

*Article***Are preoperative CT findings useful for predicting postoperative intraabdominal abscess in the patients with acute appendicitis?**

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Ethics statement: This retrospective study is for academic communication only and is not for other purposes. This paper does not disclose the personal information of any

patients and informed consent was waved for this retrospective study. The study protocol was approved by the institutional review board and the need for informed consent was waived for this retrospective study. The study does not include any animal experiments.

Abstract

Background: To investigate the preoperative clinical and radiological factors that predict the development of a postoperative intraabdominal abscess (IAA) in patients with acute appendicitis who were treated by laparoscopic appendectomy (LA). **Methods:** Two hundred sixteen patients with pathologically proven acute appendicitis underwent LA between January 2013 and March 2018 in our department. Of these, 147 patients were diagnosed with complicated appendicitis (CA) (CA group), while the other 69 patients were diagnosed with simple appendicitis (SA) (SA group). We compared the perioperative clinical and radiographic factors between the two groups and investigated the predictive factors of postoperative IAA. **Results:** Sixteen patients developed postoperative IAA in the CA group, while no patients did in the SA group. The univariate analysis revealed that time from onset to surgery more than 3 days ($p = 0.011$), the preoperative CT finding of periappendiceal fluid ($p = 0.003$), abscess ($p < 0.001$), and free air ($p < 0.001$), operation time more than 120 minutes ($p = 0.023$) and placement of a drainage tube ($p < 0.001$) were significantly associated with the development of IAA. Multivariate analysis revealed that the preoperative CT finding of free air was independently associated with the development of IAA ($p = 0.007$, odds ratio = 5.427). **Conclusions:** IAA was developed predominantly in the patients with CA. Preoperative CT findings of free air was found to be an independent predictor for the development of

IAA. Surgeons should be meticulous in managing the postoperative course of patients with this finding.

Key words: acute appendicitis, complicated appendicitis, laparoscopic appendectomy, intraabdominal abscess

1. Introduction

Recent meta-analyses revealed the feasibility of laparoscopic appendectomy (LA) for acute appendicitis, even in those with complicated appendicitis (CA) [1,2].

Postoperative intraabdominal abscess (IAA) is one of the most severe complications after appendectomy. A few of the patients who developed IAA required second surgery and/or percutaneous drainage, while some were treated conservatively [3-5]. Therefore, the development of postoperative IAA is a major cause of morbidity, not only for the patients who underwent appendectomy but also for the surgeons. To make a well-considered perioperative strategy associated with preventing or detecting the postoperative development of IAA, the perioperative prediction of risk factors for developing IAA is essential for surgeons.

Previously, some risk factors associated with IAA had been reported [6-8]. However, the number of previous reports that revealed the preoperative computed tomography (CT) findings suggesting development of IAA is limited. The aim of this study is to determine the predictive features of the patients with a high risk for developing IAA after LA, identified on their preoperative CT images.

2. Materials and Methods

2.1. Study population

Two hundred sixty-four patients, preoperatively diagnosed with acute appendicitis, underwent LA between January 2013 and March 2018 in our department. Of these, 38 patients underwent interval appendectomy, eight patients were pathologically diagnosed with appendiceal tumor (two were appendiceal cancer, six were mucinous neoplasm), one patient had a preoperatively percutaneous drainage performed, and one patient did not have a preoperative CT. These 48 patients were all excluded from this retrospective study, and the other 216 patients met the study criteria and were included; 69 patients were classified as having simple appendicitis (SA group; n=69), and 147 patients were classified as having complicated appendicitis (CA group; n=147). In this study, all the included patients had performed a preoperative CT, underwent emergency LA, and acute appendicitis was pathologically proven. We retrospectively reviewed and compared the preoperative clinical and radiographic factors between the groups and investigated the risk factors predicting postoperative IAA in these 216 patients. The study protocol was approved by the institutional review board and the informed consent was waived for this retrospective study.

