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RESEARCH ARTICLE

Preoperative undernutrition predicts postoperative complications of acute empyema

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Abstract

Introduction: Surgery for acute empyema is associated with postoperative complications and relapse. Establishing a predictor for postoperative complications may improve prognosis.

Objectives: To demonstrate undernutrition as a predictor of complications after surgery for acute empyema.

Methods: We retrospectively analyzed 52 consecutive patients who underwent surgery for acute empyema from 2004 to 2019 and validated the correlation of undernutrition with serum albumin level, patient characteristics, hospital stay, and postoperative complications.

Results: The median preoperative serum albumin level was 2.4 g/dL (range: 1.1-3.4). The levels in all patients were lower than the standard value (3.5 g/dL). Patients were divided into two groups based on the median serum albumin levels: the low serum albumin level group (group L, n = 28) and the high serum albumin level group (group H, n = 24). Group L patients were significantly older (64.5 vs 52.9 years, P = .002), had lower median body mass index (21.0 vs 24.2, P = .008), and significantly had *Streptococcus anginosus* group as the causative bacteria (50% vs 21%, P = .044). Their hospitalization duration was significantly longer (28.1 vs 14.8 days, P < .001), and postoperative complications were significant or tended to be more frequent (all incidence; 11 (39%) vs 2 (8%), P = .012, respiratory-related; 7 (25%) vs 1 (4%), P = .056) in group L. Further analyses revealed that other undernutrition indicators also correlated with postoperative complications.

Conclusions: Preoperative serum albumin level is a valid predictor of complications after surgery for acute empyema. Preoperative nutrition management for empyema patients may reduce the occurrence of postoperative complications.

KEYWORDS
complications, empyema, thoracic surgery, undernutrition

1 | INTRODUCTION

Empyema is defined as pleural effusion due to the spread of infection to the thoracic cavity.[1] The most common origin is an intrapulmonary infection, such as pneumonia or lung abscess. However, its etiology varies from chest trauma, infection of the mediastinitis, head, or neck, to postoperative infection after surgery, secondary to abscess of other organs to the performance of medical practices such as chest puncture.[1,2] Furthermore, the duration from onset to appearance of symptoms, severity, and causative bacteria widely vary. Thus, empyema can generally occur in patients with various conditions.

Recently, aspiration of bacteria in the oral cavity has been reported to be one of the etiologies of empyema.[3,4] *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Streptococcus pyogenes* are frequently reported as causative bacteria of empyema,[5] while the *Streptococcus anginosus* group, an oral bacteria group, has been reported as the causative bacteria of intrathoracic abscess.[4,6] Empyema often develops in patients with immunodeficiency, who are termed "immunocompromised hosts."[7] Patients with diabetes mellitus, chronic kidney disease, and malignancy history, as well as those undergoing any cancer therapies, may be at risk for empyema; however, a detailed analysis has not been performed due to its complex conditions and rarity.[8]

Empyema is classified as acute empyema and chronic empyema. Acute empyema is defined as infectious pleural effusion with symptoms appearing within 3 months.[9] Its treatment differs depending on its classification, which is based on the findings of pleural effusion and imaging examination.[10] Empyema may be cured by non-surgical therapy, which includes drainage, chest tube irrigation, and intrapleural fibrinolytic therapy.[11-13] On the other hand, surgical therapy is effective for empyema, because a separated area of pleural effusion is formed in non-acute empyema, and drainage may be ineffective for the entire cavity.[1,14] The surgical procedure is selected according to the thoracic cavity's condition and duration from the onset, and thoracic reconstruction or filling technique may be selected for chronic empyema.[15]

Prognosis of empyema remains poor, and surgery has a high frequency of postoperative complications and relapse after treatment, especially in patients with a long duration between onset and treatment.[8,12,16] Identifying high-risk patients may be effective at reducing the rate of complications, as preventative measures can be taken prior to surgery. Some facilities have previously reported that preoperative serum albumin level was a good predictor for postoperative complications of acute empyema.[17,18] Albumin, one of the indices of nutrition, may be a good predictor of postoperative complications for empyema because patients often have nutrition problems due to long-term morbidity and being immunocompromised.

Hence, we investigated the correlation between undernutrition and postoperative complications for acute empyema, and validated the serum albumin level as a predictor of perioperative complications of acute empyema.

