Therapeutic Consideration of Periappendiceal Abscess: an Evaluation of Non-surgical Treatment Followed by Minimally Invasive Interval Appendectomy

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Purpose: Periappendiceal abscess (PAA) is a severe complicated appendicitis with high morbidity. Non-surgical treatment followed by interval appendectomy (IA) is associated with lower complication rate compared with emergency surgery (ES) and minimally invasive surgery (MIS) can be done more often. The purpose of this study is to assess the incidence and factors predictive of complications of surgery for PAA and to evaluate the clinical effectiveness of IA as a treatment policy to increase MIS.

Methods: Retrospectively, we reviewed 171 patients undergoing surgery for PAA between 2011 and 2016 at Ulsan University Hospital. The incidence and influence of different factors were assessed by univariate and multivariate analyses.

Results: In 171 patients, 28 (16.4%) developed postoperative complications, which included: wound complications (7.6%), intra-abdominal abscess (4.1%) and ileus (2.9%). In both analyses, only ES was independently associated with postoperative complications: (Relative risk, 15.0; 95% Confidence interval, 2.4~92.5). Comparing the IA and ES groups revealed that operative time, complication rate, laparoscopic approach, postoperative hospitalization, postoperative antibiotic use and bowel resection rate were significantly different. The postoperative complication rate of patients with PAA in ES group was 28.7%, which was statistically higher than that of IA group (3.6%). Especially, MIS rate was more than 9-times greater in the IA group (98.8% vs. 10.3%, $p < 0.001$). Although the IA group required additional hospitalization, there was no statistical difference between the two groups in total length of hospital stay.

Conclusion: Morbidity was high for patients who had emergency surgery for PAA. ES was the only factor associated with postoperative morbidity. IA can reduce the postoperative complication rate and allowed MIS to be used more often as a useful treatment policy for PAA.

Keywords: Periappendiceal abscess, Non-surgical treatment, Minimal invasive surgery, Interval appendectomy

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INTRODUCTION

Acute appendicitis should be considered first for adult or pediatric patients who present with acute abdominal symp-

oms. Most will need surgery. A meta-analysis of 61 observational studies in which periappendiceal abscess (PAA) or phlegmon was present in 3.8% of patients with appendicitis found that emergency surgery (ES) as associated with mor-

bidity in 35.6% compared with that in 13.5% with nonsurgical treatment, which has considerable influence on treatment policy and cost remarkably.¹

Conservative management using antibiotics alone and image-guided percutaneous drainage for patients with PAA has achieved high success rates of 76% to 97%, with a low incidence of complications.²⁻⁸

After achieving complete resolution of the inflammatory mass with non-surgical treatment, interval appendectomy (IA) is a less hazardous and less challenging operation, compared with ES. However, IA requires extra hospitalization for surgery and can take a long time from the time of illness to the end of treatment.^{9,10}

In this study, we tried to assess the incidence and the type of postoperative complications in patients who underwent surgery for PAA, and evaluated the risk factors of postoperative morbidity. In addition, we explored the clinical usefulness of non-surgical treatment followed by IA to increase the rate of minimally invasive surgery (MIS).

MATERIALS AND METHODS

A total of 2,392 patients underwent a surgery for appendicitis at OOO Hospital between January 2010 and May 2016. Of these 2,392 patients, we identified 180 consecutive patients who underwent surgery for established acute appendicitis accompanied by PAA and retrospectively reviewed our prospectively collected database of patients with PAA. We excluded patients diagnosed as malignancy (1), who were pregnant (1), or received other combined operations (3) and already had Crohn's disease (4). Finally, total of 171 patients

met the study criteria (Fig. 1). The OOO Hospital Institutional Review Board approved this study. Patients with appendicitis with well-circumscribed abscess were indicated to have non-surgical treatment followed by IA. Between January 2010 and March 2011, patients with PAA underwent emergency surgery because non-surgical treatment strategies were not applied in our center. After performing the first case of non-surgical treatment followed by IA in 2011, non-surgical treatment strategy was adopted between April 2011 and May 2016 (Fig. 1). We excluded patients diagnosed as malignancy (1), who were pregnant (1), or received other combined operations and already had Crohn's disease. Finally, we selected 171 patients.

The diagnosis of complicated appendicitis with abscess was based on the patient's history, physical examination, and imaging modality (computed tomography (CT) or ultrasonography) findings showing a well circumscribed abscess. In cases of negative CT findings and highly suspicious signs and symptoms, ultrasonography was considered for further evaluation. CT was also considered in cases of negative ultrasonography findings. All ultrasonographic examinations and image readings were performed by radiologists. All operations were performed by four surgeons (two residents and two colorectal surgeons). All of them were qualified, experienced surgeons who performed more than 100 cases of appendicitis including complicated appendicitis. All residents performed surgery under the supervision of a colorectal surgeon.

