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Early mortality in patients with community-acquired pneumonia: causes and risk factors

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ABSTRACT: The first 48 h of evolution of patients with community-acquired pneumonia (CAP) are critical. The aim of the present study was to determine the frequency, causes and factors associated with early mortality in CAP.

Nonimmunocompromised adults hospitalised with CAP were prospectively observed from 1995 to 2005. Early deaths, defined as death due to any cause ⩽48 h after admission, were compared with all patients who survived >48 h. Furthermore, early deaths were compared with late deaths (patients who died >48 h) and with survivors.

Of 2,457 patients, 57 (2.3%) died ⩽48 h after admission. Overall mortality was 7.7%. The main causes of early mortality were respiratory failure and septic shock/multiorgan failure. Independent factors associated with early deaths were increased age, altered mental status at presentation, multilobar pneumonia, shock at admission, pneumococcal bacteraemia and discordant empiric antibiotic therapy.

Currently, early mortality is relatively low and is caused by pneumonia-related factors. It occurs mainly among the elderly and in patients presenting with altered mental status, multilobar pneumonia and septic shock. Pneumococcal bacteraemia and discordant antibiotic therapy, mainly due to lack of coverage against *Pseudomonas aeruginosa* are also significant risk factors.

KEYWORDS: Community-acquired pneumonia, early mortality, *Pseudomonas aeruginosa*, shock, *Streptococcus pneumoniae*

Community-acquired pneumonia (CAP) continues to be a major health problem worldwide [1–3]. Despite more accurate aetiological diagnosis, effective antibiotic therapy and advances in supportive care, the morbidity and mortality rates associated with this infection remain high. Recent studies report complications in 15–50% of hospitalised patients and overall mortality rates that range from ~10% for patients treated in a hospital setting to >30% for patients treated in an intensive care unit [4–7]. According to these studies, most deaths occurring within 30 days of presentation appear to be pneumonia related. A substantial number of identifiable risk factors may influence mortality, and some of the factors associated with mortality within the first days may differ from those associated with mortality occurring later.

In this setting, information regarding the causes and factors related to mortality within the first 48 h of pneumonia are scarce and there is no clear consensus on whether this very early mortality is modifiable by medical intervention [8–10].

The aim of the present study was to determine the frequency, causes and factors associated with early mortality in a large prospective cohort of hospitalised patients with CAP.

MATERIALS AND METHODS

Study subjects and design

The study was carried out in a 900-bed university hospital for adults in Barcelona, Spain. The hospital serves an area with 1,100,000 inhabitants and admits ~24,000 patients per year. All nonimmunocompromised patients with CAP who were admitted to the hospital from February 1995 to December 2005 were prospectively recruited and followed up. Patients with neutropenia or HIV infection and those who had undergone transplantation were not included. For the purposes of the present study, patients were divided into two groups: those who died due to any cause ⩽48 h after admission (early

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STATEMENT OF INTEREST
None declared.

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deaths), and those who survived the first 48 h after admission. In addition, the latter group was divided into two: patients who died >48 h after admission (late deaths) and survivors. This prospective, longitudinal and observational study was approved by the Hospital University of Bellvitge (Barcelona, Spain) Ethical Committee.

Clinical evaluation and follow-up

At the initial visit, and before starting empirical antibiotic therapy, patients underwent a complete clinical history and physical examination. Basic chemistry and haematology tests, arterial blood gas determinations and chest radiography were performed. Two sets of blood samples were obtained and cultured and, when available, a sputum sample was evaluated by use of Gram staining and culture. Invasive procedures and urinary antigen detection for *Streptococcus pneumoniae* and *Legionella pneumophila* were performed if indicated by the attending physician. Paired serum samples obtained during the acute and convalescent phases of infection (separated by a 3–8 week interval) were also obtained for serological studies.

