Predictive Factors of Acute Complicated Appendicitis: A Retrospective Study

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Abstract

Background: Complicated appendicitis is an indication for emergency surgery. Therefore, the predictive factors for appendicitis based on the patient background needs identification. Previously, factors predicting non-complicated and complicated appendicitis were reported. However, most of those reports were deemed unsuitable as a standard for emergency use, since those comprised too many items as predictors. We previously reported three items that preoperatively predicted complicated appendicitis (body temperature, C-reactive protein, and fluid retention around the appendix). In this study, we re-evaluated different cases to confirm the usefulness of these three items can for accurately predicting complicated appendicitis preoperatively. In addition, we compared the effectiveness of these predictor items with those reported by other researchers.

Methods: We retrospectively evaluated 417 adult patients who underwent surgery for acute appendicitis between January 2013 and December 2019, and compared our predictor items with those used in previous reports on the preoperative prediction of complicated appendicitis (criteria A consisting of eight predictor items and criteria B consisting of seven predictor items).

Results: The area under the receiver operating characteristic curve (AUC) for the sensitivity to diagnose complicated appendicitis according to our criteria, criteria A, and criteria B were 0.823, 0.839, and 0.856, respectively. The AUC of our criteria and criteria A were similar ($P = 0.356$); those of criteria A and B were also similar ($P = 0.352$). However, the AUC of criteria B was statistically higher than that of our criteria ($P < 0.05$).

Conclusion: Diagnostic criteria B were statistically the best predictor items for characterizing complicated and uncomplicated appendicitis. However, like criteria A and B, the AUC of our criteria exceeded 0.8, and only involved three predictor items; therefore, they can be considered useful predictors.

Background

Acute appendicitis is the most common acute abdominal disease. Annually, an estimated 43,000 cases occur in Japan; US accounts for 250,000 cases, and the UK for 50,000 cases (1). The lifetime incidence was 8.6% for men and 6.7% for women (2). In general, catarrhal appendicitis and phlegmonous appendicitis are classified as non-complicated appendicitis, and gangrenous/perforated appendicitis is classified as complicated appendicitis. There is no dispute that early surgery is the principle treatment for patients diagnosed with acute appendicitis (3). Perforated appendicitis and necrotic appendicitis with a high risk of perforation require prompt emergency surgery. Conversely, catarrhal appendicitis and phlegmonous appendicitis have a low risk of perforation in a short period of time and can be treated by quasi-emergency/quasi-waiting surgery with conservative treatment under appropriate medical supervision. Conservative treatment may be sufficient depending on the course. However, the preoperative distinction between non-complicated and complicated appendicitis is challenging. In addition, cases of complicated appendicitis, including perforated appendicitis and gangrenous appendicitis, may progress

to acute peritonitis, a condition that necessitates emergency surgery regardless of the time of development. There is a need for clinical indicators that accurately predict complicated appendicitis for which emergency surgery is indicated.

Studies by Avanesov et al. (4) and Atema et al. (5) report factors that predict complicated appendicitis. Avanesov et al. reported seven items as predictors: age, body temperature, elapsed time from onset, appendix diameter, fluid retention around the appendix, free air, and abscess. Atema et al. reported eight items as predictors: age, body temperature, elapsed time from onset, leukocyte count C-reactive protein (CRP), free air, fluid retention around the appendix, and appendicolith.

These are useful preoperative predictive factors; however, they involve many predictor items and are complicated. Therefore, there may be difficulties using these predictive factors in the field of emergency medical care. We have previously reported three predictor items of complicated appendicitis, body temperature $\geq 37.4^{\circ}\text{C}$, CRP ≥ 4.7 mg/dL, and fluid collection surrounding the appendix on computed tomography (CT), and reported on their usefulness^{6,7}.

In this study, we confirmed the usefulness of our criteria by comparing them with other criteria for predicting complicated appendicitis preoperatively.

Methods

In this study, we retrospectively evaluated 417 patients who underwent surgery for acute appendicitis between January 2013 and December 2019 in our institution. Blood tests and CT were performed in all cases. Patients who were successfully treated with antibiotics were excluded.

