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Original Article

Clinical Significance of Pleural Lactate Measurement in Critically Ill Patients with Parapneumonic Pleural Effusion

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Abstract

OBJECTIVE: Pleural fluid pH measurement is recommended for tube thoracostomy decisions in complicated parapneumonic pleural effusions. However, pleural fluid pH may be affected by blood pH in critically ill patients with common systemic acid-base disorders. We aimed to investigate the use of pleural fluid lactate to distinguish culture-positive parapneumonic effusions from other pleural effusions.

MATERIAL AND METHODS: This prospective observational study included 121 eligible patients (51 female and 70 male). All patients with pleural effusion who underwent thoracentesis were assessed. Pleural fluid lactate was measured by a blood gas analyzer.

RESULTS: Of the 121 patients, 30 (24.8%) were transudate and 91 (75.2%) were exudate. Of the 91 patients with exudative pleural effusion, 61 were diagnosed as culture-negative parapneumonic, 13 as culture-positive parapneumonic, 9 as malignant, and 8 as other exudative effusion. There was a strong positive linear association between serum pH and pleural fluid pH ($R = 0.77$, $P < .001$). The post hoc tests for pleural fluid lactate revealed there was a significant difference between culture-positive parapneumonic versus culture-negative parapneumonic groups ($P = .004$), culture-positive parapneumonic versus transudative effusion groups ($P < .001$), culture-negative parapneumonic versus transudative effusion groups ($P = .008$) and lastly; malignant effusion versus transudative effusion groups ($P = .001$). Receiver operating characteristics curve analysis for culture-positive parapneumonic indicated a cutoff of 4.55 mmol/L for pleural fluid lactate to have a sensitivity of 76.9% and a specificity of 84.3% (positive predictive value: 37%, negative predictive value: 96.8%).

CONCLUSION: A cutoff of 4.55 mmol/L of pleural fluid lactate can be used as a useful tool to distinguish culture-positive parapneumonic effusions from other effusions in critically ill patients.

KEYWORDS: Pleural effusion, complicated parapneumonic pleural effusion, pleural fluid lactate, critical illness
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INTRODUCTION

Parapneumonic effusion is the exudative pleural fluid accumulation related to ipsilateral lung infection, primarily pneumonia.[1] Parapneumonic pleural effusions are a common finding that affects mortality in intensive care unit (ICU) patients.[2,3] Chest tube drainage is required for optimal management when parapneumonic effusions are complicated.[4,5] However, it may be difficult to distinguish patients with complicated parapneumonic effusion from patients with simple parapneumonic effusion on the basis of clinical presentation.[5] Therefore, pleural fluid analysis and pleural fluid pH measurement are recommended by guidelines to aid in the management of parapneumonic effusions.[4,5] In complicated parapneumonic effusions and empyema, the increased metabolic activity of leukocytes and bacteria in the pleural fluid increases acid generation.[6] Acid generation is a result of glucose metabolism and its end products, lactic acid and carbon dioxide.[6] A parapneumonic effusion with a pleural fluid pH <7.2 predicts a complicated clinical course that necessitates tube thoracostomy.[4,5,7]

In an experimental study conducted on normal rabbits without pleural effusions, the pleural fluid pH was around 7.66.[8] In patients with pleural effusions, the pH of pleural fluid usually approaches that of the blood.[9] Recommendations using pleural fluid pH <7.2 are based on the assumption that patients have no systemic acid-base disorders.[4,5] However, almost half of the intensive care patients have systemic acid-base disorders.[10] As the blood pH affects pleural fluid pH,[9] the guidance of pleural fluid pH in critically ill patients with potential acid-base disorders may be confusing.

In this study, we aimed to (i) examine the diagnostic utility of pleural fluid pH in critically ill populations, (ii) investigate the correlation of pleural fluid pH with systemic pH, (iii) describe the level of pleural fluid lactate in pleural effusions due to different causes, and (iv) determine a cutoff level of pleural fluid lactate to distinguish culture-positive parapneumonic effusions from other pleural effusions.