Patients were seen daily during their hospital stay by one or more of the investigators, who provided medical advice when requested and recorded: demographic characteristics; underlying disease; clinical features; vaccination status; causative agents; therapy; and outcomes in a computer-assisted protocol.

Definitions

CAP was defined as the presence of a new infiltrate on chest radiography plus at least one of the following: fever (temperature $\geqslant$38.0°C) or hypothermia (temperature $\leqslant$35.0°C); new cough, with or without sputum production; pleuritic chest pain; dyspnoea; or altered breath sounds on auscultation. The diagnosis of septic shock was based on a systolic blood pressure of <90 mmHg and peripheral hypoperfusion with clinical or bacteriological evidence of uncontrolled infection. Complications were defined as any untoward circumstance occurring during hospitalisation, with the exception of side-effects from medication. Antibiotic therapy was administered according to the hospital guidelines, which recommended the administration of a β-lactam (ceftriaxone or amoxicillin clavulanate) with or without a macrolide (erythromycin or clarithromycin) or a fluoroquinolone. Combination therapy was recommended for patients with clinical suspicion of Legionella or an atypical pathogen, or in the absence of a demonstrative sputum Gram stain. From February 2000 onwards, levofloxacin monotherapy was permitted in selected cases. Concordance of antibiotic therapy was examined for all cases with an aetiological diagnosis according to susceptibility test criteria for classic respiratory pathogens. Early death was defined as death due to any cause $\leqslant$48 h after hospitalisation; late death was defined as a death due to any cause >48 h <30 days after hospitalisation. Overall, mortality was defined as death due to any cause <30 days after hospitalisation. The severity of illness at presentation was quantified using the validated Pneumonia Outcome Research Team prediction rule for 30-day mortality and medical complications in CAP [4].

Microbiological studies

The aetiological diagnosis of CAP was established as described elsewhere [11]. Isolation of Legionella was attempted in sputum and other respiratory samples by using selective media (buffered charcoal-yeast extract medium-α). Detection of *L. pneumophila* serogroup I antigen in urine was performed by an immunoenzymatic commercial method (Legionella Urinary Antigen; Binax, Portland, ME, USA). Detection of the *S. pneumoniae* antigen in urine was performed by a rapid immunochromatographic assay (Now™; Binax). Standard serological methods were used to determine antibodies against the following pathogens: *Mycoplasma pneumoniae* (indirect agglutination), *Chlamydia psittaci* (immunofluorescence (IF)), *Chlamydia pneumoniae* (micro-IF), *Coxiella burnetii* (IF), and *L. pneumophila* (serogroups 1–6; enzyme immunoassay (EIA)). The Centers for Disease Control and Prevention criteria [12] were used for *Chlamydia pneumoniae* (micro-IF) serology. Serologies for respiratory syncytial virus (EIA), parainfluenza 3 virus (EIA) and influenza A virus (EIA) were performed as part of a research protocol during the first years of the study.

The antibiotic sensitivity of all isolates was determined at the Laboratory of the Microbiology Service, Bellvitge University Hospital (Barcelona, Spain), by using a commercial microdilution panel (STRHAEl, Sensititre; Trek Diagnostic Systems Ltd, East Grinstead, England) in accordance with the National Committee for Clinical Laboratory Standards guidelines [13]. The National Committee for Clinical Laboratory Standards 2001 criteria were used to define susceptibility of pneumococcal isolates [14].

Analysis

In order to assess factors associated with early mortality, early deaths were compared with the remaining patients. Early deaths were compared with late deaths in order to more accurately discern risk factors for early mortality and late mortality. To detect significant differences between groups the following were used: Chi-squared test with continuity correction for categorical variables and paired t-test for continuous variables. All the significant variables detected in the univariate analysis and considered clinically relevant were involved in the multivariate analysis. The analysis was performed with a stepwise logistic-regression model. In all analyses, $p<0.05$ was considered to be statistically significant. All reported p-values are two tailed.

