JOURNAL OF THE
ANUS, RECTUM AND COLON
dx.doi.org/10.23922/jarc.2022-029
http://journal-arc.jp

Original Research Article

Delayed Presentation and Referral Time from General Practitioners Contribute to Increased Complicated Appendicitis during the Initial COVID-19 Pandemic Period in Japan

Tadataka Takagi, Shoichi Kinoshita, Chihiro Kawaguchi and Takao Ohyama

Department of Surgery, Heisei Memorial Hospital, Kashihara, Japan

Abstract

Objectives: This study aims to investigate the impact of the coronavirus disease 2019 (COVID-19) pandemic on the situation of acute appendicitis (AA) with respect to patients' and general practitioners' behaviors in a general community hospital in Japan.

Methods: The surgical outcomes and periods from symptom onset to medical presentation besides practitioners' referral time for consecutive AA patients were compared between the control (January 2016 to March 2020) and COVID-19 periods (April 2020 to April 2021).

Results: Eighty-three patients who underwent emergency surgery for AA were reviewed. Complicated appendicitis significantly increased in the COVID-19 period (63.6% vs. 31.2%, $P = 0.023$). In the COVID-19 period, the time from symptom onset to the medical presentation (2.2 vs. 0.9 days, $P < 0.001$) was significantly longer than in the control period. Among the patients who first presented to a general practitioner, the referral time from the practitioner to our hospital was significantly longer in the COVID-19 period (1.6 vs. 0.7 days, $P = 0.017$). Furthermore, among patients with a fever of higher than 38°C at medical presentation, the time from symptom onset to medical presentation was significantly longer in the COVID-19 period (3.0 vs. 0.7 days, $P = 0.015$). There was no difference in severe postoperative complications.

Conclusions: Hesitation to seek surgical treatment for AA was seen in both the patients and practitioners in the COVID-19 period. The delay in surgical treatment presumably led to the increase in severe AA. In a pandemic era, timely care for emergent conditions is a crucial challenge.

Keywords

complicated appendicitis, COVID-19, delayed presentation

J Anus Rectum Colon 2023; 7(1): 17-24

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has impacted many lives and has affected healthcare systems worldwide. As the pandemic unfolded, healthcare professionals have had to rapidly and fundamentally restructure healthcare systems in an unprecedented way to cope with the COVID-19 surge. In Japan, the first wave of COVID-19 struck in March 2020. In response, the Japanese government declared a state of emergency on April 7. Additionally, the Japan Surgical Society recommended that given the global spread of COVID-19, surgical treatment should be limited to patients requiring emergency surgery for life-threatening conditions and that elective surgery for patients with a nonfatal or nonurgent disease should be postponed[1]. Consequently, various noncritical surgeries showed significant declines in case volume after the first outbreak of COVID-19[2,3].

Corresponding author: Tadataka Takagi, t.takagi@naramed-u.ac.jp
Received: June 10, 2022, Accepted: September 14, 2022

The COVID-19 outbreak had also influenced patients' behavior toward seeking emergent medical care. Some hospitals in the United States reported as high as a 50% decrease in emergency department volume after the first shelter-in-place policy took effect[4]. Alarmingly, many reports suggested that even patients requiring urgent and critical medical care, such as cardiac disease or stroke, tended to wait longer before seeking emergent care due to fear of contracting COVID-19[5,6]. The delayed medical presentation resulted in the loss of opportunity to perform critical interventions, such as tissue plasminogen activator therapy[4]. Additionally, for abdominal emergencies which required surgery, the delay in presentation to the emergency department due to the COVID-19 pandemic was associated with increased postoperative complications[7].