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MATERIAL AND METHODS

Study Population

After approval from the local ethics committee (with date July 13, 2020, and number 2020/16-07), this prospective observational study was conducted in the adult intensive care units of our center. All participants provided written informed consent. Between July 2020 and February 2022, all patients with pleural effusion (18 years and older) who underwent thoracentesis were assessed. Only the patients who underwent both blood gas analysis and pleural fluid gas analysis after thoracentesis were included. Patients with a history of acute trauma, patients with a loculated pleural effusion detected by ultrasound or chest CT, and patients with frank pus were excluded. Patients who received local lidocaine before thoracentesis were excluded from the study, as it may artificially alter the pleural fluid pH.

Pleural Fluid Sample Collection

The pleural effusion was collected by a physician using ultrasound-guided thoracentesis. Thoracentesis was performed for diagnostic and/or therapeutic reasons. In our center, 4 pleural fluid samples are routinely collected according to international recommendations[4]: (1) a sample for biochemistry, (2) a sample for pH and lactate analysis, (3) a sample for microbiology cultures, and (4) a sample for cytology. The pleural fluid is collected into an uncoated syringe, immediately transferred to a heparinized blood gas syringe for pH analysis, and processed within a maximum of 5 minutes. The pH and lactate were measured using a gas analyzer ABL800 FLEX (Radiometer Medical ApS, Denmark).

Variables

The following data were recorded for this study: (1) the demographic data (age, sex, body mass index, smoking history, and comorbidities), Acute Physiology and Chronic Health Evaluation (APACHE) II Score, Sequential Organ Failure Assessment (SOFA) Score, and Charlson Comorbidity Index (CCI); (2) major events during ICU stay (presence of sepsis/septic shock, presence of acute kidney injury [AKI], need for renal replacement therapy [RRT], and need for invasive mechanical ventilation [IMV]); (3) the durations from hospitalization to thoracentesis and from ICU admission to thoracentesis; (4) lengths of ICU, and hospital stays, and mortality; (5) effusion-related characteristics (estimated pleural fluid volume measured by ultrasound, diuretic use before thoracentesis, side of thoracentesis, complications, and the number of tube tracheostomies); (6) biochemical test results on the day of thoracentesis (glucose, total protein, albumin, and lactate dehydrogenase) and laboratory results of pleural fluid (glucose, total protein, albumin, and lactate dehydrogenase); (7) the results of pleural fluid gas analysis (pH and lactate) and blood gas analysis (pH and lactate); and (8) results of microbiology and cytology were recorded.

MAIN POINTS

- Pleural fluid pH is strongly affected by systemic serum pH.
- A pleural fluid pH <7.20 may not be a good predictor for complicated parapneumonic effusions in the critically ill population.
- A cutoff of 4.55 mmol/L for pleural fluid lactate can be used to distinguish culture-positive parapneumonic effusions from other effusions.

Definitions

Transudative and exudative pleural effusions were defined according to Light's criteria.[11] Pleural effusions were classified as culture-negative parapneumonic, culture-positive parapneumonic, malignant, and transudative. The exudative effusions not meeting the criteria for these groups are classified under other exudative effusions. Parapneumonic effusions were defined as exudative effusions with no other cause in patients with clinical/radiological evidence of pneumonia. Parapneumonic effusions were classified as culture-negative and culture-positive parapneumonic effusions. Malignant pleural effusion was defined as effusion with positive cytological results on pleural fluid analysis or radiological evidence of malignant pleural disease in the context of a known malignancy without any other identified cause.

Statistical Analysis

Categorical variables were expressed as numbers and percentages (n, %), and continuous variables were expressed as median with interquartile range (IQR). Normal distribution was assessed based on histograms and Shapiro–Wilk test. Continuous variables between 5 pleural effusion groups were compared using Kruskal–Wallis test. If there was a significant difference, we performed post hoc Dunn's test with Bonferroni adjustment. The linear association between blood pH and pleural fluid pH was evaluated with Spearman's rank correlation test. We performed receiver operating characteristics (ROC) curve analysis to measure the diagnostic performance of pleural fluid lactate and pleural fluid/serum lactate for culture-positive parapneumonic effusion. The optimal cutoff value was determined according to the Youden index, and sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. Data analysis and visualizations were done using R version 4.2.0 (https://www.r-project.org/). Double-sided *P*-values of less than .05 were considered significant.

