

[ORIGINAL ARTICLE]

Efficacy and Safety of a Strategy for Reviewing Intravenous Antibiotics for Hospitalized Japanese Patients with Uncomplicated Diverticulitis: A Single-center Observational Study

Kazumasa Soma¹, Dai Nakamatsu¹, Tsutomu Nishida¹, Yutaro Minoura¹, Miyoung Park¹, Ryo Sugio¹, Akino Okamoto¹, Tatsuya Sakamoto¹, Yuri Tsujii¹, Sho Yamaoka¹, Naoto Osugi¹, Aya Sugimoto¹, Kaori Mukai¹, Kengo Matsumoto¹, Masashi Yamamoto¹, Shiro Hayashi^{1,2}, Sachiko Nakajima¹, Koji Fukui¹ and Masami Inada¹

Abstract:

Objective Treatment for uncomplicated diverticulitis (UD) is not well established. We evaluated the strategy of reviewing intravenous antibiotics for hospitalized Japanese patients with UD.

Methods Treatment was based on the physician's choice until August 2018; the indications for hospitalization and treatment have been standardized since September 2018. In this study, we monitored the use of intravenous antibiotics administered to patients hospitalized for UD and then reviewed the need for them on hospital day 3. We compared patients' length of antibiotic use, hospital stay, health care cost, and complications via the review strategy from September 2018 to December 2020 and via the previous physicians' choice strategy from January 2016 to August 2018.

Results Two hundred and forty-seven patients were admitted to our hospital because of acute colonic diverticulitis from January 2016 to December 2020. After excluding complicated cases, 106 individuals were enrolled during the period of physician's choice; 87 were enrolled when treatment review was employed. There were no significant differences in age, sex, inflammation site, or severity during the first hospital visit. The median duration of antibiotic use was significantly reduced from 5 to 4 days ($p=0.0075$), with no marked increase in rates of transfer to surgery, mortality, or readmission due to recurrence. A more significant proportion of patients completed 3-day antibiotic treatment with the review strategy than with the physician's choice strategy (6.6% vs. 25.3%, $p=0.0004$). However, the length of hospital stay and total medical costs did not decrease.

Conclusion The strategy of reviewing treatment on day 3 after hospitalization for UD safety reduced the duration of antibiotic use, but the hospital stay and health care costs did not decrease.

Key words: uncomplicated diverticulitis, intravenous antibiotics, healthcare costs, hospital stay, acute diverticulitis

(Intern Med 61: 3475-3482, 2022)

(DOI: 10.2169/internalmedicine.9361-22)

Introduction

The mechanism underlying acute diverticulitis remains

unknown. However, it has been proposed that obstruction of the diverticulum's neck by fecal matter can trigger a cascade of events, including bacterial proliferation, local ischemia similar to appendicitis, and sometimes perforation (1). Acute

¹Department of Gastroenterology, Toyonaka Municipal Hospital, Japan and ²Department of Gastroenterology and Internal Medicine, Hayashi Clinic, Japan

Received: January 7, 2022; Accepted: March 28, 2022; Advance Publication by J-STAGE: May 7, 2022

Correspondence to Dr. Tsutomu Nishida, tnishida.gastro@gmail.com

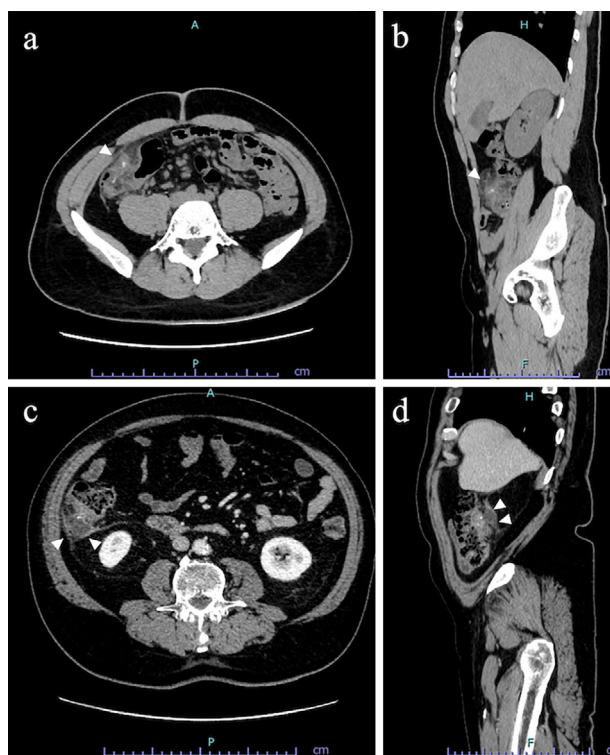


Figure 1. Computed tomography images for stage 1a (a: horizontal view, b: sagittal view) and suspected 1b (c: horizontal view, d: sagittal view) according to the modified Hinchey classification for the severity of acute diverticulitis. In the upper row, bowel wall thickening and pericolic inflammatory reactions with fat stranding pericolic fat (arrowheads, a, b) are observed, indicating stage 1a. In contrast, in the lower row, a small amount of fluid accumulation is noted around the diverticulum, which is confirmed to not be an abscess (arrowheads, c, d), without free air, indicating stage 1b.

