Assessment of Intraoperative Microbiological Culture in Patients with Empyema: Comparison with Preoperative Microbiological Culture

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Purpose: Assessing microbiological culture results is essential in the diagnosis of empyema and appropriate antibiotic selection; however, the guidelines for the management of empyema do not mention assessing microbiological culture intraoperatively. Therefore, we tested the hypothesis that intraoperative microbiological culture may improve the management of empyema.

Methods: We performed a retrospective analysis of 47 patients who underwent surgery for stage II/III empyema from January 2011 to May 2019. We compared the positivity of microbiological culture assessed preoperatively at empyema diagnosis versus intraoperatively. We further investigated the clinical characteristics and postoperative outcomes of patients whose intraoperative microbiological culture results were positive.

Results: The positive rates of preoperative and intraoperative microbiological cultures were 27.7% (13/47) and 36.2% (17/47), respectively. Among 34 patients who were culture-negative preoperatively, eight patients (23.5%) were culture-positive intraoperatively. Intraoperative positive culture was significantly associated with a shorter duration of preoperative antibiotic treatment ($p = 0.002$). There was no significant difference between intraoperative culture-positive and culture-negative results regarding postoperative complications.

Conclusions: Intraoperative microbiological culture may help detect bacteria in patients whose microbiological culture results were negative at empyema diagnosis. Assessing microbiological culture should be recommended intraoperatively as well as preoperatively, for the appropriate management of empyema.

Keywords: empyema, microbiological culture test, thoracic surgery

Introduction

Pleural empyema was known as an infectious disease of the pleural cavity even in ancient times, but outcomes remain poor, and optimal management is still undetermined. A surgical approach is often required to treat empyema, especially in fibrinopurulent stage II or organized stage III. Clinically, the 2017 American...
Association for Thoracic Surgery (AATS) guidelines and the 2015 European Association for Cardio-Thoracic Surgery (EACTS) guidelines recommend a surgical approach in patients in the above stages.\(^{2,3}\) Moreover, a recent retrospective large cohort study indicated that surgical intervention was performed in 61.9% of patients with empyema, and that 44% of the patients initially treated by chest tube drainage required subsequent surgical treatment.\(^{4}\) Therefore, a surgical approach plays an essential role in treating empyema.\(^{4,5}\)

In addition to surgical intervention, antibiotics are fundamentally essential for empyema treatment. Both the 2017 AATS guidelines and the 2010 British Thoracic Society (BTS) guidelines strongly recommend assessing microbiological culture on initial samples during aspiration or drainage procedures to select appropriate antibiotics.\(^{2,6}\) However, the positive rate of microbiological culture ranges from 40% to 70%,\(^{7,8}\) and the relatively low negative culture rate is likely related to previous antibiotic therapy. Furthermore, surgical cases of empyema are usually loculated or develop from parapneumonic effusion under antibiotic treatment for pneumonia.\(^{8,9}\)

Although it is recommended that microbiological culture is performed upon empyema diagnosis or preoperatively, no guidelines describe intraoperative culture.\(^{2,6}\) Therefore, we formulated the hypothesis that if intraoperative microbiological culture results are positive or other bacteria are newly detected in culture-negative patients at diagnosis, it is worth assessing microbiological culture intraoperatively.

The aim of this study was to investigate discrepancies in microbiological culture between preoperative and intraoperative results to determine the optimal postoperative empyema management.

### Materials and Methods

#### Patients

We retrospectively reviewed patients who underwent surgery for pleural empyema (stage II/III) from January 2011 to May 2019 at the departments of Thoracic Surgery of Saiseikai Fukuoka General Hospital (n = 39) and Saiseikai Karatsu Hospital (n = 12). Three patients who did not undergo intraoperative microbiological culture and one patient who was initially treated surgically without preoperative pleural aspiration were excluded. Thus, data for 47 patients with preoperative and intraoperative microbiological culture results were analyzed.