2.2. *Definition of simple and complicated appendicitis*

Patients with findings of abscess, free air, or small bowel obstruction in the preoperative CT image were classified as having complicated appendicitis. In addition, patients with pathologically proven gangrenous appendicitis or perforated appendicitis were also classified as having CA. All others were classified as having simple appendicitis. In the present study, 131 of the 216 patients were pathologically diagnosed with gangrenous appendicitis.

2.3. *Surgical strategy and surgical procedure*

At our institution, all patients with an acute abdomen that suggested acute appendicitis underwent enhanced CT, unless the patient had a contraindication, such as an allergy to contrast agents or impaired renal function. Patients diagnosed with acute appendicitis were treated surgically or conservatively, according to patient's tolerance and selection. For the patients with generalized peritonitis, we performed emergency operation. We generally intended to complete the operations laparoscopically for all patients who were preoperatively diagnosed with acute appendicitis after 2013.

We used a 10-mm port for the camera (30-degree oblique laparoscope) at the umbilicus incision and two 5-mm ports at the left and middle lower quadrants for

instrumentation. For the patients in whom it was difficult to keep surgical field, another 5-mm port was added at the right lower quadrant. After pneumoperitoneum, dissection around the appendix was performed. The mesoappendix was cut using an ultrasonic dissector (Sonosurg; OLYMPUS, Tokyo, Japan). The root of the appendix was closed doubly by ligation, and the appendix was cut and removed. For the patients in whom it was difficult to ligate the stump of the appendix, mobilization of the ileocecal was done, and mini-laparotomy was added at the umbilicus incision to close the stump. In the all cases with CA, intraabdominal irrigation with saline was performed after closing the stump until the contaminated fluids became clear. The drainage tube was placed on the right paracolic gutter and/or rectovesical pouch at the surgeon's discretion. In seven cases in the SA group and four cases in the CA group, a single incisional laparoscopic appendectomy was performed at the surgeon's discretion [9]. Generally, antibiotics were administered after surgery until fever and inflammatory response had subsided.

Development of postoperative IAA was confirmed by CT image which was performed selectively in the patients with persistent or recurrent fever and/or inflammatory response after surgery.

2.4. Pre- and perioperative findings

Preoperative information included sex, age, history of appendicitis, American Society of Anesthesiologists Physical Status (ASA-PS) classification, WBC level, C-reactive protein (CRP) level, radiographic findings of preoperative CT imaging (appendicolith, fluid around appendix, abscess, free air, small bowel obstruction), time from onset to admission (days), time from CT to surgery (hours), and time from onset to surgery (days). The perioperative findings included operation time, postoperative length of hospital stay, conversion to laparotomy, placement of drainage tube, incidence rate of postoperative complications and readmission. Complications were classified according to the grading system proposed by Dindo et al [10].

2.5. Imaging diagnostic modality and radiographic parameters

Among the 216 patients included in the study, all patients were preoperatively examined by abdominal MDCT in non-enhanced and/or enhanced phases using Light Speed VCT (GE Healthcare, Tokyo, Japan) until January 2017 and SOMATOM Force (Siemens Healthineers AG, Erlangen, Federal republic of Germany) after February 2017. Two experienced reviewers (a gastroenterological surgeon with twelve years of experience and a radiologist with seventeen years of experience.) retrospectively reviewed the radiographic parameters to determine the presence of appendicolith, periappendiceal fluid,

abscess, free air and small bowel obstruction (Fig. 1A-D). Measurements were performed in consensus, and both readers were blinded to the outcome at the time of performing the measurements.

2.6. Statistical analysis of the surgical outcomes and clinical and radiological factors

The clinical and radiographic factors were compared. Each cutoff value was determined according to the median value or a receiver-operating characteristic curve, adjusting to a value easy to use in practice. Pearson's chi-square test was used to assess nominal variables, and continuous data were compared using the Mann-Whitney U test. All statistical analyses were performed using the Software Package for Social Sciences, version 11.5J for Windows 1 software program (SPSS, Chicago, IL, USA). A *p* value of < 0.05 was considered significant.