Acute appendicitis (AA) is one of the most common acute abdominal diseases[8]. AA may become complicated appendicitis (CA) if not properly treated within 48-72 h after symptom onset[9]. CA is a potentially severe disease that requires urgent surgical intervention. A study that analyzed the Japanese national surgical database showed that annual surgical volume did not change for appendicitis in the first year of the COVID-19 pandemic[10]. However, the severity of appendicitis was unknown in this study. Another single-center study showed that surgical volume for abdominal emergencies and patient background at admission did not differ between the initial months of the COVID-19 pandemic and the same months in the prior year[11]. However, this study included various abdominal emergencies into one total cohort, so the disease-specific clinical characteristics were unknown. Some studies reported an increasing incidence of CA in the COVID-19 pandemic period[12,13]. However, it is still unclear why CA increased during the COVID-19 period and there was no study investigating the period regarding medical presentation and referral from general practitioners in detail. This study retrospectively investigated the AA patients in the first year after the outbreak of COVID-19 in a Japanese general community hospital with respect to patients' and general practitioners' behaviors. We compared surgical outcomes and periods from symptom onset to medical presentation besides the practitioner's referral time between the initial COVID-19 pandemic period and years prior to the pandemic.

Methods

Patients

Eighty-three consecutive patients who underwent emergency surgery for AA between January 2016 and April 2021 at Heisei Memorial Hospital were reviewed. Since the Japanese government announced the state of emergency in April 2020 in response to the first surge of COVID-19 patients, AA patients who underwent surgery from April 2020 to April 2021 were considered the COVID-19 group. The patients who underwent surgery between January 2016 to March 2020 were considered the control group. The patients' data on the following clinicopathological characteristics were obtained retrospectively from the medical records: age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) classification, comorbidity, preoperative white blood cell (WBC) count, C-reactive protein (CRP) levels, preoperative body temperature (BT), and time from symptom onset to medical presentation or surgery. The blood test data were collected within 6 h before surgery. The surgical findings included the type of surgery, duration of surgery, amount of blood loss, abscess formation, diffuse peritonitis, postoperative diagnosis, postoperative complications, duration of abdominal drainage, and hospital stay. Informed consent was obtained from all the patients. This study was conducted according to the World Medical Association Declaration of Helsinki and was approved by the ethics committee of Heisei Memorial Hospital (Approval number: 2021-010).

AA diagnosis and treatment

According to intraoperative findings, AA was categorized into uncomplicated appendicitis (UA) and CA. UA was defined as appendicitis with localized peritonitis at most, including catarrhalis or phlegmonous appendicitis. Appendicitis, such as gangrenous appendicitis, which involved perforation, abscess formation, or diffuse peritonitis upon operation, was considered CA. The basic treatment strategy of AA was laparoscopic surgery in our institution. However, in cases with severe inflammation or adhesion, we might perform laparotomy with a midline incision from the beginning of the operation. We diagnosed the degree of intraabdominal inflammation and adhesion, including abscess formation, via preoperative computed tomography. We performed a preoperative polymerase chain reaction test for COVID-19 on patients with symptoms such as fever and suspected COVID-19 infection to confirm the absence of infection preoperatively. We performed the surgery with adequate infection control measures such as double masking, considering the risk of intraoperative infection. Furthermore, we took measures to temporarily leave the operating room during induction of general anesthesia and extubation, considering the risk of infection during induction of general anesthesia, such as aerosols from the respiratory tract. A severe postoperative complication was defined as a grade III or higher complication according to the Clavien-Dindo (CD) classification[14]. Surgical site infections (SSIs) were classified as superficial incisional infection, deep incisional infection, or organ/space infection based on the criteria established by the Centers for Disease Control and Prevention's National Healthcare Safety Network (CDC/NHSN)[15]. An organ/space SSI was de-

Table 1. Patients Characteristics and Preoperative Factors.