RESULTS

A total of 2,457 hospitalised patients with CAP were included in the present study. Out of these, 57 (2.3%) were early deaths ($\leqslant$48 h), 131 (5.4%) were late deaths and 2,269 (92.3%) were survivors. Overall mortality (<30 days) was 7.7% (188 patients). Demographic characteristics and the main clinical features of patient groups are compared in table 1. Early deaths were older and more often classified as having a high-risk pneumonia, compared with the remaining patients. Altered mental status, renal failure, tachycardia, increased respiratory rate, high fever, multilobar infiltrates, respiratory failure and shock were more frequently found at baseline in early deaths. Late deaths had greater comorbidity than early deaths, mainly chronic heart disease and chronic renal disease. Conversely, shock at admission and bacteraemic pneumonia was more frequent in early deaths.

TABLE 1 Main demographic and clinical characteristics of 2,457 patients hospitalised for community-acquired pneumonia

Characteristic	Early deaths ⩽48 h	Early survivors >48 h					
		Late deaths	p-value#	Survivors at 30 days	p-value¶	All	p-value+
Subjects n	57	131		2269		2400	
Demographics							
Age yrs	71.74 ±16.79	73.01±13.19	0.564	64.69±16.95	0.001	65.23±16.86	0.004
⩾70 yrs	40 (70.2)	92 (46.1)	0.994	1048 (70.2)	<0.001	1140 (47.8)	0.001
Male	45 (78.9)	95 (72.5)	0.352	1579 (69.6)	0.169	1674 (70.2)	0.396
Current smoker	10 (19.6)	22 (16.8)	0.899	636 (28.0)	0.208	658 (27.7)	0.267
Heavy drinking	8 (15.4)	19 (14.5)	0.887	420 (18.5)	0.591	439 (18.5)	0.718
Vaccination status							
Influenza vaccine (season)	24 (42.4)	65 (49.6)	0.342	934 (41.2)	0.886	999 (45.5)	0.861
Pneumococcal vaccination§	4 (11.1)	10 (7.6)	0.882	267 (11.8)	1	277 (12.6)	1
Underlying disease	43 (78.2)	115 (87.7)	0.033	1721 (75.8)	0.932	1836 (77.0)	1
COPD	12 (22.2)	41 (31.3)	0.112	616 (27.1)	0.382	657 (28.0)	0.361
Diabetes mellitus	13 (23.6)	32 (24.4)	0.810	391 (17.2)	0.357	423 (18.8)	0.383
Cancer	10 (18.2)	19 (14.5)	0.595	183 (8.0)	0.20	202 (9.0)	0.031
Cerebrovascular disease	3 (5.5)	9 (6.8)	0.678	95 (4.1)	0.737	104 (4.7)	0.783
Chronic heart disease	11 (20.0)	49 (37.4)	0.014	579 (25.5)	0.283	628 (27.8)	0.225
Chronic renal disease	1 (1.8)	16 (12.2)	0.043	89 (3.9)	0.384	105 (4.5)	0.313
Chronic liver disease	4 (7.3)	7 (5.3)	0.653	126 (5.5)	0.570	133 (6.0)	0.686
Dementia	3 (5.5)	12 (9.1)	0.539	77 (3.4)	0.483	89 (4.0)	0.588
Others	17 (29.8)	40 (30.5)	0.922	625 (27.5)	0.817	665 (27.7)	0.765
High severity risk PSI class (IV–V)	52 (91.2)	119 (90.8)	0.848	1174 (51.7)	<0.001	1293 (54.1)	<0.001
Clinical features							
Altered mental status on admission	23 (41.1)	45 (34.4)	0.431	246 (10.8)	<0.001	291 (12.2)	<0.001
Renal failure (Cr >150 mmol·L^{-1})	17 (42.5)	48 (36.6)	0.366	267 (11.7)	<0.001	315 (13.3)	<0.001
Heart rate (beats·min^{-1})	107.82±22.89	104.09±24.01	0.402	98.37±19.49	.003	98.71±19.83	0.005
Respiratory rate	34.88±7.54	33.89±8.123	0.441	28.12±7.53	<0.001	28.51±33.1	<0.001
Temperature	37.64±1.37	37.7±1.06	0.779	38.1±1.01	0.001	38.1±1.02	0.021
Leukocytes	6140±3380.4	6320±3420.4	0.396	12060±5145.5	0.397	12158±5213	0.395
$P_{O_2}/F_{I,O_2}$ <300 mmHg	44 (88.8)	111 (84.7)	0.211	1210 (53.3)	<0.001	1321 (67.2)	<0.002
Multilobar infiltrates	31 (56.4)	70 (53.4)	0.904	713 (31.4)	<0.001	783 (32.1)	<0.001
Shock at admission	16 (29.1)	19 (14.5)	0.028	66 (2.9)	<0.001	85 (3.5)	<0.001
Pleural effusion	11 (20.0)	27 (20.6)	0.836	402 (17.7)	0.894	429 (18.0)	0.722
Bacteraemia	21 (40.4)	28 (21.4)	0.026	258 (11.4)	<0.001	286 (12.4)	<0.001

