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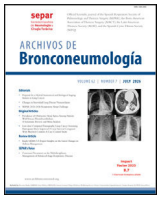

Scientific Letter

Diagnostic Yield of Ultrasound-Guided Percutaneous Pleural Biopsy in Pleural Infection

To the Director,

The incidence of infectious pleural effusions (IPE) has increased in recent years, and associated mortality remains substantial [1–3]. However, both blood cultures and pleural fluid (PF) cultures have limited diagnostic yield [4]. This may lead to suboptimal patient management, including prolonged empirical antibiotic therapy, the emergence of antimicrobial resistance, and complications related to antibiotic exposure [5]. Therefore, improving the diagnostic sensitivity of microbiological testing represents a clinical priority. A recent small study involving 20 patients with IPE demonstrated that pleural tissue culture may increase the diagnostic yield of standard microbiological culture methods [6].

Our objective was to evaluate whether the culture of ultrasound-guided percutaneous pleural biopsy (PPB) specimens, using Cope or Abrams needles, increases the diagnostic sensitivity of conventional PF culture in patients with IPE.

We conducted a prospective study including all consecutive patients diagnosed with IPE over a 4-year period. Pleural infection was defined according to British Thoracic Society criteria as bacterial infection of the pleural space, including empyema and complicated parapneumonic effusion [7]. Exclusion criteria were age under 18 years, refusal to participate, contraindications to thoracentesis or PPB, and tuberculous pleural effusion.

Two sets of blood cultures were obtained, and thoracic ultrasound was performed in all cases. Ultrasound-guided PPB was performed under real-time guidance, with 6–8 samples obtained per patient when a PF depth of at least 3 cm was present. PF samples were sent to the microbiology laboratory both in standard sterile containers and in BACTEC blood culture bottles. Pleural tissue specimens were transported in sterile containers with saline solution. Demographic, clinical, radiological, and pleural fluid biochemical parameters were evaluated (see Table 1).

Descriptive statistics were used to summarize the data. Qualitative variables are expressed as absolute frequencies and percentages, whereas quantitative variables are reported as mean ± standard deviation or median (interquartile range), depending on their distribution. Diagnostic yield was assessed by calculating sensitivity. Comparisons between diagnostic sensitivities were performed using McNemar's test for paired data. A two-sided p-value < 0.05 was considered statistically significant. It was estimated that the final sample size should include at least 84 patients to detect a 25-percentage-point difference in diagnostic sensitivity between techniques, with 90% statistical power, a two-sided alpha level of 0.05, and a 5% attrition rate. The protocol was approved by the Ethics Committee (code 2018/320).

Table 1
Characteristics of the patients studied.

Clinical variables	
Patients (n)	91
Age (median, IQR) (years)	68 (54, 82)
Men (n, %)	71 (78)
Time elapsed from the diagnosis of pleural effusion to thoracentesis (median, IQR) (days)	2 (1, 7)
Cough (n, %)	43 (47.3)
Purulent sputum (n, %)	26 (28.6)
Fever (n, %)	38 (41.8)
Dyspnea (n, %)	52 (57.1)
Previous antibiotics	54 (59.3)
Pleural infection	
Community (*n*, %)	65 (71.4)
Nosocomial (*n*, %)	26 (28.6)
Radiological variables	
Pulmonary consolidation (n, %)	65 (71.4)
Size of pleural effusion (n, %)	
<1/3 of the hemithorax	30 (33)
>1/3 and <2/3 of the hemithorax	38 (41.8)
>2/3 of the hemithorax	23 (25.2)
Side of pleural effusion (R/L/B) (n, %)	51 (56)/39 (42.9)/1 (1.1)
Septations (n, %)	28 (30.8)
Pleural fluid	
Purulent aspect (n, %)	30 (33)
pH (median, IQR)	7.36 (7.10, 7.41)
pH ≤ 7.20 (n, %)	31 (34.1)
Lactate dehydrogenase (UI/L) (median, IQR)	670 (379, 3219)
Lactate dehydrogenase > 1000 (n, %)	35 (38.5)
Glucose (median, IQR) (median, IQR) (mg/dL)	79 (59, 104)
Glucose ≤ 60 (n, %)	26 (28.6%)
Proteins (median, IQR) (mg/dL)	3.8 (3.2, 4.21)
C-reactive protein (median, IQR) (mg/dL)	1.03 (0.77, 1.93)
Leukocytes (median, IQR) (cells/μL)	3890 (1200, 6430)
% neutrophil count (median, IQR)	60 (47, 70)
% ≥70	30 (33)
RAPID score	
Points 0–2 (low risk) (n, %)	5 (5.5)
Points 3–4 (moderate risk) (n, %)	41 (45.1)
Points 5–7 (high risk) (n, %)	45 (49.4)