diverticulitis can be classified as uncomplicated or complicated based on clinical, laboratory, and radiological findings, although most cases of diverticulitis are uncomplicated. Based on standard treatment, intravenous antibiotics should be continued until abdominal pain and tenderness are resolved, typically 3 to 5 days, followed by oral antibiotics for 10 to 14 days (2). Indeed, the need for antibiotics in cases of uncomplicated diverticulitis is acceptable in current clinical practice, according to the 2017 Japanese Colonic Diverticulosis Guidelines. However, the efficacy of antibiotic therapy among Japanese patients remains unclear. In addition, there are no specific descriptions regarding the dosage, administration route, or duration of antibiotics (3).

In clinical practice in Japan, patients with acute uncomplicated diverticulitis and moderate to severe symptoms are usually hospitalized for bowel rest, intravenous fluids, and intravenous antibiotics until their symptoms resolve, and this process does not always include a step down to oral antibiotics. Therefore, previous Japanese studies on patients with diverticulitis showed that hospital stays were approximately 8-10 days (4, 5). Although recent randomized controlled studies of uncomplicated diverticulitis have revealed no sig-

nificant differences in outcomes with or without antibiotics (6, 7), a rapid change to a no-antibiotic strategy is unacceptable because of the lack of evidence in Asian countries (3). In general, the duration of antibiotic treatment depends on the physician's judgment. However, how long antibiotics should be administered for uncomplicated diverticulitis in Japanese patients remains unclear, as there is insufficient evidence despite decades of clinical experience with antibiotic treatment for the condition.

Since September 2018, we have adopted a clinical pathway reviewing the need for intravenous antibiotics on hospital days 3 and 5 for patients with uncomplicated diverticulitis who require hospitalization. The practice was determined by a consensus meeting of board certified gastroenterologists at our hospital.

In this study, we evaluated whether or not reviewing treatment with intravenous antibiotics on hospital day 3 is safe and whether or not it reduces the length of hospital stay and medical costs for acute uncomplicated diverticulitis compared with the physician's choice strategy previously employed at the same hospital.

Materials and Methods

This was a single-center, retrospective study of patients with acute uncomplicated diverticulitis who were hospitalized at Toyonaka Municipal Hospital from January 2016 to December 2020. Our hospital is a mid-sized hospital with 613 beds that provides secondary care in an urban area of Osaka Prefecture, Japan.

Acute diverticulitis was diagnosed based on computed tomography (CT) findings showing consistent bowel wall thickening and fat stranding, abdominal pain, elevated white blood cell (WBC) counts, and C-reactive protein (CRP) levels during the first hospital visit. Cases of diverticulitis were classified as uncomplicated or complicated. Complicated diverticulitis was defined as the presence of complications associated with inflamed or infected diverticula, including bowel perforation, intra-abdominal abscess, intestinal obstruction, and fistula. We used the modified Hinchey classification for the severity of acute diverticulitis (8) and evaluated inflammatory sites according to specific CT findings. In this study, suspected cases with stage 1b disease were classified as uncomplicated cases (Fig. 1). We recommend that patients with diverticulitis be hospitalized when they are systemically unwell, immunosuppressed, or have significant comorbidities.

We excluded patients with complicated diverticulitis, those treated on an outpatient basis due to mild symptoms or no significant comorbidities, and those with suspected diverticulitis whose condition had not yet been confirmed by blood tests or CT. We enrolled patients with uncomplicated diverticulitis who were hospitalized for treatment in this study.

After admission, bowel rest, intravenous fluid infusion, and intravenous antibiotics were administered. Treatment for

patients with uncomplicated diverticulitis was based on the physician's choice until August 2018; since September 2018, we have used standardized criteria for hospitalization based on findings of ≥ 1 of the following characteristics: ≥ 75 years old, low activities of daily living, severe spontaneous pain, severe tenderness, peritonitis findings, a fever of $\geq 37.5^\circ\text{C}$, WBC count $\geq 10,000/\mu\text{L}$, and CRP level > 3 mg/dL.

After hospitalization, we followed a typical treatment strategy. We reviewed the treatment effect and antibiotic use; if antibiotics were not contraindicated, we administered cefmetazole 1 g intravenously twice a day as an empirical regimen under bowel rest for three days. On the third day of hospitalization, we reviewed antibiotics for discontinuation and began allowing the patient to eat solid foods if they showed all of the following findings of improvement: resolution of spontaneous pain, WBC count below its peak, and CRP level < 5 mg/dL. If a patient's condition had not improved, intravenous antibiotic therapy was continued, and the case was reviewed again on day 5. If the clinical condition deteriorated during treatment (e.g. deterioration of symptoms, reincrease in CRP level of > 2 mg/dL from the previous level and WBC count above the normal limit, or no improvement for more than 1 week), we reviewed the CT findings with or without contrast medium to evaluate the presence of complications.

