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ORIGINAL ARTICLE

Patient backgrounds and short-term outcomes of complicated appendicitis differ from those of uncomplicated appendicitis

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Abstract

Background: Appendicitis is classified as either complicated (CA) or uncomplicated (UA). Some authors have shown that the epidemiologic trends of CA and UA may differ. The aim of this study was to clarify differences in backgrounds and surgical outcomes between CA and UA patients.

Methods: This study was a cohort study. We extracted case data from the Japanese Diagnosis Procedure Combination (DPC) database from January 2014 to December 2017. Patients were classified into three groups, depending on whether they underwent emergency appendectomy for CA (CA group), emergency appendectomy for UA (UA group), or elective appendectomy (EA group). We evaluated patient characteristics and surgical outcomes for each group.

Results: We included 89,355 adult patients in the study, comprising 29,331 CA, 48,691 UA, and 11,333 EA patients. Old age, larger body mass index, smoking, and medication with antidiabetic drugs, oral corticosteroids, oral antiplatelet drugs, and oral anticoagulant drugs were independent risk factors for CA. The percentage of CA increased with age. In-hospital mortality (0.15%, 0.02%, and 0.00%) and 30-d mortality (0.09%, 0.01%, and 0.00%), respectively, of CA patients were significantly higher than those of the UA and EA groups. The duration of postoperative antibiotic administration, duration of fasting, and time before removal of a prophylactic drain were significantly longer in the CA group than in the UA and EA groups.

Conclusion: Backgrounds and treatment outcomes of CA and UA patients after emergency surgery are entirely different. Thus, the treatment strategy of CA and UA patients should differ accordingly.

KEYWORDS

complicated appendicitis, DPC, interval appendectomy, nationwide database, uncomplicated appendicitis

Takuya Oba and Takeshi Yamada contributed equally to this work.

1 | INTRODUCTION

Acute appendicitis is one of the most common general surgical emergencies worldwide, with an estimated lifetime risk of 7%–8%.[1] Emergency appendectomy has been the standard of care for treating acute appendicitis. Recently, appendicitis has been classified into two categories: complicated appendicitis (CA), involving perforation or peritoneal abscess, and uncomplicated appendicitis (UA), which does not. Some authors have shown that epidemiologic trends of CA and UA may differ,[2,3] and that emergency surgery for CA may involve more frequent and more serious morbidity than that of UA. A systemic review found that CA has a 3-fold higher morbidity rate than UA after emergency surgery,[4] which we confirmed in a previous study using the Japanese National Clinical Database (NCD).[5] To decrease morbidity after emergency surgery for CA, interval appendectomy (IA), which involves antibiotic therapy with or without percutaneous peritoneal drainage, followed by elective surgery, is often performed. However, there has been no evidence for the efficacy of IA in adult patients.

Another important question concerns the etiology of CA. CA has traditionally been viewed as untreated or deteriorating UA that develops into CA. However, large[6,7] and even nationwide studies,[8] as well as a meta-analysis,[9] have shown that CA patients are older and comprise a higher American Society of Anesthesiologists (ASA) class than UA patients. In the MUSTANG study, the prevalence of risk factors, including cigarette smoking, was significantly higher in CA patients than in UA patients.[6] If the etiology of CA is actually different from that of UA, the most appropriate treatment may differ as well.

Using the NCD, which was initiated in 2011 in collaboration with the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) in order to create a standardized surgery database for quality improvement, we showed that the morbidity rate, the readmission rate, and the mortality rate of CA after emergency surgery are all higher than in UA.[5] In that study, patients classified as ASA3 or higher were far more numerous in CA than in UA. However, the NCD does not contain data regarding kinds of comorbidity; thus, we could not identify the risk factors of CA. Also, the NCD does not record kinds of morbidity occurring after surgery, the need for a prophylactic drain, fasting duration, or duration of antibiotic therapy after surgery. In the present study we sought to clarify the differences between CA and UA in terms of patient background (comorbidity), kind of morbidity, and treatment after surgery (the need for a prophylactic drain, fasting duration, or duration of antibiotic therapy) using the Japanese Diagnosis Procedure Combination (DPC) database.

2 | MATERIALS AND METHODS

2.1 | DPC

The DPC database is a Japanese diagnosis-dominant, case-mix system maintained by the Ministry of Health, Labor, and Welfare of Japan. Approximately 90% of all acute care hospitals (>1000) and all 82 university hospitals in Japan participate in the DPC.[10] It contains discharge abstracts and administrative reimbursement claim data from inpatient cases collected at participating hospitals, and it has been used in various studies.[11,12] Details of this database have been reported by Yamana et al.[13] The database includes the following data: disease names, hospitalization costs, urgent or planned hospital admission, comorbidities at admission and during hospitalization, coded according to the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10), age, sex, length of hospital stay (LOS), medical procedures including surgery, names and quantities of medicines administered, and discharge status (including in-hospital deaths). Medical procedures are indexed with a Japanese code (K-code, Table S1),[14] assigned by the Ministry of Health, Labor, and Welfare of Japan. All data that could identify patients were deleted. This study was approved by the Ethics Committee for Medical Care and Research at the University of Occupational and Environmental Health Japan (R1-067).

2.2 | Patient selection

This retrospective cohort study of short-term surgical results of patients who underwent appendectomies was approved by the Ethics Committee of University of Occupational and Environmental Health, Kitakyushu, Japan. In this study, we included patients who underwent appendectomies between January 1, 2014, and December 31, 2017. Patient characteristics and surgical outcomes were obtained from DPC data.

