Preoperative MRI for predicting pathological changes associated with surgical difficulty during laparoscopic cholecystectomy for acute cholecystitis

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Background: Severe inflammation with necrosis and fibrosis of the gallbladder in acute cholecystitis increases operative difficulty during laparoscopic cholecystectomy. This study aimed to assess the use of preoperative MRI in predicting pathological changes of the gallbladder associated with surgical difficulty.

Methods: Patients who underwent both preoperative MRI and early cholecystectomy for acute cholecystitis between 2012 and 2018 were identified retrospectively. On the basis of the layered pattern of the gallbladder wall on MRI, patients were classified into three groups: high signal intensity (HSI), intermediate signal intensity (ISI), and low signal intensity (LSI). The endpoint was the presence of pathological changes of the gallbladder associated with surgical difficulty, such as necrosis, abscess formation and fibrosis.

Results: Of 229 eligible patients, pathological changes associated with surgical difficulty were found in 17 (27 per cent) of 62 patients in the HSI group, 84 (85 per cent) of 99 patients in the ISI group, and 66 (97 per cent) of 68 patients in the LSI group (P < 0.001). For detecting these changes, intermediate to low signal intensity of the gallbladder wall had a sensitivity of 90 (95 per cent c.i. 84 to 94) per cent, specificity of 73 (60 to 83) per cent and accuracy of 85 (80 to 90) per cent.

Conclusion: Preoperative MRI predicted pathological changes associated with surgical difficulty during laparoscopic cholecystectomy for acute cholecystitis.

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Introduction

Surgical difficulty during laparoscopic cholecystectomy (LC) for acute cholecystitis (AC) differs, depending on the degree of inflammation and fibrosis of the gallbladder.1 Severe local inflammation and fibrosis of the gallbladder wall increase both operative difficulty and frequency of intraoperative complications during LC1,2. The Tokyo Guidelines from 20181 proposed that intraoperative findings such as necrosis, abscess formation and fibrosis of the gallbladder are considered to be novel, objective and direct indicators for measuring surgical difficulty in LC for AC. Indicators such as open conversion rate and duration of surgery are not considered appropriate because they depend substantially on surgeons’ skills and experiences3,4. However, in clinical practice, preoperative predictions of these pathological changes in the gallbladder wall are also crucial in deciding a treatment strategy to reduce severe complications.

These histopathological changes of the gallbladder wall in AC develop with time within the following stages: first stage, oedematous cholecystitis (2−4 days); second stage, necrotizing cholecystitis (3−5 days); third stage, suppurrative cholecystitis (7−10 days); and fourth stage, chronic cholecystitis (repeated occurrence of cholecystitis)5. The second and third stages comprise gangrenous changes, and the third and fourth stages comprise fibrosis of the gallbladder wall5.

However, it is difficult to determine precisely the time that has passed since disease onset6. In addition, some cases of AC occur as a result of exacerbations of chronic cholecystitis6. Therefore, it is difficult to predict the pathological condition of the gallbladder in AC, and surgeons...
often discover unpredictable severe necrosis and fibrosis of 
the gallbladder wall during early surgery, sometimes even 
within 48 h of disease onset. Although many studies have 
tried to identify indicators of surgical difficulty in LC, only 
a few have focused on preoperative assessment to predict 
pathological changes of the gallbladder wall associated with 
increased surgical difficulty.

Some studies have reported that the gallbladder wall 
showed various signal intensities and layered patterns on 
MRI; the MRI findings correlated well with the pathologi-
ical findings and were useful for diagnosis of gallbladder 
disease, such as AC, gangrenous cholecystitis, chronic 
cholecystitis and gallbladder carcinoma. The present 
authors have assumed that layered patterns of the gall-
bladder wall in AC before surgery are also associated with 
pathological changes associated with surgical difficulty, 
such as necrosis, abscess formation and fibrosis.

This study aimed to assess the usefulness of preoperative 
non-contrast-enhanced MRI to predict the pathological 
changes of the gallbladder wall associated with increased 
surgical difficulty during early cholecystectomy for AC.