Before August 2018, the indication for hospitalization of a patient with diverticulitis and treatment were determined by the attending physician based on disease severity, physical examination findings, and comorbidities or age. Details of the treatment based on the physician's choice included some of the review strategies, such as use of intravenous antibiotics and bowel rest; however, the kind of antibiotic and duration of administration, timing of the review and fasting duration were inconsistent.

We compared the clinical outcomes of the physician's choice strategy with the review strategy regarding safety and efficacy. Efficacy outcomes were the length of hospital stay, antibiotic use and total medical costs. Safety outcomes were surgery, readmission, and mortality rate. In addition, we evaluated the clinical characteristics of patients with uncomplicated diverticulitis who were treated for three days with intravenous antibiotics compared with those who needed intravenous antibiotics for four or more days. In this study, these determinations were made by the attending physician (gastroenterologist) who examined the patients and evaluated their condition.

Statistical analyses

Medians and interquartile ranges (IQRs) are reported for continuous variables. Categorical variables are summarized as frequencies (percentages). Differences in categorical variables were evaluated for statistical significance by Wilcoxon's signed-rank sum test, and differences in continuous variables were evaluated by Fisher's exact tests. All calculated p values were two-sided, and a p value < 0.05 was considered statistically significant.

All statistical analyses were performed using the JMP statistical software program (ver. 15.2.1, SAS Institute, Cary, USA).

Results

A total of 229 consecutive patients with 247 episodes of acute colonic diverticulitis diagnosed by CT who were admitted to Toyonaka Municipal Hospital from January 2016 to December 2020 were enrolled in this study. We excluded 36 patients with complicated cases diagnosed by CT: 35 underwent surgery, and 1 was treated conservatively. In addition, we excluded 18 cases of recurrence in the same patients during the overall study period. Ultimately, 106 individuals were enrolled during the period of the physician's choice strategy, and 87 were enrolled during the period of the review strategy (shown in Fig. 2).

There were no significant differences in patients' age, sex, comorbidities, drug use, severity of disease, WBC count, CRP level, or inflammation site at the first visit to the hospital between the physician's choice strategy and review strategy groups. However, the patients in the physician's choice strategy cohort showed higher first episode of diverticulitis and suspected stage 1b according to the modified Hinchey classification (6.6% vs. 0%, $p=0.0170$) (Table 1), although the median hospital stay with suspected stage 1b severity was 8 days, which was equal to that in cases of stage 1a during the study period (data not shown).

Efficacy and safety outcomes

Compared with the physician's choice strategy, the review strategy was associated with a significantly shorter duration of antibiotic use (median 5 vs. 4 days, $p=0.0075$), although the length of hospital stay was not significantly shortened (median 9 vs. 8 days, $p=0.2092$). During the hospital stay, there were no significant differences in duration until the disappearance of symptoms, WBC counts, fasting duration, or rate of using antibiotics between the two strategies, but more patients in the physician's choice strategy group had a peak fever over 38°C than did those in the review strategy cohort. In addition, a more significant proportion of patients in the review strategy completed treatment with 3-day antibiotic use than did those in the physician's choice strategy group (6.6% vs. 25.3%, $p=0.0004$) (Table 2). No patient who completed the 3-day antibiotic treatment during the review strategy experienced worsened symptoms or 30-day readmission.

Regarding adverse events (AEs) during the hospital stay, there were no significant differences in antibiotic-related AEs, including eruption or drug-induced liver dysfunction. In addition, there were no marked differences in the rate of patients transferred to surgery because of progression to a complicated status re-evaluated by CT. Furthermore, there was no mortality related to diverticular disease and no marked difference in readmission rates due to recurrence (Table 3). Among patients in the physician's choice strategy

