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Relationship between the Hospital Visit-to-Operation Time Interval and the Risk of Appendiceal Perforation and Clinical Outcomes

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Purpose: The aim of this study was to investigate the relationship between the elapsed time from hospital visit to operation and perforation risk and surgical site infection (SSI).

Methods: We conducted a single-center, retrospective cohort study using 986 patients who underwent appendectomy between Jan. 2009, and Dec. 2013. We divided hospital visit-to-operation time into multiple sessions and analyzed the statistical differences in univariate and multivariate analysis.

Results: Nine-hundred and ninety-six patients were admitted due to appendicitis and 986 (98%) patients underwent an appendectomy. Perforation occurred in 13.2% (n=130) of these patients. Patients with greater than 12 hours of elapsed time between their visit to hospital and surgery demonstrated a higher perforation rate than those who underwent surgery within 12 hours from their visit to the hospital. Upon logistic regression analysis, appendectomy timing was a predictors of appendiceal perforation (adjusted odds ratio, 1.04; 95% confidence interval, 1.00~1.07; p=0.04). The SSI rate of the patients who underwent appendectomy within 12hrs was lower than those who underwent surgery more after than 12 hrs, but hospital visit-to-operation time was not a statistically significant predicting factor of SSI (adjusted odds ratio, 0.99; 95% confidence interval, 0.93~1.05; p=0.796).

Conclusion: A delay more than 12 hrs between the visit to a hospital and surgery was significantly associated with an increased risk of perforation of the appendix. However, it was not associated with an increase in the risk of SSI. Prompt surgical treatment is needed to decrease the risk of perforation.

Keywords: Appendicitis, Perforation, Appendectomy timing, SSI

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INTRODUCTION

Acute appendicitis (AA), which has a high lifetime incidence in general population, is one of the most common diseases that require emergent surgical treatment. Without immediate intervention, appendicitis can progress to appendiceal perforation with intraperitoneal contamination, which can cause complications such as peritonitis or abscess formation and may lead to prolonged hospital management. Hence, to prevent potentially significant morbidities, complete surgical excision of the inflamed appendix before rupture is important.[1-7]

Many recent studies have emphasized the importance of preventing appendiceal perforation. In particular, the time interval between hospital visit and surgery is one of the factors that can be objectively quantified and has been analyzed in many prior articles. However, the acceptable in-hospital time

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before surgical treatment that can minimize complication rates remains controversial.[8-27]

Many surgeons have stated that appendectomy should be performed without delay, irrespective of the time of day. They emphasize that longer hospital visit-to-operation time increases perforation risk.[8-13] However, several previously published retrospective series have reported conflicting relationships between the timing of surgery and the risk of morbidities. These studies reported that appendectomy timing was not associated with the risk of perforation. In addition, a common limitation of previous research was obscurity regarding the timing of appendiceal perforation, especially 'before arrival to hospital' or 'while waiting for surgery in hospital.[14-27]

The aim of this study was to investigate the relationship between elapsed time from hospital visit to operation and perforation risk and surgical site infection (SSI) in patients that were radiologically diagnosed with appendicitis with no evidence of perforation at a single medical center.

MATERIALS AND METHODS

Patients and data collection

A retrospective medical chart review of all patients who underwent an appendectomy from January 2009 to December 2013 at a single center (OO University Hospital in Seoul, Korea) was conducted. Data on clinical condition, surgery, morbidity, and timing of surgery were collected by reviewing the medical records. During this period, 996 patients visited the hospital due to appendicitis and routine radiological investigations, such as ultrasonography or computed tomography, were performed during the diagnostic process. Among them, 988 patients with no radiological evidence of perforation underwent appendectomy. Six patients were excluded because they did not undergo surgery after their diagnosis, and two patients were excluded since their pathological reports showed that they were misdiagnosed.