Data are presented as n (%) or mean±SD, unless otherwise stated. COPD: chronic obstructive pulmonary disease; PSI: Pneumonia Severity Index; Cr: creatine; P_{O_2}: oxygen tension; F_{I,O_2}: fraction of inspired oxygen. #: comparison of early deaths and late deaths; ¶: comparison of early deaths and survivors; +: comparison of early deaths and all the others; §: pneumoccocal vaccination (<5 yrs). 1 mmHg=0.133 kPa.

Causes of early mortality are shown in table 2. Acute respiratory failure secondary to pneumonia and multiorgan failure associated with septic shock were the most frequent.

As shown in table 3, *S. pneumoniae* was the most frequently identified pathogen; there were no differences between groups. Bacteraemic pneumococcal pneumonia was significantly more frequent in early and late deaths. Out of 324 *S. pneumoniae* strains isolated from the 718 patients with pneumococcal pneumonia, no significant differences were found in the rates of antibiotic resistance between groups (early deaths *versus* late deaths *versus* survivors *versus* all (late deaths and survivors)):

TABLE 2 Causes of early and late death in patients hospitalised with community-acquired pneumonia

Cause of death	Early deaths	Late deaths
Subjects	57	131
Acute respiratory failure	38 (66.6)	64 (48.8)
Septic shock / multiorgan failure	14 (24.6)	22 (16.8)
Congestive heart failure or cardiac arrhythmia	4 (7.0)	16 (12.2)
Diabetic ketoacidosis	1 (1.7)	0 (0)
Nosocomial infection	0	8 (6.1)
Others	0	21 (16.0)

Data are presented as n or n (%).

penicillin (Minimum Inhibitory Concentration (MIC) $\geqslant 4$ μg·mL^{-1}; 20.0% *versus* 8.7% (p=0.738), *versus* 8.1% (p=0.448), and *versus* 8.3% (p=0.521)), cefotaxime/ceftriaxone (MIC $\geqslant 2$ μg·mL^{-1}; 0% *versus* 0% (p=1), *versus* 6.3% (p=0.563), and *versus* 6.4% (p=0.586), erythromycin (MIC $\geqslant 1$ μg·mL^{-1}; 37.5% *versus* 15.8% (p=0.464), *versus* 13.7% (p=0.058), and *versus* 13.4 (p=0.088)), and ciprofloxacin (MIC $\geqslant 4$ μg·mL^{-1}; 0% *versus* 0% (p=1), *versus* 1.9% (p=1), and *versus* 1.75% (p=1)). Pneumonia due to Gram-negative bacilli was significantly more frequent in patients who died (early and late deaths), especially in the case of *Pseudomonas aeruginosa* pneumonia. No significant differences were observed regarding the frequency of *P. aeruginosa* between nursing home residents and the remaining patients (1.9 *versus* 0.8%; p=0.361).

