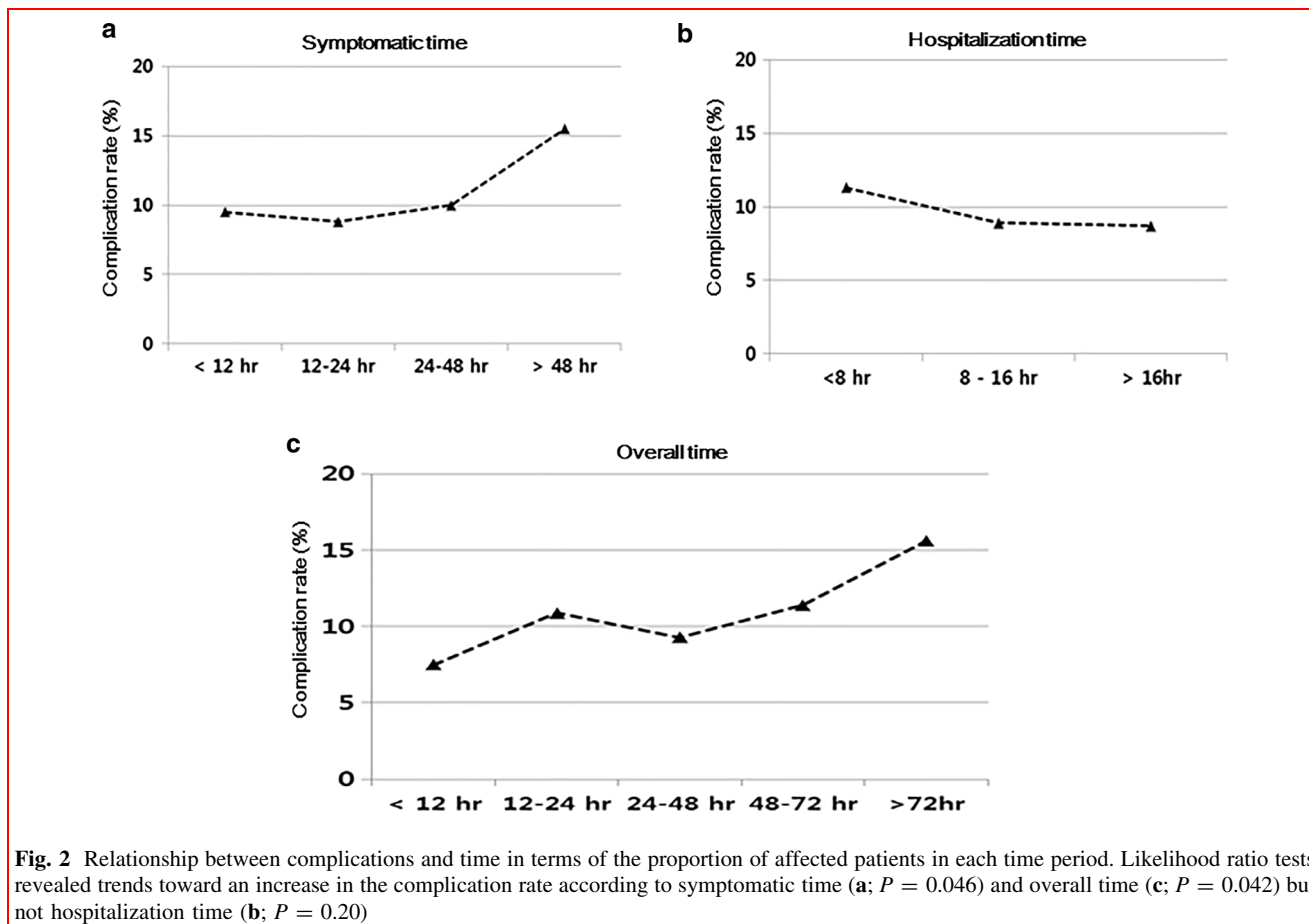
Symptomatic time was defined as the time from onset of first symptom to admission. Hospitalization time was defined as the time from admission to operation. Overall time was defined as the time from onset of first symptom to operation, which was calculated by adding the patient time and hospitalization time

antibiotic therapy without surgery is a safe treatment option for acute appendicitis [19, 20].

Several recent studies have also investigated the relationship between hospital delay (i.e., time from admission to surgery) and postoperative outcomes [7, 14, 21–25]. Because the times of admission and surgery were accurately recorded in our study, the time from admission to surgery could be quantified. Several studies found no association between delayed appendectomy and

postoperative complications [7, 21–23]. Ingrahm et al. [7] divided patients into three groups according to hospital delay ( $\leq 6$  vs. 6–12 vs.  $>12$  h) and reported that delayed appendectomy did not affect the rate of overall morbidity (5.5 vs. 5.4 vs. 6.1%;  $P = 0.33$ ) or the rate of serious morbidity/mortality (3.0 vs 3.6 vs 3.0%;  $P = 0.17$ ). A meta-analysis of 12 studies revealed that delaying surgery by  $\geq 12$  h after admission did not increase the risk of complex appendicitis (odds ratio 1.07;  $P = 0.41$ ) [24]. Meanwhile, Teixeira et al. [14] reported that although delayed appendectomy did not increase the risk of perforation, it did increase the risk of surgical site infection. Moreover, Busch et al. [25] reported that an in-hospital delay of  $>12$  h was an independent risk factor for perforation.