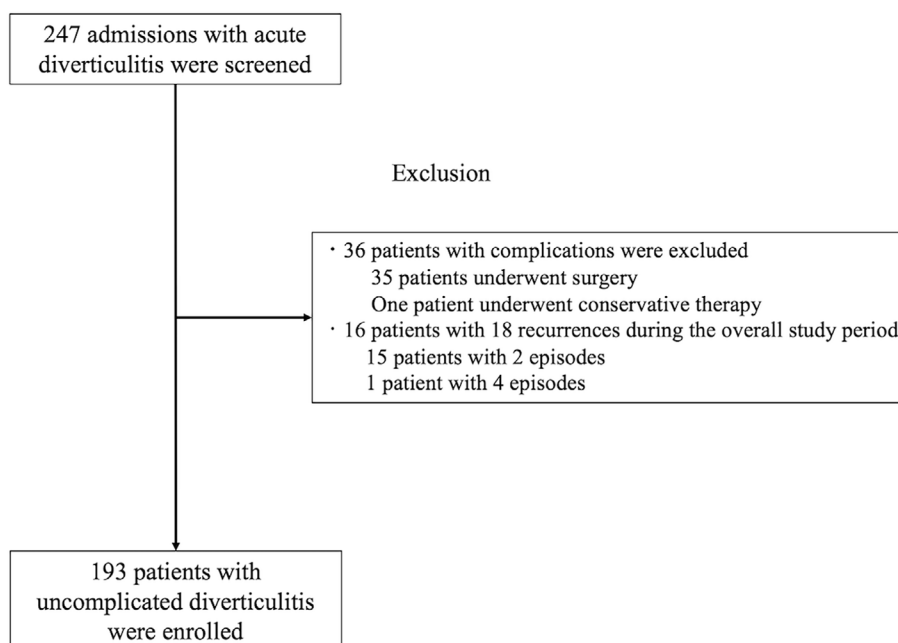


Figure 2. Flow chart of the patient inclusion and exclusion criteria.

group, one needed readmission and surgery due to complications from abscess formation within one month after discharge.

There were no significant differences between groups regarding total medical costs during the hospital stay.

Clinical characteristics of patients with uncomplicated diverticulitis who were treated for three days with intravenous antibiotics

Throughout the study period, compared with patients who needed more than four days of intravenous antibiotics, patients treated with three days of intravenous antibiotics were significantly more likely to be in the review strategy group than in the physician's choice strategy group. The short-term antibiotic use also had significantly lower temperatures at the first visit (36.8°C vs. 37.0°C, $p=0.0200$), lower WBC counts and CRP levels at the first visit, and a shorter recovery from symptoms. There were no significant differences in AEs or readmission due to recurrence of diverticulitis between the groups. Furthermore, the total medical costs in the short-term antibiotic use group did decrease significantly than in the long-term use (292,900 JPY vs. 332,090 JPY, a decrease of 11.8%, $p<0.0001$) (Table 4).

Discussion

We found that the strategy of reviewing intravenous antibiotic use on hospital day 3 for patients with uncomplicated diverticulitis reduced the interval of antibiotic use without increasing progression to a complicated status or AEs. Of note, hospital stay and total healthcare costs did not decrease significantly. However, changing treatment strategies might have increased the rate of 3-day intravenous antibiotic use from 6.6% to 25.3% for patients; with this reduced du-

ration of antibiotics administration, health care costs may also be reduced as well.

The present study showed that patients with uncomplicated diverticulitis needed approximately four days of intravenous antibiotics and hospitalization for eight days. In a previous sizeable Japanese cohort of 933 patients with uncomplicated diverticulitis, Manabe et al. reported a mean hospital stay of 9.2 ± 6.4 days (4); this was consistent with our results, although these authors did not report the details of antibiotic treatment (4). The hospital stay in Japan may be relatively long because, in clinical practice, we usually manage uncomplicated cases showing moderate to severe symptoms using intravenous antibiotics during hospitalization. In addition, we found that it was difficult to shorten the hospital stay, even when using the review of intravenous antibiotics strategy to reduce medical care costs, because we needed approximately four days to administer intravenous antibiotics based on improvements in symptoms and laboratory data.

Colonic diverticular disease is common, and the incidence is increasing. This condition is a fundamental cause of hospital admissions and a significant contributor to the healthcare burden in industrialized societies (9), and associated medical costs are estimated at \$2.6 billion USD per year (10). However, the management of patients with diverticular disease is not well established and involves administering the most clinically appropriate and cost-effective treatment.

Regarding uncomplicated diverticulitis, the Surgical Infection Society Guidelines 2002 state that treatment with intravenous antibiotics for five to seven days is as effective as more extended regimens for uncomplicated diverticulitis (11). Nevertheless, the latest revised guidelines in 2017 suggest that antibiotic therapy may not be necessary for

Table 1. Clinical Characteristics and Clinical Data of Hospitalized Patients with Diverticulitis on Admission in the Physician's Choice and Review Strategy.