In non-surgical treatment, patients with PAA were received intravenously with a combination of two antibiotics (3rd generation cephalosporin and metronidazole) until the afebrile, normalization of white blood cell count and C-reactive protein (CRP). Percutaneous drainage (PCD) can be inserted if

Fig. 1. Patient selection and study flow chart.

anatomically applicable. Patients were discharged when pain and a soft diet was tolerated. After 4 weeks of discharge, abdominal CT scan was performed to evaluate the improvement of the abscess and to exclude malignancy. Usually, an interval appendectomy was performed after 6 to 8 weeks of discharge.

Patient characteristics that were analyzed were age, gender, presence of significant comorbidities (i.e., diabetes mellitus, hypertension, coronary heart disease, respiratory disease, nephropathy and liver cirrhosis), history of previous abdominal surgery, duration of initial presenting symptoms, and operative time.

Surgical outcomes were determined by postoperative follow-up. To evaluate the rate of adverse events, we examined the complication rate occurring within 30 days and the readmission rate. Complications were defined as all events necessitating diagnostic or therapeutic measures that increased the length of stay, or required a patient to visit the outpatient clinic on more than two occasions, or led to readmission. Readmission was defined as repeated hospitalization caused by appendectomy-induced complications. Postoperative complications included wound infections, intra-abdominal abscess, intestinal obstructions, paralytic ileus, and cardiovascular problems. Intra-abdominal abscess was confirmed by percutaneous drainage or either CT scan or ultrasonography. Postoperative complications were graded according to the Clavien-Dindo classification.

Postoperative hospital stay was defined as the period of admission for appendectomy.

The main analyses were based on comparisons of patients who experienced postoperative complication with patients who

had no complication after surgery, and patients who had different procedures (ES vs. IA). The chi-squared test and Student's t-test were used for univariate analyses for categorical and continuous variables. Multivariate logistic regression models were used to identify independent predictors of morbidity following surgery. Factors with a p value <0.05 on univariate analysis were incorporated into a multivariate analysis. Statistical significance was defined as a $p < 0.05$. Statistical analysis was done using SPSS 21.0 software (SPSS, Chicago, IL, USA).

RESULTS

The study population included 94 males (54.9%) and 77 females (45.1%). The median of 171 patients in the study group was 47 years (range, 5~92 years). The median postoperative hospital stay was 5 days (range, 2~37 days).

At the time of the surgery, 62 (36.2%) patients had comorbidities including hypertension, diabetes mellitus, chronic renal disease, arrhythmia, and other cardiovascular problems. Hypertension was the most common pre-existing condition (46.0% of comorbidities), followed by diabetes mellitus, nephropathy and coronary artery disease.

In 171 patients, 28 (16.4%) developed postoperative complications. Incidence and type of postoperative complications in patients with PAA are shown in Fig. 2. There was no mortality. In the Clavien-Dindo classification, grade II complications (7.0%) were the most common, followed by grade III (5.3%) and grade I (4.1%). There were no grade IV or V complications. Of the 28 patients who experienced postoperative complications, wound infection (7.6%) had the highest incidence in

Fig. 2. Incidence and type of postoperative complications in patients with peri-appendiceal abscess (flow chart).

the total patient, followed by intra-abdominal abscess (4.1%), paralytic ileus (2.9%), and small bowel obstruction (1.2%). More rarely, small bowel obstruction caused by postoperative adhesion and cardiovascular problem (atrial fibrillation) occurred. Seven patients (4.1%) were re-admitted with wound complications (1.8%), intra-abdominal abscess (1.2%), paralytic ileus (0.6%), and small bowel obstruction (0.6%), respectively. There were 8 patients (4.7%) who underwent reoperation and, four of them received reoperation during hospitalization before discharge. Six (3.5%) patients developed complications that required reoperations due to wound complication (wound infection and dehiscence). And two (1.2%) patients required reoperation due to small bowel obstruction.