Histopathologically, catarrhal appendicitis was defined as the apparent enlargement of lymphoid follicles in the appendix mucosa, and cellulitis appendicitis was defined as neutrophil infiltration into all layers. Gangrenous appendicitis was defined as neutrophil infiltration and muscle layer necrosis, and perforated appendicitis was defined as necrosis and perforation in all the layers. Complicated appendicitis was defined as a pathologically proven gangrenous or perforated appendix. We classified all cases as complicated or non-complicated appendicitis. We compared each of the physical findings, blood test findings, CT image findings, and surgical results. We determined the proportions of complicated appendicitis and non-complicated appendicitis, respectively, depending on the degree to which the criteria we reported previously (body temperature $\geq 37.4^{\circ}\text{C}$, CRP ≥ 4.7 mg/dL, and fluid collection surrounding the appendix on CT) were met.

Next, we compared our criteria with previously reported preoperative predictor items of complicated appendicitis. The predictor items reported by Avanesov et al. in 2018 were defined as A criteria, while those reported by Atema et al. in 2015 were defined as B criteria. All statistical analyses were carried out using the JMP® Pro 15.0.0 (SAS Institute Inc.). The sensitivity performance for diagnosing complicated appendicitis was evaluated in terms of the area under the curve of the receiver operating characteristic curve (AUROC), homogeneity, discriminatory ability, and Akaike information criterion (AIC). The AUROC

was compared between the two models using the DeLong method. Homogeneity was defined using the likelihood ratio, χ^2 , calculated using the Cox regression model. Discriminatory ability, defined as the large differences in survival among patients in different grades within each system, was determined using the linear trend χ^2 -test. The AIC, which shows the effect of the grading systems of sensitivity to diagnose complicated appendicitis, also estimated the results of the Cox regression model in each system. A model with a lower AIC was more explanatory and informative. Statistical significance was set at $P < 0.05$.

All study participants provided informed consent, and the study design was approved by the ethics review board of our institution. The identities of the patients were protected.

Results

There were 237 cases of non-complicated appendicitis and 180 cases of complicated appendicitis. We compared the patient backgrounds (Table 1), and patients with complicated appendicitis had significantly higher body temperature and CRP levels than patients with non-complicated appendicitis, in addition to significant fluid collection surrounding the appendix. Moreover, the group with complicated appendicitis required ileocecal resection, and there were many open operations, and the operation time was long. In addition, the complicated appendicitis group had significantly longer postoperative hospital stays (Tables 1 and 2). We applied the risk factors reported in the past (body temperature $\geq 37.4^\circ\text{C}$, CRP ≥ 4.7 mg/dL, and fluid collection surrounding the appendix on CT) to the target cases. Complicated appendicitis occurred in 86% of patients who met all three criteria. Of the patients who met two factors, 69.6% had complicated appendicitis. Of the patients who met only one factor, 31.5% had complicated appendicitis. Only 7.3% of patients who did not meet any of the factors had complicated appendicitis.

Table 1
Patient Background

	Non-complicated appendicitis	Complicated appendicitis	<i>p</i> -value
	(n = 237)	(n = 180)	
Age(years)	39(11–86)	56(12–90)	0.0001
Gender			0.1058
Male	141(59.5%)	121(67.2%)	
Female	96(40.5%)	59(32.8%)	
Onset time			0.0001
≥ 48hours	65(27.4%)	104(57.8%)	0.0001
Physical findings			
Body temperature (°C)	37.2(35.3–40.2)	37.6(35.5–40.1)	0.0001
Rebound tenderness	100(42.2%)	90(50%)	0.1129
Muscular guarding	75(31.7%)	81(45.0%)	0.0052
WBC(/μL)	12350(2600–27100)	12400(2900–30100)	0.8139
CRP(mg/dL)	2.2(0.01–30.8)	10.7(0.2–45.07)	0.0001
Computed tomography			
Appendix minor Diameter(mm)	11(6–20)	13(4–23)	0.0001
Increased adipose tissue concentration	178(75.1%)	166(93.3%)	0.0001
Periappendiceal fluid	26(11.0%)	98(54.4%)	0.0001
Appendicolith	87(36.9%)	86(48.0%)	0.0221
Douglas fossa ascites	34(14.4%)	51(28.3%)	0.0005
Our criteria.	1(0–3)	2(0–3)	0.0001
Criteria A	1(0–5)	3(0–9)	0.0001
Criteria B	4(0–14)	10(2–20)	0.0001
Our criteria: body temperature ≥ 37.4°C:1point, C-reactive protein ≥ 4.7mg.dl,:1point, fluid collection surrounding the appendix on computed tomography (CT):1point (Maximum score.3points)			