Empyema was diagnosed according to the presence of any of the following: purulent or opaque pleural fluid; positive Gram’s stain or positive microbiological fluid culture; loculated effusion detected by computed tomography (CT); or specific characteristics of pleural fluid analysis according to the AATS guidelines.\(^{2}\) Empyema was staged according to the BTS guidelines.\(^{6}\) Empyema related to postoperative thoracic surgery, carcinomatous pleurisy, bronchopleural fistula, or mediastinitis was excluded. Once diagnosed with empyema, patients received empirical treatment with broad-spectrum intravenous antibiotics effective against anaerobic beta-lactamase producing bacteria, and drainage procedures were attempted.

Patients were classified into three groups—those with community-acquired empyema, healthcare-associated empyema, or hospital-acquired empyema—based on the 2005 guidelines from the American Thoracic Society/Infectious Disease Society of America.\(^{10}\) Patients with community-acquired empyema were defined as those who did not meet criteria for healthcare-associated empyema. Patients with healthcare-associated empyema were defined as those who meet at least one of the following criteria: hospitalization for 2 days during the previous 90 days; residence in a nursing home; outpatient antibiotic infusion; and receiving chronic dialysis. Patients with hospital-acquired empyema were defined as those who developed empyema 48 hours or more after admission.

This study was approved by the institutional review board (IRB) of Saiseikai Fukuoka General Hospital (IRB No 2020-9) and Saiseikai Karatsu Hospital (IRB No-33).

#### Surgical procedure

All surgical procedures were performed under general anesthesia using a double-lumen endotracheal tube for single-lung ventilation and initially, with video-assisted thoracoscopic surgery (VATS). However, if we encountered difficulty evacuating the infected pleural fluid and debris due to firm adhesions, VATS was converted to open thoracotomy. Pleural debris samples were submitted for microbiological culture, which was defined as intraoperative microbiological culture. After lavage of the thoracic cavity with 3–5 L of warm saline, 1–3 chest tubes (28 Fr or 32 Fr) were inserted into the thoracic cavity. Thoracic tubes were removed under the following conditions: no air leak, clear yellow drainage fluid, and drainage volume <50 ml per day. Preoperative antibiotics were continued postoperatively and changed if necessary. Intravenous antibiotics were continued until the day of hospital discharge. Most patients continued oral antibiotics after discharge and until the outpatient examination. Patients were discharged from the hospital when
their inflammatory status improved and their condition was confirmed as good, after removing the chest tubes.

**Microbiological culture**

Preoperative and intraoperative microbiological cultures were assessed at the diagnosis of empyema and during surgery, respectively. Patients were classified into four groups according to preoperative and intraoperative microbiological culture results, respectively, as follows: negative/negative (N/N); negative/positive (N/P); positive/negative (P/N); and positive/positive (P/P). In addition, postoperative microbiological cultures, or suction drainage fluid cultures, were assessed at postoperative days 3–7 for some patients, although this assessment was not routinely performed for all patients.

**Data collection**

The following radiological variables were analyzed from the chest CT images: number of loculations; thickened parietal pleura; and maximum primary diameter and deepest diameter of the empyema cavity measured on the axial plane. We collected the following preoperative laboratory data within 48 hours of surgery: total white blood cell counts, percentages of neutrophils and lymphocytes, and serum C-reactive protein concentration. The definitions of the clinical milestones and time intervals are as follows (Supplementary Fig. 1). All supplementary figures and table are available Online.): illness duration: interval between symptom onset and surgery; preoperative antibiotic duration: interval between initial medical examination, when antibiotics were started, and surgery; empyema treatment duration: interval between diagnosing empyema, when preoperative microbiological culture was assessed, and surgery; and postoperative chest tube duration: interval between surgery and removing the chest tube. Prolonged air leak (>5 days), surgical site infection, re-expanding pulmonary edema, and recurrent empyema were considered complications.

**Statistical analysis**

Continuous variables were expressed as mean ± standard deviation or median and interquartile range (IQR). Clinical continuous variables were compared with Student’s t-test if normally distributed, or with Wilcoxon’s signed-rank test, for non-normal distribution. Categorical variables were analyzed by Fisher’s exact test. The relationships between preoperative antibiotic duration and perioperative microbiological culture were presented graphically using mosaic plots. All statistical analyses were performed with JMP software, version 13 (SAS Institute, Cary, NC, USA). P values <0.05 were considered statistically significant.

