

ORIGINAL RESEARCH ARTICLE

## Prediction of Negative Outcomes in Non-Surgical Treatment for Appendiceal Abscess in Adults

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### Abstract:

**Objectives:** Non-surgical treatment is an acceptable approach for managing appendiceal abscess in adults. However, it is only applicable for selected patients, and conversion to surgery is mandatory for failed conservative treatment. This study aimed to determine the predictive factors for unsuccessful outcomes. **Methods:** Of 594 patients with acute appendicitis, 34 (5.7%) diagnosed with appendiceal abscess were initially treated conservatively. Patients were divided into two groups: the conservative group, which was successfully treated with antibiotics and percutaneous abscess drainage, and the conversion group, which comprised patients who had surgical conversion despite conservative treatment. Risk factors for the conversion group were investigated by comparing clinical and radiological parameters between the two groups. **Results:** Eight (23.4%) patients were converted to surgical management at an average of 5.5 days of non-surgical treatment. An abscess size greater than 40 mm and a lower rate of improvement in the white blood cell (WBC) count were significant factors for predicting conversion in multivariate analysis. The conversion group had a long operative time and high morbidity and operative conversion rates (change of proposed initial operation). Early conversion to operation group, i.e., less than 5 days of treatment, contributed to a significantly shorter hospital stay, lower hospital cost, and relatively shorter operative time ( $p = 0.02$ ,  $p = 0.04$ , and  $p = 0.11$ , respectively). **Conclusions:** Contributing factors in predicting unsuccessful outcomes for non-surgical treatment include an abscess size greater than 40 mm and a low rate of improvement in WBC count on the first day of antibiotic treatment.

### Keywords:

appendiceal abscess, non-surgical treatment, antibiotics treatment, unsuccessful outcomes, adults

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### Introduction

Acute appendicitis is one of the most common surgical diseases. Traditionally, management of patients with simple appendicitis is immediate appendectomy<sup>1)</sup>. However, in cases of appendiceal abscess, initial non-surgical management with or without interval appendectomy (IA) is selected because of its safety and effectiveness<sup>2,3)</sup>. This approach was

initially reported by Janik et al. in pediatric patients presenting with appendiceal mass<sup>4)</sup>. After their report, the indication for a non-surgical approach has expanded to adults as well, yet with more careful attention and consideration for malignancy.

The rationale of this approach is to avoid perioperative complications and the possibility of a more extensive operation such as hemicolectomy or ileocecectomy<sup>5)</sup>. Successful

rates for the initial non-surgical treatment have been reported to be high. However, the non-surgical approach is not always effective in all patients with appendiceal abscess. Non-surgical treatment has been shown to be unsuccessful in 7.2% of patients with appendiceal abscess and phlegmon in review studies<sup>5,6</sup>. Furthermore, some patients had to undergo an operation earlier than initially planned due to intractable infection<sup>7</sup>. These unsuccessful outcomes are associated with an increased complication rate and longer length of hospital stay.

Some studies examined this particular sub-set of failed non-surgical management in children and reported several predictors that affect negative outcomes, which include the following: presence of an abscess rather than phlegmon<sup>8</sup>, appendicolith<sup>9</sup>, and small bowel obstruction<sup>7,9</sup>. However, their results are varied and disparate. Furthermore, the population in these analyses was composed of children only. The treatment strategy for appendiceal abscess in adult patients is different from that in children due to the possibility of malignancy. This study aimed to clarify the predictors of conversion in non-operative management of appendiceal abscess in adults. In addition, we determined the operative outcomes of the conversion group compared with those of the conservative group with IA.