Non-complicated appendicitis	Complicated appendicitis	<i>p</i> -value
Criteria A: age $\geq$ 52 years: 1 point, temperature $\geq$ 37.5°C: 1 point, duration of symptoms $\geq$ 48 h: 1 point, diameter $\geq$ 14 mm: 1 point, periappendiceal fluid: 1 point: 2 points, extraluminal air present: 1 point, abscess present: 3 points (Maximum score 10 points)		
Criteria B: age $\geq$ 45 years: 2 points, temperature $\leq$ 37.0: 0 point, 37.1–37.9: 2 points, $\geq$ 38.0: 4 points, duration of symptom $\geq$ 48 h: 2 points, WBC count $> 13 \times 10^9/l$: 2 points, C-reactive protein (mg/l) $\leq$ 50: 0 point, 51–100: 2 points, > 100 : 3 points		
Extraluminal free air on imaging: 5 points, periappendiceal fluid on imaging: 2 points, appendicolith on imaging: 2 points		
(Maximum score 22 points)		
Data are expressed as median(range) for continuous and n (%) for categorical variables. WBC, White blood cell CRP, C-reactive protein		

The AUROC for the sensitivity to diagnose complicated appendicitis according to our criteria, criteria A, and criteria B were 0.823, 0.839, and 0.856, respectively. The areas under the curve of our criteria and criteria A were similar ($P = 0.356$). The A and B criteria were also similar ($P = 0.352$). However, those of the criteria B were statistically higher than those of our criteria ($P < 0.05$) (Fig. 1). The discriminatory ability linear trend χ^2 calculated using the Cox regression of our criteria and criteria A and B were 128.9, 121.1, and 142.5, respectively. The likelihood ratios χ^2 calculated using the Cox regression model, which indicate homogeneity, were 146.4, 143.6, and 172.8, respectively. The AIC of each criterion was 397.0, 345.8, 369.0, respectively (Table 3). Criteria B was the best statistical indicator.

Table.2 Surgical result

Data are expressed as median(range) for continuous and n (%) for categorical variables.

	Non-complicated appendicitis (n=237)	Complicated appendicitis (n=180)	<i>p</i> -value
Surgery			0.0001
Appendectomy	233(98.3%)	154(87.5%)	
Colectomy	4(1.7%)	22(12.5%)	
Laparoscopic surgery	174(73.4%)	50(29.2%)	0.0001
Surgery time(min)	76(32-240)	94(46-266)	0.0001
Bleeding volume(ml)	5(0-401)	23(1-911)	0.0001
Complications ($\geq$ Grade)	3(1.3%)	9(5.0%)	0.0244
Hospital stays (days)	4(2-40)	8(2-47)	0.001

Table.3 Performance evaluation of our criteria, Criteria A and Criteria B

Criteria	Discriminatory ability (Linear trend χ^2 test)	Homogeneity (likelihood ratio χ^2 test)	Akaike information Criterion (AIC)
Our criteria	128.9	146.4	397.0
Criteria A	121.1	143.6	345.8
Criteria B	142.5	172.8	369.0

Higher discriminatory ability and homogeneity, and lower Akaike information criterion (AIC) statistics associated with better performance of the grading system.

Discussion

In our hospital, we perform emergency or quasi-emergency surgery on all patients within 24 h after admission as the standard treatment for patients with a definitive diagnosis of acute appendicitis. Complicated appendicitis, including gangrenous appendicitis and perforated appendicitis, progresses to peritonitis when it becomes severe; thus, immediate emergency surgery is required. Therefore, a method for preoperatively predicting non-complicated appendicitis and complicated appendicitis is needed. In addition to our 2016 report (6), some predictor items have been developed to distinguish non-complicated

from complicated appendicitis (4, 5). They were based on patient characteristics and diagnostic markers that are routinely collected in clinical practice, combined with imaging features.

In a previous retrospective study(2, 6), we proposed predictor items to discriminate between complicated and non-complicated appendicitis using clinical and radiological findings. Our predictor items comprised two clinical (body temperature $\geq 37.4^{\circ}\text{C}$, and C-reactive protein ≥ 4.7 mg/dL) and one radiological finding (fluid collection surrounding the appendix). Patients with complicated appendicitis had significantly higher body temperature and CRP at the time of consultation than patients with non-complicated appendicitis. CT often shows fluid retention around the appendix. However, there were no significant differences in white blood cell (WBC) scores. The average age of patients with non-complicated appendicitis was 39 yrs, and the average age of patients with complex appendicitis was 56 yrs in this survey. Patients with complicated appendicitis were found to be significantly older ($P < 0.001$). It has been reported that WBC counts are less likely to increase in the elderly compared with CRP levels.