Variables and outcome

Collected patient characteristics included age, sex, white blood cell (WBC) count, American Society of Analgesia (ASA) score, time of admission and operation, operation method (laparoscopy vs open conversion), and the time interval between the hospital visit and operation. The hospital visit-to-operation time delay was defined as an interval from the time that a patient arrived to the hospital to the time that the operation started. We divided hospital visit-to-operation time into multiple session; 6 hrs, 6~12 hrs, 12~24 hrs, over 24 hrs, and analyzed the statistical difference. To elucidate the risk factors of appendiceal perforation and SSI, we analyzed multivariate analysis. Perforated appendix was diagnosed primarily intraoperatively and confirmed on histopathological examination. The diagnostic criteria for perforated appendix included followings: visible perforation, spilling of feces.

Statistical analyses

Continuous data are described as the mean (standard deviation, S.D.) and median (range), with analysis done by Student's t-test. The significance of differences between groups of cat-

Table 1. Characteristics of patients (N = 986)

Variable	Total (N = 986)
Age (years), mean ± SD	34.2 ± 18.6
Age over 50 years old, n (%)	225 (22.8)
Sex	
Male, n (%)	527 (53.4)
ASA class	
1	564 (57.2)
2	399 (40.5)
≥ 3	23 (2.3)
Length of hospital stay (days), mean ± SD	4.3 ± 2.8
WBC count (on admission)	12,885 ± 5,737
Night hospital visit, n (%)	172 (17.4)
Night admission, n (%)	217 (22.0)
Night operation, n (%)	37 (3.8)
Operation time (min)	58.0 ± 27.4
Visit-to-operation (hr), Mean ± SD	9.4 ± 5.8
Visit-to-operation, n (%)	
Within 6 hr	353 (35.8)
6 ~ 12 hr	358 (36.31)
12 ~ 24 hr	258 (26.17)
Over 24 hr	17 (1.72)
Visit-to-operation, n (%)	
Within 12 hr	711 (72.11)
Over 12 hr	275 (27.89)
Perforation, n (%)	130 (13.2)
Laparoscopic appendectomy, n (%)	978 (99.2)
Open conversion, n (%)	7 (0.7)
Appendectomy	960 (97.4)
Drain insertion	261 (26.5)

egorical variables was tested using the χ^2 test. The significance level was set at $p<0.05$. Then, statistically significant factors were selected and a logistic regression model was developed.

RESULTS

Patient characteristics

Over 5 years, 996 patients with appendicitis visited OO University Hospital, and 986 (98%) patients underwent appendectomy for acute appendicitis. The mean age was 34.2±18.6 years, and the proportion of patients over the age of 50 was 22.3% (n=225). Of the 986 patients, 53% (n=527) were male and the mean WBC count was 12,885±5,737. Most patients were classified as American Society of Anesthesiologist (ASA) class 1 or 2 (97.5%). The mean operation time was 58.0±27.4 min, and the average time delay from hospital visit to operation was 9.4±5.8 hour. On pathology, 13.2% (n=130) of patients had perforated appendix. 99.2% of patients underwent laparoscopic appendectomy, and open conversion was done in 0.7% of cases (Table 1).

Comparison between the 'non-perforation' and 'perforation' groups

The mean age of patients was 33.1±18 and, 41.8±20.7 years

Table 2. Comparison of characteristics between non-perforated and perforated groups