| | Physician's choice strategy n=106 | Review strategy n=87 | p value |
|--|--------------------------------------|-------------------------|---------|
| Male sex, n (%) | 57 (53.8) | 49 (56.3) | 0.7721 |
| Age, (IQR), yr | 52 (41, 66.3) | 55 (43, 68.8) | 0.5280 |
| BMI, (IQR) | 22.3 (20.2, 25.3) | 22.4 (20.5, 24.9) | 0.8049 |
| First episode, n (%) | 91 (85.9) | 61 (70.1) | 0.0127 |
| Smoking habit, yes, n (%) * | 37 (43.5) | 25 (30.1) | 0.0803 |
| Drinking habit, yes, n (%) ** | 42 (49.4) | 48 (59.3) | 0.2162 |
| Comorbidities, n (%) | | | |
| Cardiovascular disease, n (%) | 7 (6.7) | 3 (3.5) | 0.3530 |
| Hypertension, n (%) | 28 (26.4) | 31 (35.6) | 0.2091 |
| Diabetes mellitus, n (%) | 6 (5.7) | 3 (3.5) | 0.5153 |
| Cerebrovascular disease, n (%) | 2 (1.9) | 4 (4.7) | 0.4115 |
| Atrial fibrillation, n (%) | 4 (3.8) | 4 (4.6) | 1.0000 |
| Lipid disorder, n (%) | 23 (21.9) | 19 (21.8) | 1.0000 |
| Drug use, n (%) | | | |
| NSAIDs, n (%) | 4 (3.8) | 3 (3.5) | 1.0000 |
| Antiplatelet drugs, n (%) | 9 (8.5) | 6 (7.0) | 0.7909 |
| Anticoagulants, n (%) | 6 (5.7) | 5 (5.9) | 1.0000 |
| Proton pump inhibitor, n (%) | 12 (11.3) | 8 (9.2) | 0.8130 |
| Laxative, n (%) | 9 (8.5) | 8 (8.9) | 1.0000 |
| Clinical symptom and laboratory data | | | |
| Body temperature at first visit, (IQR), °C | 37.1 (37.1, 38.1) | 36.9 (36.9, 37.7) | 0.1626 |
| Fever over 38°C at a hospital visit, n (%) | 11 (10.4) | 8 (9.2) | 0.8136 |
| Spontaneous pain, yes, n (%) | 106 (100) | 86 (98.9) | 0.4508 |
| Tenderness, yes, n (%) | 105 (99.1) | 86 (98.9) | 1.0000 |
| Rebound tenderness, yes, n (%) | 36 (34.0) | 23 (26.4) | 0.2758 |
| Hematochezia | 4 (3.8) | 3 (4.0) | 1.0000 |
| WBC count, (IQR),/μL | 11,450 (9,450, 13,800) | 12,600 (9,800, 14,400) | 0.2507 |
| CRP, (IQR), mg/dL | 5.49 (2.84, 9.73) | 5.12 (2.58, 9.21) | 0.7198 |
| Modified Hinchey classification, | | | |
| Stage 1a/suspected 1b | 99/7 | 87/0 | 0.0170 |
| Inflammation site, N (%) | | | 0.9385 |
| Right-sided n (%) | 70 (66.0) | 53 (60.9) | |
| Cecum, n (%) | 5 (5.8) | 4 (4.6) | |
| Cecum~ascending colon, n (%) | 7 (6.6) | 5 (5.8) | |
| Ascending colon, n (%) | 52 (49.1) | 40 (46.0) | |
| Ascending~transverse colon, n (%) | 1 (0.94) | 0 (0) | |
| Transverse colon, n (%) | 5 (4.7) | 4 (4.6) | |
| Left-sided, n (%) | 36 (33.9) | 34 (39.1) | |
| Descending colon, n (%) | 10 (9.4) | 11 (12.6) | |
| Descending sigmoid colon, n (%) | 3 (2.8) | 1 (1.2) | |
| Sigmoid colon, n (%) | 23 (21.7) | 22 (25.3) | |

IQR: interquartile range, NSAIDs: nonsteroidal anti-inflammatory drugs, WBC: white blood cell, CRP: C-reactive protein

*missing data n=25, **missing data n=27

low-risk patients with uncomplicated diverticulitis (12). In addition, based on a randomized control trial, oral antibiotics are not inferior to intravenous antibiotics in achieving a resolution of clinically diagnosed diverticulitis (13). The 2019 National Institute for Health and Care Excellence (NICE) guidelines recommend the current practice of treating an acute episode of diverticulitis with intravenous antibiotics in secondary care. If CT confirms no complications, switching to oral antibiotics does not affect outcomes. How-

ever, the guidelines recommend antibiotics for patients with uncomplicated diverticulitis because watchful waiting might increase recurrence and the probability of needing further surgery (14). Therefore, NICE recommends reviewing the need for intravenous antibiotics at a maximum of five days before deciding on further treatment.

Recently, the consensus of the underlying pathogenesis has shifted from bacterial infection to a more inflammatory process, and the use of antibiotics has recently been ques-

Table 2. Clinical Outcomes during the Hospital Stay in the Physician's Choice and Review Strategies.