**Results**

**Patients’ characteristics**

We analyzed data for 47 patients with empyema (Table 1). The average patient age was 66 years, and 37 (78.7%) patients were men; 24 (51.1%) patients had a history of smoking. In all, 29 (59.6%) patients developed empyema after or during treatment for pneumonia as a parapneumonic effusion, and the suspected cause in four (8.5%) patients was odontogenic infection. For the remaining 15 patients, an etiology was less obvious. The percentages of patients with community-acquired empyema, healthcare-associated empyema, and hospital-acquired empyema were 55.3% (26/47), 14.9% (7/47), and 29.8% (14/47), respectively. In total, 22 (46.8%) patients received preoperative antipseudomonal antibiotics, 29 (61.7%) patients presented with stage II empyema, and 18 patients (38.3%) presented with stage III empyema. VATS was performed in 34 patients (72.3%), whereas 13 patients (27.7%) were converted to thoracotomy. Out of the 13 patients who were converted to thoracotomy, 8 (61.5%) had stage III empyema. The positive rates of the preoperative and intraoperative microbiological cultures were 27.7% (13/47) and 36.2% (17/47), respectively. Multiple pathogens were detected in positive preoperative (15.4%) and intraoperative (29.5%) microbiological cultures.

**Perioperative microbiological culture**

Among 34 patients whose preoperative microbiological culture results were negative, 8 patients (23.5%) were positive intraoperatively (Table 2). The positive rate of intraoperative microbiological culture was approximately 10% higher than that of preoperative culture (36.2% vs 27.7%, respectively). The discrepancy rate for the perioperative microbiological cultures was 25.5% (12/47; 95% confidence interval, 13.9%–40.3%). Postoperative microbiological cultures were assessed for 32 patients. Of these, one culture-P/P patient (3.1%) was positive. The bacterial species detected in the perioperative microbiological cultures are listed in Supplementary Table 1. The most frequently isolated bacterial family was Streptococaceae species in both preoperative and intraoperative cultures (58.8% [10/17] and 41.6% [10/24], respectively). Intraoperative microbiological culture detected oral-type bacteria such as Parvimonas micra, Prevotella oralis, and Actinomycetaceae species in 45.8% (11/24) of the
Table 1  Preoperative characteristics of the patients with empyema (n = 47)

| Variables                                      |       |
|------------------------------------------------|-------|
| **Age (years)**                                | 66 ± 14.5 |
| **Sex**                                        |       |
| Male                                           | 37 (78.7) |
| Female                                         | 10 (21.3) |
| **Smoking history**                            |       |
| Current/former                                 | 24 (51.1) |
| Never                                          | 23 (48.9) |
| **Side**                                       |       |
| Right                                          | 20 (57.4) |
| Left                                           | 27 (42.6) |
| **Comorbidity**                                |       |
| Diabetes                                       | 10 (21.3) |
| Cardiovascular disease                         | 10 (21.3) |
| Chronic kidney disease                         | 3 (6.4) |
| Chronic obstructive pulmonary disease          | 3 (6.4) |
| **Etiology**                                   |       |
| Post-pneumonia empyema                         | 28 (59.6) |
| Odontogenic empyema                            | 4 (8.5) |
| Poorly described                               | 15 (31.9) |
| **Classification of empyema**                  |       |
| Community-acquired empyema                     | 26 (55.3) |
| Healthcare-associated empyema                  | 7 (14.9) |
| Hospital-acquired empyema                      | 14 (29.8) |
| **Preoperative feature**                       |       |
| Duration of illness (days)                     | 15 [7–23] |
| Preoperative antibiotic duration (days)        | 8 [5–13] |
| Treatment duration for empyema until surgery (days) | 5 [3–9] |
| **Preoperative antibiotics**                   |       |
| Antipseudomonal antibiotics                    | 22 (46.8) |
| Carbapenem (MEPM, DRPM)                        | 11 |
| Penicillin (PIPC/TAZ)                          | 4 |
| New quinolone (PZFX)                           | 3 |
| Third-generation cephalosporin (CAZ)           | 4 |
| Non-antipseudomonal antibiotics                | 25 (53.2) |
| Penicillin (AMPC/SBT)                          | 23 |
| Others                                         | 2 |
| **Empyema stage**                              |       |
| Stage II                                       | 29 (61.7) |
| Stage III                                      | 18 (38.3) |
| **Surgical approach**                          |       |
| Video-assisted thoracic surgery                | 34 (72.3) |
| Thoracotomy                                    | 13 (27.7) |
| **Preoperative microbiological culture**       |       |
| Negative                                       | 34 (72.3) |
| Positive                                       | 13 (27.7) |
| Single pathogen                               | 11 (84.6) |
| Multiple pathogens                             | 2 (15.4) |
| **Intraoperative microbiological culture**     |       |
| Negative                                       | 30 (63.8) |
| Positive                                       | 17 (36.2) |
| Single pathogen                               | 12 (70.5) |
| Multiple pathogens                             | 5 (29.5) |

