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Relationship between oral health and prognosis in patients with empyema: Single center retrospective study with propensity score matching analysis

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Abstract

Background

Empyema is a life-threatening infection often caused by oral microbiota. To the best of our knowledge, no reports have investigated the association between the objective assessment of oral health and prognosis in patients with empyema.

Materials and methods

A total of 63 patients with empyema who required hospitalization at a single institution were included in this retrospective study. We compared non-survivors and survivors to assess risk factors for death at three months, including the Renal, age, pus, infection, diet (RAPID) score, and Oral Health Assessment Tool (OHAT) score. Furthermore, to minimize the background bias of the OHAT high-score and low-score groups determined based on the cut-off value, we also analyzed the association between the OHAT score and death at 3 months using the propensity score matching method.

Results

The 3-month mortality rate was 20.6% (13 patients). Multivariate analysis showed that a RAPID score ≥5 points (odds ratio (OR) 8.74) and an OHAT score ≥7 points (OR 13.91) were significantly associated with death at 3 months. In the propensity score analysis, a significant association was found between a high OHAT score (≥7 points) and death at 3 months ($P = 0.019$).

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Conclusion

Our results indicated that oral health assessed using the OHAT score may be a potential independent prognostic factor in patients with empyema. Similar to the RAPID score, the OHAT score may become an important indicator for the treatment of empyema.

1. Introduction

Empyema is defined as the presence of bacteria or pus in the pleural cavity and has common clinical symptoms, including dyspnea, fever, chest pain, and cough [1]. In recent years, the incidence of empyema has increased steadily worldwide, with a high mortality rate of 10–30% despite the advancements in antibiotic therapy and widespread chest tube drainage [2–4]. Physicians must understand the risk factors, clinical features, and severity of diseases with high mortality. A clinical risk score for predicting death can facilitate the formulation of early management strategies. In 2014, the RAPID score was developed as a clinical risk score of pleural infections, including empyema [5]. This score is composed of the following five patient characteristics and clinical data: renal, age, purulence, infection source, and dietary factors. Recent reports have revealed an association between the RAPID score and 3-month death rate (low risk: 0–2 points, medium risk: 3–4 points, high risk: 5–7 points) in patients with empyema [6,7].

The most common cause of empyema is bacterial pneumonia, which is associated with oral health, including the number of oral bacteria [8,9]. Bacteria breach the visceral pleura to establish an infected parapneumonic effusion, resulting in empyema. Many studies have reported that oral bacteria, including *Streptococcus spp*., *Staphylococcus aureus*, and *Fusobacterium spp*. Have been detected as the main causative bacteria of empyema [10–12]. In addition, a recent report presented direct genetic evidence that some bacteria in empyema are derived from the oral flora [13]. Therefore, oral health may be associated with the onset or prognosis of empyema. To the best of our knowledge, no reports have investigated the association between the objective assessment of oral health and prognosis in patients with empyema. The Oral Health Assessment Tool (OHAT) score system is widely recognized as an objective tool for assessing oral health [14–17]. In 2015, this scoring system was developed for non-dental professionals such as nurses and allied health personal care attendants [14]. This score consists of the following eight categories on a 3-point scale: lips, tongue, gums and mucosa, saliva, natural teeth, dentures, oral cleanliness, and dental pain, with higher total scores indicating poorer overall oral health. Recently, many researchers, including dentists, have used the OHAT score to evaluate the oral health of patients in various fields [15–17]. This study aimed to investigate the association between oral health assessed using the OHAT score and prognosis in patients with empyema.

2. Patients and methods

2.1. Patients

This study included 63 patients hospitalized for empyema treatment between January 2017 and July 2022 at Kakogawa Central City Hospital. Light's classification was used to diagnose empyema [18]. In brief, 1) aspiration of grossly purulent material on thoracentesis and 2) at least one of the following: a) thoracentesis fluid with a positive Gram stain or culture, b) pleural fluid glucose $<$40 mg/dL, c) pH $<$7.2, or d)- lactate dehydrogenase $>$1000 IU/L [18]. The exclusion criteria were as follows: patients under 20 years old, those who did not undergo pleural puncture for some reason, those who did not wish to participate after the publication of this study, and those with missing data that were needed in this study. Patients with confirmed empyema underwent various tests such as blood tests, and were treated with antibiotics and chest tube drainage. They also underwent dental examinations, including panoramic dental radiography and oral photography, within days after hospitalization and dental treatments, if needed, during hospitalization.

This study was performed in accordance with the 1964 Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Boards (IRB) of Kakogawa Central City Hospital (Authorization number: 2020–46). The ethics committee approved the study and gave administrative permissions to access the data used in this study. As this was a retrospective study, the research plan was published on the homepage of the hospital according to the instructions of the IRB in accordance with the guaranteed opt-out opportunity.

2.2. Study design

The present study is a retrospective cohort study. Patients were divided into two groups: non-survivors and survivors at 3 months. The following variables from medical records were investigated: (1) patient factors (sex, presence of dysphagia, compromised-host, smoking history); (2) clinical findings factors, such as CRP, WBC, blood urea nitrogen (BUN), age, purulence of pleural fluid, infection source (community-acquired/hospital-acquired), serum albumin, OHAT score, and etiology (monomicrobial/polymicrobial/no growth); and (3) treatment methods. Dysphagia was defined as coughing when taking a meal or decreasing swallowing ability on evaluation by physicians and speech-language-hearing therapists [7]. Data on treatment and outcomes were also evaluated for each patient during hospitalization. A compromised-host was defined as a patient with any of the following diseases: rheumatoid arthritis, chronic kidney disease, malignancy, diabetes, cardiovascular diseases, neurological diseases, and steroid use. We used two clinical risk scores: RAPID (total score; min:0 point, max:7 points) and OHAT (total score; min:0 point, max:16 points). The RAPID score was based on five common parameters (Table 1) [6]. Based on the results of the dental examinations, the presence of teeth with poor prognosis was retrospectively investigated using panoramic dental

Table 1. RAPID score.

