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Multilobar bilateral and unilateral chest radiograph involvement: implications for prognosis in hospitalised community-acquired pneumonia

To the Editor:

Community-acquired pneumonia (CAP) remains a leading cause of morbidity and mortality worldwide [1]. Studies from the USA and Europe suggest that severe CAP patients requiring admission to the intensive care unit (ICU) reach a mortality of up to 39% [2, 3].

Since potential poor prognosis is known to contribute to increased ICU admissions, anticipating complications through the use of supporting measurements becomes essential. The 2007 Infectious Diseases Society of America (IDSA)/American Thoracic Society (ATS) guidelines [1] have redefined severe CAP and indications for ICU admission, with a rule consisting of major and minor clinical criteria. The rule is considered positive if one major or three minor criteria are present [1]. The presence of multilobar infiltrates is included among the minor criteria. However, multilobar pneumonia can be bilateral or unilateral and this difference may be of some importance. Our hypothesis was that radiographical bilateral pneumonia is an independent risk factor for mortality and that the prognosis for bilateral involvement is worse than that for multilobar unilateral involvement. We, therefore, studied the clinical characteristics and outcomes of bilateral pneumonia (at admission) compared to unilateral multilobar and localised pneumonia.

We performed a prospective observational study at Hospital Clínic, Barcelona, Spain. The study population consisted of adults with a diagnosis of CAP, consecutively examined from 2000 to 2013. In the initial visit, patients underwent a complete history and physical examination and laboratory testing. Patients were stratified into risk classes using the pneumonia severity index [4] and the CURB-65 scores (CURB-65: confusion, urea, >7mmol·L^{-1} respiratory rate ⩾30 breaths·min^{-1}, blood pressure, 90 mmHg (systolic) ⩽60 mmHg (diastolic), age ⩾65 years) [5]. All surviving patients were seen between 30 and 40 days after discharge. Multilobar pneumonia was defined as chest-radiograph infiltrates involving ⩾2 lobes; bilateral when the involved lobes were in both the right and left lungs, unilateral when the affected involved lobes were in the same lung, and localised when only a single pulmonary lobe was involved. Patients were categorised into three groups according to the presence of infiltrates: bilateral, multilobar unilateral and localised pneumonia. All CAP patients had lateral and anteroposterior (PA) projections to categorise radiographic involvement. All chest radiographs were reviewed by one specialist in lung radiology (M. Sánchez) to evaluate the radiographical pattern of infiltrate, number of lobes involved, and the presence of pleural effusion and atelectasis; the specialist was blinded to the clinical data.

Of the 5084 CAP patients screened, 4644 were included in this study. Of these, 1069 (23%) had multilobar pneumonia and 585 (13%) presented bilateral infiltrates; unilateral infiltrates were present in 484 (45%) patients. Localised infiltrates were present in 3575 patients (77%).

Patients from the bilateral group were younger, more frequently former alcohol consumers, had more often received previous antibiotic treatment, but less frequently influenza vaccine and inhaled corticosteroids, presented less frequently with chronic respiratory disease, chronic cardiovascular disease, or diabetes mellitus as a comorbidity, and pleuritic pain at admission. Patients from the unilateral multilobar group had a higher rate of chronic liver disease at admission. According to arterial oxygen tension (P_{aO_2}) inspiratory oxygen fraction F_{IO_2} ratio (P_{aO_2}/F_{IO_2}) and the presence of infiltrates on the chest radiograph, we found significant differences between localised group *versus* unilateral multilobar group median (interquartile range) of 267 (226–314) *versus* 292 (252–335), p=0.001 and between localised *versus* multilobar bilateral of 292 (252–335) *versus* 257 (219–300), p=0.001. Interestingly we did not find differences between multilobar bilateral *versus* unilateral multilobar was 257 (219–300) *versus* 267 (226–314), p=0.28.

Confirmed aetiology was found in 1821 (39%) patients. The most frequent pathogens were *Streptococcus pneumoniae* (n=768, 42%). Pathogens did not differ between groups, except for *S. pneumoniae*, which was

less frequent in bilateral patients (bilateral 34%, unilateral multilobar 44%, and localised 43%; p=0.013), and *Staphylococcus aureus* was more frequent in the unilateral multilobar group (bilateral 3%, unilateral multilobar 5% and localised 2%; p=0.025).