	Control period $n = 61$ (%)	COVID-19 period $n = 22$ (%)	P value
Age, years*	43 (24.5–57)	54 (34–64.5)	0.065
Sex			0.443
Female	23 (37.7%)	6 (27.3%)	
Male	38 (62.3%)	16 (72.7%)	
BMI, kg/m^2*	21.6 (19.6–24.0)	20.7 (19.0–27.4)	0.897
ASA classification			0.070
1	51 (83.6%)	14 (63.6%)	
2	10 (16.4%)	8 (36.4%)	
Comorbidity			
Diabetes mellitus	3 (4.9%)	4 (18.2%)	0.076
Hypertension	5 (8.2%)	2 (9.1%)	1.000
History of abdominal surgery	0 (0 %)	2 (9.1%)	0.068
Laboratory data			
Preoperative WBC, $\times 10^3/\mu L$**	139 ± 35	121 ± 41	0.058
Preoperative CRP, mg/L*	4.7 (0.4–9.0)	4.4 (1.2–12.7)	0.635
BT at medical presentation, °C**	37.1 ± 0.9	37.8 ± 1.0	0.003

BMI, body mass index; ASA, American Society of Anesthesiologists; WBC, white blood cell; CRP, C-reactive protein; BT, body temperature

*Data are expressed as median with interquartile range

**Data are expressed as mean ± standard deviations

fined as the presence of purulent discharge from a drain or intraabdominal fluid collection identified on computed tomography associated with clinical symptoms, such as a fever, abdominal pain, and elevated numbers of WBC.

Statistical analysis

If our data were normally distributed, we performed a T-test to compare continuous variables. If our data were not normally distributed, we performed the Mann-Whitney U test. Categorical variables are presented as numbers and percentages, and the groups were compared using Fisher's exact test. $P < 0.05$ was considered significant. All statistical analyses were performed using the JMP software program ver. 13.2 (SAS Institute Inc. Cary, NC, USA).

Results

Patients characteristics

The mean annual surgical volume for AA in our hospital did not differ between the control and COVID-19 periods. Sixty-one patients in the control period and 22 patients in the COVID-19 period were included. There were no significant differences in patients' characteristics including age, sex, BMI, ASA classification, comorbidity, history of abdominal surgery, and preoperative laboratory data between the two periods. The mean age, ASA status, and history of diabetes mellitus tended to be higher in the COVID-19 period. All the patients with diabetes mellitus had mild diabetes mellitus without the need for insulin therapy, and their levels of HbA1c were controlled below 6.5 with oral medication. The preoperative WBC levels tended to be higher in the control period. The BT at medical presentation was significantly higher in the COVID-19 period (37.8°C vs. 37.1°C, $P = 0.003$) (Table 1). No patient developed COVID-19 during hospitalization nor had COVID-19 on admission for AA.

Seeking medical and surgical care

In all the patients, the time from symptom onset to medical presentation was significantly longer in the COVID-19 period than in the control period (2.2 vs. 0.9 days, $P < 0.001$). Furthermore, the time from symptom onset to surgery was significantly longer in the COVID-19 period than in the control period (3.3 vs. 1.5 days, $P < 0.001$) (Figure 1 a). Among the patients who first presented to a general practitioner, the time from symptom onset to practitioner was significantly longer in the COVID-19 period (n = 13) than in the control period (n = 39) (1.9 vs. 0.8 days, $P = 0.009$). Furthermore, the practitioner's referral time to our hospital was significantly longer in the COVID-19 period than in the control period (1.6 vs. 0.7 days, $P = 0.017$) (Figure 1b). Additionally, in patients with a fever of higher than 38°C at medical presentation, the time from symptom onset to medical presentation was significantly longer in the COVID-19 period (n = 10) than in the control period (n = 10) (3.0 vs. 0.7 days, $P = 0.015$). In these patients, the time from symptom onset to surgery was significantly longer in the COVID-