RAPID score		
Parameter	**Measure**	**Score**
Renal		
BUN (mg/dL)	<14	0
	14–22.4	1
	>22.4	2
Age (years)	<50	0
	50–70	1
	>70	2
Purulence of pleural fluid	Purulent	0
	Non-purulent	1
Infection source	Community-acquired	0
	Hospital-acquired	1
Dietary factors		
Alb (g/dL)	≥2.7	0
	<2.7	1
Risk categories	Score 0–2	Low risk
	Score 3–4	Medium risk
	Score 5–7	High risk

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radiography. They were defined as teeth with abnormal radiographic findings (e.g., apical radiolucency larger than 3 mm in diameter, alveolar bone loss around more than half of the root, untreated root remnants, or vertically fractured roots) [19,20]. Medical records were used whether those teeth were extracted. Pleural fluid was collected by pleural puncture at the time of admission, and microbiological examinations were performed. Anaerobic containers were used to collect pleural fluid to detect anaerobic bacteria, and Gram staining and pleural fluid cultures were performed. Blood agar (Kohjin Bio Co., Ltd., Saitama, Japan) and chocolate agar media (Kohjin Bio Co., Ltd.) were used to detect general bacteria. Anaero Columbia agar medium with hemin and vitamin K1 (Nippon Becton Dickinson Co., Ltd., Tokyo, Japan) was used to detect anaerobic bacteria; any anaerobic bacteria were then cultivated at 35˚C and 9% CO_2. The causative pathogens were then identified in the pleural fluid culture.

2.3. OHAT score

The OHAT score consists of eight categories with three possible scores (0 = healthy, 1 = some changes, and 2 = unhealthy) (Table 2) [14]. The total score is the sum of the various sub-scores. Based on the results of the dental examinations, including oral photographs and medical records, OHAT score of each patient was retrospectively evaluated by two observers (EI and KS). EI is an oral and maxillofacial surgeon with $\geq$ 10 years of experience, and KS is a dental hygienist with $\geq$ 10 years of experience. The OHAT-J, which includes images of each category and point scale in Japanese, is well-known among dentists and dental hygienists in Japan [21,22]. In this study, the dentist (EI) and dental hygienist (KS) evaluated the OHAT score after visual training and calibration by using this picture (S1 Data). Finally, the OHAT score of each patient was determined through discussion among the observers.

2.4. Statistical analyses

Statistical analyses were performed using SPSS (version 26.0; IBM Corp., Armonk, NY, USA) and Ekuseru-Toukei 2012 (Social Survey Research Information Co., Ltd., Tokyo, Japan). A receiver operating characteristic (ROC) curve was used to determine the cut-off values for the RAPID and OHAT scores. The area under the ROC curve was used to measure the accuracy of

Table 2. OHAT score.

OHAT score			
Category	**0 = healthy**	**1 = changes**	**2 = unhealthy**
Lips	Smooth, pink, moist	Dry, chapped, or red, at corners	Swelling or lump, white/red/ulcerated patch; bleeding/ulcerated at corners
Tongue	Normal, moist, rough, pink	Patchy, fissured, red, coated	White/red patches, ulcerated, swollen
Gums and tissues	Pink, moist, smooth, no bleeding	Dry, shiny, rough, red, swollen, one ulcer/sore spot under dentures	Swollen, bleeding ulcers, white/red patches, generalized redness under dentures
Saliva	Moist tissues, watery and free flowing saliva	Dry sticky tissues, little saliva present, resident thinks they have a dry mouth	Tissue parched and red, very little/no saliva present, saliva thick, resident thinks they have a dry mouth
Natural teeth	No decayed or broken teeth/ roots	1–3 decayed or broken teeth/roots or very worn-down teeth	≥4 decayed or broken teeth/roots, or very worn-down teeth, or <4 teeth
Dentures	No broken areas or teeth, dentures regularly worn and named	1 broken area/tooth or dentures only worn for 1–2 h daily, or dentures not named or loose	More than 1 broken area/tooth, denture missing or not worn, loose and needs denture adhesive, or not named
Oral cleanliness	Clean and no food Particles or tartar in mouth or dentures	Food particles/tartar/plaque in 1–2 areas of the mouth or on a small area of dentures or halitosis (bad breath)	Food particles/tartar/plaque in most areas of the mouth or on most areas of dentures or severe halitosis (bad breath)
Dental pain	No behavioral, verbal, or physical signs of dental pain	Verbal and/or behavioral signs of pain present, such as pulling at face, chewing lips, not eating, aggression	Physical pain signs (swelling of cheek or gum, broken, ulcers) present, as well as verbal and/or behavioral signs (pulling at face, not eating, aggression)

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discrimination. The area under the ROC curve was used to measure the accuracy of discrimination (range, 0.5 to 1). The association of each variable with death at 3 months was analyzed using the non-parametric Mann-Whitney U test for ordinal variables and either the Fisher's exact test or the chi-squared test was used for categorical variables. Statistical significance was set at $P<0.05$. The selected variables were included in a multiple logistic regression model using the forced-entry method. Odds ratios (Ors) and 95% confidence intervals (Cis) were calculated. Furthermore, to minimize selection bias associated with the comparison of retrospective data analysis, propensity score matching was performed between the high and low OHAT score groups using cut-off values. Subsequently, propensity score-matched cases (36) were evaluated to determine an association between a high OHAT score and death at 3 months. Reliability assessments for the stability of OHAT scores were assessed in a test-retest of observers using Cohen's kappa statistic for the individual categories and intraclass correlation (ICC) for the total OHAT score [14]. The Kappa statistic indicated the degree of departure between the actual observed and chance percentage agreement and was not weighted. In interpreting the Kappa statistic, values of 0.41–0.60 were considered moderate, 0.61–0.80 substantial, and 0.81–1.0 almost perfect agreement [14].