Inclusion criteria were as follows: over 18 y old, inpatient status and, admission for acute appendicitis (ICD-10 code: K350, K351, K359). Exclusion criteria were cancer of the appendix and insufficient data. Patients who underwent emergency appendectomy for CA (K-code: K7182, K718-22) comprised the CA group. Patients who underwent emergency appendectomy for UA (K-code: K7181, K718-21) comprised the UA group. Patients who were admitted as per scheduled and underwent appendectomy (K-code: K7181, K718-21, K7182, K718-22) comprised the elective appendectomy (EA) group.

2.3 | Endpoints

Endpoints were as follows: in-hospital mortality, 30-d postoperative mortality, executing rate of laparoscopic surgery, duration of postoperative antibiotic administration, duration of fasting, use of a prophylactic drain, time to remove a prophylactic drain, necessity of a postoperative trans-nasal long decompression tube, necessity of postoperative percutaneous peritoneal drainage, LOS, and total hospitalization cost.

2.4 | Statistical analysis

Age, body mass index (BMI), LOS, duration of postoperative antibiotic administration, fasting duration, time to a remove a prophylactic drain, and admission cost were analyzed using the Kruskal–Wallis method with the Mann–Whitney *U*-test. Sex, smoking rate, use of antidiabetic drugs, oral corticosteroid drugs, oral antiplatelet drugs, and oral anticoagulant drugs, surgical method (laparoscopic or open surgery), use of a prophylactic drain, necessity of a postoperative trans-nasal long decompression tube, necessity of postoperative peritoneal drainage, and mortality were analyzed using the chi-square test.

$P < .05$ was considered statistically significant. The Bonferroni correction was used to adjust *P*-values because of the increased risk of a type I error when making multiple statistical tests.

3 | RESULTS

3.1 | Patients

During the study period, 103,856 patients who were over 18 y of age and underwent appendectomies were registered in the DPC database. Patients who had cancer of the appendix (58), or who lacked sufficient data (14,443) were excluded, resulting in inclusion of 89,355 patients (29,331 CA, 48,691 UA, and 11,333 EA patients) (Figure 1). Patient backgrounds and surgical outcomes are shown in Table 1 and an intergroup comparison is found in Table 2. Of 89,355 patients, 49,429 (55.3%) were male, 3272 patients (3.7%) were taking antidiabetic drugs, 655 (0.7%) were taking oral corticosteroids, 2153 (2.4%) were receiving oral antiplatelet drugs, and 1072 patients (1.2%) were taking oral anticoagulant drugs.

Median age, the proportion of men, median BMI, the proportion of smokers, and use of antidiabetic drugs, oral corticosteroid drugs, antiplatelet drugs, and anticoagulant drugs were higher in the CA group than in the UA and EA groups. Multivariate analysis showed that old age (odds ratio [OR]: 2.83, 95% confidence interval [CI]: 2.72–2.94, $P < .001$), men (OR: 1.14, 95% CI:1.10–1.18, $P < .001$), large BMI (OR: 1.24, 95% CI:1.19–1.29, $P < .001$), smoking (OR: 1.11, 95% CI:1.07–1.14, $P < .001$), antidiabetic drugs (OR: 1.93, 95% CI:1.77–2.09, $P < .001$), oral corticosteroid drugs (OR: 1.55, 95% CI:1.30–1.84, $P < .001$), oral antiplatelet drugs (OR: 1.39, 95% CI:1.26–1.54, $P < .001$), oral anticoagulant drugs (OR: 1.68, 95% CI:1.45–1.94, $P < .001$) were all independent risk factors for CA (Table 3). In the analysis of Table 3, patients in the EA group were not included. The percentage of CA increased with age (Figure 2).

3.2 | Surgical outcomes

A total of 62,092 patients (69.5%) received laparoscopic appendectomies, and prophylactic drains were inserted in 24,531 patients (27.5%). After surgery, 425 patients (0.5%) required trans-nasal long decompression tubes, and peritoneal drainage after surgery was performed on 125 patients (0.1%). The median LOS was 6 d, the in-hospital mortality rate was 0.06%, and the 30-d mortality rate was 0.04%.

The surgical outcomes of each group are shown in Table 1. The rate of laparoscopic surgery was significantly lower in the CA group than in the UA and EA groups (64.6%, 67.5%, and 90.4%, respectively, $P < .001$). Although CA patients needed prophylactic drains significantly more often than UA and EA patients (65.4%, 8.9%, and 9.0%, respectively, $P < .001$), they also required peritoneal drainage at a significantly higher rate than UA and EA patients (0.3%, 0.05%, and 0.03%, respectively, $P < .001$). CA patients also needed trans-nasal long decompression tube after surgery far more often than UA and EA patients (1.2%, 0.1%, and 0.08%, respectively, $P < .001$); however, there was no statistical difference between UA and EA patients. Durations of postoperative

