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LETTER

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Management of parapneumonic pleural effusion and empyema in children: A tale of two cities

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To the Editor,

The management of parapneumonic pleural effusion and pleural empyema (PPE/PE) is controversial.[1–3] Although fibrinolytics are considered to have similar efficacy to video-assisted thoracoscopic surgery,[4,5] it is unknown when a drainage procedure for PPE/PE is beneficial, and many patients recover satisfactorily with antibiotic treatment alone.[6–8] Because of the potential severity and possible need for interventional procedures, pediatric patients with PPE/PE are often transferred to tertiary referral centers for treatment. The two hospitals participating in this study (HA and HB) are tertiary centers equipped with pediatric intensive care units (PICUs) as well as pediatric surgery and interventional radiology services. Both centers are located in southeast Spain, about 90 km apart, and serve as reference centers for the other hospitals in their respective provinces, each covering a population of just over 250,000 children under 15 years of age. Despite these similarities and both hospitals' extensive experience caring for pediatric patients with PPE/PE, their treatment policies for this condition diverged in 2010, when HA adopted a more conservative (less interventional) approach,[8] while HB continued with a more traditional interventional policy according to the main international guidelines. This situation offers the opportunity to compare the clinical characteristics, treatments, and outcomes observed in two adjacent and contemporaneous cohorts of patients with PPE/PE treated with different criteria by analyzing the use of chest drainage and the length of hospital (LOS) stay.

1 | MATERIALS AND METHODS

All patients under 15 years of age, who were hospitalized between 2010 and 2018 in the two study hospitals, and were diagnosed with a primary or secondary pleural effusion or empyema, were eligible. Exclusion criteria were: noninfectious cause of the effusion; tuberculosis; nosocomial pneumonia; unknown date of admission; patients transferred to finish their treatment in a center other than HA or HB; and patients with previous or concomitant severe comorbidities that could markedly interfere with the course, treatment or LOS, specifically patients with oncological diseases, immunodeficiencies, severe encephalopathies and myopathies, significant heart or lung diseases, or Down's syndrome.

Medical records of the included patients were reviewed to register the date of admission and discharge, age, sex, previous diseases, days of fever, analytical and microbiological results in blood and pleural fluid, radiological characteristics of the effusion, and treatments used. Vaccination status and pneumococcal serotypes were not retrieved. The size of the effusion was considered a surrogate of severity,[9] and was classified according to the maximum thickness observed on any imaging test performed during admission, as less than 10 mm (PPE/PE−) or greater than or equal to 10 mm (PPE/PE+). Patients with PPE/PE+ were further divided into two groups according to the thickness of the effusion: 10–20 mm (PPE/PE + 1) or greater than 20 mm (PPE/PE + 2). The primary outcome measures were the proportion of patients undergoing pleural drainage and LOS. Total LOS was defined as the number of days between the date of the patient's first admission to a hospital with a diagnosis of PPE/PE and the date of final discharge from

TABLE 1 Analysis of the main variables, according to size of parapneumonic pleural effusion and pleural empyema (PPE/PE)

Variable	PPE/PE < 10 mm		PPE/PE ≥ 10 mm		PPE/PE 10–20 mm		PPE/PE > 20 mm	
	HA (*n* = 32)	HB (*n* = 42)	HA (*n* = 100)	HB (*n* = 170)	HA (*n* = 24)	HB (*n* = 64)	HA (*n* = 76)	HB (*n* = 106)
Drainage, *n* (%)	0 (0.0%)	0 (0.0%)	32 (32.0%)	99 (58.2%)	1 (4.2%)	21 (32.8%)	31 (40.8%)	78 (73.6%)
p	*1*		*<0.001*		*0.005*		*<0.001*	
Median total LOS (IQR), days	5.5 (4.7–9.2)	7 (6.0–10.0)	12.0 (9.0–17.0)	18.0 (13.2–23.0)	9.5 (7.0–13.0)	14.5 (8.7–19.2)	13.0 (10.0–17.0)	19.0 (15.0–25.0)
p	*0.073*		*<0.001*		*0.007*		*<0.001*	
Median LOS in reference hospital (IQR), days	5.5 (4.7–7.0)	7 (6.0–10.0)	9.0 (7.0–13.2)	16.0 (11.0–22.0)	7.0 (5.7–8.0)	12.0 (7.0–18.0)	10.0 (7.7–15.2)	18.0 (14.0–23.0)
p	*0.035*		*<0.001*		*<0.001*		*<0.001*	

Abbreviations: IQR, interquartile range; LOS, length of stay.

the tertiary hospital. LOS in the tertiary reference hospital was defined as the number of days between admission to the reference hospital (from the emergency department or transferred from another center) and definitive discharge for this condition. In the case of patients who had been discharged from hospital but required a new admission for the same process, LOS included the days that the patient remained at home between the two hospitalizations. Other secondary variables were duration of fever and duration of intravenous antibiotic treatment.

The data collected were entered into a database for statistical analysis using the SPSS v.22 program. Statistical analyses were carried out using R software, version 4.0.2 (R Foundation for Statistical Computing; http://www.R-project.org). Bilateral statistical tests were applied with a significance level set at 0.05. Normal distribution of the continuous variables was checked using the Kolmogorov–Smirnov test. Qualitative variables were described using frequencies and percentages, and quantitative variables using median and interquartile range, given that they were not normally distributed. To evaluate differences in the characteristics between the two hospitals, we applied the Chi-square test or Fisher's exact test (categorical variables) or the Mann–Whitney *U*-test (continuous variables). The study was approved by the research ethics committees at HA and HB.