3. Results

The 3-month mortality rate was 20.6% (13 out of 63 patients). The median age of non-survivors was 84.0 years and that of survivors was 72.0 years, which showed a significant difference ($P<0.001$). All non-survivors and 42 of the 50 survivors were male.

Table 3 shows patient characteristics and the results of the univariate analysis. In the univariate analysis, the rate of dysphagia ($P = 0.047$), RAPID score ($P<0.001$), and OHAT score ($P<0.001$) were significantly higher in non-survivors than in survivors. Of the five factors assessed by the RAPID score, BUN level, and age were significantly higher in non-survivors than in survivors, while serum albumin level was lower in non-survivors than in survivors. Of the eight categories of OHAT score, lip ($P<0.001$), tongue ($P = 0.021$), gums and tissues ($P = 0.007$), and saliva ($P = 0.014$) were unhealthier in non-survivors than survivors. More than half of the non-survivors (69.2%) and survivors (54.0%) had teeth with a poor prognosis. Of them, some non-survivors (22.2%) and survivors (55.6%) underwent extraction of those teeth. Non-survivors tended to have a lower frequency of oral care than survivors ($P = 0.135$).

RAPID score ≥5 points had a sensitivity of 61.5%, a specificity of 88.0%, and an area under curve (AUC) of 0.81 (Fig 1A). OHAT score ≥7 points had a sensitivity of 76.9%, a specificity of 74.0%, and an AUC of 0.79 (Fig 1B). After applying a logistic regression model and forced entry method, we found that RAPID score ≥5 points (OR 8.74) and an OHAT score ≥7 points (OR 13.91) were significant risk factors for death at 3 months (Table 4). Table 5 includes the intra- and inter-rater reliability data for the OHAT scores. Intra-rater reliability ranged from 84.1% for oral cleanliness to 100% for dental pain. Kappa statistics were in the range considered substantially perfect (0.61–0.80) for saliva and oral cleanliness, and for all other categories in the range of 0.81–1.00 (almost perfect). Inter-rater reliability ranged from 82.5% for oral cleanliness to 100% for dental pain. Kappa statistics were in the range of substantially perfect (0.61–0.80) for lips, saliva, and oral cleanliness, and for all other categories in the range of 0.81–1.00 (almost perfect). The ICC for the OHAT total scores was 0.94 for intra-rater and 0.92 for inter-rater reliability.

Table 6 shows the results of the pleural fluid culture test. In both groups, oral bacteria were detected in many patients. The most frequently detected bacteria were *Streptococcus species*, followed by *facultative* anaerobic *Staphylococcus* spp., obligate anaerobic *Prevotella* spp., *Parvimonas micra*, and *Porphyromonas gingivalis*.

Table 3. Distribution of variables between non-survivors and survivors.

Variables		Non-survivors Survivors (n = 13) (n = 50)		*P* value
Sex	Male	13 (100.0%)	42 (84.0%)	0.188 [b]
Dysphagia	Yes	12 (92.3%)	31 (62.0%)	**0.047*** [b]
Compromised host	Yes	6 (46.2%)	19 (38.0%)	0.752 [b]
Smoking history	Yes	10 (76.9%)	47 (74. 0%)	1.000 [b]
CRP (mg/dL)	Median (range)	23.7 (7.1–30.3)	21.4 (2.1–41.0)	0.425 [a]
WBC (10^3/μL)	Median (range)	15.6 (10.8–24.8)	15.4 (5.5–39.2)	0.663 [a]
RAPID score	Median (range)	5.0 (2–6)	3.0 (0–5)	<**0.001*** [a]
BUN (mg/dL) Age (years)	Median (range) Median (range)	43.4 (9.4–95.4) 84.0 (65–96)	16.3 (4.6–67.5) 72.0 (43–90)	<**0.001*** [a] <**0.001*** [a]
Purulence of pleural fluid	Purulent Non-purulent	13 (100.0%) 0 (0.0%)	42 (87.3%) 8 (12.7%)	0.188 [b]
Infection source	Community-acquired	12 (92.3%)	45 (90.0%)	1.000 [b]
	Hospital-acquired	1 (7.7%)	5 (10.0%)	
Serum albumin (g/dL)	Median (range)	2.1 (1.2–2.9)	2.5 (1.7–4.2)	**0.025*** [a]
OHAT score	Median (range)	7.0 (4–13)	5.0 (0–11)	<**0.001*** [a]
Lips	Median (range)	1.0 (0–2)	0.0 (0–2)	<**0.001*** [a]
Tongue	Median (range)	1.0 (0–2)	1.0 (0–2)	**0.021*** [a]
Gums and tissues	Median (range)	1.0 (0–2)	0.5 (0–2)	**0.007*** [a]
Saliva Natural teeth	Median (range) Median (range)	1.0 (0–2) 1.0 (0–2)	0.0 (0–2) 1.0 (0–2)	**0.014*** [a] 0.697 [a]
Teeth with a poor prognosis	Presence	9 (69.2%)	27 (54.0%)	0.365 [b]
With tooth extraction	Yes (/presence)	2/9 (22.2%)	15/27 (55.6%)	0.128 [b]
Dentures Oral cleanliness Frequency of oral care Dental pain	Median (range) Median (range) Median (range) Median (range)	0.0 (0–2) 2.0 (0–2) 2.0 (0–3) 0.0 (0)	0.0 (0–2) 2.0 (0–2) 2.0 (1–4) 0.0 (0–2)	0.913 [a] 0.055 [a] 0.135 [a] 0.384 [a]
Etiology	Monomicrobial	5 (38.5%)	22 (44.0%)	1.000 [b]
	Polymicrobial	2 (15.3%)	11 (22.0%)	
	No growth	6 (46.2%)	17 (34.0%)	
Treatment	Antibiotic therapy only	4 (30.8%)	4 (8.0%)	0.120 [c]
	+ drainage	2 (15.4%)	5 (10.0%)	
	+ drainage, urokinase	7 (53.8%)	39 (78.0%)	
	+ surgery	0 (0.0%)	2 (4.0%)	