Continuous data are shown as mean ± standard deviation or median (interquartile range), and categorical data as number (%). AMPC/SBT: sulbactam/ampicillin; CAZ: ceftazidime; DRPM: doripenem; MEPM: meropenem; PIPC/TAZ: piperacillin/tazobactam; PZFX: pazufloxacin
Intraoperative Microbiological Culture of Empyema

Anaerobic bacteria families constituted *Prevotellaceae*, *Peptostreptococcaceae*, and *Bacteroidaceae*, and *Actinomycetaceae* species were more likely to be detected in intraoperative vs preoperative cultures (54.2% vs 29.4%, respectively). Multidrug-resistant bacteria such as methicillin-resistant *Staphylococcus aureus* or other multidrug-resistant bacteria were not isolated. Among the nine cases of culture-P/P, detected pathogens were consistent between preoperative and intraoperative cultures. Postoperatively, among the eight patients with culture-N/P, antibiotics in two patients were changed to ampicillin sulbactam from carbapenem while the other patients continued with the same antibiotics, to which the detected bacteria were sensitive.

### Table 2: Discrepancies between preoperative and intraoperative microbiological culture results

| Intraoperative microbiological culture | Preoperative microbiological culture |
|---------------------------------------|--------------------------------------|
|                                       | Positive | Negative | Total |
| Positive                              | 9        | 8        | 17    |
| Negative                              | 4        | 26       | 30    |
| Total                                 | 13       | 34       | 47    |

Discrepancy rate: 25.5% (12/47; 95% CI: 13.9–40.3) Coincidence rate: 74.5% (35/48; 95% CI: 59.7–86.1) CI: confidence interval

### Table 3: Patients’ characteristics according to the intraoperative microbiological culture results

| Characteristics | Intraoperative microbiological culture | p Value |
|-----------------|---------------------------------------|---------|
| Age (years)     |                                       | 0.162   |
| Male            |                                       | 0.727   |
| Right           |                                       | 0.362   |
| Etiology        |                                       | 0.227   |
| Post-pneumonia  | 8 (47.1)                              |         |
| Others          | 9 (52.9)                              |         |
| Comorbidity     |                                       | 0.135   |
| Smoking         | 6 (35.3)                              |         |
| Diabtes         | 3 (17.6)                              |         |
| Cardiovascular disease | 2 (11.8)  | | 0.727   |
| Preoperative antibiotics | | |
| Antipseudomonal | 9 (52.9)                              | 0.558   |
| Non-antipseudomonal | 8 (47.1)  | |         |
| Preoperative feature | | |
| Illness duration (days) | 12 [5–23]   | 15 [10–25] | 0.094* |
| Preoperative antibiotic duration (days) | 7 [3–10]   | 12 [7–16]  | 0.020* |
| Empyema treatment duration (days) | 4 [2–7]    | 8 [3–12]   | 0.053* |
| Preoperative blood test | | |
| WBC count (/µl) | 14141 ± 4844 | 12412 ± 4303 | 0.241* |
| Neutrophil (%) | 80.8 ± 7.9 | 80.5 ± 6.8 | 0.557* |
| Lymphocyte (%) | 10.6 ± 6.9 | 11.2 ± 5.2 | 0.762 |
| CRP (mg/DL) | 17.5 ± 9.1 | 15.3 ± 9.8 | 0.459 |
| Empyema findings | | |
| Multiloculated empyema | 13 (76.5) | 17 (56.7) | 0.218 |
| Number of incapsulates | 2.4 ± 1.0 | 1.8 ± 0.8 | 0.059* |
| Largest thickness of parietal pleura (mm) | 3.7 ± 1.3 | 3.5 ± 1.3 | 0.634* |
| Largest diameter of empyema cavity (cm) | 11.3 ± 1.9 | 12.0 ± 2.0 | 0.290 |
| Largest depth of empyema cavity (cm) | 5.6 ± 1.8 | 5.0 ± 1.8 | 0.280 |
| Empyema stage | | |
| Stage II | 9 (52.9) | 20 (66.7) | 0.371 |
| Stage III | 8 (47.1) | 10 (33.3) |         |