3. Results

3.1. Comparison of the clinical factors between the patients in the SA group and CA group

A total of 216 patients included 135 males and 81 females. The mean age was 37.1 ± 22.9 (range 5 to 91). Clinical characteristics of the SA and CA groups are shown in Table 1. The mean age of the CA group was significantly higher than that of the SA group ($p = 0.008$). The presence of a history of appendicitis was significantly lower in the CA group ($p < 0.001$). The number of the patients with an ASA-PS classification of 2 or 3 was significantly higher in the CA group ($p < 0.001$). There were no significant differences in the preoperative WBC, while the mean CRP level was significantly higher in the CA group. Regarding preoperative CT findings, appendicolith, periappendiceal fluid, abscess and free air were found significantly more often in the CA group ($p < 0.001$ respectively). The CT finding of small bowel obstruction was also significantly found more often in the CA group ($p < 0.003$). The time from operation to surgery was significantly longer in the CA group ($p < 0.001$).

Perioperative outcomes are shown in Table 2. The operation time was significantly longer in the CA group ($p = 0.005$) and the postoperative length of stay was significantly longer in the CA group ($p < 0.001$). The incidence rate of conversion to laparotomy was

not statistically significant. The number of patients who had drainage tubes placed was significantly higher in the CA group ($p < 0.001$). Regarding postoperative complications, the incidence rate of Grade 2 or more and Grade 3 were significantly higher in the CA group ($p = 0.002$, $p = 0.009$, respectively). Intraabdominal abscess developed in 16 patients (10.8%) of the CA group, while no patients developed it in the SA group ($p = 0.004$). Three of these 16 patients required a second operation, and nine patients required percutaneous drainage, while the other four patients were treated conservatively. The incident rate of superficial infection and paralytic ileus was not significantly different. Readmission associated with the first operation was required for 11 patients in the CA group ($p = 0.019$) within one year after discharge. The reason for readmission included IAA (n = 7), superficial infection (n = 1), strangulated ileus (n = 1), ventral hernia (n = 1), and abdominal pain (n = 1).

3.2. Perioperative prediction of IAA in the whole patients.

Univariate analysis revealed that time from onset to surgery more than 3 days ($p = 0.011$), the preoperative CT finding of periappendiceal fluid ($p = 0.003$), abscess ($p < 0.001$), and free air ($p < 0.001$) were significantly associated with the development of IAA. In addition, operation time more than 120 minutes ($p = 0.023$), placement of a drainage tube (p

<0.001) was significantly associated with the development of IAA (Table 3). Multivariate analysis revealed that the preoperative CT finding of free air was independently associated with the development of IAA ($p = 0.007$, odds ratio = 5.427). Patients with a preoperative CT finding of free air showed a 50.0% sensitivity, 93.0% specificity and 89.8% accuracy for the development of IAA.

4. Discussion

Previously, LA had been reported to imply a higher risk for developing IAA compared to that of conventional open appendectomy [11,12]. On the other hand, recent reports suggest that the risk for IAA is comparable between LA and open appendectomy [1,2,13-16]. These reports suggest that LA is already a treatment of choice for acute appendicitis, including CA. According to a recent meta-analysis, the incident rate of IAA in patients with CA after LA was 8.0% [1]. In the present study, 18 out of 147 patients with CA (12.2%) developed complications of Grade 3 and, notably, 12 of these 18 (66.6%) were derived from IAA. In addition, three patients required a second operation due to IAA. These results suggest that IAA is a major complication after LA.