2 | RESULTS

We included 344 patients, 132 at HA and 212 at HB, of whom 74 (21.5%) had a PPE/PE− and 270 (78.5%) a PPE/PE+, with no significant difference in this proportion between the two hospitals ($p = 0.35$). In patients with PPE/PE+, the proportion of PPE/PE + 1 and PPE/PE + 2 was slightly different between HA (24.0% and 76.0%) and HB (37.6% and 62.4%; $p = 0.023$).

Characteristics of the patients attended in the two hospitals were similar, with no significant differences in age, sex, year or month of admission, comorbidities, duration of fever, antibiotic treatment before admission to the referral hospital, affected side, peak leukocytes, neutrophils and C-reactive protein in blood, or proportion of patients with a pathogen identified by culture (Supporting Information: Tables 1 and 2). The only initial difference was that PPE/PE+ patients seen in HA were hospitalized with fewer days of fever (median 4 vs. 5 days; $p = 0.003$) and were more often transferred from another center (73.0% vs. 42.9%; $p < 0.001$) compared to those in HB.

Table 1 shows the results of the analysis of the main variables, percentage of drained patients and LOS, stratified by effusion size. No patient with PPE/PE− was drained. The percentage of drained PPE/PE+ patients was significantly smaller in HA compared to HB, and LOS was significantly shorter in HA than in HB. Supporting Information: Table 1 presents a detailed analysis of other treatments and patient outcomes. Although cefotaxime was the most common antibiotic in both centers, more amoxicillin (alone or with clavulanic acid) was used in HA, and more clindamycin in PPE/PE + 2 patients in HB. The duration of antibiotic treatment (intravenous and oral) was shorter in HA (Supporting Information: Table 1). There were no differences between the two centers in the use of fibrinolytics in patients who underwent pleural drainage, the administration of oxygen therapy or mechanical ventilation, the presence of pneumothorax, or the need for surgical treatment. PPE/PE+ patients were admitted to the PICU more frequently in HB than in HA. Fever lasted longer during hospitalization in HA patients than in HB patients, both in PPE/PE− and PPE/PE+, but the total duration of fever from the onset of disease was longer only in PPE/PE + 2 (Supporting Information: Table 1).

3 | DISCUSSION

Our results show a remarkable difference in the use of pleural drainage in two comparable hospitals caring for similar pediatric populations with PPE/PE. Unexpectedly, LOS was longer in the center that performed pleural drainage more frequently. Differences in both the use of pleural drainage and LOS appeared to be independent of disease severity. In fact, LOS was also different in patients with PPE/PE−, none of whom required pleural drainage.

The only initial difference was that HA patients with PPE/PE+ were admitted earlier and transferred more frequently from peripheral hospitals, while HB patients spent more time with fever and oral antibiotics before hospital admission, and admissions originated more frequently from its own emergency department. These differences are possibly due to social and geographical factors, and we do not believe that they had a significant impact on the main outcome measures, given

that the duration of fever and antibiotic treatment before admission to the tertiary hospital were similar between centers. The similar needs for oxygen therapy, mechanical ventilation, surgery, and the presence of pneumothorax also suggest that disease severity was comparable in the two centers. Pleural drainage was always managed in the PICU in HB, but not necessarily in HA, which explains the differences observed in the proportion of patients admitted to the PICU. The duration of antibiotic treatment was longer in HB, which probably contributed to the longer hospital stay.

The shorter duration of fever during hospitalization in HB patients might suggest that pleural drainage accelerates healing. However, fever was often intermittent and particularly difficult to account for retrospectively. Data on fever could have been recorded differently in the two hospitals, as suggested by the fact that its median duration was shorter in HB, including in the PPE/PE− patients who did not require drainage. On the other hand, when quantifying the total duration of fever from the onset of disease, before hospitalization, differences were only observed in PPE/PE + 2 patients, who may have benefited most from pleural drainage. Therefore, differences in the duration of fever between the two centers should be interpreted with caution. Prolonged fever is common in patients with PPE/PE. Although it is often interpreted as a sign of treatment failure, it may also be due to underlying inflammation, prompting the addition of corticosteroids to the treatment.[10,11]

In conclusion, this study adds weight to others[6–8,12] suggesting that restricting the use of pleural drainage is safe and does not prolong LOS, which may be more conditioned by the routines at each center. Controlled studies are needed to identify patients who may benefit from the use of pleural drainage procedures, as many treatment decisions seem to be based on subjective interpretation of data and local habits.

AUTHOR CONTRIBUTIONS

Luis Moral: Conceptualization; methodology; data curation; investigation; validation; formal analysis; supervision; funding acquisition; project administration; writing – original draft; writing – review and editing. **Susana Reyes:** Conceptualization; methodology; data curation; investigation; validation; writing – review and editing. **Teresa Toral:** Data curation; investigation; writing – review and editing; validation; writing – original draft. **Amalia Ballesta:** Data curation; investigation; validation; writing – review and editing. **Eloísa Cervantes:** Data curation; investigation; validation; writing – review and editing.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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