Methods

An institutional surgery database was searched to iden-
tify patients who had undergone cholecystectomy at Toy-
ohashi Municipal Hospital in Japan from January 2012 to 
December 2018. Patient information was collected retro-
spectively from the electronic medical records. Eligibility 
criteria were: patients with AC diagnosed clinically accord-
ing to the Tokyo Guidelines of 2007, 2013 and 2018, who 
underwent cholecystectomy 7 days or less after disease 
onset (early cholecystectomy), and had MRI and magnetic 
resonance cholangiopancreatography (MRCP) 24 h or less 
before surgery. Exclusion criteria were: gallbladder wall 
thickness less than 3 mm on MRI, and clinical suspicion 
of gallbladder cancer. The ethics committee of Toyohashi 
Municipal Hospital approved the study protocol.

MRI and MRCP procedure

Non-contrast-enhanced MRI and MRCP on a 3-T 
superconducting instrument (MAGNETOM Skyra; 
Siemens, Erlangen, Germany) were performed routinely 
to assess the presence of common bile duct stones and 
abnormal anatomical variations in the bile duct before 
surgery. After initial T1-weighted images, HASTE 
(Half-Fourier-Acquired Single-shot Turbo spin Echo) 
T2-weighted images sequence were applied in the axial, 
coronal, and oblique sagittal planes. The oblique sagittal 
plane was applied parallel to the course of the common 
bile duct, as demonstrated on initial coronal scout views.

Images were acquired in each imaging plane. MRCP 
was performed using a HASTE sequence. The following 
parameters were used: prospective acquisition correction 
technique; repetition time, 86 ms; thickness, 3 mm; gap, 0 mm; flip angle, 130°; matrix size, 256 × 256; 
phase partial Fourier 4/8; field of view, 300 × 300 mm; 
and fat saturation (spectral-attenuated inversion recovery). 
Data from the MRCP and original HASTE MRI of each 
patient were routinely stored in the electronic medical 
records.

Interpretation of MRI

The previously obtained preoperative MRI and MRCP 
data for all patients were assessed retrospectively and 
individually by two surgeons blinded to the clinical 
information and type of surgery but aware of the presence 
of cholecystitis. HASTE T2-weighted images captured 
during MRCP were assessed, and gallbladder wall thick-
ness was measured from the section showing the thickest 
part of the wall. The layered pattern of the thickened wall 
was classified into three groups: a high signal intensity 
(HSI) group (two layers with a discrete margin composed 
of a thin inner layer (3 mm or less) with low signal and a 
relatively thick outer layer with high signal); an interme-
diate signal intensity (ISI) group (two layers with a partially 
ill-defined margin composed of a partially thickened inner 
layer (more than 3 mm) with low signal and an outer layer 
with high or partially heterogeneous intermediate signal); 
and a low signal intensity (LSI) group (ill-defined layers 
composed of a diffusely thickened inner layer (more than 
3 mm) with low signal and an outer layer with intermediate 
to low signal). Examples of images from the three groups 
are shown in Fig. 1. Signal intensities were determined by 
using standardized regions of interest (ROI). The ROI size 
was similar for all measurements and patients, and varied 
between 0-03 and 0-06 cm². LSI lesions of the gallbladder 
wall were judged in comparison with the signal intensity 
of the renal parenchyma.

Histopathological examination

Details of histopathological findings in the surgical spec-
imens of each patient were obtained from the pathology 
reports. These reports were made within 2 weeks of surgery 
by a staff pathologist who was aware of the presence of 
cholecystitis and type of surgery but not informed about 
the radiological findings.

Endpoint

The endpoint of this study was the presence of pathological 
changes predictive of surgical difficulty, such as necrosis,
MRI prediction of pathology of acute cholecystitis

Statistical analysis

Median (range) values are presented. Fisher’s exact test was used to test differences between categorical variables, and the Mann-Whitney U test and the Kruskal–Wallis rank sum test for differences between continuous variables. All P values were two-sided, and associations were considered significant at P < 0.050. If there was a significant difference among the three groups, pairwise comparisons for all groups were performed, with P values adjusted by the Holm method. All statistical analyses were performed using R version 3.5.2 (The R Foundation for Statistical Computing, Vienna, Austria) and EZR (Saitama Medical Centre, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R.