As shown in table 4, most patients were initially treated with a single antimicrobial agent. Concordance of antibiotic therapy could be determined in 38 out of 57 early deaths, 85 out of 131 late deaths, and 1,223 out of 2,269 survivors. Overall, early deaths received discordant antibiotic therapy more frequently than all others. Discordant empirical antibiotic therapy in early deaths was mainly due to lack of coverage against *P. aeruginosa* infection (five out of six patients; 83%). All these five patients were aged >70 yrs and were classified into the Pneumonia Severity Index (PSI) risk class V; three of them had bacteraemia and septic shock and two had chronic obstructive pulmonary disease (COPD), but none had bronchiectasis or were receiving chronic steroid therapy.

Table 5 shows factors associated with early mortality by multivariate analyses. After adjustment, factors associated with early death ($\leqslant$48 h) were increased age, altered mental status, multilobar pneumonia, shock at admission, pneumococcal bacteraemia and discordant empiric antibiotic therapy. No significant differences were found in these factors associated with death when analysing 5-day instead of 2-day mortality, by univariate and multivariate analyses. Among all 188 patients who died, shock at admission was independently associated with early deaths (odds ratio (OR) 2.683, 95% confidence interval (CI) 1.014–7.097), whereas chronic heart disease was associated with late deaths (OR 0.382, 95% CI 0.153–0.956).

TABLE 3 Aetiology of community-acquired pneumonia of 2,457 patients hospitalised for community-acquired pneumonia

Aetiology	Early deaths $\leqslant$48 h	Early survivors >48 h					
		Late deaths	p-value#	Survivors at 30 days	p-value¶	All	p-value+
Subjects n	57	131		2269		2400	
Streptococcus pneumoniae	16 (28.1)	39 (29.7)	0.813	663 (29.2)	0.967	702 (29.3)	1
Bacteraemic pneumococcal pneumonia	13 (22.8)	21 (16)	0.257	210 (9.2)	0.001	231 (7.6)	0.003
Legionella pneumophila	4 (7.0)	6 (4.5)	0.740	162 (7.1)	0.965	168 (7.0)	1
Haemophilus influenzae	1 (1.8)	11 (8.4)	0.165	140 (6.2)	0.169	151 (6.3)	0.259
Bacteraemic *H. influenzae* pneumonia		1 (0.8)	1	18 (0.8)	1	19 (0.8)	1
Aspiration pneumonia	5 (8.8)	20 (15.3)	0.331	122 (5.4)	0.228	142 (5.9)	0.387
Atypical agents		3 (2.2)	0.604	122 (5.4)	0.112	125 (5.2)	0.116
Gram negative bacilli	7 (12.3)	11 (8.3)	0.405	20 (0.1)	<0.001	31 (5.3)	<0.001
Bacteraemic Gram-negative bacilli	5 (8.7)	6 (4.6)	0.736	6 (0.3)	<0.001	12 (0.5)	0.003
Pseudomonas aeruginosa	6 (10.5)	5 (3.8)	0.143	11 (0.1)	<0.001	16 (0.7)	<0.001
Bacteraemic *P. aeruginosa* pneumonia	4 (7)	3 (2.3)	0.415	2 (0.04)	<0.001	5 (0.2)	0.002
Other aetiologies	4 (7.1)	7 (5.3)	0.911	63 (2.8)	0.085	70 (2.9)	0.086
Unknown aetiology	19 (33.3)	43 (32.8)	0.945	1050 (46.3)	0.071	1093 (45.5)	0.080

Data are presented as n (%), unless otherwise stated. #: comparison of early mortality and late deaths; ¶: comparison of early deaths and survivors. +: comparison of early deaths and all the others.