| | Physician's choice strategy n=106 | Review strategy n=87 | p value |
|--|--------------------------------------|-------------------------|---------|
| Length of stay (IQR), days | 9 (7, 10) | 8 (7, 10) | 0.2092 |
| Peak body temperature, (IQR), °C | 37.5 (37.1, 38.1) | 37.2 (37.0, 37.7) | 0.0090 |
| Peak fever over 38°C, n (%) | 33 (32.7) | 15 (17.7) | 0.0282 |
| Time until the disappearance of spontaneous pain | 3 (2, 4) | 2 (2, 3) | 0.2352 |
| Time until the disappearance of abdominal tenderness | 3 (2, 5) | 4 (2, 5) | 0.1264 |
| Peak levels of WBC count, (IQR), μ L | 11,900 (9,450, 13,925) | 12,600 (9,900, 14,700) | 0.2215 |
| Peak levels of CRP, (IQR), mg/dL | 8.47 (5.25, 13.5) | 7.92 (4.72, 13.7) | 0.6843 |
| Reevaluation on CT, n (%) | 13 (12.3) | 14 (16.1) | 0.5329 |
| Treatment | | | |
| Bowel resting, yes, n (%) | 104 (98.1) | 85 (97.7) | 1.000 |
| Days of the fasting period, days | 4 (3, 5) | 4 (3, 5) | 0.5664 |
| Antibiotics | | | |
| Cefmetazole/others/none, n (%) | 88 (84.9)/16/2 | 80 (92.0)/7/0 | 0.1306 |
| Days of antibiotics-use, n (%) | 5 (4, 6) | 4 (3, 6) | 0.0075 |
| Use period for 3 days or no-use, n (%) | 7 (6.6) | 22 (25.3) | 0.0004 |
| Changes of antibiotics | 10 (9.8) | 9 (10.3) | 1.0000 |

IQR: interquartile range, WBC: white blood cell, CRP: C-reactive protein, CT: computed tomography

Table 3. Adverse Events and Medical Costs in the Physician's Choice and Review Strategies.

| | Physicians' choice strategy n=106 | Review strategy n=87 | p value |
|---|--------------------------------------|----------------------------|---------|
| Adverse events during the hospital stay | 11 (10.4) | 9 (10.3) | 1.000 |
| Eruption, n (%) | 2 (1.9) | 0 (0) | 0.5023 |
| Liver dysfunction, n (%) | 2 (1.9) | 3 (3.5) | 0.6592 |
| Transferred to surgery, n (%) | 3 (2.8) | 4 (4.6) | 0.7030 |
| Mortality, n (%) | 0 | 0 | N.A. |
| Readmission due to diverticulitis | | | |
| 1-wk readmission, n (%) | 0 (0) | 0 (0) | N.A. |
| 30-day readmission, n (%) | 1 (0.9)* | 0 (0) | 1.000 |
| 1-year readmission, n (%) | 3 (2.8) | 4 (4.6) | 0.7030 |
| Total medical costs, JPY | 328,727 (291,226, 376,680) | 324,850 (292,900, 375,118) | 0.8908 |

*Readmission within 30 days after discharge due to developing abscess formation.

tioned (15). Two retrospective studies with 311 and 272 patients with uncomplicated diverticulitis found that treatment without antibiotics appears to be safe (16, 17). A more recent double-blind, randomized controlled trial revealed the noninferiority of placebo compared with antibiotic management for uncomplicated acute diverticulitis, which supports omitting antibiotics in some patients presenting with uncomplicated acute diverticulitis (7). In secondary-care clinical practice in Japan, most cases of diverticulitis are evaluated by CT at the first visit. In the future, we should assess whether or not a strategy of oral antibiotics for patients with uncomplicated diverticulitis is feasible and safe for the Japanese population.

A recent meta-analysis revealed that the management of uncomplicated, right-sided diverticulitis is safe and feasible and that complications requiring urgent surgery are uncommon (18). Recent guidelines based on Western populations separate right- and left-sided uncomplicated acute diverticu-

litis (19). Right-sided diverticulitis is common in Asia, and the present study showed a higher rate of right-sided diverticulitis, accounting for approximately 60% of cases. There are no directions in the Japanese guidelines regarding the side of the affliction because there is a lack of relevant evidence in non-Western population. Therefore, we analyzed both sides of diverticulitis in this study. As evidence accumulates in the future, we may reduce antibiotic use for patients with right-sided diverticulitis without comorbidities. It is difficult to omit antibiotics in the real world, as intravenous antibiotics are practically a community standard in Japan. Regardless, we should assess the validity of omitting antibiotics for select patients in our region to shift toward a strategy of omitting or reducing antibiotics for patients without significant comorbidities in an effort to lower medical costs.

There are several limitations associated with this single-center retrospective study. First, the study cohort was small.

Table 4. Comparison of Clinical Outcomes of Short-term (≤ 3 Days) and Long-term (≥ 4 Days) Antibiotic Use.