RESULTS

General Characteristics

A total of 121 eligible patients were included in the study. The median age of the study population was 73.0 (63.0-81.0) years, and 57.9% (n = 70) were male. Table 1 provides the general characteristics of the study population. Common comorbidities were hypertension (59.5%), diabetes mellitus (39.7%), and congestive heart failure (29.8%). Chest tube drainage was performed in 76.9% (n = 93) of the patients. The ICU mortality rate was 62.8% (n = 76).

Results of Serum and Pleural Fluid Analysis

Of the 121 patients, 30 (24.8%) were transudate and 91 (75.2%) were exudate (Table 2). Of the 91 patients with exudative pleural effusion, 61 were diagnosed as culture-negative parapneumonic, 13 as culture-positive parapneumonic, and 9 as malignant. Eight patients with exudative pleural effusion could not reach a definitive diagnosis and were classified under the other exudative effusion group. Three

Table 1. Baseline Characteristics of Patients

Characteristics	Value
Age, years	73.0 (63.0-81.0)
Gender	
Female	51 (42.1)
Male	70 (57.9)
Smoking history	29 (24.0)
Body mass index, kg/m²	24.2 (20.9-28.3)
Comorbidities	
Hypertension	72 (59.5)
Diabetes mellitus	48 (39.7)
Congestive heart failure	36 (29.8)
Chronic kidney disease	23 (19.0)
Coronary artery disease	19 (15.7)
Dementia	17 (14.0)
COPD	16 (13.2)
Liver cirrhosis	8 (6.6)
APACHE II score	24.0 (16.0-29.0)
SOFA[a] score	7.0 (5.0-9.5)
CCI	6.0 (4.0-8.0)
Events/therapies during ICU stay	
IMV	100 (82.6)
Sepsis/septic shock	80 (66.1)
Acute kidney injury	63 (52.1)
Renal replacement therapy	29 (24.0)
Diuretic use before hospitalization	43 (35.5)
Diuretic use before thoracentesis[b]	89 (73.6)
Estimated pleural fluid volume measured by Ultrasound, mL	
Right sided	600 (200-800)
Left sided	300 (145-750)
Side of thoracentesis	
Right sided	77 (63.6)
Left sided	44 (36.4)
Tube thoracostomy	
Yes	93 (76.9)
No	28 (23.1)
Complications	
No	116 (95.9)
Hemothorax	3 (2.5)
Pneumothorax or emphysema	2 (1.7)
Diagnosis of pleural effusion according to Light's criteria	
Transudate	30 (24.8)
Exudate	91 (75.2)
Positive pleural fluid microbiology	13 (10.7)
Acinetobacter baumannii	5 (4.1)
Klebsiella pneumoniae	3 (2.5)
Staphylococcus aureus	2 (1.7)
Pseudomonas aeruginosa	2 (1.7)
Burkholderia cepacia	1 (0.8)
Duration from hospitalization to thoracentesis, days	9.0 (2.0-22.5)
Duration from ICU admission to thoracentesis, days	2.0 (0.0-8.5)
Length of ICU stay, days	11.0 (6.0-22.5)
Length of hospital stay, days	26.0 (13.0-42.5)
ICU mortality	76 (62.8)
Hospital mortality	79 (65.3)

All values are expressed as numbers (percentages) or median (interquartile range).
APACHE II, Acute Physiology and Chronic Health Evaluation II; CCI, Charlson Comorbidity Index; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; IMV, invasive mechanical ventilation; SOFA Score, The Sequential Organ Failure Assessment Score.
[a]Calculated on the day of ICU admission.
[b]Includes patients using oral diuretics before hospital admission and patients receiving intravenous diuretics before thoracentesis at hospital follow-up.

of 8 patients died without a definitive diagnosis. Five of the 8 patients were clinically expected to be transudative, while the analysis resulted in exudative.