Several risk factors for developing IAA, such as obesity, leukocytosis, perforated appendicitis, longer operation time and peritoneal irrigation had been suggested previously [6-8]. On the other hand, preoperative CT findings that predict the postoperative development of IAA had not been investigated in detail. Kim et al. investigated the association between preoperative CT findings was and 30-day adverse events. In their study, a presence of extraluminal air was not significantly associated with 30-day adverse event [17]. However, in their study, presence of extraluminal air showed tendency to be found in the patients with postoperative adverse event ($p = 0.059$ in

univariate analysis). In addition, as opposed to our study, they included not only IAA but also peritonitis and small bowel obstruction as adverse event and their study population was limited to the patients with appendiceal inflammatory mass.

Our study also revealed that postoperative IAA is predominantly develop in the patients with CA. Although preoperative CT finding is considered as useful for distinguish CA from SA [18-21], the definition of CA includes pathological findings which is proved postoperatively. Then, we retrospectively reviewed the preoperative CT findings of whole study patients with acute appendicitis, and our study demonstrated that the presence of free air was found to be independently associated with the development of IAA, while the presence of abscess or periappendiceal fluid was not an independent predictor. We suppose that the presence of free air reflects the presence of an apparent perforation of the appendix wall, causing bacterial adhesion that is not cleared by irrigation.

In our study, the placement of a drainage tube was also significantly associated with the development of IAA in patients with CA. However, in our study, we placed a drainage tube depending on the surgeon's discretion; that is, we placed them in the patients who were considered high risk for developing IAA according to intraoperative findings. Therefore, this result might imply a strong bias. It remains controversial whether a

drainage tube is useful for preventing IAA. Some authors advocate that a drainage tube should be placed after peritoneal irrigation in order to prevent IAA [6]. On the other hand, according to a recent report, there is no clinical improvement by using an abdominal drainage after LA for CA [22,23]. An additional validation study is required regarding this agenda.

Regarding intraoperative irrigation, Cho et al. reported that irrigation was a risk factor for developing IAA [6]. Actually, irrigation implies a risk for spreading contamination. However, it was not demonstrated in the recent meta-analysis [24]. In our study, all of the patients in the CA group performed irrigation until the contaminated ascites became cleared. Therefore, we could not validate whether irrigation could be a risk factor for IAA.

Our study was not without limitations. First, this study was a retrospective and single-center experience. Another limitation was that the number of the patients who developed IAA was small and postoperative CT was selectively performed. Additional external validation is necessary to confirm that these findings are applicable to other patient groups. In addition, in our study, the patients were not distinguished according to their age, ranging 5 to 91 years. Furthermore, two readers obtained CT findings via a consensus read. It was desirable to perform measurement by several readers independently.

In conclusion, we found that the presence of free air on preoperative CT in the patients with acute appendicitis was an independent predictor for postoperative development of IAA. Surgeons should be meticulous in managing the postoperative course of patients with this finding.

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Author Contributions:

A.K. wrote the manuscript and performed data analysis. All authors contributed to acquire data and revise the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest:

The authors declare no conflicts of interest.

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Versus Suction Alone in Laparoscopic Appendectomy: Is Dilution the Solution to

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Figure legends:

Fig. 1A~D: Each figure shows presence of periappendiceal fluid (A), abscess (B), free air (C), and paralytic ileus (D). Arrows indicate each finding (A~C).