Variable	Non-perforation (N=856)	Perforation (N=130)	*p* value
Age (years), mean±SD	33.1±18.0	41.8±20.7	<0.0001
Age over 50 yrs old, n (%)	175 (20.4)	50 (38.5)	<0.0001
Sex			
Male, n (%)	457 (53.4)	70 (53.9)	0.9222
ASA class			
1	511 (59.7)	53 (40.8)	<0.0001
2	335 (39.1)	64 (49.2)	0.0289
≥3	10 (1.2)	13 (10)	<0.0001
Length of hospital stay (day), mean±SD	4.0±2.4	6.3±4.4	<0.0001
WBC count (on admission)	12,909±5,865	12,726±4,824	0.6952
Night hospital visit, n (%)	143 (16.7)	29 (22.3)	0.1168
Night admission, n (%)	185 (21.6)	32 (24.6)	0.4412
Night operation, n (%)	33 (3.9)	4 (3.1)	0.6635
Operation time (min)	54.8±24.7	79.1±34	<0.0001
Visit-to-operation (hr), Mean±SD	9.2±5.6	11±6.3	0.001
Visit-to-operation, n (%)			
Within 6 hr	322 (37.62)	31 (23.85)	0.0023
6∼12 hr	308 (35.98)	50 (38.46)	0.5837
12∼24 hr	212 (24.77)	46 (35.38)	0.0103
Over 24 hr	14 (1.64)	3 (2.31)	0.4814
Visit-to-operation, n (%)			
Within 12 hr	630 (73.60)	81 (62.31)	0.0075
Over 12 hr	226 (26.40)	49 (37.69)	
Laparoscopic appendectomy, n (%)	853 (99.7)	125 (96.2)	0.0015
Open conversion, n (%)	2 (0.2)	5 (3.9)	<0.0001
Drain insertion	174 (20.3)	87 (66.9)	<0.0001

Table 3. Complications overall and comparison between 'non-perforated' and 'perforated' groups

Outcomes	Total (N=986)	Non-perforation (N=856)	Perforation (N=130)	OR (95% CI)	*p* value
Mortality	0	0	0	-	-
SSI, n (%)	43 (4.36)	33 (3.86)	10 (7.69)	2.08 (1 ~ 4.33)	0.050
Wound infection, n (%)	30 (3.04)	24 (2.8)	6 (4.62)	1.68 (0.67 ~ 4.19)	0.268
Intra-abdominal abscess, n (%)	13 (1.32)	9 (1.05)	4 (3.08)	2.99 (0.91 ~ 9.85)	0.072
Stump appendicitis, n (%)	2 (0.2)	2 (0.23)	0 (0)	<0.001 (<0.001 ~ >999.9)	0.988
Ileus, n (%)	8 (0.81)	3 (0.35)	5 (3.85)	11.37 (2.69 ~ 48.17)	0.001
Intra-abdominal fluid collection, n (%)	8 (0.81)	5 (0.58)	3 (2.31)	4.03 (0.95 ~ 17.05)	0.059
Intervention, n (%)	6 (0.61)	4 (0.47)	2 (1.54)	3.33 (0.6 ~ 18.36)	0.168
Readmission, n (%)	16 (1.62)	12 (1.4)	4 (3.08)	2.23 (0.71 ~ 7.03)	0.170
Reoperation, n (%)	3 (0.3)	1 (0.12)	2 (1.54)	13.36 (1.2 ~ 148.39)	0.035
Hydronephrosis, n (%)	1 (0.1)	1 (0.12)	0 (0)	<0.001 (<0.001 ~ >999.9)	0.987
Sepsis, n (%)	1 (0.1)	0 (0)	1 (0.77)	>999. 9 (<0.001 ~ >999.9)	0.980

Table 4. Predictors of perforated appendicitis after logistic regression

Factor	Adjusted OR (95% CI)	*p* value
Age	1 (0.99 ~ 1.02)	0.592
Male sex	1.06 (0.69 ~ 1.63)	0.795
ASAclass 3	3.77 (1.14 ~ 12.43)	0.029
Operation time (min)	1.01 (1.01 ~ 1.02)	0.000
Visit-to-operation (each 1-h increase)	1.04 (1 ~ 1.07)	0.043
Visit-to-operation time		
Within 12 hr	0.59 (0.40 ~ 0.87)	0.008
Over 12 hr		

(p<0.0001) in non-perforation and perforation groups, respectively. The proportion of patients older than 50 years was 20.4% and, 38.4% (p<0.0001) and the percentage of patients who were classified as ASA class 2 or 3 was 40.3% and, 59.2% (p<0.0001), respectively, in each group. The mean hospitalization period in each group was 4±2.4 and, 6.3±4.4 days, respectively (p<0.0001).