TABLE 4 Antibiotic therapy of 2,457 patients hospitalised for community-acquired pneumonia

Therapy	Early deaths ⩽48 h	Early survivors >48 h					
		Late deaths	p-value#	Survivors at 30 days	p-value¶	All	p-value+
Subjects	57	13		2269		2400	
Initial antibiotic therapy							
Monotherapy	36 (63.2)	91 (69.5)	0.402	1755 (77.3)	0.018	1846 (76.9)	0.025
β-Lactams	32	80	0.879	1284	0.027	1364	0.027
Macrolides	2	3	0.987	159	0.766	162	0.379
Quinolones		6	0.233	255	0.007	261	0.004
Other	2	2	0.752	57	0.235	59	0.735
Combination therapy	21 (36.8)	40 (30.5)	0.402	514 (22.7)	0.018	554 (23.1)	0.025
β-lactams + macrolides	12	20	0.331	197	0.093	201	0.003
β-lactams + quinolones	7	19	0.860	278	0.099	297	.146
Other combinations	2	1	0.454	55	0.849	56	0.642
Initial antibiotic therapy in high severity risk population§	52	119		1174		1293	
Monotherapy	33 (63)	89 (74.8)	0.4.83	862 (73.4)	0.146	951 (73.5)	0.113
β-Lactams	31	76	0.735	735	0.210	811	0.124
Macrolides		3	0.553	41	0.395	44	0.394
Quinolones		9	0.312	60	0.160	69	0.086
Other	2	1	0.177	26	0.276	27	0.583
Combination therapy	19 (36.5)	30 (25.2)	0.483	312 (26.6)	0.146	342 (26.5)	0.113
β-lactams + macrolides	11	14	0.636	110	0.046	124	0.010
β-lactams + quinolones	7	16	0.404	190	0.396	206	0.846
Other combinations	1	0	0.400	12	0.815	12	0.815
Initial antibiotic therapy in pneumoccocal pneumonia	16	39		663		702	
Combination therapy	4 (25)	13 (33.3)	0.749	140 (21.1)	0.757	153 (21.8)	0.763
β-lactams + macrolides	1	3	1	283	0.122	31	0.525
β-lactams + quinolones	3	10	1	112	1	122	1
Other combinations	0	0		3	1	3	1
Discordant initial therapy§	6/38 (15.8)	5/85 (5.9)	0.092	18/1223 (1.5)	<0.001	23/1308 (1.7)	<0.001

Data are presented as n or n (%), unless otherwise stated. Data for discordant initial therapy are presented as n/n of patients for whom concordance could be determined (%). #: comparison of early mortality and late deaths; ¶: comparison of early deaths and survivors; +: comparison of early deaths and all the others; §: concordance of antibiotic therapy was examined in 1,346 patients with an aetiological diagnosis, 38 patients in early deaths and 1,308 patients in all the others.

DISCUSSION

It is widely recognised that the evolution of patients with CAP within the first 48 h is crucial [1, 15, 16]. In fact, once clinical stability is achieved, substantial clinical deterioration owing to pneumonia is rare [17]. In a previous study, the current authors analysed the causes and factors associated with early failure in hospitalised patients with CAP [11]. In the definition of early failure as ''lack of response or worsening of clinical or radiological status at 48–72 h requiring changes in antibiotic therapy or invasive procedures,'' patients who had died within the first 48 h of admission were specifically excluded. The current prospective study offers a comprehensive evaluation of this group of patients in order to establish the causes of, and risk factors for, early mortality in CAP.

In the present series of patients admitted according to predefined criteria [18], in which the severe immunosuppressed population is excluded, the early mortality rate was 2.3%; that is, one third of the total patients with CAP who died during hospital admission. This figure, though relatively low in the current authors' view, is difficult to compare with others obtained in previous series, owing to differences in definitions and study populations.