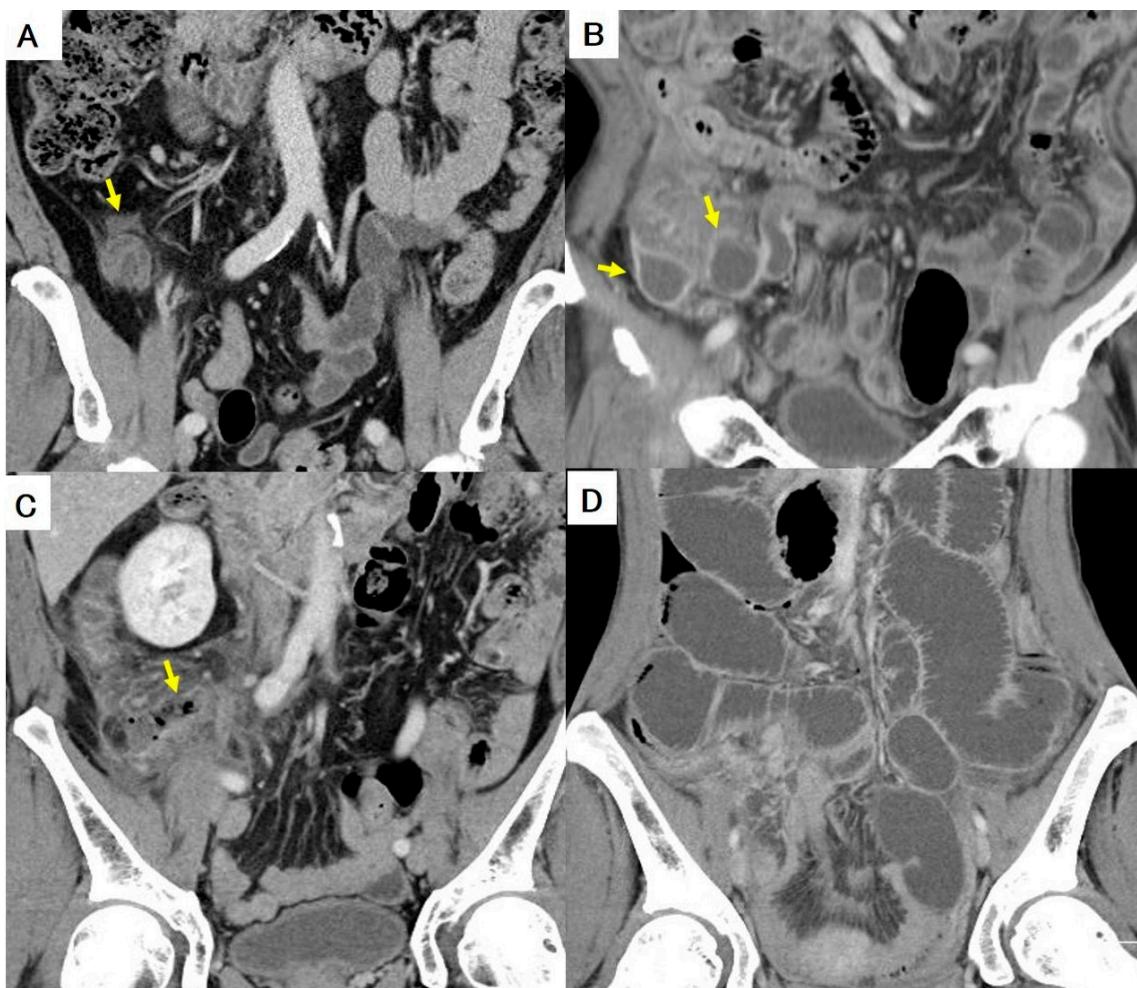


Table 1. The results of the univariate analyses of preoperative clinical factors between SA and CA in the patients who underwent LA.

	SA group (n = 69)	CA group (n = 147)	Univariate Analysis <i>P</i>
Gender ; Male / Female	42/27	93/54	0.734
Age (years)	30.5 ± 19.5	40.2 ± 23.8	0.008
History of appendicitis	16 (23.1%)	8 (5.4%)	<0.001
ASA-PS score; class 1/class 2 or 3	58/11	91/56	0.001
Preoperative WBC (/μl) mean	13400 ± 4600	15076 ± 8412	0.139
Preoperative CRP (mg/dl) mean	2.6 ± 4.5	9.0 ± 10.0	<0.001
Preoperative CT findings			
Appendicolith	16 (23.1%)	77 (52.3%)	<0.001
Periappendiceal fluid	19 (27.5%)	80 (54.4%)	<0.001
Abscess	0	27 (18.3%)	<0.001
Free air	0	22 (14.9%)	<0.001
Small bowel obstruction	0	17 (11.4%)	0.003
Time from onset to surgery (days)	1.5 ± 1.6	2.8 ± 3.8	<0.001

SA, simple appendicitis; CA, complicated appendicitis; LA, laparoscopic appendectomy; ASA-PS, American society of anesthesiologists physical status;

Table 2. The results of the univariate analyses of perioperative outcomes between SA and CA in the patients who underwent LA.