Comparisons of demographics and preoperative charac-

teristics between patients with and without complications are shown in Table 1. Univariate analysis revealed that preoperative factors significantly associated with postoperative complication were open surgery and ES ($p < 0.001$, both). No other preoperative factor was associated with an increased risk of postoperative complication, including patient age, sex, comorbidities, past operative history, and use of percutaneous drainage. There were no statistical differences in duration between the first presentation of symptom and operation (three or more days; five or more days; seven or more days). There was also no difference in the diameter of intra-abdominal abscess in CT (≥ 3 cm; ≥ 5 cm; ≥ 7 cm). In multivariate analysis, ES was identified as the only independent factor of postoperative complication (Relative risk, 15.0; 95% Confidence interval, 2.4~92.5) (Table 2).

Operative characteristics and postoperative outcomes according to the treatment strategies (IA and ES), that display significant differences included laparoscopic approach, postoperative hospital stay, total antibiotics use, and postoperative use of antibiotics (Table 3). The postoperative complication rate of patients with PAA in ES group was 28.7%, which was statistically higher than that of IA group (3.6%). Especially, laparoscopic surgery was performed more frequently in the IA group. There was only one case (1.2%) of open conversion due to severe adhesion in the IA group, which was the only open case in the IA group. Of the 17 cases that were initiated with laparoscopic surgery in the ES group, 8 cases (47.1%) were converted to open surgery. Among these parameters, except for total antibiotics use, negative outcomes were evident in the ES group. Although the number of days of antibiotics use after surgery was statistically significantly shorter in the IA group ($p < 0.001$), the total number of days of antibiotics use including the preoperative admission period was longer in the IA group ($p < 0.001$). There was no statistically significant difference between the two groups during the entire hospitalization period, although there was additional preoperative admission period for antibiotic treatment in the IA group (9.7 ± 4.2 vs. 9.7 ± 5.6 , $p = 0.949$) (Table 3).

Table 1. Demographic and clinical characteristics

Characteristics	No. of patients (%)		<i>p</i> value ^a
	No complication (n = 143)	Complication (n = 28)	
Age (mean $\pm$ standard deviation)	46.5 $\pm$ 21.1	44.7 $\pm$ 21.6	0.681
Age (≥ 60 years)	39 (27.3%)	5 (17.9%)	0.353
Gender (male)	80 (55.9%)	14 (50.0%)	0.679
Comorbidity	55 (38.5%)	7 (25.0%)	0.203
Cardiovascular disease	41 (28.7%)	6 (21.4%)	0.496
Previous operative history	22 (15.4%)	2 (7.1%)	0.375
PCD insertion	13 (9.1%)	1 (3.6%)	0.471
Symptom			
≥ 3 days	115 (80.4%)	21 (75.0%)	0.608
≥ 5 days	78 (54.5%)	17 (60.7%)	0.678
≥ 7 days	61 (42.7%)	12 (42.9%)	1.000
Abscess			
≥ 3 cm	92 (64.3%)	18 (64.3%)	1.000
≥ 5 cm	42 (29.4%)	7 (25.0%)	0.820
≥ 7 cm	17 (11.9%)	5 (17.9%)	0.366
Surgical approach			
Open surgery	57 (72.2%)	6 (6.5%)	< 0.001
Laparoscopic surgery	86 (93.5%)	22 (27.8%)	
Treatment method			
Emergency surgery	62 (43.4%)	25 (89.3%)	< 0.001
Interval appendectomy	81 (56.6%)	3 (10.7%)	

^aCross-table analysis using Fisher's exact test; PCD = percutaneous drainage. Bold print, $p < 0.05$.

Table 2. Multivariate analysis of risk factors

Parameters	Relative risk	95% confidential interval	<i>p</i> value ^a
Age (≥ 60 years)	2.992	0.928 ~ 9.642	0.066
Gender (male)	0.667	0.275 ~ 1.616	0.370
Open surgery	1.306	0.293 ~ 5.819	0.726
Emergency surgery	15.074	2.456 ~ 92.505	0.003

^aMultivariate analysis using the binary logistic regression analysis. Bold print, $p < 0.05$.

Table 3. Operative characteristics and postoperative outcomes according to the treatment strategies