Of the 585 patients with bilateral involvement, 198 (34%) were admitted to the ICU; 81 (16%) patients required invasive mechanical ventilation more frequently than the unilateral multilobar (n=39, 10%) and localised groups (n=97, 3%), (p<0.001). Patients with bilateral involvement had a longer stay in hospital than the localised group (bilateral 8 days; unilateral multilobar 9 days and localised 6 days; p<0.001). A total of 260 (6%) patients died and a 30-day mortality was significantly higher among bilateral patients (bilateral 11%, unilateral multilobar 7% and localised 4%; p<0.001).

In the multivariate analysis, age (⩾65 years), neurological disease, chronic liver disease, altered mental status, P_{aO_2}/F_{IO_2} <250, acute renal failure, septic shock, interstitial pattern, and bilateral involvement were

TABLE 1 Significant univariate and multivariate logistic regression analyses of predictors for 30-day mortality

	Univariate[#]		Multivariate[¶]	
	OR (95% CI)	**p-value**	**OR (95% CI)**	**p-value**
Age ⩾65 years	4.37 (3.08–6.20)	<0.001	4.37 (2.46–7.75)	<0.001
Sex male	1.34 (1.02–1.75)	0.036		
Influenza vaccine	1.34 (0.97–1.84)	0.074		
Chronic cardiovascular disease	1.74 (1.28–2.36)	<0.001		
Chronic renal disease	2.26 (1.54–3.30)	<0.001		
Chronic liver disease	1.85 (1.18–2.89)	0.007	3.40 (1.75–5.03)	<0.001
Diabetes mellitus	1.42 (1.06–1.92)	0.021		
Neurologic disease	3.84 (2.94–5.03)	<0.001	3.35 (2.23–5.03)	<0.001
Pleuritic pain	0.42 (0.31–0.57)	<0.001		
Altered mental status	3.92 (3.01–5.10)	<0.001	1.63 (1.10–2.430	0.015
Creatinine ⩾1.5 mg·dL^{-1}	4.06 (3.14–5.23)	<0.001		
S_{aO_2} <92%	2.44 (1.80–3.30)	<0.001		
P_{aO_2}/F_{IO_2} <250	4.79 (3.55–6.46)	<0.001	3.24 (2.20–4.76)	<0.001
CURB-65 risk class 3–5	6.12 (4.69–7.99)	<0.001		
PSI risk class IV–V	10.91 (7.19–16.55)	<0.001		
Multilobar[+]		<0.001		0.006
Bilateral	2.71 (2.01–3.67)	<0.001	2.13 (1.33–3.41)	0.002
Unilateral multilobar	1.61(1.10–2.37)	0.014	1.09 (0.64–1.86)	0.75
Localised	1		1	
Patterns of infiltrate[§]		0.015		0.046
Alveolar	1		1	
Interstitial	1.39 (0.69–2.79)	0.35	3.11 (1.24–7.78)	0.015
Mixed	2.00 (1.23–3.26)	0.005	0.89 (0.43–1.84)	0.75
Acute renal failure	4.63 (3.58–6.00)	<0.001	2.90 (1.97–4.28)	<0.001
Septic shock	10.02 (7.38–13.61)	<0.001	6.30 (4.02–9.86)	<0.001
Aetiology[f]		<0.001		
Unknown	1			
Bacterial	1.04 (0.77–1.39)	0.80		
Respiratory virus or atypical bacterial	0.34 (0.16–0.69)	0.003		
Mixed	1.86 (1.20–2.90)	0.006		