In 16.5% (n = 20) of all cases, blood pH was <7.20. In all cases, 26 (21.5%) patients had pleural fluid pH <7.2. In the culture-negative parapneumonic group, the proportion of patients with a pleural fluid pH <7.20 was 13.1% (n = 8), while the proportion of patients with a blood pH <7.20 was the same as 13.1% (n = 8). In the culture-positive parapneumonic group, the proportion of patients with a pleural fluid pH <7.20 was 53.8% (n = 7), while the proportion of patients with a blood pH <7.20 was 15.4% (n = 2). In the transudative pleural fluid group, 20.0% (n = 6) of patients had a pleural fluid pH <7.20. The proportion of patients with a blood pH <7.20 was 23.3% (n = 7) in this group. The comparison of pleural fluid pH levels across the groups is indicated in Figure 1. There was no statistically significant difference between the groups in terms of pH levels ($P = .079$).

Correlation between Blood pH and Pleural Fluid pH

There was a strong positive linear association between serum pH and pleural fluid pH ($R = 0.77$, $P < .001$; Figure 2).

Pleural Fluid Lactate Levels in Different Pleural Effusions

Comparisons of pleural fluid lactate and pleural fluid/serum lactate across the effusion groups depicted a statistically significant difference (in both, $P < .001$; Figure 3). The post hoc tests for pleural fluid lactate revealed there was a significant difference between culture-positive parapneumonic versus culture-negative parapneumonic groups ($P = .004$), culture-positive parapneumonic versus transudative

Table 2. Serum and Pleural Fluid Analysis Data Based on Pleural Effusion Type and Final Diagnosis

Characteristics	All Cases	Overall Parapneumonic	Culture-Negative Parapneumonic	Culture-Positive Parapneumonic	Malignant	Other Exudative*	Transudative
	(n = 121)	(n = 74)	(n = 61)	(n = 13)	(n = 9)	(n = 8)	(n = 30)
Serum							
LDH, U/L	314 (222-454)	319 (229-463)	315 (225-463)	353 (290-470)	507 (252-753)	304 (218-518)	251 (207-327)
Total protein, g/L	5.25 (4.81-5.83)	5.18 (4.84-5.87)	5.13 (4.83-5.92)	5.33 (4.98-5.86)	5.40 (4.32-6.45)	5.81 (4.70-6.72)	5.29 (4.78-5.66)
Albumin, g/L	2.48 (2.22-2.70)	2.52 (2.27-2.66)	2.53 (2.30-2.67)	2.39 (2.15-2.56)	2.28 (1.92-3.04)	2.67 (2.21-3.65)	2.41 (2.19-2.91)
Glucose, mg/dL	141 (114-194)	149 (112-196)	156 (116-207)	120 (100-151)	138 (123-186)	125 (89-146)	147 (118-202)
pH	7.37 (7.27-7.45)	7.38 (7.29-7.45)	7.38 (7.29-7.45)	7.38 (7.26-7.48)	7.25 (7.02-7.42)	7.39 (7.32-7.43)	7.36 (7.22-7.42)
pH <7.20	20 (16.5)	10 (13.5)	8 (13.1)	2 (15.4)	3 (33.3)	0 (0.0)	7 (23.3)
Lactate, mmol/L	1.80 (1.20-2.40)	1.60 (1.10-2.20)	1.60 (1.10-2.10)	1.90 (1.15-3.85)	3.30 (1.65-6.05)	2.30 (1.93-2.98)	1.55 (1.20-2.20)
Pleural fluid							
LDH, U/L	246 (111-473)	354 (216-662)	321 (202-579)	654 (317-4773)	298 (211-600)	228 (141-321)	92 (55-106)
LDH > 1000 U/L	14 (11.6)	12 (16.2)	6 (9.8)	6 (46.2)	1 (11.1)	1 (12.5)	0 (0.0)
Total protein, g/L	2.39 (1.65-3.24)	2.90 (2.00-3.30)	2.92 (2.00-3.35)	2.69 (2.36-3.25)	3.10 (1.68-4.50)	2.59 (2.23-3.98)	1.62 (1.38-2.02)
Albumin, g/L	1.23 (0.81-1.58)	1.39 (1.00-1.63)	1.39 (1.00-1.69)	1.33 (1.09-1.56)	1.64 (0.93-2.29)	1.47 (1.15-2.05)	0.79 (0.67-0.99)
Glucose, mg/dL	138 (105-182)	136 (102-183)	156 (120-192)	86 (12-118)	136 (92-148)	140 (98-174)	148 (112-188)
Glucose < 40 mg/dL	7 (5.8)	7 (9.5)	2 (3.3)	5 (38.5)	0 (0.0)	0 (0.0)	0 (0.0)
pH	7.33 (7.23-7.41)	7.33 (7.23-7.43)	7.34 (7.25-7.43)	7.16 (6.85-7.41)	7.19 (7.06-7.36)	7.36 (7.28-7.40)	7.35 (7.24-7.40)
pH <7.20	26 (21.5)	15 (20.3)	8 (13.1)	7 (53.8)	5 (55.6)	0 (0.0)	6 (20.0)
Lactate, mmol/L	2.40 (2.00-4.25)	2.95 (2.10-4.60)	2.40 (2.05-4.00)	10.10 (4.00-13.80)	4.10 (3.70-6.05)	3.20 (1.60-4.55)	1.60 (1.20-2.10)
Pleural fluid/ serum lactate, mmol/L	1.33 (1.00-2.35)	1.70 (1.14-3.04)	1.61 (1.10-2.57)	3.10 (1.57-8.15)	1.27 (0.89-1.80)	1.21 (0.70-2.67)	1.07 (0.88-1.25)