The mean operation time was 54.8±24.7 minutes and 79.1 ±34.0 minutes, respectively. Patients who underwent surgery more than 12 hours after hospital visit included 26.4% of the non-perforation group patients and 37.7% of the perforation group patients (p=0.0075). Also, the mean hospital visit-to-operation time was 9.2±5.6, 11±6.3 hours, respectively in non-perforation group and perforation group (p<0.0001). Open conversion was conducted in 0.2% of non-perforation group patients and in 3.9% of perforation group patients (p<0.0001). The drain insertion rate was 20.3% in non-perforation group and 67% in perforation group (p<0.0001) (Table 2). The SSI rate was 3.86% in non-perforation group, 7.69% in perforation group, respectively. Ileus rate was 0.35% in non-perforation group, 3.85% in perforation group, respectively. Other complications such as intra-abdominal abscess, intra-abdominal fluid collection, intervention, readmission, reoperation, hydronephrosis, or sepsis were not significantly different in both groups (Table 3).

Predictors of perforated appendicitis after logistic regression analysis

Using logistic regression analysis, several factors were identified as predictors of perforated appendicitis: the operation time [odds ratio (OR) (95% confidence interval) (95% CI), 1.01 (1.01~1.02); p=0.001] and, hospital visit-to-operation time [OR (95% CI), 1.04 (1~1.07); p=0.043] were identified as predictors, and every hour increase between the time from Emergency Department triage and the time of appendectomy was independently associated with an increase in odds of perforation by 4% (p=0.04; adjusted OR, 1.04; 95% CI, 1.00~1.07; Table 4).

Characteristics of the patients 'with' or 'without' SSI

When we compared between the patients with SSI and without SSI, there were no significant differences in age, sex, ASA class, or WBC count between two groups. On the other hand, a longer operation time was significantly associated with the occurrence of SSI (74±30.1 minutes vs. 57.3±

Table 5. Characteristics of the patients 'with' or 'without' SSI

Variable	No SSI (N=943)	SSI (N=43)	*p* value
Age (years), mean±SD	34.1±18.5	36.21±20.4	0.4771
Age over 50 yrs old, n (%)	212 (22.5)	13 (30.2)	0.2362
Sex			
Male, n (%)	500 (53.0)	27 (62.8)	0.2092
ASA class			
1	545 (57.8)	19 (44.2)	0.0778
2	376 (39.9)	23 (53.5)	0.0753
≥3	22 (2.3)	1 (2.3)	0.9975
Length of hospital stay (days), mean±SD	4.3±2.8	5±4.2	<0.0001
WBC count (on admission)	12,918±5,808	12,169±3,821	0.2271
Night hospital visit, n (%)	160 (17)	12 (28)	0.0645
Night admission, n (%)	206 (21.9)	11 (25.6)	0.563
Night operation, n (%)	36 (3.8)	1 (2.3)	0.6146
Operation time (min)	57.3±27	74±30.1	<0.0001
Visit-to-operation time (hr), mean±SD	9.5±5.8	9.2±5.1	0.7642
Visit-to-operation time, n (%)			
Within 6 hr	336 (35.63)	17 (39.53)	0.6015
6～12 hr	345 (36.59)	13 (30.23)	0.3969
12～24 hr	245 (25.98)	13 (30.23)	0.5351
Over 12 hr	17 (1.8)	0 (0)	0.3745
Laparoscopic appendectomy, n (%)	936 (99.3)	42 (97.7)	0.2577
Open conversion, n (%)	6 (0.6)	1 (2.3)	0.1969
Drain insertion	244 (25.9)	17 (39.5)	0.0471
Perforation	120 (12.7)	10 (23.3)	0.0459

Table 6. Predicting factors of SSI development after logistic regression analysis

Factor	Adjusted OR (95% CI)	*p* value
Age	1.00 (0.98～1.02)	0.862
Male sex	1.47 (0.77～2.80)	0.229
Operation time (min)	1.01 (1.00～1.02)	0.004
Visit-to-operation time (each 1-hr increase)	0.99 (0.93～1.05)	0.796
Drain insertion	1.14 (0.46～2.31)	0.755
Perforation	1.43 (0.62～3.27)	0.403

27, in SSI and non-SSI groups, respectively; $p<0.0001$). Also, the occurrence of SSI was increased significantly with drain insertion (39.5% vs. 25.9%, respectively; $p=0.0471$). The presence of perforation higher in SSI group as two-fold regardless of the timing of appendectomy (23.3% vs. 12.7%, respectively; $p=0.0459$). Mean hospital visit-to-operation time in SSI group was lower than visit-to-operation time in No SSI group (9.2 vs. 9.5%, respectively. $p=0.7642$), but this difference was not statistically significant (Table 5).