We have previously confirmed that our three predictor items can correctly stratify complicated and non-complicated appendicitis. As a result, we reported that these three items are suitable predictors for complicated appendicitis preoperatively. In the present retrospective study, we examined whether our three predictor items were more effective than other predictors reported by other researchers. To distinguish complicated appendicitis from non-complicated appendicitis, Atema et al. reported eight predictor items (age ≥ 45 yrs, body temperature ≤ 37.0 – 37.1 – 37.9 – $\geq 38.0^{\circ}\text{C}$, duration of symptoms ≥ 48 h, WBC count $> 13 \times 10^9/\text{L}$, CRP (mg/L), extraluminal air present, abscess present) (criteria A)(5), while Avanesov et al. reported seven predictor items (age ≥ 52 yrs, body temperature $\geq 37.5^{\circ}\text{C}$, duration of symptom ≥ 48 h, diameter ≥ 14 mm, fluid collection surrounding the appendix, extraluminal air present, abscess present) (criteria B) (4). However, both these criteria are complicated because they consist of seven and eight predictor items, respectively, that require assessment. The criteria we adopt consists of only three factors, thus making it simpler than predictor items reported in the past. They can be used universally by both experienced and inexperienced healthcare professionals. This is a major difference from previously reported predictor items.

The analysis showed that criteria B was more effective in distinguishing between complicated and non-complicated appendicitis. Criteria A and B implemented a combined clinical and radiological score. Both criteria included age as an evaluation item. Certainly, elderly people are more likely to have severe disease. However, elderly people often have a poor onset of symptoms, and WBC counts tend to elevate later than CRP. As mentioned above, there were no significant differences in WBC scores. Therefore, we adopted only CRP as a criterion.

Furthermore, criteria A includes the appendix diameter. However, in the case of an appendix that has already been perforated, this is often impossible to measure because of the influence of surrounding abscesses and fluids, and it is doubtful that it is appropriate.

Criteria A and B assess free air and abscess formation, which may be seen in other diseases, such as diverticulum perforation; thus, it is doubtful whether they are appropriate as criteria. In addition, criteria A did not include the periappendiceal fluid. However, these CT findings were 99% specific for appendiceal perforation.

In addition, criteria A and B are time consuming as they assign different points for each item.

We believe that the predictor items for acute appendicitis should be simple. Acute appendicitis is a major disease, and doctors who do not specialize in abdominal emergencies are more likely to encounter it in their daily practice. Since our predictors are simple, they may be useful universal criteria that even inexperienced practitioner can easily use. Although our predictor assessments are limited by the retrospective nature of the study, their accuracy has been validated and their usefulness demonstrated.

Conclusions

In conclusion, the three items, body temperature $\geq 37.4^{\circ}\text{C}$, C-reactive protein ≥ 4.7 mg/dL, and fluid collection surrounding the appendix on CT, are useful in predicting cases of complicated appendicitis preoperatively. Our predictor items can be used to quickly and appropriately predict complicated appendicitis, even by those with little experience in the settings of busy emergency care.

Abbreviations

AIC

Akaike information criterion; AUC:Area under the receiver operating characteristic curve; AUROC:Area under the curve of the receiver operating characteristic curve; CT:Computed tomography; CRP:C-reactive protein; WBC:White blood cells

Declarations

Ethics approval and consent to participate

Informed consent was obtained from all patients or their caregivers.

Consent for publication

Not applicable.

Availability of data and materials

The data and materials are not available because consent for such an action was not taken from the participants.

Competing interests

There are no competing interests to declare.

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Author contributions

S.H. and M.H. performed the research/study, analyzed the data, and wrote the manuscript. M.M., T.M., Y.Y., S.I., Y.M., H.N., and T.I. performed the research/study and analyzed the data. T.I. designed the study and interpreted the results. All authors read and approved the final manuscript.

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Figures

	Δ AUC	P value
Our criteria vs. Criteria A	0.016	0.356
Our criteria vs. Criteria B	0.033	0.032
Criteria A vs. Criteria B	0.017	0.352

Figure 1

Receiver operating characteristic curve for diagnosing complicated appendicitis according to Criteria A and B. Receiver operating characteristic curve with 95% for the final adjusted regression model. AUC, area under the curve