	SA group (n = 69)	CA group (n = 147)	Univariate Analysis <i>P</i>
Operation time (min)	72.8±25.3	85.8±34.8	0.005
Postoperative length of stay (day)	4.6±2.2	8.5±13.2	<0.001
Conversion to laparotomy	1 (1.4 %)	6 (4.0%)	0.477
Placement of drainage tube	8 (11.5%)	52 (35.3%)	<0.001
Postoperative complications			
Grade 2 or more in C-D classification	6 (8.6 %)	39 (26.5 %)	0.002
Grade 3 \ddagger in C-D classification	1 (0.5%)	18 (12.2%)	0.009
Intraabdominal abscess	0	16 (10.8 %)	0.004
Superficial infection	0	7 (4.7%)	0.065
Paralytic ileus	2 (1.7 %)	10 (6.8%)	0.242
Readmission	0	11 (7.4 %)	0.019

SA, simple appendicitis; CA, complicated appendicitis; LA, laparoscopic appendectomy; C-D, Clavien-Dindo;

\ddagger SA group included leakage from appendix stump (n = 1). CA group included intraabdominal abscess (n = 12), superficial infection (n = 1), hematoma (n = 1), paralytic ileus (n = 1), strangulated ileus (n = 1), ventral hernia (n = 1) and respiratory failure (n = 1)

Table 3. The results of the univariate and multivariate analyses of prognostic factors associated with developing intraabdominal abscess in the patients with simple and complicated appendicitis.

	No	IAA	IAA	Univariate Analysis P	Multivariate Analysis	
		Positive n=16	Negative n=200		Odds ratio (95% CI)	P
Gender				0.283		
	Male	135	12	123		
	Female	81	4	77		
Age				0.304		
	< 40	121	7	114		
	≥ 40	95	9	86		
ASA-PS classification				0.983		
	1	149	11	138		
	2 or 3	67	5	62		
Onset to surgery				0.011		0.708
	< 3 days	154	7	147		1
	≥ 3 days	62	9	53	1.282(0.349, 4.707)	
Preoperative WBC				0.237		
	< 18000 / μl	173	11	162		
	≥ 18000 / μl	43	5	38		
Preoperative CRP				0.205		
	< 20 mg/dl	195	13	182		
	≥ 20 mg/dl	21	3	18		
Appendicolith †				0.102		
	Absent	123	6	117		
	Present	93	10	83		
Periappendiceal fluid †				0.003		0.371
	Absent	117	3	114		1
	Present	99	13	86	1.960(0.448, 8.577)	
Abscess †						0.599
	Absent	189	9	180	<0.001	1
	Present	27	7	20	1.449(0.363, 5.780)	
Free air †				<0.001		0.007
	Absent	194	8	186		1
	Present	22	8	14	5.427(1.586, 18.57)	
SBO †				0.093		

	Absent	199	13	186		
	Present	17	3	14		
Operation time					0.023	0.971
	< 120 min	188	11	177		1
	≥ 120 min	28	5	23		1.027(0.247, 4.261)
Placement of drainage tube					<0.001	0.081
	Absent	156	4	152		1
	Present	60	12	48		3.675(0.849, 15.92)

IAA, intraabdominal abscess; CI, confidence interval;†

ASA-PS, American Society of Anesthesiologists physical status;

† judged by preoperative CT image