2 | MATERIALS AND METHODS

2.1 | Patients

Between January 2004 and May 2019, a total of 70 consecutive patients underwent surgery for clinically diagnosed acute empyema in Toho University Omari Medical Center. Acute empyema was defined as "infectious pleural effusion with symptoms appearing within 3 months," according to previous studies. All patients underwent initial treatment with chest tube placement and antibiotic therapy, and underwent surgery at our hospital as the initial treatment was not sufficiently effective in controlling the infection. All thoracotomy procedures were performed using the two-port approach. A comprehensive informed consent was obtained from all participants, and the study protocol was approved by the Ethics Committee of Toho University Omari Medical Center (approval number; M19218).

The inclusion criterion included those undergoing surgery for clinically diagnosed acute empyema. To unify patients under acute empyema caused by head, neck, and intrathoracic infection, we excluded those cases where the empyema was caused by a surgical procedure or medical practice as the etiology, causative bacteria, and surgical procedure would otherwise be quite different. We also excluded *Aspergillus* infection and chronic empyema diagnosed upon surgery because the corresponding surgical procedure is different to acute empyema. Thus, we retrospectively analyzed the remaining 52 patients.

We reviewed the patients' clinical characteristics, treatment, clinical course, and prognosis by referring to their medical records. Clinical characteristics included age, sex, body mass index, smoking status, affected side, causative disease, bacteria, and treatment. Comorbidities such as diabetes mellitus, malignancy history, brain ischemic stroke, and surgery for head and neck illness, which were previously reported to be associated to acute empyema, were also reviewed. Data on the duration from appearance of symptoms, hospitalization, chest-tube placement, until the surgery, as well as from surgery to discharge were also collected. When the accurate date of the initial appearance of symptoms was unclear, the median date of the range in which the symptoms were considered to have appeared was set as the start date.

2.2 | Indicator of undernutrition

To validate the correlation between undernutrition and the noted complications, we selected the serum albumin level as an indicator because of its comprehensibility in accordance to previous studies.[17,18] The preoperative serum albumin level was determined on the day of the surgery or 1 day before surgery. We divided the patients into two groups: low serum albumin level group (group L) and high serum albumin level group (group H) using the median serum albumin level.

Other indicators, which were previously reported, were also compared. Each indicator of undernutrition, prognostic nutritional index

TABLE 1 The clinical characteristics of the patients (n = 52)

Characteristics (n = 52)		
Age	60	(27-84)
Male	48	(92)
Smoker	39	(75)
Body mass index	22	(13-33)
Comorbidity/anamnesis		
Diabetes mellitus	21	(40)
Ischemic stroke	9	(17)
History of head and neck surgery	7	(13)
History of malignancy	4	(8)
Symptoms of onset		
Chest or back pain	29	(56)
Dyspnea	7	(13)
Fever	7	(13)
Cough	6	(12)
Malaise	3	(6)
Preoperative blood test		
Hospitalization		
Albumin (g/dL)	2.7	(1.6-3.9)
C-reactive protein (mg/dL)	25.7	(3.7-41.1)
White blood cell (/μL)	13 900	(5000-45 400)
Before surgery		
Albumin (g/dL)	2.4	(1.1-3.4)
C-reactive protein (mg/dL)	9.4	(1.0-34.6)
White blood cell (/μL)	9900	(2100-27 600)
Neutrophils (/μL)	7054	(672-20 700)
Lymphocytes (/μL)	1360	(536-3360)
Platelet cell (*10 000/μL)	42.3	(11.8-95.7)

Note: All variables are median ± SD (range) or number (%).

TABLE 2 Course and type of the empyema, treatment of the patients (n = 52)

Variables (n = 52)		
Side: right	24	(46)
Primary disease		
Pneumonia/pulmonary abscess	24	(46)
Caries/gingivitis	5	(10)
Trauma	2	(4)
Pyogenic spondylitis	1	(2)
Not pointed out	20	(38)
Causative bacteria		
Streptococcus anginosus group	19	(37)
Other *streptococci*	3	(6)
Propionibacterium	3	(6)
Staphylococcus aureus	3	(6)
Others	6	(12)
Not detected	22	(42)
First dose antibiotics		
Penicillin and β-lactamase	27	(52)
Cephems	3	(6)
Piperacillin/tazobactam	7	(13)
Carbapenem	15	(29)
Drainage before surgery	52	(100)
Intracavitary instillation of urokinase	14	(27)
Duration (days)		
From appearance of symptoms to hospitalization	8	(0-39)
From appearance of symptoms to surgery	23	(5-62)

Note: All variables are median ± SD (range) or number (%).