B, bilateral; IQR, interquartile range; L, left; R, right; RAPID, renal, age, purulence of pleural fluid, infection source and dietary factors.

Pleural biopsy culture was proposed to 185 patients to determine the etiology of pleural infection. Ninety-nine patients agreed to participate (53.5%) and 91 were ultimately included in the analysis; 8 patients were excluded because of missing data. Baseline clinical, radiological, and PF characteristics are summarized in Table 1. Common presenting symptoms included cough, purulent sputum, fever, and dyspnea. Prior antibiotic therapy had been administered in 54 patients (59.3%). Pleural infection was community-acquired in 65 cases (71.4%) and nosocomial in 26 (28.6%). Pulmonary consolidation on chest radiography was present in 65 patients (71.4%). On thoracic ultrasound, pleural

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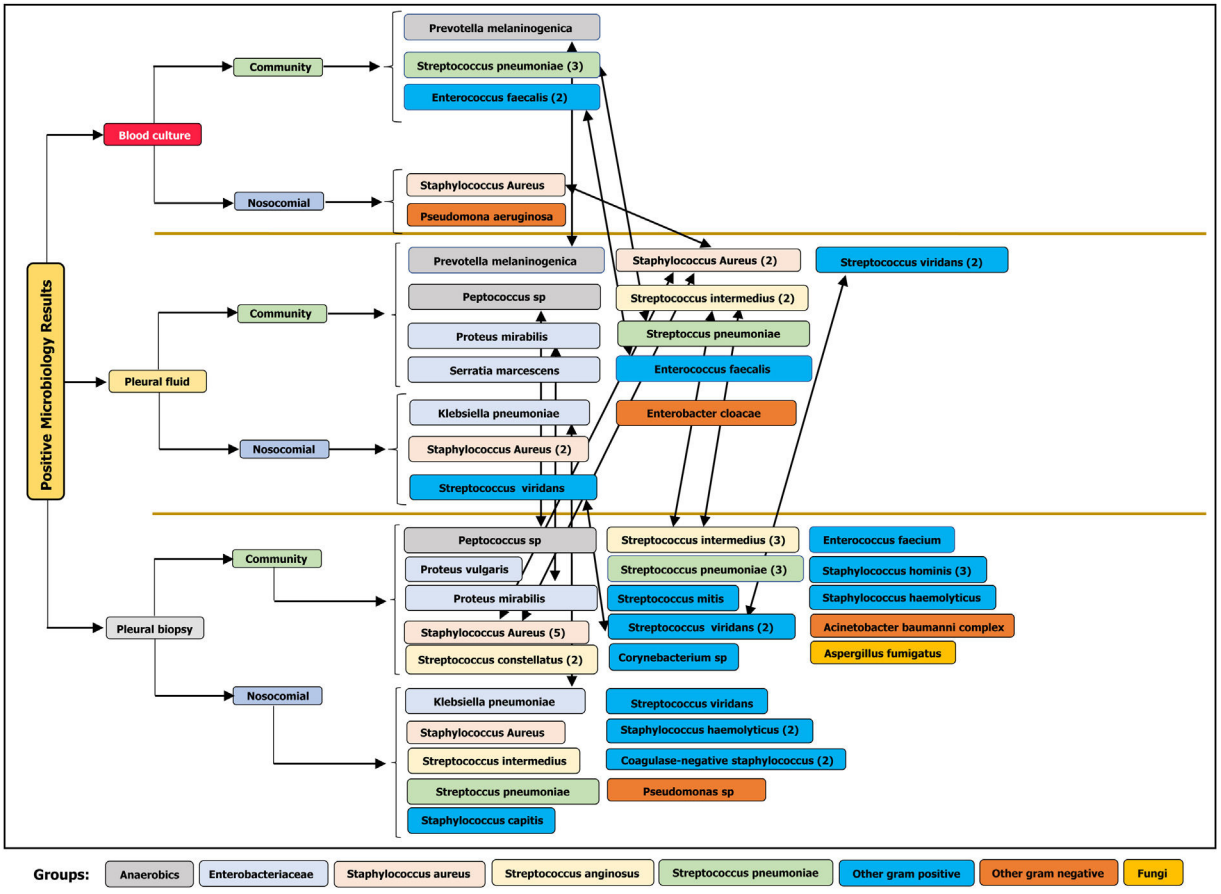