Parameters	No. of patients (%)		<i>p</i> value ^c
	IA ^a (n=84)	ES ^b (n=87)	
Operative time (min)	64.1 ± 30.5	106.6 ± 41.3	<0.001
Laparoscopy (number)	83 (98.8)	9 (10.3)	<0.001
Hospital stay for non-surgical treatment	6.9 ± 3.5	0	-
Postoperative stay (day)	2.7 ± 1.6	9.7 ± 5.6	<0.001
Total stay (day)	9.7 ± 4.2	9.7 ± 5.6	0.949
Postoperative antibiotics use (day)	7.8 ± 2.8	12.6 ± 8.8	<0.001
Total antibiotics use (day)	26.3 ± 10.3	12.6 ± 8.8	<0.001
Re-admission	0 (0.0)	7 (8.0)	0.008
Re-operation	0 (0.0)	8 (9.2)	0.004
Bowel resection	1 (1.2)	4 (4.6)	0.186
Extended incision	0 (0.0)	5 (5.7)	0.026
Postoperative complication	3 (3.6)	25 (28.7)	<0.001
Wound complication	3 (3.6)	10 (11.5)	0.046
Intra-abdominal Abscess	0	7 (8.0)	0.008
Paralytic ileus	0	5 (5.7)	0.026
Mechanical obstruction	0	2 (2.3)	0.162
Cardiovascular problem	0	1 (1.1)	0.324
Clavien-Dindo Classification (≥3)	0	9 (10.5)	0.002
Postop hospital visit (time)	1.1 ± 0.7	1.6 ± 1.4	0.008

^aIA = Interval appendectomy; ^bES = Emergency surgery; ^cCross-table analysis using Fisher's exact test. Bold print, *p* < 0.05.

Fig. 3. Annual variation in the number of postoperative complications according to treatment strategy. (A) Number of annual surgeries for patient with periappendiceal abscess. (B) Number of annual postoperative complications in patients with periappendiceal abscess. ES = emergency surgery; IA = interval appendectomy.

The annual variation in the number of postoperative complications according to treatment strategy is shown in Fig. 3. The annual number of ES and IA are shown in Fig. 3A. Beginning with the first case in 2011, we performed IA for all patients who had perforated appendicitis with PAA in 2013 and 2014, and also performed IA for the most of patients similarly diagnosed disease in 2015 and 2016. The number of postoperative complications was higher in 2011 and 2012, with no complications experienced in 2013 (Fig. 3B). The number of postoperative complications was dramatically decreased after the beginning in earnest of IA for the patients who had perforated appendicitis with PAA in 2013.

DISCUSSION

In our study of 171 consecutive patients who underwent surgery for PAA, 28 (16.4%) experienced complications within 30 days of surgery. Wound infection and intra-abdominal abscess were the most common postoperative complications. Only ES was associated with postoperative complications in univariate and multivariate analysis.

Emergency surgery may be technically demanding in patients with PAA or phlegmon formed after acute perforated appendicitis, because of the adhesive loops of the bowel, distorted anatomy, and the difficulties in closing the appendiceal stump due to the inflammation within a wide area of the abdominal cavity. Under these circumstances, appendectomy often requires extensive dissection and may lead to injury of adjacent structures. Complications such as postoperative abscess or enterocutaneous fistula may ensue, necessitating an ileostomy or cecostomy. When an emergency surgery is performed in such patients, the incidence of complications is reported to be up to 36%.^{1,11-14} In our study, the postoperative complication rate was 28.7% and reoperation rate was 9.2% in the IS group which is in line with the published data.

Complicated appendicitis has long been considered a significant factor in longer hospitalization and requirement for extended antibiotic coverage due to its close relationship with higher incidence of postoperative complications.^{15,16} Our study also showed that the length of hospital days and the duration of antibiotics use after IS were protracted (9.7 days and 12.6 days, respectively).

Non-surgical treatment followed by IA has been associated with significantly fewer perioperative complications, such as intraoperative visceral damage, postoperative abdominal and pelvic abscesses, and wound infections, which sometimes require re-intervention.¹⁷

Non-surgical treatment also allowed a significantly shorter operative time in removing of a diminished inflammatory or normal appendix without adherence than in IA, reducing

overall hospitalization time.¹⁸

In line with the literature, presently there were significantly fewer complications and shorter operative time in non-surgical treatment followed IA compared with in IS. As shown in Fig. 1 and Fig. 2, the rate of postoperative complications of PAA has decreased dramatically since IA was introduced in our center. In addition, although an additional hospitalization (non-surgical treatment+IA) was needed to treat PAA in non-surgical treatment followed by IA, the overall hospitalization time was not statistically different between the IA and ES groups. Previous studies reported a high success rate of 76~97% for non-surgical treatment.²⁻⁸ In the present study, there were 3 cases (3.6%) of treatment failure in non-surgical management. Two of them underwent emergent surgery under septic condition due to deterioration of inflammation despite initial antibiotic treatment. The remaining one was improved after initial antibiotic treatment and discharged, but underwent an operation because the inflammation re-exacerbated while waiting for interval appendectomy.