We also divided the duration of symptoms into the symptomatic pre-hospitalization period and the hospitalization period to evaluate its association with perforation and complications of appendicitis. However, there is controversy regarding the associations between the symptomatic period and hospitalization period with complications. Eldar et al. [26] reported that delayed admission was associated with increased rates of infectious



**Table 6** Logistic regression analysis of predictors associated with complication

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
Age >55 years	0.654 (0.337–1.268)	0.21	0.527 (0.255–1.091)	0.08
Male	1.038 (0.758–1.421)	0.82	1.067 (0.774–1.471)	0.69
ASA ≥ 2	0.953 (0.610–1.488)	0.83	1.024 (0.626–1.675)	0.92
BT > 38 °C	1.365 (0.746–2.499)	0.31	1.085 (0.575–2.049)	0.80
WBC > 1.3 × 10 <sup>3</sup> /μl	1.089 (0.797–1.487)	0.59	1.119 (0.814–1.537)	0.49
Neutrophil ratio >80%	2.124 (1.536–2.938)	<0.001	2.326 (1.658–3.262)	<0.001
Perforation	1.106 (0.787–1.554)	0.563	0.958 (0.669–1.373)	0.82
Symptomatic time ≤12 h	Reference		Reference	
12–24 h	0.871 (0.580–1.308)	0.51	0.891 (0.590–1.346)	0.58
24–48 h	1.024 (0.648–1.618)	0.92	1.057 (0.659–1.697)	0.82
>48 h	1.727 (1.120–2.662)	0.013	1.997 (1.263–3.156)	0.003
Hospitalization time ≤8 h	Reference		Reference	
8–16 h	0.784 (0.551–1.115)	0.18	0.789 (0.551–1.129)	0.20
>16 h	0.677 (0.397–1.154)	0.15	0.686 (0.399–1.179)	0.17

ASA American Society of Anesthesiologists, BT body temperature, WBC white blood cell count, h hour

complications ( $P < 0.001$ ) and advanced appendicitis ( $P < 0.001$ ), but the hospital delay (termed ‘physician delay’ in that study) was not associated with the stage of disease. Maroju et al. [27] reported that postoperative complications for acute appendicitis are associated with a delay in treatment, which was not due to in-hospital delay (with vs. without complications: 8.6 vs 8.3 h,  $P =$  not significant) but rather patient delay (63.3 vs 24.3 h,  $P < 0.001$ ). Ditillo et al. reported that longer times from symptom onset to admission and from admission to surgery were associated with increased severity of acute appendicitis. They also reported a positive correlation between the patient-to-hospital interval ratio with the severity of complications, which suggests that delayed admission is strongly associated with advanced pathology of appendicitis [13]. In the present study, the increased rates of perforation ( $P < 0.001$ ) and complications ( $P = 0.046$ ) were primarily related to a longer symptomatic period before admission, rather than with delayed surgery after admission.

Previous studies suggested that a higher proportion of elderly patients than younger patients present with perforated appendicitis [21, 25, 28]. One of the possible explanations might be that the incidence of perforating appendicitis was stable across age groups, but the incidence of non-perforating cases decreased sharply with increasing age. Therefore, the high proportion of perforation among the elderly patients may be due to the decreased incidence of non-perforated appendicitis in the elderly [29, 30].

Another possible explanation is that elderly patients sometimes present with ambiguous features, and the fewer elderly patients report right lower quadrant pain [31]. These atypical symptoms may make it longer to reach a diagnosis because other diseases such as acute cholecystitis and urinary stone must be considered in the differential diagnosis. Another explanation relates to the physiologic changes in elderly patients, including decreased immunity [32]. Therefore, it takes longer to prepare preoperative management and fully evaluate the patient’s cardiac, pulmonary, and renal functions. In the present study, multivariable analysis showed that age was not associated with perforation ( $P = 0.30$ ) or complications ( $P = 0.08$ ). This discrepancy could be explained by the difference in inclusion criteria. For example, some studies defined elderly as >55 years of age, while other studies, including our study, defined elderly as >65 years of age.