| | Short-term use n=29 | Long-term use n=164 | p value |
|--|----------------------------|----------------------------|---------|
| Male sex, n (%) | 12 (41.4) | 94 (58.6) | 0.1557 |
| Physicians' choice/review strategy | 7/22 | 99/65 | 0.0004 |
| Age, (IQR), yr | 51 (38, 62) | 55 (42.5, 67.5) | 0.2440 |
| BMI, (IQR) | 22.0 (19.5, 24.5) | 22.4 (20.3, 25.0) | 0.5468 |
| First episode, n (%) | 21 (72.4) | 131 (79.9) | 0.4592 |
| Smoking habit, yes, n (%) * | 8 (30.8) | 54 (38.0) | 0.5172 |
| Drinking habit, yes, n (%) ** | 12 (46.2) | 78 (55.7) | 0.3979 |
| Comorbidities, n (%) | | | |
| Cardiovascular disease, n (%) | 1 (3.5) | 9 (5.5) | 1.000 |
| Hypertension, n (%) | 10 (34.5) | 49 (29.9) | 0.6639 |
| Diabetes mellitus, n (%) | 1 (3.5) | 8 (4.9) | 1.000 |
| Cerebrovascular disease, n (%) | 1 (3.5) | 5 (3.1) | 1.000 |
| Atrial fibrillation, n (%) | 1 (3.5) | 7 (4.3) | 1.000 |
| Lipid disorder, n (%) | 5 (17.2) | 37 (22.7) | 0.6304 |
| Drug use, n (%) | | | |
| NSAIDs, n (%) | 0 (0) | 7 (4.3) | 0.5970 |
| Antiplatelet drugs, n (%) | 2 (7.1) | 13 (7.9) | 1.000 |
| Anticoagulants, n (%) | 1 (3.6) | 10 (6.1) | 1.000 |
| Proton pump inhibitor, n (%) | 3 (10.3) | 17 (10.4) | 1.000 |
| Laxative, n (%) | 0 (0) | 16 (10.1) | 0.1340 |
| Clinical symptom and laboratory data | | | |
| Body temperature at first visit, (IQR), °C | 36.8 (36.6, 37.1) | 37.0 (36.6, 37.1) | 0.0200 |
| Spontaneous pain, yes, n (%) | 29 (100) | 163 (99.4) | 1.000 |
| Tenderness, yes, n (%) | 29 (100) | 162 (98.8) | 1.000 |
| Rebound tenderness, yes, n (%) | 8 (27.6) | 51 (31.1) | 0.8283 |
| WBC count, (IQR),/μL | 10,700 (8,650, 12,850) | 12,150 (9,900, 14,300) | 0.0455 |
| CRP, (IQR), mg/dL | 3.71 (0.81, 7.9) | 5.71 (3.08, 9.81) | 0.0209 |
| Length of stay, (IQR), days | 7 (5, 8) | 9 (7, 10) | <0.0001 |
| Fever over 38°C at a hospital visit, n (%) | 0 (0) | 19 (11.6) | 0.0832 |
| Peak fever over 38°C, n (%) | 2 (7.1) | 46 (29.1) | 0.0173 |
| Time until disappearance spontaneous pain, (IQR) | 2 (1, 2) | 3 (2, 4) | 0.0002 |
| Time until disappearance abdominal tenderness, (IQR) | 2 (1, 3) | 4 (2, 5) | 0.0012 |
| Peak levels of WBC count, (IQR),/μL | 11,000 (8,900, 13,000) | 12,250 (10,025, 14,850) | 0.0573 |
| Peak levels of CRP, (IQR), mg/dL | 5.01 (2.41, 8.46) | 8.83 (5.85, 13.98) | 0.0002 |
| Adverse events during the hospital stay | | | |
| Eruption, n (%) | 0 (0) | 2 (1.2) | 1.000 |
| Liver dysfunction, n (%) | 1 (3.5) | 4 (2.4) | 0.5611 |
| Transferred to surgery, n (%) | 0 (0) | 7 (4.3) | 0.5970 |
| Mortality, n (%) | 0 (0) | 0 (0) | N.A. |
| Readmission due to diverticulitis | | | |
| 1-wk readmission, n (%) | 0 (0) | 0 (0) | N.A. |
| 30-day readmission, n (%) | 0 (0) | 1 (0.61) | 1.000 |
| 1-year readmission, n (%) | 3 (10.3) | 4 (2.4) | 0.0705 |
| Total medical costs, JPY, (IQR) | 292,900 (230,387, 322,974) | 332,090 (296,158, 382,451) | <0.0001 |

IQR: interquartile range, BMI: body mass index, NSAIDs: nonsteroidal anti-inflammatory drugs, WBC: white blood cell, CRP: C-reactive protein

*missing data n=25, **missing data n=27

Second, the background of the patients managed with the physician's choice strategy might not have been the same as those managed with the review strategy because the indication of hospitalization was not unified, as judged by the physician. Patients with first episodes, smoking habits, a slightly higher body temperature at the first visit, and suspected stage 1b disease according to the modified Hinchey

classification were more likely to have been in the physician's choice strategy group than in the review strategy group. However, there were no marked differences in the sex, age, body mass index, comorbidities, drug use, other clinical symptoms, or laboratory data between groups. Therefore, we suspect that there was no significant impact on the results. Third, we did not decelerate to oral antibiot-

ics in this study. Recent guidelines recommend reviewing intravenous antibiotics within 48 hours or after scanning if sooner and dropping down to oral antibiotics when possible (14). In addition, the entire course of antibiotic treatment should be for a maximum of five days. In fact, NICE has determined five days as the optimum duration of antibiotic use based on current clinical practice, as the duration of antibiotics used in many studies is variable. Our study may support a shorter treatment duration with the review strategy, as our median duration of intravenous antibiotic use was four days. Next, we plan to adopt an oral antibiotic strategy or shorten the fasting duration to reduce medical costs where possible.