All values are expressed as numbers (percentages) or median (interquartile range).
*Three of 8 patients with exudative pleural fluid died without a definitive diagnosis. Although clinically transudative, 5 of 8 patients had exudative pleural effusion according to Light's criteria.
LDH, lactate dehydrogenase.

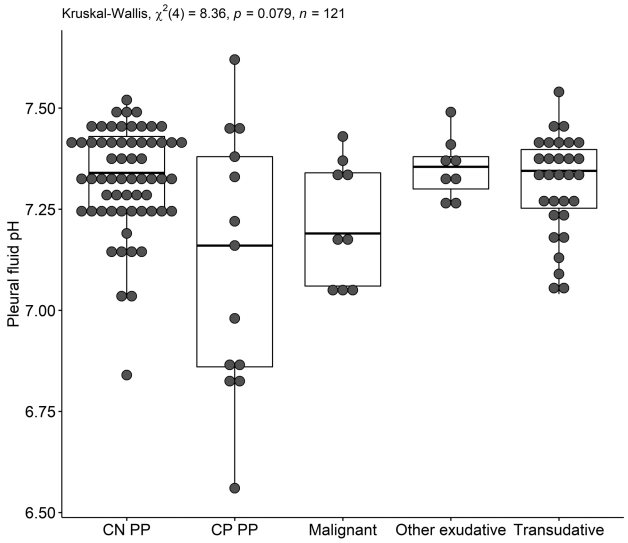

Figure 1. The comparison of pleural fluid pH levels between culture-negative parapneumonic (CN PP), culture-positive parapneumonic (CP PP), malignant, other exudative and transudative effusion groups.