Results

Data were collected for 651 patients who had undergone cholecystectomy after diagnosis of AC. Of these patients, 258 had undergone early cholecystectomy and 393 had had delayed cholecystectomy. Some 231 of the patients who underwent early cholecystectomy had MRI and MRCP within 24 h of surgery. Two patients were excluded owing to gallbladder wall thickness of less than 3 mm on MRI. Ultimately, 62, 99 and 68 patients respectively were selected for the HSI, ISI and LSI groups (Fig. 2).

Table 1 shows baseline patient characteristics, preoperative findings and type of operation. Baseline characteristics were similar among the three groups. Gallbladder wall thickness measured on MRI was significantly greater in the ISI and LSI groups than in the HSI group (HSI versus ISI, P < 0.001; ISI versus LSI, P = 0.277; LSI versus HSI, P < 0.001). Preoperative C-reactive protein (CRP) level was significantly higher in decreasing order of LSI, ISI and HSI in pairwise comparisons (HSI versus ISI, P < 0.001; ISI versus LSI, P < 0.001; LSI versus HSI, P < 0.001). The rate of planned open cholecystectomy was significantly higher in decreasing order of LSI, ISI and HSI (HSI versus ISI, P = 0.022; ISI versus LSI, P = 0.022; LSI versus HSI, P < 0.001).

Outcomes

Pathological gallbladder changes associated with surgical difficulty were identified in 27 per cent of patients in the HSI group, 85 per cent of patients in the ISI group, and 97 per cent of those in the LSI group (P < 0.001) (Table 2). In the pairwise comparisons, the proportion of patients with any pathological change associated with surgical difficulty was significantly higher in decreasing order of LSI, ISI and HSI (Table 2).
With regard to the types of pathological change, necrosis in the gallbladder wall was detected in 15 per cent of patients in the HSI group, 52 per cent of patients in the ISI group, and 72 per cent of those in the LSI group. In the pairwise comparisons, the proportion of patients with necrosis of the gallbladder was significantly higher in decreasing order of LSI, ISI and HSI (Table 2). Fibrosis in the gallbladder wall was detected in 16 per cent of the HSI group, 51 per cent of the ISI group, and 54 per cent of the LSI group. In the pairwise comparisons, the proportion of patients with fibrosis of the gallbladder was significantly higher in the ISI and LSI groups than in the HSI group (Table 2). Abscess formation in the gallbladder wall was found in 3, 8 and 13 per cent of patients in the HSI, ISI and LSI group respectively, but the differences were not significant (Table 2).

**Use of MRI to predict gallbladder wall changes associated with surgical difficulty**

As the outcomes were relatively similar between ISI and LSI groups, intermediate to low signal intensity in the gallbladder wall was defined as positive and high signal intensity as negative. The sensitivity, specificity, accuracy, LR+ and LR− of MRI for predicting pathological changes associated with surgical difficulty were 90 (95 per cent c.i. 84 to 94) per cent, 73 (60 to 83) per cent, 85 (80 to 90) per cent, 3.28 (95 per cent c.i. 2.18 to 4.93) and 0.14 (0.09 to 0.23) respectively. Because preoperative CRP concentration was significantly higher in the decreasing order of LSI, ISI and HSI (Tables 1 and 3), an additional analysis was performed for the utility of CRP level in predicting pathological change; this was later compared with MRI scans. The resulting Mann–Whitney U test highlighted a significant difference between preoperative CRP level and pathological changes. However, as with all cut-off points, the accuracy, LR+ and LR− values of CRP for predicting pathological changes associated with surgical difficulty were inferior to those of MRI.

**Subgroup analysis**

A total of 184 patients who had surgery within 48 h of disease onset were eligible for subgroup analysis. Pathological changes associated with surgical difficulty, such as necrosis, abscess formation and fibrosis, were detected in 130 (70.7 per cent) of these patients: 55 in the HSI group, 78 in the ISI group and 51 in the LSI group. Subgroup results are shown in Table 4. For each group, the proportion of patients with pathological changes associated with surgical difficulty was similar to that in analysis of the whole cohort.
### Table 1 Characteristics of the three groups