*Wilcoxon’s signed-rank test. Values are presented as number (%), mean ± standard deviation, or median (interquartile range). CRP: C-reactive protein; WBC, white blood cell.
Clinical findings and intraoperative microbiological culture

There were no significant differences in age, sex, comorbidities (smoking history, diabetes, cardiovascular disease), and preoperative regimens between the intraoperative culture-positive group and culture-negative group (Table 3). The values for preoperative inflammatory markers such as white blood counts, neutrophil and lymphocyte counts, and C-reactive protein did not differ significantly between the two groups; \( p = 0.241, p = 0.557, p = 0.762, \) and \( p = 0.459, \) respectively. The mean number of loculations in the pleural cavity in the culture-positive group was slightly higher than that of the culture-negative group; \( p = 0.050 \) while the size of the cavity did not differ significantly between the groups. The only factor differing significantly between the groups was preoperative antibiotic duration \( (p = 0.002) \). Specifically, the median preoperative antibiotic duration in the culture-positive group was 7 days (IQR: 3–10 days) and 12 days (IQR: 7–16 days) in the culture-negative group, \( p = 0.020 \). Although the result was not significant, illness duration and treatment duration for empyema until surgery were shorter in the positive group than in the negative group \( (p = 0.094 \) and \( p = 0.053, \) respectively).

Preoperative antibiotic duration and perioperative microbiological culture

Univariate logistic regression analysis revealed that the odds ratio for intraoperative positive culture per day of preoperative antibiotic duration was 0.867 (95% confidence interval: 0.86–0.98; \( p = 0.013 \)). Short preoperative antibiotic duration was associated with a significantly higher possibility of positive culture. According to the receiver operating characteristic curve analysis (Supplementary Fig. 2), the value for the area under the curve for preoperative antibiotic duration was 0.734, and the best cutoff value was 7 days. Based on this analysis, we classified patients into three groups according to the preoperative antibiotic duration: 1–7 days \( (n = 19) \); 8–13 days \( (n = 18) \); and ≥14 days \( (n = 10) \) (Fig. 1). There was a higher proportion of intraoperative culture-positive patients as well as culture-N/P patients early in the preoperative antibiotic treatment period. In addition, culture-N/P patients were still found even after 1 week of preoperative antibiotic treatment. In contrast, there were no culture-P/N patients within 1 week of preoperative antibiotic treatment (Fig. 1). All preoperative culture-positive patients were culture-negative after 2 weeks of treatment (Fig. 1).

Intraoperative microbiological culture and relationship with surgical outcomes

Intraoperative culture-positive status did not affect the surgical approach or the surgical time. Specifically, VATS was performed in approximately 70% of the patients in each group. Postoperatively, complications were not significantly different between the intraoperative culture-positive group and the culture-negative group \( (11.8% \text{ vs } 10.0%, \text{ respectively}; p = 1.000) \) (Table 4). The patient who was culture-positive postoperatively did not experience any complications. Although the results were not significantly different, the median postoperative stay was 12 days (IQR: 10–22 days) in the culture-positive group and 16 days (IQR: 11–30 days) in the culture-negative group \( (p = 0.072) \). Additionally, the median duration of hospital stay was significantly shorter in the culture-positive group than in the culture-negative group \( (15 \text{ days vs } 24 \text{ days, respectively}; p = 0.004) \).