## Methods

An institutional review board approved the retrospective review of all initial non-surgical treatment for complicated appendicitis at the JCHO Kyushu Hospital of Japan. This study was designed as a retrospective study at a single tertiary care center. From January 2007 to December 2015, 594 adult patients were diagnosed with acute appendicitis in our institution. In order to confirm the diagnosis of acute appendicitis, a patient was subjected to a contrast computed tomography (CT) using a 64-slice multidetector-row CT scanner with reconstructed slice thickness (5 mm) (Aquilion Prime, Toshiba Medical Systems, Japan). If contrast CT imaging studies revealed appendiceal abscess suggesting complicated appendicitis, a non-surgical approach was approved. Patients below 15 years old or with signs and symptoms of generalized peritonitis, sepsis, or shock were immediately excluded from this study. Maximum abscess diameter (which includes the body of the appendix), presence of appendicolith, and identification of the appendix were precisely confirmed in the initial CT scan. If symptoms did not improve in 3-5 days after antibiotic treatment, then the treatment was determined to be non-effective. Those patients underwent a repeat imaging study (either a CT scan or ultrasonography). Percutaneous abscess drainage (PAD) was performed in some select patients, especially in those with increased abscess size on re-evaluation. However, if the abscess was inaccessible through PAD or if PAD was ineffec-

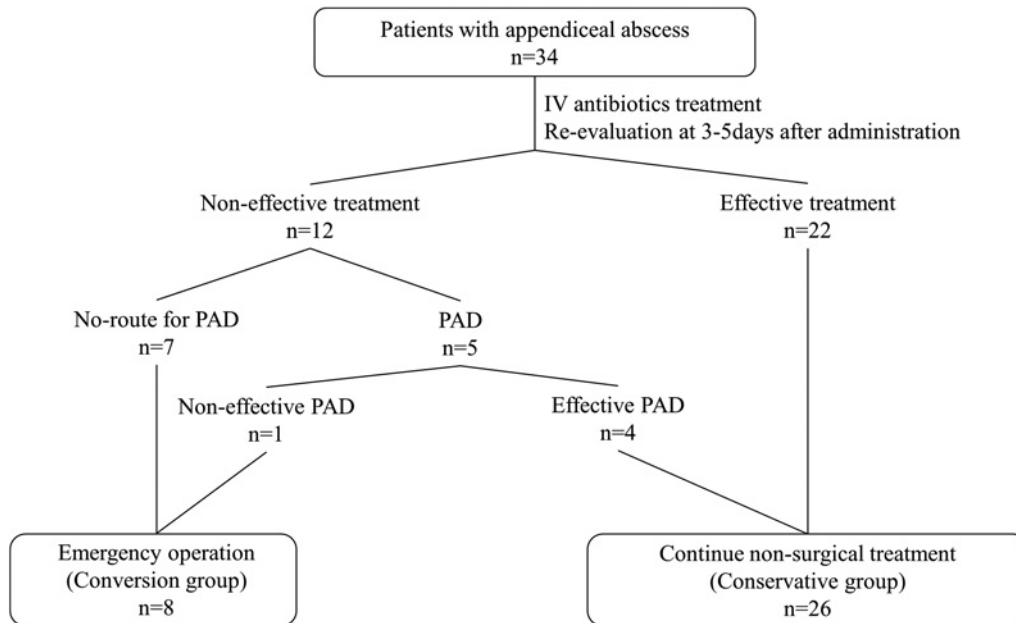
tive, the procedure was converted to a more invasive approach, e.g., laparoscopic or open surgery. These patients were classified as the “conversion group” and patients with manageable infection were classified as the “conservative group.” Some patients in the conservative group required IA a few months after the initial diagnosis and management.

Patient’s identifying data, including history of present illness and past medical histories, and physical examination findings were collected from clinical records. White blood cell (WBC) count (/ $\mu$ l), axillary body temperature (BT) ( $^{\circ}$ C), serum albumin levels (g/dl), and C-reactive protein (CRP) levels (mg/dl) were recorded at pretreatment, and on the first and third or fourth days of antibiotic treatment in each patient. The rate of improvement (%) in each parameter was calculated by dividing the posttreatment differential value by the pretreatment value. Statistical analysis was performed using the JMP Pro 12.2.0 software (SAS, Cary, NC, USA). A value of  $p < 0.05$  was considered statistically significant. Continuous and categorical variables were analyzed using the Wilcoxon signed-rank test and the Fisher’s exact test, respectively. The target variables in multivariate analysis were selected using the stepwise method. The cutoff value was determined using receiver operating characteristic analysis.