(PNI),[19] and controlling nutritional status (CONUT score)[20] were calculated based on the previous reports.

2.3 | Outcomes

Outcomes were determined based on patient characteristics, length of hospital stay, and postoperative complications. Postoperative complications within 30 days were evaluated using the standardized Clavien-Dindo classification.[21]

2.4 | Statistics

Continuous variables were analyzed using *t* analysis, and categorical variables were analyzed by χ^2 test or Fisher's exact test, as appropriate. All *P* values were determined using two-sided analyses, and statistical significance was set at <.05. All statistical analyses were performed using IBM SPSS statistics version 22 (SPSS Inc., Chicago, Illinois).

3 | RESULTS

3.1 | Patients' characteristics

Table 1 shows the clinical characteristics of the patients. The median age was 60 years (range: 27-84), 48 patients (92%) were men, and 39 patients (75%) were smokers. Twenty-one patients (40%) had diabetes mellitus, nine patients (17%) had a history of ischemic stroke, seven patients (13%) had a history of head or neck surgery, and four patients (8%) had a history of malignancy. Chest or back pain was the most frequent complaint (29 patients, 56%).

The median preoperative serum albumin level was 2.4 g/dL (range 1.1-3.4), and the level in all patients was below the standard value (3.5 g/dL).

TABLE 3 Comparison of the clinical characteristics between low-albumin level group (Group L, n = 28) and high-albumin level group (Group H, n = 24)

Variables	Group L	Group H	*P*-value
Age	64.5 ± 13.4	52.9 ± 12.3	.002
Male	26 (93)	22 (92)	1.000
Body mass index	21.0 ± 3.7	24.2 ± 4.5	.008
Smoker	20 (71)	18 (75)	1.000
Side: right	15 (54)	9 (38)	.278
Comorbidity/anamnesis			
Diabetes mellitus	10 (37)	11 (44)	.778
Ischemic stroke	6 (21)	3 (13)	.480
History of head and neck surgery	1 (4)	6 (25)	.040
History of malignancy	4 (14)	0 (0)	.115
Symptoms of onset: dyspnea	6 (21)	1 (4)	.107
Primary disease: pneumonia	14 (50)	10 (42)	.588
Oral infection	15 (54)	13 (54)	1.000
Causative bacteria: *streptococcus anginosus* group	14 (50)	5 (21)	.044
First dose antibiotics: carbapenem	10 (36)	5 (21)	.358
Intracavitary instillation of urokinase	6 (21)	8 (33)	.366
From appearance of symptoms to surgery (days)	22.8 ± 13.1	23.7 ± 13.9	.819
Intraoperative bleeding	260 ± 348	119 ± 145	.071
Operation time	201 ± 65.8	168 ± 56.6	.059

Note: All variables are mean ± SD (range) or number (%).

TABLE 4 Comparison of the surgical outcomes between low-albumin level group (Group L, n = 28) and high-albumin level group (Group H, n = 24)

Variables	Group L	Group H	*P*-value
Postoperative complications (CTCAE grade > 3)	11 (39)	2 (8)	.012
Respiratory complications	7 (25)	1 (4)	.056
Pneumonia	5 (18)	0 (0)	-
Respiratory failure	2 (7)	1 (4)	-
Other complications	4 (14)	0 (0)	-
Days of hospitalization after surgery	28.1 ± 24.4 (8-132)	14.8 ± 4.7 (7-42)	.006
Recurrence of empyema	0	0	-
Mortality	0	0	-

Note: All variables are mean ± SD (range) or number (%).

Table 2 shows the detailed characteristics, cause, and treatment of the empyema patients. Pneumonia and pulmonary abscess were observed most frequently as a previous infection in 24 patients (46%), while previous infection was not detected upon imaging and physical examination in 20 patients (38%). The *S. anginosus* group was detected most frequently in pleural effusion in 19 patients (37%) and was therefore declared a causative bacterium. Sulbactam and ampicillin were selected as initial antibiotic agents for 27 patients (52%). The median number of days from appearance of symptoms to hospitalization and from appearance of symptoms to surgery were 8 (range: 0-39) and 23 (range: 5-62), respectively.