Discussion

Microbiological culture is essential for the management of empyema; in particular, for the appropriate use of antibiotics. Although the necessity of intraoperative microbiological culture is not mentioned in the guidelines, intraoperative culture may be routinely assessed clinically. To our knowledge, no study has compared preoperative and intraoperative microbiological cultures. In this study, we found that 23.5% of patients had intraoperative positive culture results among patients with negative results at empyema diagnosis. The intraoperative microbiological culture-positive rate was 10% higher versus the preoperative rate. Moreover, shorter preoperative antibiotic duration was associated with a higher culture-positive rate.
One possible reason for newly detected bacteria intraoperatively or for the increased positive rate of intraoperative microbiological culture may be the presence of multiple loculated effusions. This hypothesis is based on our data showing that CT images in the patients in the intraoperative culture-positive group were more likely to show loculation than the culture-negative patients. Indeed, 63% (5/8) of patients whose perioperative microbiological cultures were N/P had multiloculated empyema. Maskell et al. demonstrated that pleural effusion may be heterogeneous in different locules by measuring the biochemical properties of fluid from different locules. Furthermore, multiple locules can cause inadequate drainage, which might allow bacterial proliferation. Therefore, heterogeneity in pleural effusion caused by the presence of multiple locules may result in inconsistent microbiological culture results from preoperative and intraoperative samples, and surgical drainage of multiple locules may increase the rate of bacterial detection.

Considering the trend toward early surgery for empyema, we recommend intraoperative microbiological culture. Surgery plays a vital role in treating empyema, and is often required. According to the results of an analysis of a database of hospitalizations for empyema, 61.9% of patients received surgical management with either VATS (32.1%) or open thoracotomy (29.8%). Although the optimal surgical approach is controversial, depending on the empyema stage, both the AATS and EACTS guidelines recommend that patients with stage II/III empyema undergo VATS as the first-line approach, especially in fibrinopurulent stage II empyema, because of the potential benefits of decreased pain and shorter length of stay compared with open thoracotomy. Some studies demonstrated that a longer delay in referral to a thoracic surgeon or longer symptom duration before surgery was associated with a higher conversion rate to thoracotomy as well as a higher risk of mortality and morbidity. Therefore, early VATS treatment is recommended in the treatment of empyema. As a consequence of the trend toward early VATS treatment, we may expect positive culture results during surgery, especially in preoperative culture-negative patients. In this study, we demonstrated that shorter durations of preoperative antibiotics were associated with higher positive intraoperative microbiological culture rates.

We also found that the postoperative stay was shorter in the culture-positive group than in the culture-negative group, although the result was not significant. In contrast to the findings in our study, Okiror et al. reported that intraoperative positive culture had a worse impact on surgical outcomes. However, the patient cohort in the study differed from ours in that it consisted of patients with stage III empyema treated by open thoracotomy. Practically, difficulty in comparing studies of empyema often arises because of heterogeneity in treatment and inconsistencies in the staging of empyema, clinically. One possible explanation that could account for this is that culture-positive patients underwent early surgery, which could be

| Characteristics                                      | Intraoperative microbiological culture | p Value |
|------------------------------------------------------|---------------------------------------|---------|
|                                                      | Positive n = 17                       | Negative n = 30 |
| Surgery                                              |                                       |         |
| Video-assisted thoracic surgery                       | 12 (70.6)                             | 22 (73.3) | 1.000 |
| Surgical time (min)                                  | 141 ± 44                              | 146 ± 56 | 0.912* |
| Postoperative complication                           |                                       |         |
| Total                                                | 2 (11.8)                              | 3 (10.0) | 1.000 |
| Prolonged air leak (>7 days)                         | 1                                    | 1        |
| Surgical site infection                              | 1                                    | 0        |
| Re-expanding pulmonary edema                         | 0                                    | 1        |
| Recurrent empyema                                    | 0                                    | 1        |
| Postoperative feature                                |                                       |         |
| Postoperative transfusion                            | 3 (17.6)                             | 5 (16.7) | 1.000 |
| Postoperative chest tube duration (days)             | 7 [6–9]                              | 7 [6–11] | 0.928* |
| Postoperative hospital stay (days)                   | 12 [10–22]                           | 16 [11–30] | 0.072* |
| Postoperative antibiotic treatment (days)            | 21 [16–29]                           | 20 [13–27] | 0.503* |
| Hospital days (days)                                 | 15 [11–23]                           | 24 [18–39] | 0.004* |