Several studies have analyzed the relationships between serologic markers and the severity of appendicitis [33, 34]. Qi et al. [33] reported that the neutrophil ratio and C-reactive protein (CRP) were risk factors for gangrenous appendicitis based on logistic regression analysis. Xharra et al. [34] analyzed the relationships with a variety of biomarkers, including CRP, WBC count, and neutrophil ratio, and reported that these markers increased in correlation with the severity of inflammation. In the present study, although the WBC count level were only associated with perforation, the neutrophil ratio was associated with both outcomes.

Perforated appendicitis generally increases the risk of postoperative complications [35]. However, in the present study, perforation was not significantly associated with complications ( $P = 0.82$ ). There might be several explanations. First, the present study only included the patients who underwent laparoscopy surgery. This minimized the wound size, and we used an endoscopic bag to extract the appendix, limiting contact between infected tissue and the wound. Accordingly, the rate of complications is unlikely to increase despite perforated appendicitis. Another explanation might involve differences in the definitions of perforation and postoperative complications between studies. The perforation rate of 28.2% in the present study is higher than the previously reported rates of 16.6–23.7% [6, 7, 13, 20, 23, 28]. In earlier studies, the rate of advanced appendicitis (gangrenous + perforated appendicitis) ranged from 32 to 44.1% [22, 26], which are much higher than the rate reported in our study. Nevertheless, the overall complication rate of 10.0% in the present study is similar to the rates of complications of 5.5–14.0% in earlier studies [7, 26, 27, 36]. In terms of complication type, the rate of infectious complications was 8.6% in our study, which is higher than the previously reported rates of 3.2–7.9% [13, 22, 23, 25]. Therefore, the different conclusion that perforation is not associated with complications in our study could be due to the differences in the rates of perforation and complications between our study and prior studies.

There are several limitations to the present study. First, this study was performed retrospectively, introducing the possibility of selection and recall bias. However, because the data collector retrieved these data from the medical records without knowledge of the primary endpoint, the results were less likely to be affected by data collection bias. Second, although the present study was conducted at two hospitals, the number of patients was still too small to reach a definitive conclusion. Third, because both of the participating hospitals were secondary, university-affiliated hospitals, a large number of patients were transferred to our hospitals from other hospitals. Unfortunately, we did not have complete information regarding the patient's arrival time at the prior hospital or the types and doses of antibiotics. Although Similis et al. [37] reported the feasibility of using antibiotics to treat acute appendicitis, perforation and postoperative complications are influenced by various factors, such as age, gender, and pre-hospital time. Therefore, inaccurate information could skew the results in terms of the association between delayed surgery and the risks of perforation and complications.

The present study showed that untreated acute appendicitis frequently progresses to perforated appendicitis with an increased risk of complications. The time from symptom onset to surgery was associated with the risk of perforation

and complications, and this association was due to the symptomatic period before admission, not the time between admission and surgery. In other words, administration of intravenous antibiotics and fluid hydration followed by elective appendectomy the day after admission did not adversely affect the patients' outcomes. However, because the severity of acute appendicitis progresses over time, surgeons should avoid excessively delaying surgery. Instead, surgery should be performed in a semi-elective manner.

**Acknowledgements** This research was supported by Hallym University Research Fund 2016(HURF-2016-52).

#### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

## References

- Owings MF, Kozak LJ (1998) Ambulatory and inpatient procedures in the United States, 1996. *Vital Health Stat* 139:1–119
- Scher KS, Coil JA Jr (1980) Appendicitis: factors that influence the frequency of perforation. *South Med J* 73:1561–1563
- Karp MP, Caldarola VA, Cooney DR et al (1986) The avoidable excesses in the management of perforated appendicitis in children. *J Pediatr Surg* 21:506–510
- David IB, Buck JR, Filler RM (1982) Rational use of antibiotics for perforated appendicitis in childhood. *J Pediatr Surg* 17:494–500
- Yardeni D, Hirschl RB, Drongowski RA et al (2004) Delayed versus immediate surgery in acute appendicitis: do we need to operate during the night? *J Pediatr Surg* 39:464–469
- Kearney D, Cahill RA, O'Brien E et al (2008) Influence of delays on perforation risk in adults with acute appendicitis. *Dis Colon Rectum* 51:1823–1827
- Ingraham AM, Cohen ME, Bilimoria KY et al (2010) Effect of delay to operation on outcomes in adults with acute appendicitis. *Arch Surg* 145:886–892
- Bufo AJ, Shah RS, Li MH et al (1998) Interval appendectomy for perforated appendicitis in children. *J Laparoendosc Adv Surg Tech A* 8:209–214
- Eriksson S, Granstrom L (1995) Randomized controlled trial of appendectomy versus antibiotic therapy for acute appendicitis. *Br J Surg* 82:166–169
- Taffinder NJ, McManus IC, Gul Y et al (1998) Effect of sleep deprivation on surgeons' dexterity on laparoscopy simulator. *Lancet* 352:1191
- Steinbrook R (2002) The debate over residents' work hours. *N Engl J Med* 347:1296–1302
- Wesnes KA, Walker MB, Walker LG et al (1997) Cognitive performance and mood after a weekend on call in a surgical unit. *Br J Surg* 84:493–495
- Ditillo MF, Dziura JD, Rabinovici R (2006) Is it safe to delay appendectomy in adults with acute appendicitis? *Ann Surg* 244:656–660
- Teixeira PG, Sivrikoz E, Inaba K et al (2012) Appendectomy timing: waiting until the next morning increases the risk of surgical site infections. *Ann Surg* 256:538–543