OR: odds ratio; S_{aO_2}: arterial oxygen saturation; P_{aO_2}: arterial oxygen tension; F_{IO_2}: inspiratory oxygen fraction; P_{aO_2}/F_{IO_2}; P_{aO_2} and F_{IO_2} ratio; CURB-65: confusion, urea, >7mmol·L^{-1} respiratory rate ⩾30 breaths·min^{-1}, blood pressure, 90 mmHg (systolic) ⩽60 mmHg (diastolic), age ⩾65 years; PSI: pneumonia severity index. [#]: the variables included in the univariate analysis were age, sex, smoking, alcohol consumption, previous antibiotic, influenza vaccine, pneumococcal vaccine, inhaled corticosteroids, systemic corticosteroids, chronic pulmonary disease, chronic cardiovascular disease, diabetes mellitus, neurological disease, chronic liver disease, pleuritic pain, altered mental status, creatinine, C-reactive protein level, white blood cell count, S_{aO_2}, P_{aO_2}/F_{IO_2}, CURB-65 risk class, PSI risk class, multilobar, pattern of infiltrate, septic shock, acute renal failure, and aetiology. [¶]: Hosmer–Lemeshow goodness-of-fit test, p=0.17. Internal validation of the final logistic regression model was conducted using bootstrapping with 1000 samples. The nine variables included in the model showed robust results, with small 95% CIs around the original coefficients. [+]: the p-value corresponds to the differences between the three groups (bilateral, unilateral multilobar, or localised). [§]: the p-value corresponds to the differences between the three groups (alveolar, interstitial, or mixed). [f]: the p-value corresponds to the differences between the four groups (unknown, bacterial, respiratory virus or atypical bacterial, or mixed).

risk factors for 30-day mortality. Unilateral multilobar involvement was not an independent factor associated with 30-day mortality (table 1). The area under the receiver operating characteristic (ROC) curve of the predictive model was 0.88 (95% CI 0.85–0.90).

In a large population of CAP patients, we showed that 23% of patients with CAP had multilobar infiltrates and 13% showed bilateral multilobar involvement on the chest radiograph. Our main findings are: 1) the clinical course of the bilateral group was severe, with more patients requiring admission to the ICU and mechanical ventilation compared to patients with unilateral multilobar and localised disease; and 2) more importantly, the presence of bilateral involvement was an independent predictive factor for mortality, while unilateral multilobar disease was not.

The association of multilobar involvement with prognosis has been previously investigated in some studies [6–8], as it is one of the IDSA/ATS minor criteria for ICU admission in CAP [1]. Many studies have evaluated these criteria, especially the minor criteria [6, 7, 9–12], with conflicting results. In the study by Chalmers *et al.* [10], the predictive value of multilobar shadowing was strong, with an OR of 4.20 (95% CI 2.56–6.88) for mechanical ventilation/vasopressor support (MV/VS) and an OR of 5.63 (95% Cl 3.09–10.3) for 30-day mortality.

Aliberti *et al.* [13] in a multicentre observational study of CAP cases observed the highest in-hospital mortality among CAP patients with acute respiratory failure, severe sepsis and multilobar infiltrates (26%).

Rello *et al.* [14], in a study evaluating 428 ICU patients with CAP, including 126 chronic obstructive pulmonary disease (COPD) patients, reported that ICU mortality in COPD patients with adequate therapy was associated with bilateral infiltrates and shock. In fact, their study and that of Walden *et al.* [15], which included patients with severe CAP, looked at bilateral involvement as a predictor of mortality.

Similarly, the meta-analysis by Mannu *et al.* [16] has shown multilobar involvement to be associated with unfavourable outcomes, such as a significantly increased risk of mortality (OR 2.57, 95% CI 1.83–3.61) in all seven studies analysed. Bilateral involvement was not analysed separately.

We also examined the mortality factors in the group of patients with bilateral and unilateral multilobar pneumonia and found that bilateral, but not unilateral involvement was an independent predictive factor for 30-day mortality in CAP patients.

The strengths of this study are the large number of patients enrolled over a long period of time, its prospective design, and the comprehensive clinical and microbiological data gathered. Limitations include the fact that it is a single-centre study, therefore the results need to be validated in external cohorts, and the lack of computed tomography (CT) scan data to compare chest radiographs with. Recently, Claessens *et al.*[17] highlighted specificity and sensitivity problems of chest radiographs compared to CT scans in CAP. However, performing CT scans for CAP is unfeasible in routine clinical practice.

In summary, bilateral chest radiographs involvement was an independent factor associated with higher mortality, whereas unilateral multilobar pneumonia was not. We suggest including bilateral instead of multilobar pneumonia in the scores for prognosis and ICU admission in CAP.

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Bilateral but not unilateral multilobar pneumonia is an independent risk factor for mortality in CAP http://ow.ly/ZNLD4

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