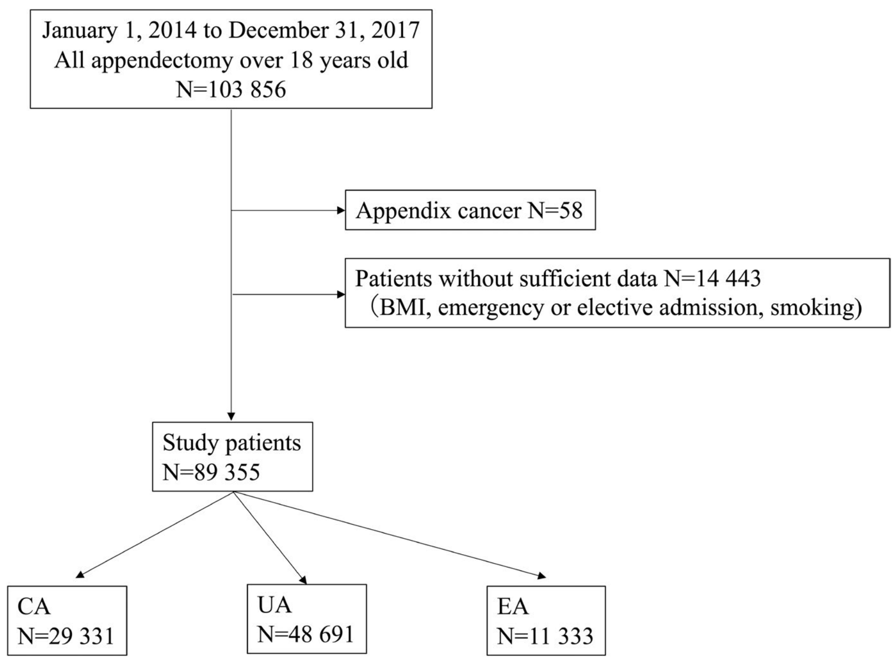

FIGURE 1 Flow diagram. Between 2014 and 2017, 103,856 adult patients who underwent appendectomy were registered in the DPC. Patients with cancer of the appendix (n = 58) or without sufficient data (n = 14,443) were excluded, leaving 89,355 patients in the study: 29,331 complicated appendicitis (CA), 48,691 uncomplicated appendicitis (UA), and 11,333 patients who received an elective appendectomy (EA)

TABLE 1 Patient characteristics and surgical outcome

	Complicated appendicitis (N = 29,331)	Uncomplicated appendicitis (N = 48 691)	Elective appendectomy (N = 11,333)	*P* value
Patients' characteristics				
Age (median [IQR])	52 [38, 68]	39 [28, 52]	44 [32, 61]	<.001
Male (%)	17 370 (59.2)	26 384 (54.2)	5675 (50.1)	<.001
BMI (median [IQR])	22.2 [20.2, 24.5]	21.8 [19.9, 24.1]	21.9 [20.0, 24.0]	<.001
Smoker (%)	12 500 (42.6)	19 241 (39.5)	4325 (38.2)	<.001
Antidiabetic drugs (%)	1927 (6.6)	1038 (2.1)	307 (2.7)	<.001
Oral corticosteroid drugs (%)	339 (1.2)	252 (0.5)	64 (0.6)	<.001
Oral antiplatelet drugs (%)	1250 (4.3)	670 (1.4)	233 (2.0)	<.001
Oral anticoagulant drugs (%)	646 (2.2)	291 (0.6)	135 (1.2)	<.001
Surgical outcome				
Laparoscopic surgery (%)	18 958 (64.6)	32 890 (67.5)	10 244 (90.4)	<.001
Duration of antibiotics medication (day) (median [IQR])	6 [4, 8]	3 [2, 4]	2 [1, 3]	<.001
Fasting duration (day) median [IQR]	3 [2, 4]	2 [2, 3]	2 [2, 2]	<.001
Prophylactic drain (%)	19 184 (65.4)	4325 (8.9)	1022 (9.0)	<.001
Duration of drain insertion (day) median [IQR]	6 [4, 8]	4 [3, 6]	4 [3, 5]	<.001
Trans-nasal long decompression tube (%)	350 (1.2)	66 (0.1)	9 (0.08)	<.001
Peritoneal drainage (%)	99 (0.3)	23 (0.05)	3 (0.03)	<.001
LOS (day) (median [IQR])	9 [6, 12]	5 [4, 7]	5 [5, 7]	<.001
Admission cost (dollar) (median)	6365	4490	3840	<.001
In-hospital Mortality (%)	43 (0.15)	12 (0.02)	0 (0.00)	<.001
30-d mortality (%)	27 (0.09)	5 (0.01)	0 (0.00)	<.001

Abbreviations: IQR, interquartile range; LOS, length of hospital stay.

antibiotic administration (6, 3, and 2 d, respectively, $P < .001$) and fasting (3, 2, and 2 d, respectively, $P < .001$), and time to remove a prophylactic drain (6, 4, and 4 d, respectively, $P < .001$) were significantly longer in the CA group than in the UA and EA groups. The duration of postoperative antibiotic administration, fasting duration, and LOS were significantly shorter in the EA group than in the other groups.

LOS of CA patients was significantly longer than of UA and EA patients (9, 5, and 5 d, respectively, $P < .001$). In-hospital (0.15, 0.02, and 0.00%, respectively, $P < .001$) and 30-d mortality (0.09, 0.01, and 0.00%, respectively, $P < .001$) rates of CA patients were significantly higher than those of the UA and EA groups. LOS of UA patients was significantly longer than that of EA patients; however, there were no significant differences in in-hospital or 30-d mortality rates between the UA and EA groups. Mean admission cost of the CA group was significantly higher than those of the UA and EA groups. ($6365, $4490, and $3840, respectively, $P < .001$).

3.3 | Elderly patients (≥65 y)

Patient characteristics and surgical outcomes of elderly patients are shown in Table 4.

In elderly patients, the same results were observed. Compared with younger CA patients (<65 y), rates of elderly CA patients who took antidiabetic drugs (13.6% vs 3.4%, $P < .001$), oral corticosteroids (2.2% vs 0.7%, $P < .001$), oral antiplatelet drugs (11.1% vs 1.2%, $P < .001$), and anticoagulant drugs (5.9% vs 0.5%, $P < .001$) were higher. In addition, the rate of laparoscopic surgery in elderly patients was lower (56.7% vs 68.2%, $P < .001$), and the rate of prophylactic drain insertions was higher (74.6% vs 61.3%, $P < .001$) among CA patients. In-hospital (0.4% vs 0.04%, $P < .001$) and 30-d mortality (0.2% vs 0.03%, $P < .001$) of elderly CA patients were higher than those of younger CA patients.