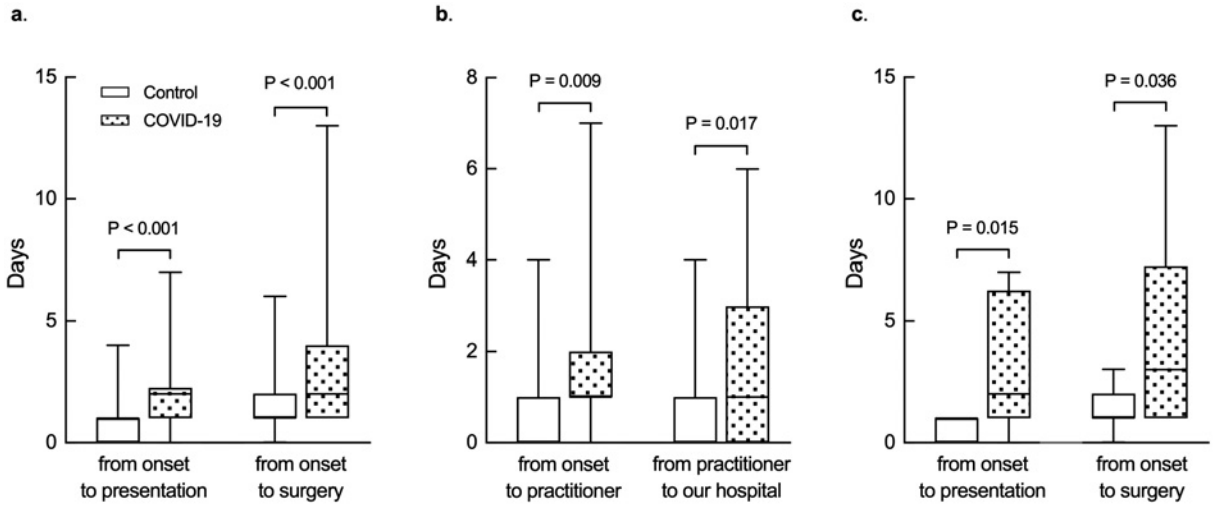

Figure 1. Time to seek medical attention in a.) all patients, b.) patients who first consulted a general practitioner, and c.) patients who presented with a high fever.

19 period than in the control period (4.3 vs. 1.4 days, P = 0.036) (Figure 1c).

Severity of AA

Most notably, we observed a significant increase in CA during the COVID-19 pandemic period compared with the control period (63.6% vs. 31.2%, P = 0.023). Perforated AA significantly increased in the COVID-19 period (40.9% vs. 14.8%, P = 0.016), contributing to the increase of CA. Perforated AA comprised 64.3% of CA in the COVID-19 period compared with 47.4% in the control period. Additionally, the rate of abscess formation (72.7% vs. 24.6%, P < 0.001) and diffuse peritonitis (18.2% vs. 1.6%, P = 0.016) was significantly higher in the COVID-19 period than in the control period (Table 2).

Surgical outcome

There were no differences in laparoscopic surgery and laparotomy conversion rates between the two periods. One patient in the COVID-19 period underwent only abdominal drainage surgery, whereas all other patients underwent appendectomy. In the COVID-19 period, the operation time was significantly longer (79.5 vs. 52.0 min, P = 0.003), and abdominal drainage during surgery tended to be more performed than in the control period (40.9% vs. 21.3%, P = 0.094). Intraoperative abdominal drainage meant intraoperative procedures such as intraperitoneal lavage or drain placement. There were no differences in the postoperative complications with C-D ≥ III, organ/space SSI, and the duration of abdominal drainage between the two periods. In the control period, the postoperative complications with C-D ≥ III (n = 3) included organ/space SSI required additional abdominal drainage (n = 2) and replacement of drainage tube (n = 1). In the COVID-19 period, those (n = 2) included organ/space SSI required additional abdominal drainage (n = 1) and replacement of drainage tube (n = 1). The postoperative additional abdominal drainage did not increase in the COVID-19 period. Conversely, superficial incisional SSI was significantly frequent (36.4% vs. 6.6%, P = 0.002). Accordingly, the length of hospital stay was significantly longer in the COVID-19 period than in the control period (7 vs. 4 days, P = 0.045) (Table 2).