Values are expressed as absolute numbers, with the corresponding percentage of the total in parentheses. Values in the right-hand column indicate the statistical significance of the difference between subgroups. Most variables expressed as the median (range) in a non-parametric ratio scale.

[a]Mann-Whiteny U test;

[b]Fisher's exact test;

[c]Chi-squared test.

*$P < 0.05$.

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We compared patient characteristics between the OHAT high-score (≥ 7 points) and low-score (< 7 points) groups (Table 7). Propensity score matching was performed for an unbiased analysis of the OHAT score using seven variables (sex, dysphagia, compromised host, smoking history, CRP, WBC, and RAPID score). After propensity score matching, the characteristics of the two groups were balanced in seven variables, and the rate of non-survivors was significantly higher in the OHAT high-score group than in the low-score group ($P = 0.019$) (Table 8).

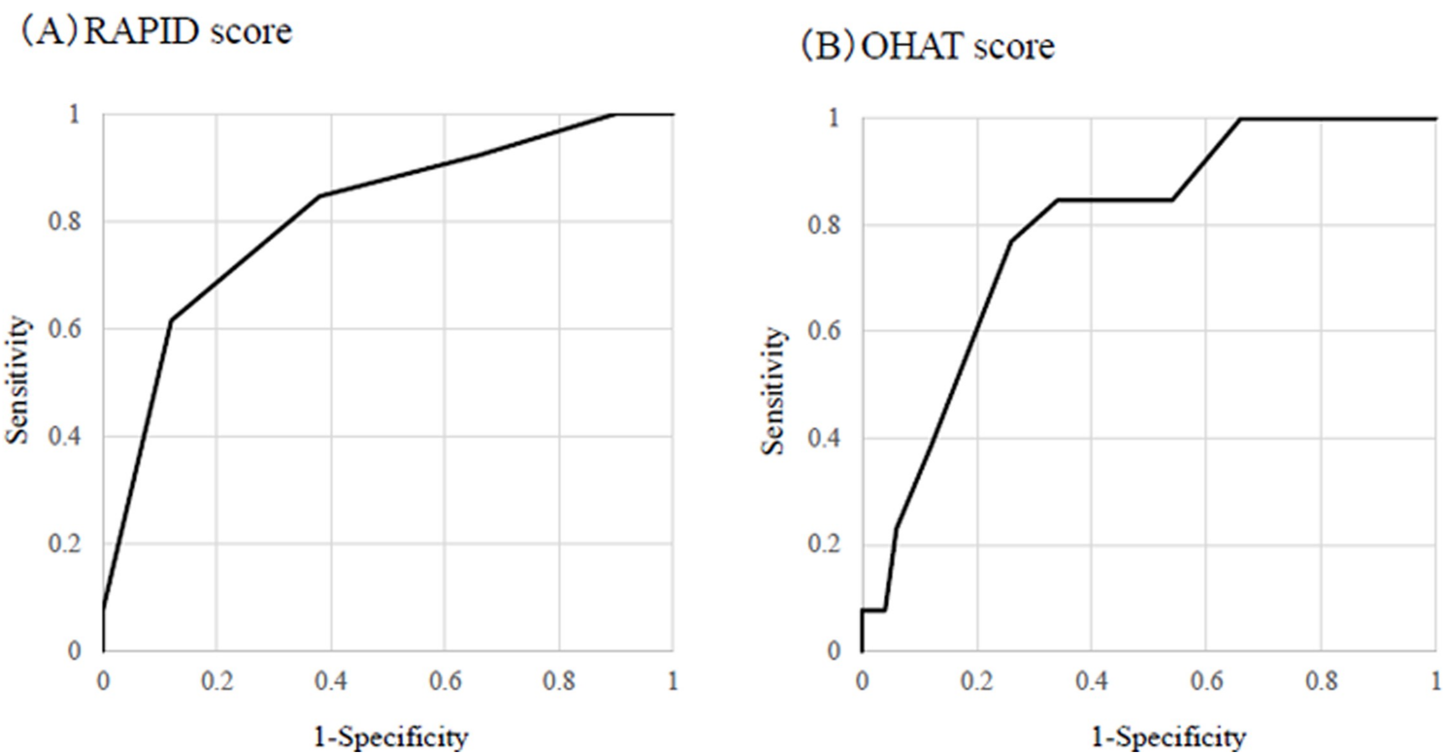

Fig 1. (A) The ROC curve for accuracy of RAPID score. The AUC for our model was 0.810 (95% confidence interval 0.675 to 0.945). (B) The ROC curve for accuracy of OHAT score. The AUC for our model was 0.790 (95% confidence interval 0.664 to 0.91.