3.4 | Use of prophylactic drains and surgical outcomes

Prophylactic drains were inserted in 65.4% of CA patients. Patients with prophylactic drains required longer antibiotic courses (6 vs 4 d, $P < .001$), longer fasting (3 vs 2 d, $P < .001$), and experienced higher rates of trans-nasal long decompression tube insertion (1.8% vs 0.1%, $P < .001$), peritoneal drainage (0.5% vs 0.02%, $P < .001$), longer LOS (11 vs 7 d, $P < .001$), higher admission costs (¥767,173 vs ¥637,900, $P < .001$), and higher in-hospital (0.2% vs

TABLE 2 Comparison among groups

	CA vs UA	UA vs EA	CA vs EA
Patients' characteristics			
Age	$P < .001$	$P < .001$	$P < .001$
Male	$P < .001$	$P < .001$	$P < .001$
BMI	$P < .001$	$P = .231$	$P < .001$
Smoker	$P < .001$	$P = .008$	$P < .001$
Antidiabetic drugs	$P < .001$	$P < .001$	$P < .001$
Oral corticosteroid drugs	$P < .001$	$P = .532$	$P < .001$
Oral antiplatelet drugs	$P < .001$	$P < .001$	$P < .001$
Oral anticoagulant drugs	$P < .001$	$P < .001$	$P < .001$
Surgical outcome			
Laparoscopic surgery	$P < .001$	$P < .001$	$P < .001$
Duration of antibiotics medication	$P < .001$	$P < .001$	$P < .001$
Fasting duration	$P < .001$	$P < .001$	$P < .001$
Prophylactic drain	$P < .001$	$P = .649$	$P < .001$
Duration of drain insertion	$P < .001$	$P = .061$	$P < .001$
Trans-nasal long decompression tube	$P < .001$	$P = .128$	$P < .001$
Peritoneal drainage	$P < .001$	$P = .339$	$P < .001$
LOS	$P < .001$	$P < .001$	$P < .001$
Admission cost	$P < .001$	$P < .001$	$P < .001$
In-hospital mortality	$P < .001$	$P = .095$	$P = .001$
30-d mortality	$P < .001$	$P = .281$	$P < .001$

Abbreviations: CA, complicated appendicitis; EA, elective appendectomy; LOS, length of hospital stay; UA, uncomplicated appendicitis.

TABLE 3 Multivariate analysis of risk factor for complicated appendicitis

	Odds ratio	95% CI	*P* value
Age			
18–64	Reference		<.001
65+	2.83	2.72–2.94	
Sex			
Women	Reference		<.001
Men	1.14	1.10–1.18	
BMI			
0–18.4	1.00	0.95–1.05	.906
18.5–24.9	Reference		
25-	1.24	1.19–1.29	<.001
Smoking			
No	Reference		<.001
Yes	1.11	1.07–1.14	
Antidiabetic drugs			
No	Reference		<.001
Yes	1.93	1.77–2.09	
Oral corticosteroid drugs			
No	Reference		<.001
Yes	1.55	1.30–1.84	
Oral antiplatelet drugs			
No	Reference		<.001
Yes	1.39	1.26–1.54	
Oral anticoagulant drugs			
No	Reference		<.001
Yes	1.68	1.45–1.94	

Abbreviation: CI: confidence interval.

0.02%, $P < .001$) and 30-d mortality (0.1% vs 0.01%, $P < .001$, Table 5).

3.5 | Difference in outcomes between laparoscopic and open surgery

CA patients who received laparoscopic surgery had more favorable outcomes than those who received open surgery, with the exception that laparoscopic surgery required peritoneal drainage just as frequently, and incurred higher admission costs. In UA patients, most outcomes of laparoscopic surgery were significantly better, but there were no differences with regard to in-hospital and 30-d mortality (Table 6).

4 | DISCUSSION

In the present study, the in-hospital mortality rate of CA was significantly higher than that of UA and EA, as in previous reports.[15,16] In addition, the CA morbidity rate was worse and hospital charges were higher. Using the Japanese nationwide database (DPC), we made three valuable findings and overcame several limitations in our previous study, which used the NCD.[5] First, elderly patients and patients receiving diabetes, antiplatelet, or anticoagulant drugs are more likely to develop CA. Second, CA patients developed ileus and intraperitoneal abscesses after surgery more frequently than UA patients or EA patients. The fasting duration and length of antibiotic use were also longer in CA patients than in the other two groups. Third, CA patients need prophylactic drains more frequently and CA patients with inserted prophylactic drains experienced worse outcomes than CA patients who did not require prophylactic drains.