## Results

Of 594 adult patients with acute appendicitis, 34 (5.7%) patients were diagnosed with acute appendicitis with appendiceal abscess. These patients were initially treated with antibiotics and were re-evaluated 3 to 5 days from the initial treatment. Figure 1 shows the treatment algorithm of this study. Of the 34 subjects, 12 did not respond well to conservative treatment and, therefore, were placed in the “non-effective” treatment group. Among the “non-effective” treatment group, five underwent PAD; however, one of the patients was eventually converted to surgery (conversion group) due to inadequate PAD treatment. The initial seven conversion-group patients underwent surgery due to the following: inaccessible abscess wall, target area in close proximity to the intestine, and patient’s preference (informed consent). In summary, twenty-six (76%) patients in the conservative group treatment arm were successfully treated with antibiotics (with or without PAD), while eight (24%) patients eventually underwent surgery and were included in the conversion group due to inadequate and ineffective initial treatment during the observation period.

Table 1 shows the patient characteristics, which include clinical data, imaging studies, treatment, and hospital admission details of the study population. There were 18 males and 16 females, with a mean age of  $63.0 \pm 17.5$  years and body mass index of  $23.1 \pm 4.5$  kg/m<sup>2</sup>. History of diabetes mellitus and smoking were also recorded. No significant differences among the above-mentioned data were noted. CT



**Figure 1.** Study flow chart and treatment strategy for appendiceal abscess.

**Table 1.** Characteristics of the Patients at Admission.

Parameter	Population (N = 34)	Conservative Group (N = 26)	Conversion Group (N = 8)	<i>p</i> -value
Characteristics				
Age, mean ± SD, yr	63.0 ± 17.5	61.9 ± 18.2	66.5 ± 15.5	0.7
Sex (male/female)	18/16	14/12	4/4	1.00
Smoking history	4 (11.8%)	3 (11.5%)	1 (12.5%)	1.00
Diabetes mellitus	5 (14.7%)	5 (19.2%)	0 (0.0%)	0.31
Body mass index, mean ± SD, kg/m <sup>2</sup>	23.1 ± 4.5	23.6 ± 4.9	21.6 ± 2.7	0.26
CT parameters				
Appendicolith	8 (23.5%)	5 (19.2%)	3 (37.5%)	0.36
Abscess size >40 mm	20 (58.8%)	12 (46.2%)	8 (100.0%)	0.01*
Identification of appendix	26 (76.4%)	22 (84.6%)	4 (50.0%)	0.07
Treatment parameters				
PAD	5 (14.7%)	4 (15.4%)	1 (12.5%)	1.00
Antibiotics				
Carbapenem/lincomycin	10	7	3	0.56
Carbapenem	21	16	5	
Cephem	3	3	0	
Hospital stay, mean ± SD, days	14.5 ± 6.6	12.8 ± 5.4	19.9 ± 7.7	0.014*
Hospital cost, mean ± SD, US \$	6,936 ± 4,331	5,063 ± 1,825	13,024 ± 4,600	<0.001*

The *p*-value with an asterisk indicates statistical significance.

Abbreviations: CT, computed tomography; PAD, percutaneous abscess drainage

scan detected appendicolith in eight patients. At the same time, the appendix was not detected in eight patients due to complex abscess formation. Presence of appendicolith and non-detection of appendix did not show any significant differences. However, an abscess size greater than 40 mm was significantly associated with the conversion group ( $p = 0.01$ ). As initial treatment, most patients were administered the antibiotic carbapenem, while others received either a

combination of carbapenem/lincomycin, or a cephalosporin (Cephem). The type of antibiotic did not seem to have significance in the study. For patients requiring PAD after initial antibiotic treatment, also no significant difference was noted. The conversion group had a longer hospital stay and higher hospital cost than the conservative group ( $p = 0.014$  and  $p < 0.001$ , respectively).