| Baseline characteristics | HSI group (n = 62) | ISI group (n = 99) | LSI group (n = 68) | P† |
|--------------------------|-------------------|-------------------|-------------------|----|
| Age (years)* | 59 (46–68) | 65 (51–73) | 67 (57–75) | 0.068§ |
| Sex ratio (M : F) | 36 : 26 | 67 : 32 | 45 : 23 | 0.439 |
| BMI (kg/m²)* | 25.0 (21.3–28.1) | 24.3 (21.8–27.4) | 24.8 (22.4–27.1) | 0.878§ |
| ASA physical status | | | | |
| I | 28 (45) | 34 (34) | 21 (31) | 0.037 |
| II | 34 (55) | 59 (60) | 39 (57) | |
| III | 0 (0) | 6 (6) | 8 (12) | |
| Diabetes mellitus | 11 (18) | 14 (14) | 15 (22) | 0.418 |
| Previous diagnosis of gallstones | 17 (27) | 34 (34) | 22 (32) | 0.793 |
| Past gallbladder attack | 13 (21) | 17 (17) | 14 (21) | 0.790 |
| Past acute cholecystitis | 3 (5) | 7 (7) | 7 (10) | 0.530 |
| Preoperative findings | | | | |
| Body temperature (°C)* | 36.7 (36.3–37.2) | 37.0 (36.6–37.5) | 37.0 (36.6–37.6) | 0.029§ |
| Preoperative gallbladder drainage | 0 (0) | 2 (2) | 1 (1) | 0.789 |
| Thickness of gallbladder wall on MRI (mm)* | 5 (4–7) | 7 (6–8) | 7 (6–9) | <0.001§ |
| Gallstones recognized on MRI | 53 (85) | 83 (84) | 53 (78) | 0.117 |
| WBC (cells/μl)* | 10 135 (8445–13 960) | 10 670 (8835–14 615) | 12 715 (9470–15 512) | 0.054§ |
| CRP (mg/dl)* | 0.31 (0.08–1.05) | 0.60 (0.14–5.99) | 6.51 (1.18–15.14) | <0.001§ |
| AST (units/l)* | 24 (19–37) | 24 (18–33) | 24 (19–34) | 0.721§ |
| ALT (units/l)* | 26 (18–39) | 23 (17–41) | 25 (16–52) | 0.519§ |
| ALP (units/l)* | 213 (163–283) | 223 (184–289) | 221 (183–282) | 0.442§ |
| Total bilirubin (mg/dl)* | 0.7 (0.5–1.0) | 1.0 (0.7–1.6) | 1.0 (0.7–1.5) | <0.001§ |
| Severity grade† | | | | |
| I | 60 (97) | 86 (87) | 57 (84) | |
| II | 2 (3) | 13 (13) | 11 (16) | |
| Surgical details | | | | |
| Type of surgery | | | | <0.001 |
| Laparoscopic | 60 (97) | 81 (82) | 42 (62) | |
| Open conversion | 0 (0) | 8 (8) | 14 (21) | |
| Open | 2 (3) | 10 (10) | 12 (18) | |
| Time from disease onset to surgery (h) | | | | 0.114 |
| ≤ 48 | 55 (89) | 78 (79) | 51 (75) | |
| > 48 | 7 (11) | 21 (21) | 17 (25) | |

Values in parentheses are percentages unless indicated otherwise; *values are median (range). †Assessed according to Tokyo Guidelines of 2007, 2013 and 2018. HSI, high signal intensity; ISI, intermediate signal intensity; LSI, low signal intensity; WBC, white blood cell; CRP, C-reactive protein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase. ‡Fisher’s exact test, except §Kruskal–Wallis test.

### Table 2 Pathological outcomes in the three groups

| Pathological change associated with surgical difficulty | HSI group (n = 62) | ISI group (n = 99) | LSI group (n = 68) | P* |
|-------------------------------------------------------|-------------------|-------------------|-------------------|----|
| Necrosis | 17 (27) | 84 (85) | 66 (97) | <0.001† |
| Abscess formation | 2 (3) | 8 (8) | 9 (13) | 0.126 |
| Fibrosis | 10 (16) | 50 (51) | 37 (54) | <0.001† |