Predicting factors of the SSI after logistic regression analysis

After logistic regression analysis, operation time was the only factor that was found to significantly increase SSI risk with every minute [OR (95% CI), 1.01 (1.00~1.02); $p=0.004$],

after adjusting for age, sex, hospital visit to operation time, drain insertion and presence of appendiceal perforation (Table 6).

In stratification analysis, there was no significant difference in the SSI rate between the hospital visit-to-operation and SSI.

DISCUSSION

Acute Appendicitis (AA) is one of the most common disease in emergency clinics.[1-7] In this study, we analyzed appendectomy timing as a risk factor of complications of appendicitis, especially perforation and SSI. We demonstrated that a delay of more than 12 hours before appendectomy was significantly associated with an increased risk of perforation of the appendix.

Patients whose appendix perforated while waiting for appendectomy in hospital had much greater morbidity rates. Perforation was significantly associated with a higher re-intervention rate, conversion rate, and longer length of hospital stay (LOS). Specifically, some authors have previously hypothesized that increasing time delay before surgical intervention concomitantly increases perforation risk. Therefore, many surgeons have stated that appendectomy should be performed without delay.[8-13] Busch et al. found that there was a significantly higher rate of perforation when comparing rates between patients whose appendectomy timing was greater than 12 hours versus those whose timing was less than 12 hours after visit to hospital.[11] Bonadio et al. also concluded that an in-hospital delay of more than 9 hours from Emergency Department visit to the operating room (OR) was associated with an approximately six-fold greater risk for developing appendiceal perforation in children.[12]

However, several recently published retrospective series have reported conflicting relationships between delayed appendectomy and the risk of complications. Eko et al. assessed the effects of time delay to the OR for uncomplicated acute appendicitis and found that timing of surgery did not affect the incidence of perforation when comparing patients who had a time to the OR of less than 18 hours to patients with a greater than 18 hour time delay from the hospital visit.[14] Some studies reported that time delay before appendectomy in children did not increase the rate of histopathologic perforation.[26]

Our data showed that patients with appendiceal perforation required a significantly longer hospitalization period and a greater number of radiographic imaging procedures during hospitalization. One of the interesting findings of this study is the fact that delayed appendectomy was associated with a significant increase in perforation rates, whereas no such negative effect was observed in the rate of SSI.

Univariate analysis showed a significant difference in visit-to-operation time within 12-hrs between perforation group and non-perforation group. This cut-off has been used in several prior studies; thus, we can compare the results of these studies directly.[11] Multivariable analysis also showed statically significant results. This study revealed that in-hospital delays prior to appendectomy are associated with a significantly higher perforation rate. The hospital visit-to-operation delay increased the perforation rate in every hour statistically, especially when the delay was greater than 12 hours.

In addition, we evaluated the relationship between the timing of appendectomy and SSI rates. In some previous articles including studies by Burjonrappa et al. and Teixeira et al., an increased risk of SSI was associated with delayed appendectomy timing.[15,27] However, we could not find any relationship between appendectomy timing and SSI rates.

In conclusion, an increased in-hospital time delay from the Emergency Department to the OR is associated with an increased risk of perforation, especially in patients with a greater than 12-hour delay in hospital visit-to-operation among those patients who presented with radiologically confirmed non-perforated appendicitis preoperatively.

However, this study has limitations that these conclusions are derived from retrospective, single-centered, uncontrolled data. A prospective, multi-centered, randomized controlled study is needed to generalize our results.

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