Table 2 shows pretreatment and re-evaluation BT and

**Table 2.** Analysis of Parameters of the Conservative and Conversion Groups.

Parameter		Conservative Group (N = 26)	Conversion Group (N = 8)	p-value
Albumin (g/dl)	Pretreatment	3.6 ± 0.56	3.4 ± 0.80	0.95
WBC (µl)	Pretreatment	13,419 ± 4,112	13,750 ± 1,654	0.78
	1 <sup>st</sup> day	11,384 ± 3,698	13,200 ± 1,146	0.10
	3 <sup>rd</sup> -4 <sup>th</sup> days	8,165 ± 2,497	13,462 ± 3,361	<0.005*
CRP (mg/dl)	Pretreatment	14.5 ± 7.2	12.7 ± 4.3	0.51
	1 <sup>st</sup> day	13.8 ± 5.3	16.4 ± 8.8	0.71
	3 <sup>rd</sup> -4 <sup>th</sup> days	8.81 ± 4.72	14.6 ± 6.01	0.02*
BT (°C)	Pretreatment	37.9 ± 0.86	37.9 ± 0.54	0.88
	1 <sup>st</sup> day	37.4 ± 0.88	38.3 ± 0.78	0.014*
	3 <sup>rd</sup> -4 <sup>th</sup> days	36.9 ± 0.78	37.8 ± 0.70	<0.005*

Improving Rate (%)		Conservative Group (N = 26)	Conversion Group (N = 8)	p-value
WBC (µl)	1 <sup>st</sup> day	14.4 ± 17.3	3.1 ± 7.9	0.04*
	3 <sup>rd</sup> -4 <sup>th</sup> days	34.0 ± 28.2	1.56 ± 23.5	<0.005*
CRP (mg/dl)	1 <sup>st</sup> day	-16.0 ± 68.4	-17.8 ± 31.3	0.42
	3 <sup>rd</sup> -4 <sup>th</sup> days	9.6 ± 93.8	-18.7 ± 46.3	0.03*
BT (°C)	1 <sup>st</sup> day	1.24 ± 2.41	-0.99 ± 1.61	0.02*
	3 <sup>rd</sup> -4 <sup>th</sup> days	2.44 ± 2.32	-0.02 ± 2.68	0.03*

The p-value with the asterisk indicates statistical significance.

Abbreviations: WBC, white blood cell; CRP, C-reactive protein; BT, body temperature

**Table 3.** Multivariate Analysis for Negative Outcomes in Non-surgical Treatment.

Parameter	Odds Ratio	95% CI	p-value
Abscess size > 40 mm	18.3	1.46-727	0.022*
Improving rate in WBC at the 1 <sup>st</sup> day (%) (<10%)	27.4	2.38-1035	0.006*
BT at the 1 <sup>st</sup> day (>37.5°C)	11.4	0.90-435	0.06

The p-value with an asterisk indicates statistical significance

Abbreviations: WBC, white blood cell count; BT, body temperature; CI, confidence interval

laboratory results (serum albumin, WBC count, CRP). We recorded these data in order to analyze and predict parameters that affect negative outcomes. Results revealed that the WBC count, CRP levels, and BT in the conversion group were significantly higher than those in the conservative group on the third to fourth days of antibiotic treatment ( $p < 0.005$ ,  $p = 0.02$ , and  $p < 0.005$ , respectively). These findings correlated with a low rate of improvement in the WBC count, CRP levels, and BT in the conversion group on the same treatment days. Interestingly, these trends were also observed in the rate of improvement of the WBC count and BT on the first day of antibiotic treatment. These findings suggested that it might be possible to predict negative outcomes of the non-surgical treatment in the early phase. In the multivariate analysis, an abscess size greater than 40 mm and a lower rate of improvement in the WBC count (<10%) were significant factors for predicting negative outcomes ( $p = 0.02$  and  $p = 0.006$ , respectively; Table 3).