Fig. 1. Positive microbiological findings obtained from each culture performed, according to the type of culture and the location of the pleural infection, taking into account the assignment of each microorganism to its corresponding classification group. Cell color corresponds to the assigned classification group. Double-headed arrows between cells indicate that the microorganism is the same in two different samples.

septations were observed in 28 patients (30.8%). PF appeared purulent in 30 patients (33%). Median values (IQR) for PF biochemical parameters, including pH, lactate dehydrogenase, glucose, proteins, C-reactive protein, and leukocyte count with neutrophil percentage, are reported in Table 1. According to the RAPID score, patients were classified as low risk [5 cases (5.5%)], intermediate risk [41 (45.1%)], and high risk [45 (49.4%)] (Table 1).

Blood cultures were positive in 8 patients (8.8%), PF cultures in 17 patients (18.7%) ($p = 0.049$), and pleural biopsy cultures in 38 patients (41.8%) ($p < 0.001$ compared with the latter). In total, 63 positive samples were obtained. At least one of the three culture techniques yielded a positive result in 50 patients (54.9%), whereas all microbiological tests were negative in the remaining 41 patients (45.1%). Pleural biopsy culture was the only positive microbiological test in 29 patients (31.9%). Fig. 1 shows the distribution of microorganisms isolated across all cultures, stratified by culture type and grouped according to predefined microbiological categories. Polymicrobial infections were not observed in any case. When microorganisms were classified by groups, pleural infection was attributed to anaerobic organisms in 2 cases, *Enterobacteriaceae* in 4, *Staphylococcus aureus* in 8, *Streptococcus anginosus* in 6, *Streptococcus pneumoniae* in 7, other Gram-positive organisms in 18, other Gram-negative organisms in 4, and fungi in 1 case.

Complications related to closed pleural biopsy occurred in 7 patients (7.7%). Pneumothorax developed in 4 patients (4.4%), although none required the placement of an additional chest tube. Two patients (2.2%) reported severe chest pain, and one patient (1.1%) experienced a vasovagal reaction after completion of the procedure. No serious adverse events were recorded.

This study shows that pleural biopsy culture significantly increases microbiological diagnostic sensitivity compared with blood cultures and PF cultures. Furthermore, pleural biopsy culture was the only positive microbiological test in nearly one-third of patients, consistent with previous studies [6].