Values in parentheses are percentages. HSI, high signal intensity; ISI, intermediate signal intensity; LSI, low signal intensity. *Fisher’s exact test. †In pairwise comparisons: P < 0.001 (HSI versus ISI), P = 0.010 (ISI versus LSI) and P < 0.001 (LSI versus HSI); ‡In pairwise comparisons: P < 0.001 (HSI versus ISI), P = 0.640 (ISI versus LSI) and P < 0.001 (LSI versus HSI) (Fisher’s exact test with adjustment by Holm method).
Table 3 Characteristics of the subgroups of patients undergoing surgery within 48 h of disease onset

| Baseline characteristics          | HSI group (n = 55) | ISI group (n = 78) | LSI group (n = 51) | P† |
|-----------------------------------|-------------------|-------------------|-------------------|----|
| **Preoperative findings**         |                   |                   |                   |    |
| Body temperature (°C)*            | 36.6 (36.2–37.2)  | 36.9 (36.3–37.5)  | 36.9 (36.5–37.7)  | 0.038§ |
| Preoperative gallbladder drainage | 0 (0)             | 1 (1–3)           | 0 (0)             | 1.000 |
| Thickness of gallbladder wall on MRI (mm)* | 5 (4–7) | 7 (6–8) | 7 (6–9) | < 0.001§ |
| Gallstones recognized on MRI      | 47 (85)           | 67 (86)           | 42 (82)           | 0.869 |
| WBC (cells/μl)*                   | 11 260 (8 850–14 140) | 10 595 (8 873–14 060) | 12 690 (9 440–15 835) | 0.141§ |
| CRP (mg/dl)*                      | 0.25 (0.08–0.85)  | 0.52 (0.12–5.12)  | 3.18 (0.47–11.39) | < 0.001§ |
| AST (units/l)*                    | 24 (19–34)        | 25 (18–33)        | 25 (19–42)        | 0.972§ |
| ALT (units/l)*                    | 25 (18–38)        | 23 (17–43)        | 25 (16–54)        | 0.919§ |
| ALP (units/l)*                    | 206 (161–272)     | 222 (182–288)     | 217 (174–285)     | 0.240§ |
| Total bilirubin (mg/dl)*          | 0.6 (0.2–0.9)     | 1.0 (0.7–1.6)     | 1.0 (0.7–1.5)     | < 0.001§ |
| Severity grade†                   | 0.499             |                   |                   |    |
| Type of surgery                   |                   |                   |                   | < 0.001 |
| Laparoscopic                      | 55 (100)          | 66 (85)           | 33 (65)           |    |
| Open conversion                   | 0 (0)             | 6 (8)             | 11 (22)           |    |
| Open                              | 0 (0)             | 6 (8)             | 7 (14)            |    |

Values in parentheses are percentages unless indicated otherwise; *values are median (range). †Assessed according to Tokyo Guidelines of 2007, 2013 and 2018. HSI, high signal intensity; ISI, intermediate signal intensity; LSI, low signal intensity; WBC, white blood cell; CRP, C-reactive protein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase. ‡Fisher’s exact test, except §Kruskal–Wallis test.

Table 4 Pathological outcomes in the subgroup of patients undergoing surgery within 48 h of disease onset

| Pathological change associated with surgical difficulty | HSI group (n = 55) | ISI group (n = 78) | LSI group (n = 51) | P* |
|--------------------------------------------------------|-------------------|-------------------|-------------------|----|
| Necrosis                                               | 14 (25)           | 66 (85)           | 50 (98)           | < 0.001† |
| Abscess formation                                      | 8 (15)            | 36 (46)           | 37 (73)           | < 0.001† |
| Fibrosis                                               | 2 (4)             | 5 (6)             | 7 (14)            | 0.149 |

Values in parentheses are percentages. HSI, high signal intensity; ISI, intermediate signal intensity; LSI, low signal intensity. *Fisher’s exact test. †In pairwise comparisons: P < 0.001 (HSI versus ISI), P = 0.015 (ISI versus LSI) and P < 0.001 (LSI versus HSI); ‡in pairwise comparisons: P < 0.001 (HSI versus ISI), P = 0.004 (ISI versus LSI) and P < 0.001 (LSI versus HSI); §in pairwise comparison: P < 0.001 (HSI versus ISI), P = 1.000 (ISI versus LSI) and P < 0.001 (LSI versus HSI) (Fisher’s exact test with adjustment by Holm method).
The sensitivity, specificity, accuracy, LR+ and LR− of MRI in identifying pathological changes associated with surgical difficulty of gallbladder wall in patients with AC who had surgery within 48 h of disease onset were 89 (95 per cent c.i. 83 to 94) per cent, 76 (62 to 87) per cent, 85 (79 to 90) per cent, 3.71 (95 per cent c.i. 2.30 to 5.98) and 0.14 (0.09 to 0.24) respectively.