Influence of CA on surgical outcome in the COVID-19 period

In both periods, BT at medical presentation, operation time, and length of hospital stay were significantly higher in CA than in UA. Among the UA patients, the time from symptom onset to surgery was significantly longer in the COVID-19 period than in the control period (2 vs. 1 day, P = 0.013). Accordingly, the time from symptom onset to surgery was longer, but not significant, in CA than in UA in the COVID-19 period. Among the CA patients, the BT at medical presentation was significantly higher (38.4°C vs. 37.6°C, P = 0.023), and the operation time was longer (92.5 vs. 71 min, P = 0.134) in the COVID-19 period than in the control period. However, more severe than C-D grade III postoperative complications did not increase, and the length of hospital stay was similar among both UA and CA patients (Table 3).

Discussion

In line with reports from various countries[16-18], this study showed a significant increase in CA, especially perforated AA, during the initial COVID-19 pandemic. However, to our knowledge, this is the first detailed study for AA in adults in a general community hospital with respect to spe-

Table 2. Surgical Findings and Postoperative Outcomes.

	Control period $n = 61$ (%)	COVID-19 period $n = 22$ (%)	P value
Surgical approach			1.000
Laparoscopy	51 (83.6%)	19 (86.4%)	
Laparotomy	10 (16.4%)	3 (13.6%)	
Conversion to laparotomy	0 (0%)	1 (4.6%)	0.265
Surgical procedure			0.250
Appendectomy	61 (100%)	21 (95.4%)	
Abdominal drainage	0 (0%)	1 (4.4%)	
Intraoperative abdominal drainage	13 (21.3%)	9 (40.9%)	0.094
Intraoperative findings			
Operation time, min*	52 (41–73)	79.5 (55.5–101)	0.003
Blood loss, ml*	10 (5–20)	10 (5–25)	0.905
Abscess formation	15 (24.6%)	16 (72.7%)	<0.001
Diffuse peritonitis	1 (1.6%)	4 (18.2%)	0.016
Postoperative diagnosis			
Complicated appendicitis	19 (31.2%)	14 (63.6%)	0.023
Perforated appendicitis	9 (14.8%)	9 (40.9%)	0.016
Gangrenous appendicitis	10 (16.4%)	5 (22.7%)	0.528
Postoperative complications			
C–D classification ≥ III	3 (4.9%)	2 (9.1%)	0.605
Superficial incisional SSI	4 (6.6%)	8 (36.4%)	0.002
Organ/space SSI	3 (4.9%)	2 (9.1%)	0.605
Postoperative additional drainage	2 (3.3%)	1 (4.6%)	1.000
Duration of drainage, days*	5 (4.5–7)	10 (7.5–13.5)	0.037
Length of hospital stay, days*	4 (3–6)	7 (3.5–11)	0.045

C–D, Clavien–Dindo; SSI, surgical site infection

*Data are expressed as median with interquartile range

Table 3. Association between CA and Surgical Outcomes.

COVID-19 period	UA $n = 8$ (%)	CA $n = 14$ (%)	P value
BT at medical presentation, °C*	37.0 ± 0.5	38.4 ± 0.9	<0.001
Time from symptom onset to surgery, days**	2 (1–2)	3 (1–7)	0.229
Operation time, min**	55 (44–79)	92.5 (71.5–111)	0.015
C–D grade ≥ III complication	0 (0%)	2 (14.3%)	0.515
Length of hospital stay, days**	2 (2–4)	10.5 (7–12.5)	<0.001

Control period	UA $n = 42$ (%)	CA $n = 19$ (%)	P value
BT at medical presentation, °C*	36.9 ± 0.8	37.6 ± 0.9	0.007
Time from symptom onset to surgery, days**	1 (1–1)	2 (1–4)	<0.001
Operation time, min**	46.5 (37.5–65.5)	71 (55–101)	<0.001
C–D ≥ grade III complication	0 (0 %)	3 (15.8 %)	0.027
Length of hospital stay, days**	3 (3–4)	8 (6–12)	<0.001

CA, complicated acute appendicitis; UA, uncomplicated acute appendicitis; BT, body temperature; C–D, Clavien–Dindo

*Data are expressed as mean ± standard deviations

**Data are expressed as median with interquartile range

cific behaviors of the patients and general practitioners in Japan. Although there was no restriction in our country to seek medical care during a state of emergency, our data highlighted both the patients' and medical practitioners' hesitancy to seek surgical care in the initial stage of the COVID-19 pandemic.