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4. Discussion

In this study, we investigated the risk factors for death at 3 months in patients with empyema. Multivariate analyses showed that a RAPID score ≥5 points (OR 8.74) and an OHAT score ≥7 points (OR 13.91) were significantly associated with death at 3 months. Additionally, using cut-off values, propensity score analysis between the high and low OHAT score groups revealed a significant association between OHAT high score (≥7 points) and death at 3 months (P = 0.019).

Table 4. The results of the multivariate logistic regression analysis of the risk factors for death at three months in empyema.

			95% CI	
Variable	***P* value**	**Odds ratio**	**Lower**	**Upper**
Sex Male	.999	390596307.6	.000	
Dysphagia	.247	4.909	.333	72.429
Compromised host	.888	.877	.142	5.413
Smoking history	.409	2.693	.256	28.314
High CRP (21.8≥)	.064	8.672	.881	85.365
High WBC (14170≥)	.128	.192	.023	1.611
High RAPID score (≥5 points)	**.019***	8.742	1.432	53.377
High OHAT score (≥7 points)	**.013***	13.905	1.755	110.160

CI. Confidence interval

Data are the p-value, OR and 95% CI for those factors found to be significantly associated with death at three months in empyema.

*$P < 0.05$.

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Table 5. Intra-rater and inter-rater reliability for individual OHAT categories and total OHAT score.

Category	Intra-rater		Inter-rater	
	Percent agreement	Kappa statistic	Percent agreement	Kappa statistic
Lips	90.5	**0.83***	87.3	**0.77***
Tongue	90.5	**0.84***	88.9	**0.81***
Gums and tissues	92.1	**0.88***	90.5	**0.83***
Saliva	88.9	**0.79***	87.3	**0.76***
Natural teeth	93.7	**0.90***	90.5	**0.86***
Dentures	96.8	**0.89***	95.2	**0.84***
Oral cleanliness	84.1	**0.76***	82.5	**0.73***
Dental pain	100.0	**1.00***	100.0	**1.00***
	Intraclass correlation		Intraclass correlation	
Total OHAT score	**0.94***		**0.92***	

*$P < 0.001$.

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The 3-month mortality rate in this study was 20.6%, which was slightly higher than or similar to that reported in previous studies [2–5,7]. In addition to the RAPID and OHAT scores, univariate analysis showed that age (*P<0.001*) out of RAPID score and presence of dysphagia (*P = 0.047*) were significantly associated with death at 3 months in patients with empyema. Pneumonia is the third leading cause of death in Japan (9.2%), and the ratio of aspiration pneumonia to total cases of pneumonia increases with age (50–59 years: approximately 30%; 60–69 years: approximately 50%; 70–79 years: approximately 70%; 80–89 years: approximately 80%; over 90 years: approximately 90%) [23]. In general, 20–40% of hospitalized patients with pneumonia have pleural effusion, and 10% progress to acute empyema [18]. A previous study reported a significant relationship between dysphagia and death at 3 months in patients with empyema [13].

Previous studies reported that the RAPID score enables the prediction of death in patients with pleural infections, including empyema at 3 months [5–7], indicating that patients with RAPID scores ≥5 were at a high risk of death at 3 months [6,7]. These results are in line with those of the present study. Of the five factors contributing to this score, BUN levels, age, and serum albumin levels were significantly different between survivors and non-survivors. High BUN levels indicate dehydration, which is expected to negatively affect the patient prognosis. A previous report showed that high BUN levels in the RAPID score were associated with death at 3 months in patients with empyema (median 53 mg/dL vs 19 mg/dL; $P<0.01$) [7] similarly to this study (median 43.4 mg/dL vs 16.3 mg/dL; $P<0.001$). Serum albumin is a reliable marker of nutritional status [24], and a previous study showed an association between low serum albumin levels and infection [25]. Additionally, Sakai et al. reported that preoperative serum albumin level is a valid predictor of complications following surgery for acute empyema (incidence of high-level group vs low-level group = 39% vs 8%; $P = 0.012$) [26].

The OHAT score has been used in various fields [15–17], and its inter-rater reliability has been discussed. Several researchers have used Cohen's kappa statistics to investigate the reliability and validity of the OHAT score per category in many fields [14,27,28], concluding that the OHAT score is a reliable and valid screening assessment tool for their research subjects. We also analyzed the intra- and inter-rater reliabilities of the OHAT scores per category using Cohen's kappa statistics in this study. The results were either almost perfect or moderately perfect and were reliable for evaluation. Furthermore, Nishizawa et al. investigated the association between the OHAT score and aspiration pneumonia [29]. They set the OHAT score cut-off

Table 6. Distribution of microorganisms as the cause of empyema.