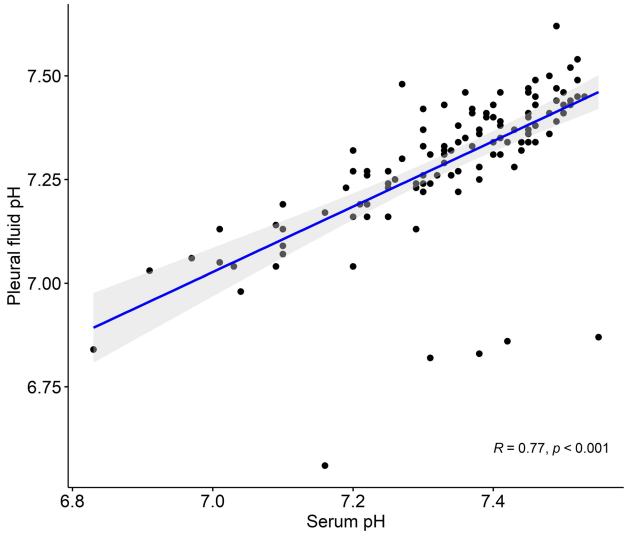

Figure 2. Correlation between blood pH and pleural fluid pH

effusion groups ($P < .001$), culture-negative parapneumonic versus transudative effusion groups ($P = .008$) and lastly; malignant effusion versus transudative effusion groups ($P = .001$). According to the post hoc tests for pleural fluid/serum lactate, comparisons between transudative effusion versus culture-positive parapneumonic groups ($P < .001$) and transudative effusion versus culture-negative parapneumonic groups ($P = .001$) were significant.

Receiver Operating Characteristic Curve Analysis

The ROC curve analysis for culture-positive parapneumonic indicated a cutoff of 4.55 mmol/L for pleural fluid lactate to have a sensitivity of 76.9% and a specificity of 84.3% (PPV: 37%, NPV: 96.8%; Table 3). The ROC analysis depicting the predictive value of the pleural fluid lactate for culture-positive parapneumonic effusions is shown in Figure 4. For the pleural fluid/serum lactate ratio, ROC curve analysis determined a 1.76 cutoff with 76.9% sensitivity and 72.2% specificity (PPV: 25%, NPV: 96.3%).

The Comparison of Pleural pH < 7.20 and Pleural Lactate > 4.55 in Patients with Culture-Positive and Culture-Negative Parapneumonic Pleural Effusions

The predictive rates of pleural pH <7.20 and pleural lactate >4.55 in patients with culture-positive and culture-negative parapneumonic pleural effusions were indicated in Table 4. In patients with blood pH <7.35 (n = 53), 5 patients were diagnosed as culture-positive parapneumonic, and 27 patients were diagnosed as culture-negative parapneumonic pleural effusions. In this population, 80.0% of patients with culture-positive parapneumonic pleural effusions and 29.6% of patients with culture-negative parapneumonic pleural effusions had a pleural pH <7.20 ($P = .053$). In the same population, 80.0% of patients with culture-positive parapneumonic pleural effusions and 14.8% of patients with culture-negative parapneumonic pleural effusions had a pleural lactate >4.55 ($P = .009$).

DISCUSSION

This prospective study evaluated the serum and pleural fluid biochemical results in critically ill patients with pleural effusion and has 3 important results. First, pleural fluid pH is strongly affected by systemic serum pH. Second, a pleural fluid pH <7.20 may not be a good predictor for complicated parapneumonic effusions in the critically ill population. Third, a cutoff of 4.55 mmol/L for pleural fluid lactate can be used to distinguish culture-positive parapneumonic effusions from other effusions.

In pleural effusion, the primary goal is to identify the underlying cause. Differentiating exudate from transudate is the

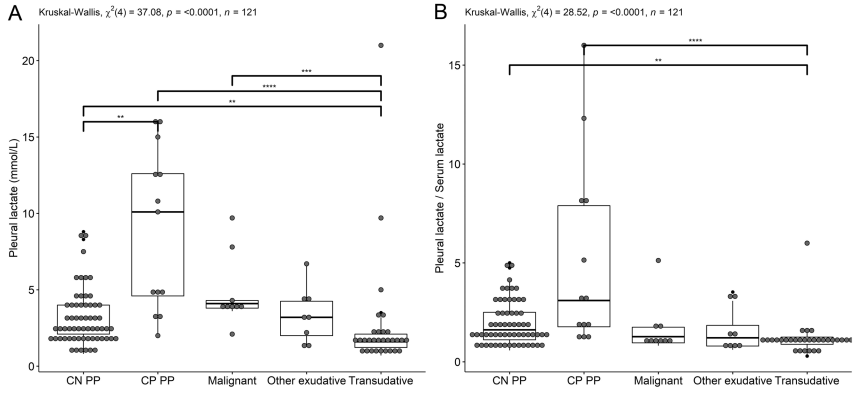

Figure 3. Pleural fluid lactate levels in different pleural effusions.