AA is the most common general surgical emergency worldwide[19]. The progression of appendiceal distention to perforation occurs in 20%-76% of cases and can impart significant morbidity[8,20]. Delay in presentation is a significant driver of perforation, with perforation rates increasing linearly with the duration of symptoms[21,22]. Previous studies showed that appendectomy delayed after 24 h from symptom onset was associated with increased postoperative complications[9,23]. This study showed that in the control period, patients who had presented within this 24 h window underwent surgery on the second day after symptom onset. In comparison, in the COVID-19 period, it took as long as 2-3 days after symptom onset to seek surgical treatment. Astonishingly, patients who resulted in CA had taken 4 days from symptom onset to undergo surgery. Therefore, the delay in medical presentation was suspected to be associated with the increased severity of AA. Furthermore, this study highlighted that the window time to intervene in a potentially preventable CA surgically had already been missed at the time of medical presentation in the COVID-19 period.

In the initial COVID-19 pandemic outbreak, Japan took the strategy to selectively test only the patients with the highest probability of contracting COVID-19 or with high-risk underlying conditions. People were encouraged to wait to see if pulmonary symptoms developed in the following few days before a medical consultation to prevent the COVID-19 outbreak in institutions with insufficient infection prevention measures. This was a potential reason that caused hesitation to seek medical attention in patients.

We have shown that not only the patients had been reluctant to seek medical treatment but also general practitioners had hesitated to introduce patients to our hospital. Regional healthcare centers had the role of deciding who could be tested and allocating where the patient should be treated. Since practitioners had to follow these instructions, they were more likely to have watched to see if the fever persisted and whether they needed to consult a healthcare center. Furthermore, since practitioners were not as easily able to test for COVID-19 as they are in 2022, when they saw patients with fever, they were unable to distinguish whether the fever was due to COVID-19 infection or appendicitis. At that time, our hospital was not equipped to treat COVID-19. These might be the reasons why practitioners hesitated to refer their patients to our hospital, even if abdominal symptoms may have been present.

Presenting with a fever was a crucial factor in surgical treatment delay. Indeed, this study showed that the time to medical presentation was significantly longer in patients with a fever of higher than 38°C. Furthermore, although CA had a significantly higher BT, it took longer to undergo surgery than UA. Among the patients with CA, the BT was significantly higher in the COVID-19 period than in the control period. Furthermore, the time from symptom onset to surgery was significantly longer in the COVID-19 period. Therefore, the severity of full-blown CA presumably worsened during the few days of wait and watch, and potentially avoidable CA may have developed in the few days of surgery delay. Fears of an unprecedented pandemic may have caused an overemphasis on fever and the ruling out of COVID-19, even in an obvious abdominal emergency such as AA.

Although many studies pointed out that the delay of medical presentation in the initial COVID-19 period was a potential cause of severity and morbidity in abdominal emergencies, only a few showed the actual time data from symptom onset to medical consultation. Cano-Valderrama et al. showed that the presentation to the emergency department was delayed for over 24 h during the COVID-19 pandemic period[7]. Willms et al. reported that medical consultation delayed over 48 h was significant in the COVID-19 risk group and the elderly[24]. This study showed detailed data on medical presentation delay in the COVID-19 period according to the route of surgical consultation or patients' symptoms.