The conservative group had a follow-up of up to 6 months after the initial treatment. A total of 15 (58%) patients eventually underwent surgery. Among these patients, three were diagnosed with malignancy and underwent radical operation with lymphadenectomy, while the other 12 patients underwent IA. Table 4 shows a comparison of the operative cases in both groups. The operative time, operative conversion rate (change of proposed initial procedure), and complication rate were significantly higher in the conversion group than in the conservative group with IA ( $p = 0.011$ ,  $p < 0.001$ , and  $p = 0.033$ , respectively). There were no significant differences in the total hospital stay and cost between the two groups. The operative details of the conversion group are shown in Table 5. Patients in the conversion group had an average preoperative hospital stay of 5.5 days. A short preoperative period of less than 5 days (Patients #5-8) contributed to a significantly shorter hospital stay, lower hospital cost, and relatively shorter operative time than a

**Table 4.** Analysis of Parameters of Patients who Had a Radical Operation in the Conservative and Conversion Groups.

	Conservative Group (N = 15)	Conversion group (N = 8)	<i>p</i> -value
Operative time, mean $\pm$ SD (min) (exclude three for revealed colon cancer)	135 $\pm$ 64	200 $\pm$ 47	0.011*
Operative conversion	0 (0.0%)	6 (75.0%)	<0.001*
Laparoscopic operation	13 (87%)	4 (50%)	0.06
Perioperative complication	1 (6.7%)	4 (50.0%)	0.033*
Surgical site infection	0	1	
Postoperative paralytic ileus	1	1	
Liver dysfunction	0	1	
Intra-abdominal bleeding	0	1	
Mortality	0 (0.0%)	0 (0.0%)	-
Malignancy	3 (20.0%)	0 (0.0%)	0.52
Total hospital stay, mean $\pm$ SD (days)	21.3 $\pm$ 7.9	19.9 $\pm$ 7.7	0.50
Total hospital cost, mean $\pm$ SD (US \$)	12,436 $\pm$ 4,625	13,024 $\pm$ 4,600	0.53

The *p*-value with an asterisk indicates statistical significance.

long preoperative period of more than 5 days (Patients #1-4) ( $p = 0.02$ ,  $p = 0.04$ , and  $p = 0.11$ , respectively).

## Discussion

The non-surgical approach is an effective strategy for managing appendiceal abscess in children and adults<sup>10-13</sup>. The success rate of this approach is relatively high, ranging from 80% to 95%<sup>2,3</sup>. However, conversion to surgery is sometimes unavoidable for patients with uncontrollable infection. In such cases, a high complication rate, extended hospital stay, and increased hospital cost are expected. Therefore, identifying predictors and parameters that affect negative outcomes of the non-surgical approach at the initial treatment is necessary. In the present study, the rate of an unsuccessful outcome (23.5%) was slightly higher than that described in a previous review (5%-20%)<sup>5</sup>. The reason for this discrepancy between studies might be partially because the present study targeted only patients with appendiceal abscess, while the review also included patients with phlegmon.

In our study, an abscess size greater than 40 mm and a low rate of improvement in the WBC count on the first day of antibiotic treatment were significant factors for predicting a negative outcome. Our findings suggest that non-surgical treatment can be abandoned at an early stage in the presence of these two factors. An abscess size greater than 40 mm is an available parameter before non-surgical treatment. Non-surgical treatment required PAD in approximately 20% of the patients<sup>5,14</sup>. In this study, PAD was performed in 14% of the patients. We could not perform PAD in some patients despite a large appendiceal abscess due to inaccessibility. Hence, we should be prudent in applying non-surgical treat-

ment for patients with a large appendiceal abscess that have no route for aspiration.