*Wilcoxon’s signed-rank test. Values are presented as number (%), mean ± standard deviation, or median (interquartile range).
expected to lead to earlier recovery, early discharge from the hospital, and a significantly shorter length of hospital stay. The results from our study are consistent with those from a previous study by Lee et al.,\textsuperscript{13} who reported that patients who underwent early VATS had shorter hospital stays than those who underwent later surgery.

Our data demonstrated that 46% of patients with empyema had oral-type bacteria detected intraoperatively. Additionally, four (8.5%) patients might have developed empyema secondary to odontogenic infection. A metagenomics study of bacterial etiology in empyema demonstrated that empyema harboring oral-type bacteria was not associated with pneumonia; therefore, Dyrhovden et al.,\textsuperscript{19} suggested that empyema harboring oral-type bacteria should be distinguished from post-pneumonia empyema. To support this suggestion, the analysis compared odontogenic-origin empyema (n = 12) with post-pneumonia empyema (n = 160) and demonstrated poor surgical outcomes with the former.\textsuperscript{20} Moreover, anaerobic bacteria, which occasionally spreads via hematogenous routes to establish empyema, are more likely to be present in patients with poor dental hygiene.\textsuperscript{2,19} Therefore, perioperative oral hygiene may lead to more effective empyema management, similar to the recommendation for preoperative oral hygiene in thoracic surgery.\textsuperscript{21}

There are several limitations in this study. First, this was a retrospective study, and the number of patients was too small to demonstrate significant differences between preoperative and intraoperative microbiological cultures. Although the positive rate of intraoperative culture was higher than that of preoperative culture in our study, a positive rate of 36% is still not high enough because the low sensitivity of microbiological culture is a problem.\textsuperscript{8} Moreover, difficulty detecting anaerobic bacteria in intraoperative samples due to exposure to air is another limitation. Therefore, more sensitive tests, namely bacterial polymerase chain reaction assay, should be considered in a prospective study comparing preoperative and postoperative results.\textsuperscript{8,22}

Second, detailed information about how specimens were collected during surgery was not available, as the retrospective nature of the study meant that it was difficult to determine from the surgical record when and from where the specimens were collected. However, our data demonstrated that the culture-positive group was more likely to exhibit multiloculated empyema than the culture-negative group, suggesting that specimens should be collected when irrigating other locules.

Third, to demonstrate the real worth of assessing microbiological cultures, we should demonstrate the impact on the treatment outcomes for empyema; for instance, early discharge, short duration of antibiotics for cost-effectiveness, or low recurrence of empyema. However, this analysis would be difficult because of the Japanese medical expense insurance system, which does not impose additional expenses on patients with longer hospital stay, and because of the relatively long antibiotic prescriptions, which result in low recurrence rates. Moreover, it is difficult to demonstrate the effectiveness of changes in the type of antibiotic or lower doses of antibiotics according to microbiological culture because broad-spectrum antibiotics covering anaerobic bacteria, such as beta-lactamase inhibitors, are usually used clinically.\textsuperscript{9} However, intraoperative microbiological culture is also essential for confirming the appropriateness of antibiotics initiated preoperatively.

Conclusion

We found that bacteria were detected more often intraoperatively than preoperatively at the drainage procedure. Therefore, intraoperative microbiological culture may help detect bacteria in patients whose microbiological culture results are negative at empyema diagnosis, indicating that intraoperative microbiological culture assessment has the potential to improve effective management of empyema.

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Disclosure Statement

The authors declare no conflicts of interest in association with this study.

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