Non-survivors	No.	Survivors	No.
[Facultative anaerobic bacteria]	5	[Facultative anaerobic bacteria]	31
Streptococcus spp.	3	*Streptococcus* spp.	22
S. constellatus	(2)	*S. intermedius*	(10)
S. intermedius	(1)	*S. anginosus*	(4)
Psudomonas aeruginosa	1	*S. constellatus*	(4)
Aspergillus fumigatus	1	*S. agalactiae*	(2)
		S. gordonii	(1)
		S. mitis	(1)
		Staphylococcus spp.	5
		S. aureus	(2)
		MRSA	(2)
		MSSA	(1)
		Psudomonas aeruginosa	2
		Citrobacter koseri	1
		Enterococcus faecalis	1
[Obligate anaerobic bacteria]	5	[Obligate anaerobic bacteria]	13
Prevotella spp.	2	*Parvimonas micra*	3
P. buccae	(1)	*Prevotella* spp.	3
P. disiens	(1)	*P. buccae*	(1)
Parvimonas micra	1	*P. disiens*	(1)
Porphyromonas gingivalis	1	*P. denticola*	(1)
Fusobacterium nucleatum	1	*Porphyromonas gingivalis*	3
		Veillonella spp.	1
		Bacteroides vulgatus	1
		Fusobacterium nucleatum	1
		Finegoldia magna	1

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value to 4 points, and few patients with aspiration pneumonia had OHAT scores of ≥7 points, which was the cut-off value determined by using ROC curve in the present study. This difference may indicate the patient's general medical condition during each disease.

Empyema is caused by obligate anaerobic bacteria such as *Prevotella* spp., *Peptostreptococcus*, or *Fusobacterium nucleatum* (30–40% responsible for mixed infections) in addition to *Streptococcus pneumoniae* and *Staphylococcus aureus* [10–12,30,31]. The detection frequency of *the Streptococcus anginosus* group (*S. anginosus*, *S. constellatus*, and S. *intermedius*), which resides in the oral cavity, is also high. Particularly in empyema, polymicrobial infections with obligate anaerobic bacteria are common [32]. In the present study, *Streptococcus pneumoniae* was not detected, and there was no significant difference between monomicrobial and polymicrobial patients, unlike the results of a previous study in which a significant difference was found [13]. The most frequently detected bacteria were *Streptococcus anginosus*, followed by *Staphylococcus* spp., *Prevotella* spp., *Parvimonas micra*, and *Porphyromonas gingivalis*. Therefore, most of the causative bacteria were derived from the oral flora. Teeth and periodontal tissues can be a route of bacterial invasion [33]. There are two possible pathways for the onset of empyema: first, descending mediastinitis by dental infection (via the cervical tissue space) spreading into the thoracic cavity; and second, the route by which bacteria reach the thoracic cavity via hematogenous circulation [33]. In this study, two out of nine non-survivors with teeth with a poor prognosis (22.2%) and 15 of 27 survivors (55.6%) underwent tooth

Table 7. Background factors of patients with high and low OHAT score.

Variables		High OHAT score (n = 23)	Low OHAT score (n = 40)	*P* value
Sex	Male	18 (78.3%)	37 (92.5%)	0.129 [b]
Dysphagia	Yes	17 (73.9%)	26 (65.0%)	0.578 [b]
Compromised host	Yes	8 (34. 8%)	17 (42.5%)	0.602 [b]
Smoking history	Yes	15 (65.2%)	32 (80.0%)	0.236 [b]
CRP (mg/dL)	Median (range)	23.7 (7.1–40.5)	21.0 (2.1–41.0)	0.589 [a]
WBC ($10^3/\mu L$)	Median (range)	16.5 (10.7–39.2)	13.7 (5.5–28.7)	0.139 [a]
RAPID score	Median (range)	4.0 (2–6)	3.0 (0–5)	**0.006*** [a]

Values are expressed as absolute numbers, with the corresponding percentage of the total in parentheses. Values in the right-hand column indicate the statistical significance of the difference between subgroups. Most variables expressed as the median (range) in a non-parametric ratio scale.

[a]Mann-Whiteny U test;

[b]Fisher's exact test.

*$P < 0.05$.

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extraction. Non-survivors tended to have a lower frequency of oral care than survivors ($P = 0.135$). Many non-survivors did not wish to improve their oral health by extracting teeth with a poor prognosis or frequent oral care, regardless of their higher OHAT score than survivors. Therefore, our dental education, might have been insufficient, especially for the OHAT high-score groups. Patients with a high OHAT score and who leave teeth with a poor prognosis untreated may have a low interest in oral health. Dentists should educate patients on the importance of improving oral health to improve the prognosis of empyema.

This study had several limitations. First, there is a possibility of unknown confounding factors as this was a retrospective study; for example, degree of underlying disease (e.g., presence of chronic obstructive pulmonary disease) or degree of smoking history (e.g., Brinkman index). Although, a propensity score matching analysis was performed to decrease the effect of confounding factors as much as possible, the possibility of selection bias could not be completely excluded. Second, the sample size was small, which might have introduced biases in the data selection and analyses. Third, no bacteria were detected in the pleural fluid cultures

Table 8. Background factors of patients with high and low OHAT score after propensity score matching.

Variables		High OHAT score (n = 18)	Low OHAT score (n = 18)	*P* value
Sex	Male	13 (72.2%)	16 (88.9%)	0.402 [b]
Dysphagia	Yes	12 (66.7%)	11 (61.1%)	1.000 [b]
Compromised host	Yes	7 (38.9%)	6 (33.3%)	1.000 [b]
Smoking history	Yes	13 (72.2%)	13 (72.2%)	1.000 [b]
CRP (mg/dL)	Median (range)	22.7 (7.1–40.0)	21.8 (2.1–31.1)	0.877 [a]
WBC ($10^3/\mu L$)	Median (range)	15.2 (10.7–39.2)	15.6 (7.9–28.7)	0.570 [a]
RAPID score	Median (range)	4.0 (2–5)	3.0 (0–5)	0.273 [a]
Outcome	Non-survivors	6 (33.3%)	0 (0.0%)	**0.019*** [b]

Values are expressed as absolute numbers, with the corresponding percentage of the total in parentheses. Values in the right-hand column indicate the statistical significance of the difference between subgroups. Most variables expressed as the median (range) in a non-parametric ratio scale.