Table 3. ROC Curve Analyses of Pleural Lactate, Pleural/Serum Lactate, and Pleural pH for Culture-Positive Parapneumonic Effusion

	AUC (95% CI)	Cutoff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
All patients, n = 121						
Pleural lactate, mmol/L	0.86 (0.74-0.97)	4.55	76.9	84.3	37.0	96.8
Pleural/serum lactate	0.81 (0.69-0.93)	1.76	76.9	72.2	25.0	96.3
Pleural pH	0.68 (0.46-0.89)*	7.01	46.2	99.1	85.7	93.9
Patients with blood pH ≥7.35, n = 68						
Pleural lactate, mmol/L	0.85 (0.68-1.00)	4.55	75.0	88.3	46.2	96.4
Pleural/serum lactate	0.83 (0.66-1.00)	3.09	75.0	85.0	40.0	96.2
Pleural pH	0.62 (0.32-0.93)*	7.24	50.0	100.0	100.0	94.0
Patients with blood pH <7.35, n = 53						
Pleural lactate, mmol/L	0.87 (0.71-1.00)	3.35	100.0	60.4	20.8	100.0
Pleural/serum lactate	0.79 (0.63-0.94)	1.32	100.0	58.3	20.0	100.0
Pleural pH	0.76 (0.41-1.00)*	7.01	60.0	97.9	75.0	95.9

*Not different from random chance.
AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value; ROC, receiver operating characteristic.

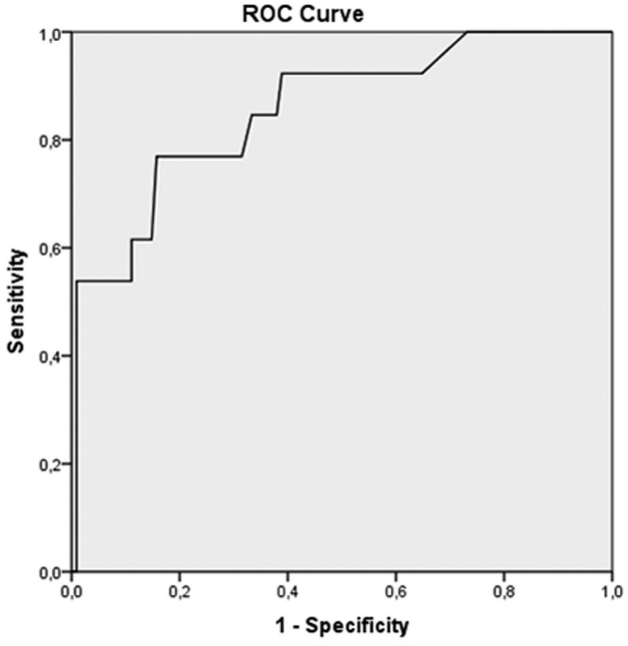

Figure 4. Receiver operating characteristic (ROC) analysis depicting the predictive value of the pleural fluid lactate for culture-positive parapneumonic effusions

first step, and Light's criteria have traditionally been used for this purpose.[11] Parapneumonic effusions are exudative effusions that can be detected in approximately 20% of hospitalized patients with pneumonia.[12] The prevalence of parapneumonic effusion increases when transthoracic ultrasonography is used.[13] The management of parapneumonic pleural effusions has gained more importance as it affects mortality in critically ill patients.[2,3] In the management of patients with parapneumonic pleural effusion, the primary decision is to drain the pleural space in addition to antibiotic therapy.[4,5]

An uncomplicated parapneumonic effusion is a sterile effusion that resolves with antibiotics alone.[14] On the other hand, frank pus in the pleural space (empyema) always requires chest tube drainage.[4,5] The main challenge is identifying patients whose fluids are not purulent but will eventually need drainage.[15] Pleural fluid pH <7.2 predicts a complicated clinical course, and this cutoff is used for the decision of the tube thoracostomy.[4,5] However, in the presence of pleural effusions, the pH of pleural fluid is affected by the pH of the blood.[9] In this study, we demonstrated that pleural fluid pH is affected by blood pH in critically ill populations. Since systemic acid-base disorders are common in critically ill patients,[10] pleural fluid pH <7.20 may not be a good indicator.