Elderly patients, smokers, and patients receiving diabetes, antiplatelet, or anticoagulant drugs are more likely to develop CA. In the present study, CA patients were significantly older than UA patients. In addition, rates of medication use and the smoking rate of CA patients were significantly higher than those of UA patients. Patients over 65 y of age experienced outcomes similar to those of patients of all ages. Some studies show that CA patients were older than UA patients.[6–9] Livingston et al reported that CA exhibits radically different epidemiologic trends than UA.[3] Our results

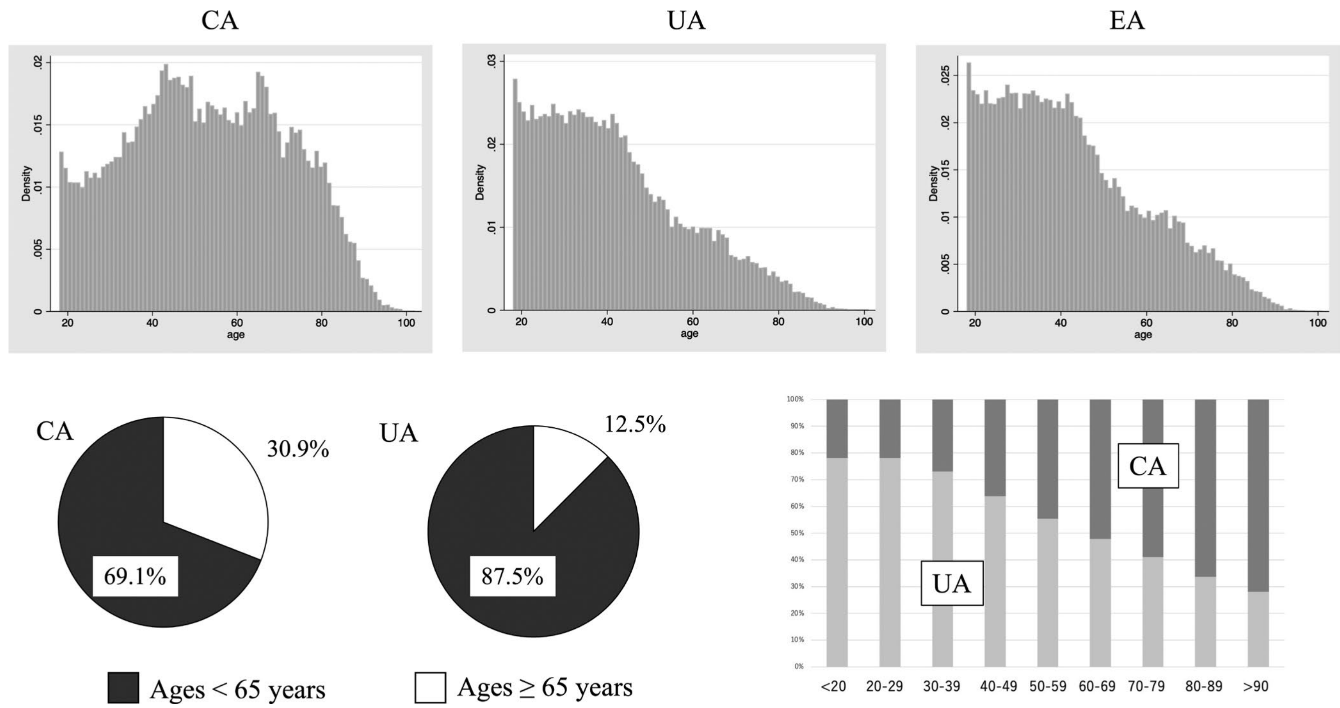

FIGURE 2 Age distribution of each group. Elderly patients (≥65 y old) comprised a much larger proportion of patients with complicated appendicitis than with uncomplicated appendicitis (30.9% vs 12.5%, $P < .001$). The percentage of CA increased with increasing age

TABLE 4 Elderly patients

	Complicated appendicitis (N = 9066)	Uncomplicated appendicitis (N = 6078)	Elective appendectomy (N = 2218)	*P* Value
Patients' characteristics				
Male (%)	5400 (59.6)	3316 (54.6)	1246 (56.2)	<.001
BMI (median [IQR])	22.2 [20.3, 24.3]	22.3 [20.3, 24.2]	22.4 [20.6, 24.2]	.007
Smoker (%)	3547 (39.1)	2204 (36.2)	852 (38.4)	.002
Antidiabetic drugs (%)	1235 (13.6)	522 (8.6)	176 (7.9)	<.001
Oral corticosteroid drugs (%)	196 (2.2)	77 (1.3)	21 (1.0)	<.001
Oral antiplatelet drugs (%)	1006 (11.1)	485 (8.0)	177 (8.0)	<.001
Oral anticoagulant drugs (%)	537 (5.9)	221 (3.6)	99 (4.5)	<.001
Surgical outcome				
Laparoscopic surgery (%)	5143 (56.7)	3559 (58.6)	1917 (86.4)	<.001
Duration of antibiotics medication (day) median [IQR]	6 [4, 9]	3 [2, 5]	2 [1, 3]	<.001
Fasting duration (day) median [IQR]	3 [2, 5]	2 [2, 3]	2 [2, 2]	<.001
Prophylactic drain (%)	6763 (74.6)	1062 (17.5)	323 (14.6)	<.001
Duration of drain insertion (day) median [IQR]	6 [5, 8]	5 [3, 7]	4 [3, 6]	<.001
Trans-nasal long decompression tube (%)	156 (1.7)	24 (0.4)	3 (0.1)	<.001
Peritoneal drainage (%)	37 (0.4)	6 (0.1)	0 (0.00)	<.001
LOS (day) (median [IQR])	10 [8, 15]	6 [5, 9]	6 [5, 8]	<.001
Admission cost (dollar) (median)	6919	4906	4177	<.001
In-hospital Mortality (%)	34 (0.4)	11 (0.18)	0 (0.00)	.003
30-d mortality (%)	20 (0.2)	5 (0.08)	0 (0.00)	.014

Abbreviations: IQR, interquartile range; LOS, length of hospital stay.