Although optimal antimicrobial therapy remains essential and microbiological identification plays a key role in guiding targeted treatment [8], the microbiological diagnosis of pleural infection remains challenging. The diagnostic sensitivity of blood cultures and the PF culture observed in our cohort is consistent with that reported in previous studies [9] and could be explained by empirical antibiotic therapy administered before diagnostic thoracentesis, or by the difficulty of bacterial growth within PF, a hypoxic medium with low pH and intense inflammatory activity. Furthermore, many pleural infections are polymicrobial and may involve anaerobic organisms that are difficult to culture [10].

The biological rationale for pleural tissue sampling in pleural infection is based on the ability of bacteria to adhere to pleural membranes and become embedded within fibrinous septations or the pleural peel [11], potentially increasing the likelihood of microbiological identification. Nonetheless, nearly half of the patients in our cohort remained without a microbiological diagnosis. This highlights the persistent limitations of conventional culture techniques and suggests that additional diagnostic strategies, such as broad-range PCR or metagenomic sequencing, may be needed to achieve a more comprehensive microbiological diagnosis of pleural infection [10,12,13]. These approaches may enable the detection of anaerobic organisms and polymicrobial communities that are not identified by conventional microbiology.

In agreement with previous epidemiological studies, Gram-positive bacteria represented the majority of isolates in our cohort. *Streptococcal* species and *S. aureus* were among the most frequently identified pathogens, reflecting the typical microbiology of community-acquired pleural infection. Gram-negative organisms and Enterobacteriaceae were less common but were more frequently observed in nosocomial infections. The low prevalence of anaerobic organisms in our series may have been underestimated because of the difficulty of cultivating these microorganisms using conventional culture methods [14]. Improving microbiological diagnostic sensitivity may contribute to better therapeutic and prognostic decision-making [2,15]. Furthermore, ultrasound-guided PPB was generally safe, with a low complication rate, consistent with previous studies [6,16].

The study has several limitations. First, it was conducted at a single center, which may limit the generalizability of the results to other settings. Second, it was not designed to assess whether this strategy leads to improved clinical outcomes or more targeted antibiotic therapy. Finally, the sample size was relatively limited.

Future research should focus on integrating pleural tissue sampling with advanced molecular diagnostics. Combining pleural biopsy with techniques such as broad-range PCR or metagenomic sequencing may further improve pathogen detection and provide a more comprehensive understanding of the microbiology of pleural infection. Multicenter studies will also be necessary to validate these findings and to determine which patient populations may benefit most from tissue-based microbiological investigation.

In conclusion, culture of specimens obtained by ultrasound-guided PPB significantly improves microbiological diagnostic sensitivity compared with conventional blood and PF cultures in patients with pleural infection. However, a substantial proportion of cases remain culture-negative despite this approach. These findings highlight both the potential value of pleural tissue sampling and the continued need for more sensitive diagnostic strategies, including molecular and metagenomic techniques, to achieve an optimal microbiological diagnosis in pleural infection. Furthermore, further studies would be needed to demonstrate that this higher diagnostic sensitivity translates into increased clinical utility.

Authors' contributions

Lucía Ferreiro. Author and drafting. Conception and design. Data acquisition. Reviewed intellectual content. Approval of the final manuscript.

Nuria Rodríguez-Núñez. Co-author. Reviewed intellectual content. Approval of the final manuscript.

Luis Valdés. Author and drafting. Conception and design. Reviewed intellectual content. Approval of the final manuscript.

Artificial intelligence involvement

The authors used ChatGPT solely to improve readability, language quality, and stylistic consistency. It was not used to generate scientific content. The authors reviewed and edited the manuscript as needed and take full responsibility for the final content.

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Conflict of interest

Authors declare no conflict of interest.

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We understand that the Corresponding Author is the sole contact for the Editorial process (including Editorial Manager and direct communications with the office). She is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs. We confirm that we have provided a current, correct email address which is accessible by the Corresponding Author (lferfer7@gmail.com).

We confirm that the manuscript has not been published elsewhere in any other language and is not currently being considered for publication in another journal.

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