In particular, the rate of open surgery was much higher in patients undergoing ES with PAA, whereas laparoscopic surgery was performed more frequently in the IA group. In addition, the conversion rate from laparoscopic to open surgery was much higher in the ES group (1.2% vs. 47.1%, $p<0.001$). With the expectation that the patient will be in danger due to serious postoperative complications, surgeons may have decided to perform open surgery rather than laparoscopic surgery in ES of PAA. In actual practice, not infrequently, even early laparoscopic surgery will be converted to a more extensive open surgical procedure, such as an ileocecal resection or a right hemicolectomy, due to technical problems or distorted anatomy.^{1,10}

The development of laparoscopic techniques offers new modalities in the treatment of complicated appendicitis and PAA. However, whether laparoscopic appendectomy should be viewed as the optimal management modality of patients with complicated appendicitis is still a contentious issue.¹⁹ Several authors have reported significant postoperative complications following laparoscopic appendectomy in patients with PAA, and suggested caution in the use of laparoscopy for complicated appendicitis.²⁰⁻²² The possible reasons for the increased incidence of postoperative intra-abdominal complications might be the spread of localized infection throughout the abdominal cavity during pneumoperitoneum or separation of the appendix within the peritoneal cavity.²³

However, since PAA are resolved after non-surgical treatment, laparoscopic surgery can be easily applied, and the rate of laparoscopic surgery may increase in IA. The success of laparoscopic IA has been reported without perioperative morbidity and the percentage of IA procedures that included

laparoscopically has markedly increased in recent years from 30% to 85%.^{3,24-26} This trend will certainly make it possible to maximize the advantages of laparoscopic surgery for PAA. The advantages include fewer wound infections, less post-operative pain, shorter hospital stay, quicker recovery, and quicker return to normal activities.²⁷⁻²⁹

After successful conservative or/and image-guided drainage management, IA is often not necessary and can safely be omitted, except in patients with recurrent symptoms.^{1,2,10,30} However, proponents of IA point to advantages of initial conservative treatment followed by IA; the approach avoids the recurrence of symptoms and the misdiagnosis of alternative pathologies, such as malignancy, tuberculosis, diverticulosis, and Crohn's disease.^{9,10}

In our study period, after non-surgical treatment, one patient had appendiceal cancer, and four had Crohn's disease. Although these patients were excluded from the analyses, we believe that IA after non-surgical treatment should be considered to exclude other pathologic causes of periappendiceal mass, especially in patients older than 40 years old age. In terms of patient safety and stress, we believe that even a slightest risk of recurrent appendicitis with abscess is still a risk for the patients. Alerting the patient to the potential risk of another acute appendicitis episode may trigger fear and anxiety, and excessive surveillance.^{31,32}

This study has several limitations. Owing to its retrospective design and based on a small number of patients in a single institute, we could not be sure whether other factors, such as surgeon's experience and laparoscopic preference, affected the rate of postoperative complications and the rate of laparoscopic surgery. Moreover, the surgeon's assessment of the state of complicated appendicitis at the time of diagnosis is important when deciding whether or not to undergo surgery. This assessment is subjective and difficult to quantify. However, all patients in this study were followed-up in the same unit by the same group of physicians, who used similar guidelines and made decisions collectively. During our study, the Korean Diagnosis-Related Groups (DRG) system was introduced. This system may have affected the number of days after surgery and the median rate of complication. However, when divided into two periods based on the introduction of the DRG system, we found the postoperative complication was still significantly reduced in the interval appendectomy group. So we are confident that the results will not be changed. Cost-effectiveness was not evaluated. Nevertheless, the high clinical effectiveness of IA indicates that it can reduce postoperative complications and the length of hospitalization, and can increase the rate of laparoscopic surgery. In our study, the total antibiotics use were longer in the IA group than in the ES group. The concept of treatment for the number of days of antibiotics use has

not yet been established. Further research should be undertaken to determine best practice in the conservative antibiotics management for PAA.

CONCLUSIONS

Our study shows that patients at the greatest risk of post-operative complication are those who have an emergency surgery for PAA, and the postoperative complication rate is high. Wound infection and intra-abdominal abscess were the most common postoperative complications. Although non-surgical treatment followed by IA has a disadvantage of a longer total antibiotics use, it can reduce the postoperative complication rate and total hospitalization days, and increase the rate of laparoscopic surgery. We recommend that IA should be considered first treatment choice for acute appendicitis accompanied by PAA. Moreover, this result suggests that further prospective randomized controlled multi-institutional trial is needed to decrease the total antibiotics use and evaluate the cost-effectiveness of non-surgical treatment followed by IA in patients with PAA.

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