[a]Mann-Whiteny U test;

[b]Fisher's exact test.

*$P < 0.05$.

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of several patients. One possible reason is that some patients may have undergone pleural puncture after antibiotic administration. Whether antibiotics were administered before hospitalization is unknown. However, strict limitations of antibiotic administration in clinics or other hospitals before admission to our hospital may be difficult because empyema is a severe disease that can result in death, and early management is important. Additionally, we did not use quantitative polymerase chain reaction or next-generation sequencing to detect the causative bacteria. Finally, the content of dental treatment may have affected the prognosis of patients with empyema. In this study, the dental treatment methods, including the standard of tooth extraction and frequency of oral care, were not unified. However, there was no significant difference between non-survivors and survivors in the rate of patients with tooth extraction and frequency of oral care. In the future, prospective studies are necessary to identify useful prognostic factors for patients with empyema.

5. Conclusion

This is the first report to investigate the association between the objective assessment of oral health and the prognosis of empyema. Our results indicate that oral health assessed using the OHAT score may be a potential independent prognostic factor in patients with empyema. However, these findings should be carefully considered because of the retrospective study design. In a prospective study, we should eliminate confounding factors as much as possible by excluding patients with the administration of antibiotics before pleural puncture and unifying dental treatment methods, such as standard of tooth extraction and frequency of oral care.

Supporting information

S1 Data. OHAT-J. Quote source: Website of Department of Oral Health Sciences for Community Welfare, Tokyo Medical and Dental University Graduate School, Tokyo, Japan http://www.ohcw-tmd.com/research/ohat.html.
(PDF)

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References

1. Corcoran JP, Wrightson JM, Belcher E, DeCamp MM, Feller-Kopman D, et al. (2015) Pleural infection: past, present, and future directions. Lancet Respir Med 3: 563–577. https://doi.org/10.1016/S2213-2600(15)00185-X PMID: 26170076
2. Asai N, Suematsu H, Hagihara M, Nishiyama N, Kato H, et al. (2017) The etiology and bacteriology of healthcare-associated empyema are quite different from those of community-acquired empyema. J Infect Chemother 23: 661–667. https://doi.org/10.1016/j.jiac.2017.04.011 PMID: 28751154
3. Bostock IC, Sheikh F, Millington TM, Finley DJ, Phillips JD. (2018) Contemporary outcomes of surgical management of complex thoracic infections. J Thorac Dis 10:5421–5427. https://doi.org/10.21037/jtd.2018.08.43 PMID: 30416790
4. Lin CW, Huang KY, Lin CH, Wang BY, Kor CT, et al. (2022) Video-Assisted Thoracoscopic Surgery in Community-Acquired Thoracic Empyema: Analysis of Risk Factors for Mortality. Surg Infect (Larchmt) 23:191–198. https://doi.org/10.1089/sur.2021.191 PMID: 35085460
5. Rahman NM, Kahan BC, Miller RF, Gleeson FV, Nunn AJ, et al. (2014) A clinical score (RAPID) to identify those at risk for poor outcome at presentation in patients with pleural infection. Chest 145: 848–855. https://doi.org/10.1378/chest.13-1558 PMID: 24264558
6. Corcoran JP, Psallidas I, Gerry S, Piccolo F, Koegelenberg CF, et al. (2020) Prospective validation of the RAPID clinical risk prediction score in adult patients with pleural infection: the PILOT study. Eur Respir J 56: 2000130. https://doi.org/10.1183/13993003.00130-2020 PMID: 32675200
7. Yamazaki A, Ito A, Ishida T, Washio Y. (2019) Polymicrobial etiology as a prognostic factor for empyema in addition to the renal, age, purulence, infection source, and dietary factors score. Respir Investig 57: 574–581. https://doi.org/10.1016/j.resinv.2019.06.008 PMID: 31427269
8. Kikutani T, Tamura F, Tashiro H, Yoshida M, Konishi K, et al. (2015) Relationship between oral bacteria count and pneumonia onset in elderly nursing home residents. Geriatr Gerontol Int 15: 417–421. https://doi.org/10.1111/ggi.12286 PMID: 25130073
9. Scannapieco FA. (2006) Pneumonia in nonambulatory patients. The role of oral bacteria and oral hygiene. J Am Dent Assoc 137: 21S–25S. https://doi.org/10.14219/jada.archive.2006.0400 PMID: 17012732
10. Ishiguro T, Takayanagi N, Ikeya T, Yoshioka H, Yanagisawa T, et al. (2010) Isolation of Candida species is an important clue for suspecting gastrointestinal tract perforation as a cause of empyema. Intern Med 49: 1957–1964. https://doi.org/10.2169/internalmedicine.49.3667 PMID: 20847498
11. Dyrhovden R, Nygaard RM, Patel R, Ulvestad E, Kommedal Ø. The bacterial aetiology of pleural empyema. A descriptive and comparative metagenomic study. Clin Microbiol Infect. (2019) 25: 981–986. https://doi.org/10.1016/j.cmi.2018.11.030 PMID: 30580031
12. Maskell NA, Batt S, Hedley EL, Davies CW, Gillespie SH, et al. (2006) The bacteriology of pleural infection by genetic and standard methods and its mortality significance. Am J Respir Crit Care Med 174: 817–23. https://doi.org/10.1164/rccm.200601-074OC PMID: 16840746
13. Katsuda R, Inubushi J, Tobata H, Eguchi T, Terada K, et al. (2022) Genetic Homology between Bacteria Isolated from Pulmonary Abscesses or Pyothorax and Bacteria from the Oral Cavity. Microbiol Spectr 10: e0097421. https://doi.org/10.1128/spectrum.00974-21 PMID: 35171020
14. Chalmers JM, King PL, Spencer AJ, Wright FA, Carter KD. (2005) The oral health assessment tool—validity and reliability. Aust Dent J 50: 191–199. https://doi.org/10.1111/j.1834-7819.2005.tb00360.x PMID: 16238218
15. Ogawa T, Koike M, Nakahama M, Kato S. (2022) Poor Oral Health Is a Factor that Attenuates the Effect of Rehabilitation in Older Male Patients with Fractures. J Frailty Aging 11: 324–328. https://doi.org/10.14283/jfa.2021.54 PMID: 35799440
16. Furuya J, Suzuki H, Hidaka R, Matsubara C, Motomatsu Y, et al. (2022) Association between oral health and advisability of oral feeding in advanced cancer patients receiving palliative care: a cross-sectional study. Support Care Cancer 30: 5779–5788. https://doi.org/10.1007/s00520-022-06984-w PMID: 35344101
17. Nomoto A, Shimizu A, Ohno T, Tohara H, Hashidume M, et al. (2022) Poor oral health and anorexia in older rehabilitation patients. Gerodontology 39: 59–66. https://doi.org/10.1111/ger.12600 PMID: 34687077