Discussion

There were three major findings from this single-centre retrospective study. First, variations in the layered pattern of the gallbladder wall on non-contrast-enhanced MRI classified by the study criteria were significantly associated with fibrosis and necrosis of the gallbladder wall in patients with AC. Second, intermediate to low signal intensity of the gallbladder wall had a sensitivity of 90 per cent and a specificity of 73 per cent for predicting pathological changes in the gallbladder wall associated with surgical difficulty during LC in AC. Third, even in patients who had early cholecystectomy within 48 h of disease onset, 70.7 per cent had pathological changes associated with surgical difficulty, and MRI findings were useful in predicting such changes. These results indicate that MRI is a promising method for predicting surgical difficulty for LC.

Many previous studies have reported predictors of surgical difficulty during LC for AC, such as preoperative radiological findings (non-visualized gallbladder on preoperative cholangiography, cystic duct length, gallbladder wall thickening, incarcerated stones in the gallbladder neck, fluid retention around the gallbladder), duration of raised CRP, white blood cell count, low albumin, high bilirubin, diabetes and male sex. These studies included factors such as open conversion rate and duration of surgery as indicators of surgical difficulty. However, some studies have indicated that the criteria for open conversion vary among surgeons and that the operating time is highly dependent on the skills and experience of the operator. Based on a Delphi consensus amongst a large number of surgeons of varying nationalities, Iwashita and colleagues reported that intraoperative findings that have a substantial effect on surgical difficulty during LC, such as necrosis, abscess formation and fibrosis of the gallbladder wall, may be novel indicators of surgical difficulty. The Tokyo Guidelines 2018 recommended the use of these intraoperative findings as objective, direct indicators that are capable of measuring surgical difficulty. As a next step, the present authors focused here on the preoperative prediction of these pathological conditions of the gallbladder wall in patients with AC.

MRCP is a non-invasive technique that has been used previously in the assessment of bile duct abnormality. The HASTE sequence captured for MRCP has already been shown to be a technique for assessing pathology of the gallbladder wall. Jung et al. reported that the thickened gallbladder wall on HASTE MRI had two layers: a low-signal inner layer and a high-signal outer layer. Pathologically, the inner layer corresponded to the mucosa and muscular layer, and the outer layer corresponded to serosal oedema. These researchers also reported that, in some cases, thickening of the low-signal layer with an ill-defined margin corresponded to sloughed mucosa or haemorrhagic necrosis, and the ISI area of the outer layer corresponded to prominent fibrosis in the muscular layer and serosa. The results of the present study may be radiologically and pathologically compatible.

In general, necrosis and fibrosis of the gallbladder wall occur approximately 3 and 7 days, respectively, after the onset of AC. Some studies assessing the appropriate timing for surgery have reported that early LC within 72 h of disease onset is relatively safe, and the Tokyo Guidelines 2013 previously recommended early cholecystectomy within 72 h of the onset of symptoms. However, in the present study, approximately 70 per cent of patients who had early surgery within 48 h after onset of AC already had either fibrosis, necrosis or abscess formation of the gallbladder wall. This finding might be because, in some cases, AC had begun some days before the patients noticed their symptoms or AC occurred in the mechanism of acute exacerbations of chronic cholecystitis. The present results indicate that MRI findings might also be useful for predicting such clinically unpredictable pathological conditions.

Several limitations of the present study should be acknowledged. First, this was a retrospective analysis. As the outcomes were assessed on the basis of the pathological report from a staff pathologist before the study protocol was devised, mild pathological changes might not have been recorded. In addition, the study included only patients who had undergone MRI within 24 h of surgery. Gangrenous change of the gallbladder wall in AC may progress day by day. Although some extension of the time between MRI and surgery might be acceptable, care should be taken when extrapolating the present results to patients under other circumstances. Furthermore, during the 2012–2018 study period, most patients who were diagnosed as having AC more than 72 h from disease onset underwent delayed surgery in the authors’ hospital, because the Tokyo Guidelines 2013 recommended early surgery only for patients with disease onset of 72 h or less. Further validation is necessary before patients diagnosed as having AC 72 h after onset can be assessed.
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