3.2 | Comparison of patients' characteristics according to the serum albumin level

Table 3 shows the comparison of the clinical characteristics between group L and group H. Group L was significantly older (64.5 vs 52.9 years, $P = .002$), and BMI was lower (21.0 vs 24.2, $P = .008$). In group L, the *S. anginosus* group was detected as the causative bacteria more frequently than in group H (50% vs 21%, $P = .044$). Intraoperative bleeding tends to be higher (260 ± 348 vs 119 ± 145, $P = .071$) and the operation time tend to be longer (201 ± 65.8 vs 168 ± 56.6, $P = .059$) in group L.

TABLE 5 Analysis between characteristics and undernutrition indicators of empyema patients and postoperative complications

Variables	Reference	Odds	95% CI	*P*-value
Age > 60	≤60	5.741	1.21-37.89	.022
Sex: male	Female	1.000	0.07-56.80	1.000
Body mass index > 22.3	≤22.3	1.353	0.32-5.87	.752
Smoker	Non-smoker	0.309	0.07-1.44	.086
Comorbidity/anamnesis				
Diabetes mellitus	No	3.124	0.73-14.81	.105
Ischemic stroke	No	0.831	0.07-5.36	.834
History of head and neck surgery	No	0.464	0.01-4.49	.664
History of malignancy	No	5.330	2.96-9.61	.003
Streptococcus anginosus group	Others	10.484	2.12-72.30	<.001
Oral infection	No	0.285	0.05-1.25	.106
Intraoperative findings				
Intraoperative bleeding > 100 mL	≤100 mL	0.536	0.15-1.93	.335
Operation time > 180 min	≤180 min	1.684	0.47-6.07	.421
Indication of nutrition				
Albumin related indications				
Serum albumin level < 2.4	≥2.4	6.865	1.25-72.06	.012
AGR > 0.48	<0.48	0.351	0.07-1.53	.199
PNI < 30	≥30	8.438	1.53-88.89	.009
CONUT score > 8	≤8	6.408	1.35-42.52	.009
CAR > 4.1	≤4.1	2.577	0.59-13.47	.205
Other indications				
NLR > 5.3	≤5.3	7.605	1.38-79.73	.010
PLR > 0.3	≤0.3	1.667	0.40-7.71	.528

Abbreviations: AGR, albumin to globulin ratio; CAR, C-reactive protein to albumin ratio; CONUT score, controlling nutritional status score; NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio; PNI, prognostic nutritional index.

3.3 | Comparison of the outcome according to the serum albumin level

Table 4 shows the comparison of the surgical outcomes between two groups. Thirteen patients had a grade over 3 within 30 days postoperatively. Five patients had pneumonia, three patients had respiratory failure, two patients had an ischemic stroke, and one patient had a wound infection. In contrast, complications were significantly more frequent in group L (11 (39%) vs 2 (8%), $P = .012$) and complications related to respiration (7 (25%) vs 1 ((4%), $P = .056$) tended to be more frequently observed in group L. There was no recorded perioperative death.

The duration of hospital stay was significantly longer in group L (28.1 ± 24.4 days [range: 8-132] vs 14.8 ± 4.7 days [range: 7-42], $P = .006$).

3.4 | Analysis of correlations between clinical variables and postoperative complications

To investigate the correlation between undernutrition and complications of acute empyema, we compared the clinical characteristics and indication of nutrition and postoperative complications via logistic analysis (Table 5). All variables were divided into two categories via the median. According to the variables, age > 60 years (odds ratio: 5.741, 95% CI: 1.21-37.89, $P = .022$), history of malignancy (odds ratio: 5.330, 95% CI: 2.96-9.61, $P = .003$), and detection of *S. anginosus* group as the causative bacteria (odds ratio: 10.484, 95% CI: 2.12-72.30, $P < .001$) were significant indicators for postoperative complications. As for indicators of nutrition, we identified not only albumin-related indications such as serum albumin level (odds ratio: 6.865, 95% CI: 1.25-72.06, $P = .012$), PNI (odds ratio: 8.438, 95% CI: 1.53-88.89, $P = .009$), and CONUT score (odds ratio: 6.408, 95% CI: 1.35-42.52, $P = .009$), but also the neutrophil/lymphocyte ratio (NLR) (odds ratio: 7.605, 95% CI: 1.38-79.73, $P = .010$), as significant indicators. Albumin/globulin ratio (AGR), C-reactive protein/albumin ratio (CAR), and platelet/lymphocyte ratio (PLR) were not found to be adequate indicators.