18. Light RW. (2006) Parapneumonic effusions and empyema. Proc Am Thorac Soc 3:75–80. https://doi.org/10.1513/pats.200510-113JH PMID: 16493154

19. Paul RA, Tamse A, Rosenberg E. (1993) Cracked and broken teeth—definitions, differential diagnosis and treatment. Refuat Hapeh Vehashinayim 24: 7–12.

20. Huumonen Sisko, Ørstavik Dag. (2002) Radiological aspects of apical periodontitis. Endodontic Topics 1: 3–25.

21. Matsuo M, Nakagawa K. Creation of oral health assessment tool Japanese version (OHAT-J) and examination of its reliability and validity. (2016) J. Jpn. Soc. Disability Oral Health 37:1–7. *in Japanese*.

22. Oral Health Assessment Tool (OHAT) Japanese version. Available from: https://www.ohcw-tmd.com/research.

23. Teramoto S, Fukuchi Y, Sasaki H, Sato K, Sekizawa K, et al. (2008) High incidence of aspiration pneumonia in community- and hospital-acquired pneumonia in hospitalized patients: a multicenter, prospective study in Japan. J Am Geriatr Soc 56: 577–579. https://doi.org/10.1111/j.1532-5415.2008.01597.x PMID: 18315680

24. Cabrerizo S, Cuadras D, Gomez-Busto F, Artaza-Artabe I, Marı´n-Ciancas F, et al. (2015) Serum albumin and health in older people: review and meta-analysis. Maturitas 81: 17–27. https://doi.org/10.1016/j.maturitas.2015.02.009 PMID: 25782627

25. Pimlott BJ, Jones CA, Beaupre LA, Johnston DW, Majumdar SR. (2011) Prognostic impact of pre-operative albumin on short-term mortality and complications in patients with hip fracture. Arch Gerontol Geriatr 53: 90–94. https://doi.org/10.1016/j.archger.2010.06.018 PMID: 20684997

26. Sakai T, Sano A, Azuma Y, Koezuka S, Otsuka H, et al. (2021) Preoperative undernutrition predicts postoperative complications of acute empyema. Health Sci Rep 4: e232. https://doi.org/10.1002/hsr2.232 PMID: 33437877

27. Klotz AL, Zajac M, Ehret J, Hassel AJ, Rammelsberg P, et al. (2020) Development of a German version of the Oral Health Assessment Tool. Aging Clin Exp Res 32: 165–172. https://doi.org/10.1007/s40520-019-01158-x PMID: 30847843

28. Simpelaere IS, Van Nuffelen G, Vanderwegen J, Wouters K, De Bodt M. (2016) Oral health screening: feasibility and reliability of the oral health assessment tool as used by speech pathologists. Int Dent J 66: 178–189. https://doi.org/10.1111/idj.12220 PMID: 26853437

29. Nishizawa T, Niikura Y, Akasaka K, Watanabe M, Kurai D, et al. (2019) Pilot study for risk assessment of aspiration pneumonia based on oral bacteria levels and serum biomarkers. BMC Infect Dis 19: 761. https://doi.org/10.1186/s12879-019-4327-2 PMID: 31477059

30. Chen KY, Hsueh PR, Liaw YS, Yang PC, Luh KT. (2000) A 10-year experience with bacteriology of acute thoracic empyema: emphasis on Klebsiella pneumoniae in patients with diabetes mellitus. Chest 117: 1685–1689. https://doi.org/10.1378/chest.117.6.1685 PMID: 10858403

31. Light RW. (2001) Pleural Diseases Fourth Edition. Lippincott Williams & Wilkins. 151–181.

32. Ahmed RA, Marrie TJ, Huang JQ. (2006) Thoracic empyema in patients with community-acquired pneumonia. Am J Med 119: 877–883. https://doi.org/10.1016/j.amjmed.2006.03.042 PMID: 17000220

33. Reyes L, Herrera D, Kozarov E, Roldán S, Progulske-Fox A. (2013) Periodontal bacterial invasion and infection: contribution to atherosclerotic pathology. J Clin Periodontol 14: S30–50.