In the COVID-19 period, there was no increase in severe morbidity and no mortality after surgery for AA compared with the control period. We showed that surgical treatment could be undergone safely despite the increase in CA. Appropriate treatment by abdominal drainage and antibiotic treatment prevented the increase of organ/space SSI and sepsis. Therefore, there was no increase in severe complications of C-D grade III or higher, which requires postoperative abdominal percutaneous intervention. Preservation of hospital resources is of utmost importance during the peak of the pandemic. Preventing an increase in postoperative complications will reduce the waste of medical resources. Therefore, this investigation demonstrates that the preservation of hospital resources could be accomplished consequently. Although CA significantly increased during the COVID-19 period, surgery was successfully undergone laparoscopically in most cases, and laparotomy conversion did not differ from the control period. Laparoscopic appendectomy for CA was associated with longer operation time, but as was reported before[25,26], it was feasible and safe and enabled versatile options such as conversion to abdominal drainage in a minimally invasive setting. So long as operation room capacity permits, laparoscopic appendectomy may be a useful procedure for CA even during a pandemic.

We acknowledge several limitations in this study. First, this was a retrospective cohort study conducted at a single

institution. To minimize selection bias, we included all patients who underwent surgery for AA in our hospital. Second, the study cohort may be too small to reach definitive conclusions. However, we included crucial details that cannot be obtained in a larger-scale study. Third, we investigated only patients who underwent surgery for AA. This did not include the patients who underwent conservative treatment. However, to our knowledge, this is the first detailed report from Japan, and our results show essential insights for all physicians treating AA in the context of our health system.

In conclusion, we highlighted the association between the delay of medical presentation and referral time followed by the increased severity of AA in the initial stages of the COVID-19 pandemic in Japan. However, CA could be safely treated. This indicated that it could be accomplished to prevent the excessive consumption of hospital capacity and medical resources. In a pandemic setting, it is all the more important to make a comprehensive assessment of abdominal emergencies to undergo surgical treatment promptly.

Acknowledgements

We appreciate Fumikazu Koyama (Nara Medical University) for his advice on useful discussions.

Conflicts of Interest

There are no conflicts of interest.

Author Contributions

Tadataka Takagi substantially contributed to the conception of the work and acquisition of the data. Tadataka Takagi and Shoichi Kinoshita drafted the work. Tadataka Takagi, Shoichi Kinoshita, Chihiro Kawaguchi, and Takao Ohyama performed the operation and final approval of the version to be published.

Approval by Institutional Review Board (IRB)