4 | DISCUSSION

This study investigated the predictors of the postoperative complications of acute empyema by analyzing the variables of patient's clinical

factors, and clarified that an indicator of undernutrition such as the serum albumin level is a valid predictor. The *S. anginosus* group was significantly associated as the causative bacteria of acute empyema in patients with low serum albumin levels, suggesting that improvement of undernutrition in patients as well as immunocompromised hosts may reduce postoperative complications.

High frequency of relapse and poor prognosis for empyema were reported in some facilities.[14,16] Patients with empyema are often immunocompromised and a long time since onset. Thus, controlling infection and improving general conditions may be difficult. Some recent studies reported good prognosis of thoracoscopic irrigation for acute empyema early onset,[22] although this disease could not be diagnosed early due to its complexity. Moreover, there are no detailed analysis reports on the predictors of postoperative complications and relapse. Therefore, predicting the complications before surgery may help in deciding on treatment strategy options and prevent further complications. Therefore, this study is useful to improve the prognosis of acute empyema patients who underwent surgery.

Reportedly, preoperative undernutrition is a predictor of postoperative complications and poor prognosis mainly in patients with malignancy, including thoracic disease.[23,24] Various parameters have been reported as indicators of nutrition, including the Glasgow prognostic score (GPS), PNI, CONUT score, serum albumin level, AGR, CAR, NLR, PLR, and sarcopenia.[19,20,25-29] These indicators, excluding sarcopenia, measure blood components/parameters albumin, total protein, total cholesterol, C-reaction protein and platelet content, and the number of leukocytes and their fractions. Moreover, undernutrition is associated with delays in wound healing and cancer immunity, and values related to the inflammatory response included the indicator because chronic inflammation related to malignancy may decrease the general condition or weaken cancer immunity.[30]

In contrast, the relationship between undernutrition and inflammatory diseases, including empyema, has not yet been reported. In this analysis, albumin-related undernutrition indicators, AGR, PNI, CAR, and CONUT score, were related to the incidence of postoperative complications. Additionally, NLR was significantly related to the incidence of postoperative complications, making the undernutrition indicator a good predictor of postoperative complications and relapse. On the other hand, PLR was not related to prognosis. Due to its special conditions that differ from cancer patients, the nutritional indicators for inflammatory diseases, including empyema, may differ from previous indicators, thereby requiring further investigation.

As all patients with empyema have a varied background, treatment, and nutrition management should be decided upon individually, rather than applying a fixed strategy. First, as the causative disease and bacteria are varied, blood test, head, neck, and chest computed tomographies, oral and neck conditions, causative bacteria search, as well as a detailed medical history taking should be undertaken preoperatively. Second, the treatment strategy should be individualized. Selection of antibiotics, oral care, and rehabilitation may improve the general condition and prevent additional infection in patients whose empyema is due to aspiration. Third, improvement of undernutrition may improve the prognosis. Generally, improvement of undernutrition in patients with malignancy is reported to be effective in some facilities. Thus, further detailed analysis on the improvement of undernutrition and prognosis for inflammation disease including empyema may improve prognosis.

In our hospital, condition of nutrition, rehabilitation, and oral care are individually planned for all empyema patients. The effectiveness for each treatment and intervention should be demonstrated. The prognosis after surgery for empyema in our hospital is relatively satisfactory despite undernutrition in patients as of the time of writing. More evidence is required to improve clinical outcomes in patients.

4.1 | Study limitations

First, this study is a single-center retrospective analysis. Though empyema is a relatively rare disease, analysis involving a larger size may help provide stronger evidence. Second, the population we analyzed was fairly biased. Most of the patients were from other hospitals because they could not be treated upon initial therapy. As empyema is a complicated disease, a multi-center analysis should be undertaken.

4.2 | Conclusion

Serum albumin level was a valid predictor of postoperative complications after acute empyema surgery. Perioperative nutrition management for acute empyema patients with low-serum albumin level may reduce postoperative complications.

CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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AUTHOR CONTRIBUTIONS

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All authors have read and approved the final version of the manuscript.

Takashi Sakai had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

TRANSPARENCY STATEMENT

Takashi Sakai affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The study protocol was approved by the Ethics Committee of Toho University Omari Medical Center (approval number; M19218) and was conducted according to the principles of the Declaration of Helsinki.

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