TABLE 5 Patients with complicated appendicitis, who had an inserted prophylactic drain during an operation or not

	Drain (+)	Drain (–)	*P* Value
Laparoscopic (%)	11 460 (59.7)	7498 (73.9)	<.001
Duration of antibiotics drugs medication (day) median [IQR]	6 [4,9]	4 [3,6]	<.001
Fasting duration (day) median [IQR]	3 [3,5]	2 [2,3]	<.001
Trans-nasal long decompression tube (%)	340 (1.8)	10 (0.1)	<.001
Peritoneal drainage after surgery (%)	97 (0.5)	2 (0.02)	<.001
LOS (day) median [IQR]	11 [9,15]	7 [6,10]	<.001
Admission cost (yen) median	767 173	637 900	<.001
In-hospital Mortality (%)	41 (0.2)	2 (0.02)	<.001
30-d mortality (%)	26 (0.1)	1 (0.01)	<.001

Abbreviations: IQR, interquartile range; LOS, length of hospital stay.

TABLE 6 Difference of outcome between laparoscopic and open surgery

	CA (N = 29,331)			UA (N = 48 691)		
	Open	Lap	*P* Value	Open	Lap	*P* Value
Duration of antibiotics medication (day) median [IQR]	6 [4,8]	5 [3,8]	<.001	3 [2,4]	3 [2,4]	<.001
Fasting (day) median [IQR]	3 [2,5]	3 [2,4]	<.001	2 [2,3]	2 [2,2]	<.001
Prophylactic drain (%)	7724 (74.5)	11 460 (60.4)	<.001	1541 (9.8)	2784 (8.5)	<.001
Duration of drain insertion (day) median [IQR]	6 [5,8]	5 [4,7]	<.001	5 [3,6]	4 [2,5]	<.001
Trans-nasal long decompression tube (%)	172 (1.7)	178 (0.9)	<.001	22 (0.14)	44 (0.13)	.878
Peritoneal drainage (%)	39 (0.4)	60 (0.3)	.401	13 (0.08)	10 (0.03)	.014
LOS (day) median [IQR]	10 [8,14]	8 [6,11]	<.001	6 [5,8]	6 [5,7]	<.001
Admission cost (yen) median	649 150	749 400	<.001	423 792	536 145	<.001
In-hospital mortality (%)	27 (0.3)	16 (0.08)	<.001	6 (0.04)	6 (0.02)	.194
30-d mortality (%)	17 (0.2)	10 (0.05)	.003	2 (0.01)	3 (0.01)	.718

Abbreviations: CA, complicated appendicitis; EA, elective appendectomy; IQR, interquartile range; Lap, laparoscopic appendectomy; LOS, length of hospital stay; Open, open appendectomy; UA, uncomplicated appendicitis.

suggest that low host immune status can cause CA. The multivariate analysis showed that smoking is an independent risk factor for CA, and the smoking rate of CA patients was ~4% higher than that of UA patients in the present study, as in previous reports.[6–17] A study of twins found that smoking is a risk factor for appendicitis, especially in women.[18]

CA patients require more postoperative interventions, such as trans-nasal long decompression tube insertion or peritoneal drainage and require longer fasting and antibiotic therapy. Our previous study using NCD data clearly showed that Clavien–Dindo Grade II or III morbidity rates of CA were higher than those of UA; however, we did not examine the details of the complications or duration of fasting and antibiotic administration. Because, on average, CA patients were significantly older than UA patients, we compared older CA patients to older UA patients and EA patients, and were still worse, indicating that the appendicitis category was the critical factor, rather than age. Various large studies have reported that CA patients have higher rates of postoperative abscesses requiring intervention[8] and longer LOS.[8,19] Emergency surgery for CA is associated with higher morbidity compared with nonoperative management.[20] CA emergency surgery had a 10% risk of bowel resection[21] and a higher risk of bowel obstruction.[22] Considering these findings, we should reconsider the safety of emergency surgery for CA and the treatment strategy for CA.

Increased morbidity and prolonged LOS of CA patients with prophylactic drains have been reported in children[23] and adults.[24] Also in patients who received laparoscopic appendectomies, it has been reported that prophylactic drains may cause prolonged LOS in all patients with or without comorbidity.[25] However, since CA is a serious disease the conclusion that prophylactic drains have a negative benefit cannot be drawn from the present nonrandomized, retrospective study. Thus, whether CA patients need prophylactic drains remains unclear.

A higher rate of open surgery in CA patients was observed in this study; however, interpreting this is difficult because the efficacy of laparoscopic appendectomies is controversial. Previous studies presented that laparoscopic appendectomies were associated with higher rates of intestinal injury, readmission, and postoperative abdominal abscess.[26,27] Moreover, a randomized, double-blind study showed that laparoscopic appendectomies do not offer significant advantages over open appendectomies[28] and that laparoscopic appendectomies were associated with more postoperative abdominal abscesses.[29] Conversely, a nonrandomized study concluded that laparoscopic appendectomies were associated with shorter LOS and fewer complications[30] and a lower late of bowel obstruction.[31] A recent meta-analysis showed that laparoscopic appendectomies for CA is associated with reduced mortality, total morbidity, wound infection, respiratory complications, and ileus without a higher incidence of postoperative abdominal abscesses.[32] A Dutch nationwide study reported that the rate of postoperative abdominal abscess formation was not significantly different following laparoscopic or open surgery.[33] In the present study, laparoscopic appendectomy for CA had the same incidence of postoperative peritoneal drainage but significantly reduced mortality, the rate of trans-nasal long decompression tube insertion, and LOS compared with open surgery for CA. Thus, the benefits of laparoscopic surgery for CA are also a matter of an ongoing debate.