The rate of improvement of the WBC count is an important factor for determining the effectiveness of antibiotic treatment. New efficient antibiotics have also provided new opportunities for non-surgical treatment of appendicitis. We used carbapenem for most patients with appendiceal abscess. An effective choice of antibiotics is important as an initial treatment for it can help decide whether to continue the non-surgical treatment or abandon it<sup>9,15</sup>.

We did not show the differences in the total hospital stay and hospital cost between the conversion and conservative groups with IA due to several factors. First, most patients were treated using antibiotics and dietary restriction alone, which can contribute to longer hospital stays. Only a few patients required PAD. Second, the Japanese public health insurance system (national health insurance) covers 70%-90% of all medical costs. Lastly, early discharge is not a priority because some patients may opt to stay longer (i.e., the average length of hospital stay for IA in this study was 8.7 days, albeit most of the operations were done laparoscopically). However, an unsuccessful non-surgical treatment contributed to longer operative time, high conversion rate, and high perioperative complication rate. The most important aspect of this study is to consider the successfulness and unsuccessfulness of non-surgical treatments in the early phase. Despite the small sample size, this study showed that the hospital stay and cost might have decreased if the conversion group abandoned the non-surgical treatment in the early stage of treatment. Further investigation, including a randomized controlled trial, may be required.

We do recognize that our study has several limitations. Firstly, it is a retrospective study and, therefore, it is limited

**Table 5.** Characteristics of the Conversion Group.

#	Sex	Age	BMI	ASA	Preoperative Periods (days)	Hospital Stay (days)	Hospital Cost (US \$)	Operation Time (min)	Operation Methods	Perioperative Complication
1	Male	62	20	1	9	27	14,909	278	LAP-Appendectomy → LAP-Ileocecal Resection	Postoperative Paralytic Ileus
2	Male	71	25	2	7	28	22,220	264	LAP-Appendectomy → Open-Appendectomy	Intra-Abdominal Bleeding
3	Female	76	21	2	7	19	11,912	199	LAP-Appendectomy	None
4	Female	75	18	3	7	31	14,456	172	Appendectomy → Ileocecal Resection	Surgical Site Infection
5	Male	61	21	2	5	14	9,117	175	LAP-Appendectomy → Open-Appendectomy	Liver Dysfunction
6	Female	41	26	1	3	11	7,921	192	LAP-Appendectomy → Open-Appendectomy	None
7	Female	54	20	1	3	13	9,325	172	LAP-Appendectomy	None
8	Male	92	22	2	3	16	14,338	147	LAP-Appendectomy → LAP-Ileocecal Resection	None

Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiologists; LAP, laparoscopy.

by the accuracy and completeness of the original documentation. Secondly, the study population was relatively small, with only 34 patients with non-surgical treatment. With these limitations acknowledged, it may still be considered that the study's findings are noteworthy for managing appendiceal abscess in adults.

On the basis of the abovementioned results, conversion to an operation in the early period contributes to a lower rate of operative complications and a decrease in the total hospital stay and cost. Factors that may allow predicting negative outcomes for non-surgical treatment include an abscess size greater than 40 mm and a low rate of improvement in the WBC count on the first day of antibiotic treatment. These findings suggest that these patients may need a modified treatment strategy.

**Author contributions**

Substantial contributions to the conception or design of the work, or acquisition, analysis, or interpretation of data for the work: YS, SD, SM, SI, SN, HK, and AS.

Drafting the work or revising it critically for important intellectual content: YS, SD, JC, MI, TK, AU, and MN.

Final approval of the version to be published: YS, SD, SM, SI, SN, HK, AS, JC, MI, TK, AU, and MN.

**Conflicts of Interest**

There are no conflicts of interest.

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