In conclusion, the strategy of reviewing treatment on day 3 after hospitalization for uncomplicated diverticulitis was able to safely reduce the duration of antibiotic use without increasing complications compared with the physician's choice treatment and might increase the proportion of patients who complete treatment with three-day antibiotic use.

This study was conducted in accordance with the Declaration of Helsinki, and approval was obtained from the Institutional Review Board of Toyonaka Municipal Hospital on April 12, 2021 (No. 2020-09-06). The requirement for informed consent was waived via the opt-out method on our hospital website.

The authors state that they have no Conflict of Interest (COI).

Acknowledgments

We thank Shigeki Hashida at Medical Professions Division, Toyonaka Municipal Hospital.

References

- Jacobs DO. Clinical practice. Diverticulitis. *N Engl J Med* **357**: 2057-2066, 2007.
- Pemberton JH. Acute colonic diverticulitis: medical management. Weiser M, Raghavendran K, Eds. UpToDate [Internet]. [cited 2021 Feb 2]. Available from: <https://www.uptodate.com/contents/acute-colonic-diverticulitis-medical-management>
- Nagata N, Ishii N, Manabe N, et al. Guidelines for colonic diverticular bleeding and colonic diverticulitis: Japan Gastroenterological Association. *Digestion* **99**: 1-26, 2019.
- Manabe N, Haruma K, Nakajima A, et al. Characteristics of colonic diverticulitis and factors associated with complications: a Japanese multicenter, retrospective, cross-sectional study. *Dis Colon Rectum* **58**: 1174-1181, 2015.
- Urabe M, Nishida T, Shimakoshi H, et al. Distinct clinical factors in hospitalized patients with diverticular bleeding and diverticulitis. *Digestion* **99**: 239-246, 2019.
- Chabok A, Pählman L, Hjern F, Haapaniemi S, Smedh K. Randomized clinical trial of antibiotics in acute uncomplicated diverticulitis. *Br J Surg* **99**: 532-539, 2012.
- Jaung R, Nisbet S, Gosselink MP, et al. Antibiotics do not reduce length of hospital stay for uncomplicated diverticulitis in a pragmatic double-blind randomized trial. *Clin Gastroenterol Hepatol* **19**: 503-510 e501, 2021.
- Kaiser AM, Jiang JK, Lake JP, et al. The management of complicated diverticulitis and the role of computed tomography. *Am J Gastroenterol* **100**: 910-917, 2005.
- Shaheen NJ, Hansen RA, Morgan DR, et al. The burden of gastrointestinal and liver diseases, 2006. *Am J Gastroenterol* **101**: 2128-2138, 2006.
- Peery AF, Dellon ES, Lund J, et al. Burden of gastrointestinal disease in the United States: 2012 update. *Gastroenterology* **143**: 1179-1187 e1173, 2012.
- Mazuski JE, Sawyer RG, Nathens AB, et al. The Surgical Infection Society guidelines on antimicrobial therapy for intra-abdominal infections: an executive summary. *Surg Infect (Larchmt)* **3**: 161-173, 2002.
- Mazuski JE, Tessier JM, May AK, et al. The Surgical Infection Society revised guidelines on the management of intra-abdominal infection. *Surg Infect (Larchmt)* **18**: 1-76, 2017.
- Ridgway PF, Latif A, Shabbir J, et al. Randomized controlled trial of oral vs intravenous therapy for the clinically diagnosed acute uncomplicated diverticulitis. *Colorectal Dis* **11**: 941-946, 2009.
- National Institute for Health and Care Excellence NICE guideline. Diverticular disease: diagnosis and management [Internet]. [cited 2021 May 11]. Available from: <https://www.nice.org.uk/guidance/ng147>
- Rezapour M, Stollman N. Antibiotics in uncomplicated acute diverticulitis: to give or not to give? *Inflamm Intest Dis* **3**: 75-79, 2018.
- de Korte N, Kuyvenhoven JP, van der Peet DL, Felt-Bersma RJ, Cuesta MA, Stockmann HB. Mild colonic diverticulitis can be treated without antibiotics. A case-control study. *Colorectal Dis* **14**: 325-330, 2012.
- Hjern F, Josephson T, Altman D, et al. Conservative treatment of acute colonic diverticulitis: are antibiotics always mandatory? *Scand J Gastroenterol* **42**: 41-47, 2007.
- Sartelli M, Catena F, Ansaloni L, et al. WSES guidelines for the management of acute left sided colonic diverticulitis in the emergency setting. *World J Emerg Surg* **11**: 37, 2016.
- Sartelli M, Weber DG, Kluger Y, et al. 2020 update of the WSES guidelines for the management of acute colonic diverticulitis in the emergency setting. *World J Emerg Surg* **15**: 32, 2020.

The Internal Medicine is an Open Access journal distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).