EA has higher safety than emergency surgery. In the present study, short-term outcomes of EA were superior to those of UA patients, and much better than those of CA. Thus, interval appendectomy (IA) is an alternative treatment for emergency surgery for CA. However, there have been no reports showing the clinical utility of IA in adults. In addition, IA raises two concerns. The success rate of nonoperative management is ~90%[1,34] and ~1% of CA patients have cancer.[20] Increasing age increases the odds of a cancer diagnosis after appendectomy[35] and age >40 is associated with a greater risk of malignancy.[36] In the present study the proportion of CA increased with increasing age. Thus, the pros and cons of IA cannot be discussed without considering these two concerns.

This study had several limitations that must be addressed in future studies. (a) The DPC does not record the morbidity rate, as the NCD does, but the DPC records the use of trans-nasal long decompression and percutaneous drainage tubes. However, we clearly showed that the morbidity rate of CA is 3-fold higher than that of UA after emergency surgery, according to data in the Japanese nationwide NCD. (b) Laboratory data were not available. (c) CA is not rigidly defined in the present study because of the study's retrospective design. Unfortunately, there is no general agreement on a definition of CA; however, the presence of a visible perforation, diffuse fibrinopurulent exudate, intra-abdominal abscess, and extraluminal fecalith are independently associated with markedly worse outcomes[37]; thus, appendicitis with any of these characteristics is generally defined as CA. (d) The EA group included not only CA patients treated with IA, but also patients initially diagnosed as UA who were treated conservatively or with chronic appendicitis not treated preoperatively with antibiotics. Surgical outcomes of IA may differ from those of EA initially diagnosed as UA or surgery for chronic appendicitis. (e) The EA group did not include patients with CA who attempted IA, but ultimately had emergency surgery because nonoperative management failed. To investigate the value of nonoperative management followed by EA, evaluation of CA patients who failed nonoperative management is essential. (f) Patients who underwent conversion surgery from laparoscopic surgery to open surgery were mostly classified as laparoscopic surgery cases, but that judgment depends on the surgeon.

In conclusion, patient backgrounds and treatment outcomes after emergency surgery for CA are entirely different from those of UA. In addition, CA patients incur greater hospital costs than UA patients. Thus, treatment strategies and issues of informed consent should differ for CA vs UA. Ultimately, a diagnosis of CA or UA is the most important criterion for treatment of appendicitis.

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REFERENCES

1. Stewart B, Khanduri P, McCord C, Ohene-Yeboah M, Uranues S, Vega Rivera F, et al. Global disease burden of conditions requiring emergency surgery. Br J Surg. 2014;101(1):e9–22.
2. Salminen P, Grönroos J, Rautio T. Complicated and uncomplicated acute appendicitis are different diseases-do not compare apples with oranges. JAMA Surg. 2019;154(8):782–3.
3. Livingston EH, Woodward WA, Sarosi GA, Haley RW. Disconnect between incidence of nonperforated and perforated appendicitis: implications for pathophysiology and management. Ann Surg. 2007;245(6):886–92.
4. Darwazeh G, Cunningham SC, Kowdley GC. A systematic review of perforated appendicitis and phlegmon: interval appendectomy or wait-and-see? Am Surg. 2016;82(1):11–5.
5. Yamada T, Endo H, Hasegawa H, Kimura T, Kakeji Y, Koda K, et al. Risk of emergency surgery for complicated appendicitis: Japanese nationwide study. Ann Gastroenterol Surg. 2021;5(2):236–42.
6. Yeh DD, Eid AI, Young KA, Wild J, Kaafarani HMA, Ray-Zack M, et al. Multicenter Study of the Treatment of Appendicitis in America: Acute, Perforated, and Gangrenous (MUSTANG), an EAST Multicenter Study. Ann Surg. 2021;273(3):548–56.
7. Drake FT, Mottey NE, Farrokhi ET, Florence MG, Johnson MG, Mock C, et al. Time to appendectomy and risk of perforation in acute appendicitis. JAMA Surg. 2014;149(8):837–44.
8. Hester CA, Pickett M, Abdelfattah KR, Cripps MW, Dultz LA, Dumas RP, et al. Comparison of appendectomy for perforated appendicitis with and without abscess: a National Surgical Quality Improvement Program Analysis. J Surg Res. 2020;251:159–67.