Pleural fluid lactic acid levels increase as a result of the increased metabolic activity of leukocytes and bacteria in the pleural fluid.[6] The use of increased lactate levels in detecting infectious pleural effusions has been investigated in various studies with conflicting results.[16-20] A small study of 57 patients with pleural effusions demonstrated that pleural fluid lactate elevation was not diagnostic for empyema.[16] Another study of 75 patients with pleural effusions showed that pleural fluid lactate can be used to distinguish bacterial

Table 4. Predictive Rates of Pleural pH <7.20 and Pleural Lactate >4.55 in Patients with Culture-Positive and Culture-Negative Parapneumonic Pleural Effusions

All Patients (n = 121)	**Culture-Positive Parapneumonic (n = 13)**	**Culture-Negative Parapneumonic (n = 61)**	***P***
Pleural pH <7.20	7 (53.8)	8 (13.1)	**.003**
Pleural lactate >4.55	10 (76.9)	10 (16.4)	**<.001**
Patients with Blood pH <7.35 (n = 53)	**Culture-Positive Parapneumonic (n = 5)**	**Culture-Negative Parapneumonic (n = 27)**	***P-***
Pleural pH <7.20	4 (80.0)	8 (29.6)	.053
Pleural lactate >4.55	4 (80.0)	4 (14.8)	**.009**
Patients with Blood pH ≥7.35 (n = 68)	**Culture-Positive Parapneumonic (n = 8)**	**Culture-Negative Parapneumonic (n = 34)**	***P***
Pleural pH <7.20	3 (37.5)	0 (0.0)	**.005**
Pleural lactate >4.55	6 (75.0)	6 (17.6)	**.004**

All values are expressed as numbers (percentages) or median (interquartile range). Bold values indicates statistical significance.

pleural inflammation from other types of pleural effusions, except malignant pleural effusions.[17] Two relatively large studies showed that lactate concentration can be used to distinguish infectious pleural effusions from other effusions.[18,19] In a recent study, pleural fluid lactate level was significantly elevated in complicated parapneumonic effusion compared with tuberculous pleural effusion.[20] Similar to the literature, we showed that pleural fluid lactate can be used to distinguish culture-positive parapneumonic effusions from other effusions. The population of our study consisted of critically ill patients and was different from these studies.[18-20] We think that the use of pleural fluid lactate to differentiate culture-positive parapneumonic effusions from other effusions is more valuable in critically ill patients as parapneumonic pleural effusions affect mortality, and a quick diagnosis and treatment are essential.[2,3]

This study has several limitations. The management of parapneumonic pleural effusions may be challenging in the ICU setting. There may be a delay in getting routine microscopy and culture results. Additionally, patients may already be on antimicrobial therapy, and cultures may result in a false negative. Measurement of pH may not guide the decision for tube thoracostomy. In these circumstances, lactate can be used as a quick and reliable aid for decisions. However, our results do not allow the clinician to use lactate as the only criterion for complicated parapneumonic effusions.

However, this study has strengths. We used culture-positive ones that more accurately demonstrate complicated parapneumonic pleural effusions, as pleural fluid cultures may give false-negative results.[21]

CONCLUSION

Pleural fluid pH is affected by blood pH in critically ill patients. Pleural fluid lactate levels can be measured quickly and easily in modern ICUs using blood gas analyzers. A cut-off of 4.55 mmol/L of pleural fluid lactate can be used as a useful tool to distinguish culture-positive parapneumonic effusions from other effusions. In addition to clinical, laboratory, and radiological assessment, lactate measurements can be particularly valuable in guiding early treatment.

Ethics Committee Approval: This study was approved by Ethics Committee of Dokuz Eylül University (approval No: 2020/16-07, date: July 13, 2020).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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