15. Fitz RH (1886) Perforating inflammation of the vermiform appendix, with special reference to its early diagnosis and treatment. *Trans Assoc Am Physicians* 1:107–144
16. Blomqvist PG, Andersson RE, Granath F et al (2001) Mortality after appendectomy in Sweden, 1987–1996. *Ann Surg* 233:455–460
17. Berry J Jr, Malt RA (1984) Appendicitis near its centenary. *Ann Surg* 200:567–575
18. Surana R, Quinn F, Puri P (1993) Is it necessary to perform appendectomy in the middle of the night in children? *BMJ* 306:1168
19. Styurd J, Eriksson S, Nilsson I et al (2006) Appendectomy versus antibiotic treatment in acute appendicitis. a prospective multicenter randomized controlled trial. *World J Surg* 30:1033–1037. doi:[10.1007/s00268-005-0304-6](https://doi.org/10.1007/s00268-005-0304-6)
20. Hansson J, Korner U, Khorram-Manesh A et al (2009) Randomized clinical trial of antibiotic therapy versus appendectomy as primary treatment of acute appendicitis in unselected patients. *Br J Surg* 96:473–481
21. Chen CC, Ting CT, Tsai MJ et al (2015) Appendectomy timing: will delayed surgery increase the complications? *J Chin Med Assoc* 78:395–399
22. Abou-Nukta F, Bakhos C, Arroyo K et al (2006) Effects of delaying appendectomy for acute appendicitis for 12 to 24 hours. *Arch Surg* 141:504–506
23. Clyde C, Bax T, Merg A et al (2008) Timing of intervention does not affect outcome in acute appendicitis in a large community practice. *Am J Surg* 195:590–592
24. Bhangu A (2014) Safety of short, in-hospital delays before surgery for acute appendicitis: multicentre cohort study, systematic review, and meta-analysis. *Ann Surg* 259:894–903
25. Busch M, Gutzwiller FS, Aellig S et al (2011) In-hospital delay increases the risk of perforation in adults with appendicitis. *World J Surg* 35:1626–1633
26. Eldar S, Nash E, Sabo E et al (1997) Delay of surgery in acute appendicitis. *Am J Surg* 173:194–198
27. Maroju NK, Robinson Smile S, Sistla SC et al (2004) Delay in surgery for acute appendicitis. *ANZ J Surg* 74:773–776
28. Augustin T, Cagir B, Vandermeer TJ (2011) Characteristics of perforated appendicitis: effect of delay is confounded by age and gender. *J Gastrointest Surg* 15:1223–1231
29. Andersson R, Hugander A, Thulin A et al (1994) Indications for operation in suspected appendicitis and incidence of perforation. *BMJ* 308:107–110
30. Luckmann R (1989) Incidence and case fatality rates for acute appendicitis in California. A population-based study of the effects of age. *Am J Epidemiol* 129:905–918
31. Burns RP, Cochran JL, Russell WL et al (1985) Appendicitis in mature patients. *Ann Surg* 201:695–704
32. Paajanen H, Kettunen J, Kostianen S (1994) Emergency appendectomies in patients over 80 years. *Am Surg* 60:950–953
33. Qi FQ, Zhang B (2015) Clinical significance of C-reactive protein levels in the determination of pathological type of acute appendicitis. *Int J Clin Exp Med* 8:13887–13890
34. Xharra S, Gashi-Luci L, Xharra K et al (2012) Correlation of serum C-reactive protein, white blood count and neutrophil percentage with histopathology findings in acute appendicitis. *World J Emerg Surg* 7:27
35. Markides G, Subar D, Riyad K (2010) Laparoscopic versus open appendectomy in adults with complicated appendicitis: systematic review and meta-analysis. *World J Surg* 34:2026–2040. doi:[10.1007/s00268-010-0669-z](https://doi.org/10.1007/s00268-010-0669-z)
36. Giraudo G, Baracchi F, Pellegrino L et al (2013) Prompt or delayed appendectomy? Influence of timing of surgery for acute appendicitis. *Surg Today* 43:392–396
37. Simillis C, Symeonides P, Shorthouse AJ et al (2010) A meta-analysis comparing conservative treatment versus acute appendectomy for complicated appendicitis (abscess or phlegmon). *Surgery* 147:818–829