9. Bhangu A. Safety of short, in-hospital delays before surgery for acute appendicitis: multicentre cohort study, systematic review, and meta-analysis. Ann Surg. 2014;259(5):894–903.
10. Tajima T, Nagata J, Akiyama Y, Torigoe T, Fujimoto K, Sato N, et al. Open colectomy vs. laparoscopic colectomy in Japan: a retrospective study using real-world data from the diagnosis procedure combination database. Surg Today. 2020;50(10):1255–61.
11. Sakamoto T, Fujiogi M, Lefor AK, Matsui H, Fushimi K, Yasunaga H. Stent as a bridge to surgery or immediate colectomy for malignant right colonic obstruction: propensity-scored, national database study. Br J Surg. 2020;107(10):1354–62.
12. Takiguchi T, Nakajima M, Ohbe H, Sasabuchi Y, Matsui H, Fushimi K, et al. Vasodilator therapy and mortality in nonocclusive mesenteric ischemia: a Nationwide Observational Study. Crit Care Med. 2020;48(5):e356–61.
13. Yamana H, Moriwaki M, Horiguchi H, Kodan M, Fushimi K, Yasunaga H. Validity of diagnoses, procedures, and laboratory data in Japanese administrative data. J Epidemiol. 2017;27(10):476–82.
14. Nakamura K. Diagnosis procedure combination database would develop Nationwide Clinical Research in Japan. Circ J. 2016;80(11):2289–90.
15. Ingraham AM, Cohen ME, Bilimoria KY, Pritts TA, Ko CY, Esposito TJ. Comparison of outcomes after laparoscopic versus open appendectomy for acute appendicitis at 222 ACS NSQIP hospitals. Surgery. 2010;148(4):625–37; discussion 35–7.
16. Kotaluoto S, Ukkonen M, Pauniaho SL, Helminen M, Sand J, Rantanen T. Mortality related to appendectomy; A population based analysis over two decades in Finland. World J Surg. 2017;41(1):64–9.
17. Sadr Azodi O, Lindström D, Adami J, Bellocco R, Linder S, Wladis A. Impact of body mass index and tobacco smoking on outcome after open appendicectomy. Br J Surg. 2008;95(6):751–7.
18. Oldmeadow C, Wood I, Mengersen K, Visscher PM, Martin NG, Duffy DL. Investigation of the relationship between smoking and appendicitis in Australian twins. Ann Epidemiol. 2008;18(8):631–6.
19. Walędziak M, Lasek A, Wysocki M, Su M, Bobowicz M, Myśliwiec P, et al. Risk factors for serious morbidity, prolonged length of stay and hospital readmission after laparoscopic appendectomy - results from Pol-LA (Polish Laparoscopic Appendectomy) multicenter large cohort study. Sci Rep. 2019;9(1):14793.
20. Andersson RE, Petzold MG. Nonsurgical treatment of appendiceal abscess or phlegmon: a systematic review and meta-analysis. Ann Surg. 2007;246(5):741–8.
21. Mentula P, Sammalkorpi H, Leppäniemi A. Laparoscopic surgery or conservative treatment for appendiceal abscess in adults? A randomized controlled trial. Ann Surg. 2015;262(2):237–42.
22. Andersson RE. Small bowel obstruction after appendicectomy. Br J Surg. 2001;88(10):1387–91.
23. Fujishiro J, Fujiogi M, Hirahara N, Terui K, Okamoto T, Watanabe E, et al. Abdominal drainage at appendectomy for complicated appendicitis in children: a Propensity-matched Comparative Study. Ann Surg. 2020. https://doi.org/10.1097/SLA.0000000000003804
24. Li Z, Zhao L, Cheng Y, Cheng N, Deng Y. Abdominal drainage to prevent intra-peritoneal abscess after open appendectomy for complicated appendicitis. Cochrane Database Syst Rev. 2018;5(5):CD010168.
25. Martínez-Pérez A, Payá-Llorente C, Santarrufina-Martínez S, Sebastián-Tomás JC, Martínez-López E, de'Angelis N. Predictors for prolonged length of stay after laparoscopic appendectomy for complicated acute appendicitis in adults. Surg Endosc. 2021;35(7):3628–35.
26. Andersson RE. Short-term complications and long-term morbidity of laparoscopic and open appendicectomy in a national cohort. Br J Surg. 2014;101(9):1135–42.
27. van Rossem CC, Schreinemacher MH, Treskes K, van Hogezand RM, van Geloven AA. Duration of antibiotic treatment after appendicectomy for acute complicated appendicitis. Br J Surg. 2014;101(6):715–9.
28. Katkhouda N, Mason RJ, Towfigh S, Gevorgyan A, Essani R. Laparoscopic versus open appendectomy: a prospective randomized double-blind study. Ann Surg. 2005;242(3):439–48; discussion 48–50.
29. Pedersen AG, Petersen OB, Wara P, Rønning H, Qvist N, Laurberg S. Randomized clinical trial of laparoscopic versus open appendicectomy. Br J Surg. 2001;88(2):200–5.
30. Guller U, Hervey S, Purves H, Muhlbaier LH, Peterson ED, Eubanks S, et al. Laparoscopic versus open appendectomy: outcomes comparison based on a large administrative database. Ann Surg. 2004;239(1):43–52.
31. Leung TTW, Dixon E, Gill M, Mador BD, Moulton KM, Kaplan GG, et al. Bowel obstruction following appendectomy: what is the true incidence? Ann Surg. 2009;250(1):51–3.
32. Quah GS, Eslick GD, Cox MR. Laparoscopic appendicectomy is superior to open surgery for complicated appendicitis. Surg Endosc. 2019;33(7):2072–82.
33. van Rossem CC, Bolmers MDM, Schreinemacher MHF, van Geloven AAW, Bemelman WA, Acker GJD, et al. Prospective nationwide outcome audit of surgery for suspected acute appendicitis. Br J Surg. 2016;103(1):144–51.
34. Vons C, Barry C, Maitre S, Pautrat K, Leconte M, Costaglioli B, et al. Amoxicillin plus clavulanic acid versus appendicectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial. Lancet. 2011;377(9777):1573–9.
35. Lu P, McCarty JC, Fields AC, Lee KC, Lipsitz SR, Goldberg JE, et al. Risk of appendiceal cancer in patients undergoing appendectomy for appendicitis in the era of increasing nonoperative management. J Surg Oncol. 2019;120(3):452–9.
36. Naar L, Kim P, Byerly S, Vasileiou G, Zhang H, Yeh DD, et al. Increased risk of malignancy for patients older than 40 y with appendicitis and an appendix wider than 10 mm on computed tomography scan: a post hoc analysis of an EAST multicenter study. Surgery. 2020;168(4):701–6.
37. Cameron DB, Anandalwar SP, Graham DA, Melvin P, Serres SK, Dunlap JL, et al. Development and implications of an evidence-based and public health-relevant definition of complicated appendicitis in children. Ann Surg. 2020;271(5):962–8.

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