Institutional review board: Ethical Committee of Heisei Memorial Hospital

Review board approval number: 2021-010

References

1. Proposals for surgical procedures for patients positive or suspected for COVID-19 [Internet]. Tokyo: Japan Surgical Society (JP). 2020 Apr - [cited 2020 Apr 29]. Available from: https://www.jssoc.or.jp/aboutus/coronavirus/info20200402.html.
2. Miyo M, Hata T, Sekido Y, et al. Colorectal surgery in the COVID-19 pandemic era. J Anus Rectum Colon. 2022 Jan; 6(1): 1-8.
3. Okuno T, Takada D, Shin JH, et al. Surgical volume reduction and the announcement of triage during the 1st wave of the COVID-19 pandemic in Japan: a cohort study using an interrupted time series analysis. Surg Today. 2021 Nov; 51(11): 1843-50.
4. Wong EL, Hawkins EJ, Langness S, et al. Where are all the patients? Addressing covid-19 fear to encourage sick patients to seek emergency care. NEJM Catalyst Innovations in Care Delivery. 2020 May; 1(3): 1-2.
5. Bersano A, Kraemer M, Touze E, et al. Stroke care during the COVID-19 pandemic: experience from three large European countries. Eur J Neurol. 2020 Sep; 27(9): 1794-800.
6. Mafham MM, Spata E, Goldacre R, et al. COVID-19 pandemic and admission rates for and management of acute coronary syndromes in England. Lancet. 2020 Aug; 396(10248): 381-9.
7. Cano-Valderrama O, Morales X, Ferrigni CJ, et al. Acute care surgery during the COVID-19 pandemic in Spain: changes in volume, causes and complications. A multicentre retrospective cohort study. Int J Surg. 2020 Aug; 80: 157-61.
8. Bhangu A, Soreide K, Di Saverio S, et al. Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. Lancet. 2015 Sep; 386(10000): 1278-87.
9. Ditillo MF, Dziura JD, Rabinovici R. Is it safe to delay appendectomy in adults with acute appendicitis? Ann Surg. 2006 Nov; 244 (5): 656-60.
10. Ikeda N, Yamamoto H, Taketomi A, et al. The impact of COVID-19 on surgical procedures in Japan: analysis of data from the National Clinical Database. Surg Today. 2022 Jan; 52(1): 22-35.
11. Nishida Y, Otagiri N, Tauchi K. Emergency abdominal surgeries remain unchanged in the COVID-19 affected environment: a single-center experience at a community hospital in Japan. Acute Med Surg. 2021 Jan; 8(1): e623.
12. Orthopoulos G, Santone E, Izzo F, et al. Increasing incidence of complicated appendicitis during COVID-19 pandemic. Am J Surg. 2021 May; 221(5): 1056-60.
13. Zaikos TD, Boudiab EM, Peshel EC, et al. Acute appendicitis severity during the early COVID-19 pandemic period. Trauma Surg Acute Care Open. 2021 Aug; 6(1): e000809.
14. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004 Aug; 240(2): 205-13.
15. Stevenson KB, Khan Y, Dickman J, et al. Administrative coding data, compared with CDC/NHSN criteria, are poor indicators of health care-associated infections. Am J Infect Control. 2008 Apr; 36(3): 155-64.
16. Fisher JC, Tomita SS, Ginsburg HB, et al. Increase in pediatric perforated appendicitis in the New York city metropolitan region at the epicenter of the COVID-19 outbreak. Ann Surg. 2021 Mar; 273(3): 410-5.
17. Orthopoulos G, Santone E, Izzo F, et al. Increasing incidence of complicated appendicitis during COVID-19 pandemic. Am J Surg. 2021 May; 221(5): 1056-60.
18. Wichmann D, Schweizer U, Wulff D, et al. Incidence of perforated appendicitis during the COVID-19 pandemic: lessons to be considered in the second wave. J Gastrointest Surg. 2021 Sep; 25 (9): 2404-6.
19. GlobalSurg Collaborative. Mortality of emergency abdominal surgery in high-, middle- and low-income countries. Br J Surg. 2016 Jul; 103(8): 971-88.
20. Newman K, Ponsky T, Kittle K, et al. Appendicitis 2000: variability in practice, outcomes, and resource utilization at thirty pediatric hospitals. J Pediatr Surg. 2003 Mar; 38(3): 372-9.
21. Narsule CK, Kahle EJ, Kim DS, et al. Effect of delay in presenta-

tion on rate of perforation in children with appendicitis. Am J Emerg Med. 2011 Oct; 29(8): 890-3.
22. Papandria D, Goldstein SD, Rhee D, et al. Risk of perforation increases with delay in recognition and surgery for acute appendicitis. J Surg Res. 2013 Oct; 184(2): 723-9.
23. Giraudo G, Baracchi F, Pellegrino L, et al. Prompt or delayed appendectomy? Influence of timing of surgery for acute appendicitis. Surg Today. 2013 Apr; 43(4): 392-6.
24. Willms AG, Oldhafer KJ, Conze S, et al. Appendicitis during the COVID-19 lockdown: results of a multicenter analysis in Germany. Langenbecks Arch Surg. 2021 Mar; 406(2): 367-75.
25. Yau KK, Siu WT, Tang CN, et al. Laparoscopic versus open appendectomy for complicated appendicitis. J Am Coll Surg. 2007 Jul; 205(1): 60-5.
26. Garg CP, Vaidya BB, Chengalath MM. Efficacy of laparoscopy in complicated appendicitis. Int J Surg. 2009 Jun; 7(3): 250-2.