Overall, although differences in the frequency and types of underlying diseases were not observed among early deaths compared with all the others, the demographic and clinical characteristics of early deaths define a group with more severe pneumonia, as shown by the fact that 91% of cases were classified in the PSI high severity risk classes.

The most frequent causes of early death were respiratory failure and shock/multiorgan failure. Indeed, a large proportion of them had bacteraemia and presented with septic shock and/or respiratory failure at admission. The vast majority of deaths were pneumonia related, in the setting of an unbalanced inflammatory response.

TABLE 5 Risk factors associated with early deaths in 2,457 patients hospitalised with community-acquired pneumonia by multivariate analysis

Risk factor	OR	95% CI
Male sex	0.538	0.254–1.140
Age ⩾70 yrs	2.727 ¶	1.394–5.337
Altered mental status at admission	2.481¶	1.276–4.822
Shock at admission	7.547¶	3.453–16.494
Respiratory failure#	2.073	0.848–5.067
Multilobar pneumonia	1.979¶	1.042–3.758
Discordant antibiotic therapy	11.281¶	3.497–36.387
Bacteraemic pneumococcal pneumonia	2.373¶	1.083–5.200

OR: odds ratio; CI: confidence interval. #: oxygen tension/inspired oxygen fraction <300 mmHg. ¶: significant values of multivariate analysis. 1 mmHg=0.133 kPa.

Both bacteraemic pneumococcal pneumonia and *P. aeruginosa* pneumonia were significantly more frequent in early deaths. In the case of *S. pneumoniae*, no relationship between mortality (early and late deaths) and drug resistance could be demonstrated. This observation is in agreement with most previous studies of bacteraemic pneumococcal pneumonia which have not shown differences in mortality between those with susceptible and those with nonsusceptible pneumococci when controlling for age, underlying disease, severity of illness on presentation, and appropriate treatment [19, 20]. In fact, all patients who died early and had pneumococcal infection were given concordant antibiotic therapy from admission. This evidence reinforces the classical concept that early deaths are less dependent on antibiotic efficacy than on other factors, including inadequate host response [21]. Recent studies suggest that modulation of the immune system could improve the outcomes of patients with severe pneumonia [22, 23]. However, further studies are warranted to evaluate the relationship among excessive host response and early deaths. Importantly, randomised clinical trials addressing the potential role of steroids as adjunctive therapy in severe CAP are needed.

Conversely, it has been shown previously that polysaccharide pneumococcal vaccination may prevent invasive pneumococcal disease in adults, and improve outcomes [24, 25]. In the present study, <10% of patients who died had received pneumococcal vaccination, despite the fact that >75% had underlying disease. These findings concur with other studies showing that current vaccination rates among target persons remain low [26, 27]. The current authors believe that a wider use of the pneumococcal polysaccharide vaccine may help to prevent bacteraemic pneumococcal pneumonia and, conceivably, lowering the rates of early deaths in CAP.

However, the present data suggest a possible relationship between early deaths and discordant therapy in cases of *P. aeruginosa* pneumonia, since five out of six patients with early deaths while receiving discordant therapy had this diagnosis. None of these patients had a previous diagnosis of bronchiectasis, nor had they received corticosteroid therapy; thus, they did not present with the major risk factors for *P. aeruginosa* pneumonia indicated in the current guidelines for the management of CAP [1]. Nevertheless, it should be borne in mind that all these patients had severe pneumonia with high risk of death, in spite of appropriate antibiotic therapy.

The clinical risk factors for early mortality identified by multivariate analysis, such as increased age, altered mental status, multilobar pneumonia and shock, have also been recognised in previous studies as factors associated with overall mortality and with mortality occurring within the initial five days after hospital admission [4–7, 28]. Such factors would be expected to influence early evolution if present at admission. In addition, the present study identified chronic heart disease as a factor associated with late mortality. Apart from age (the major driver in the PSI score) the other factors would also be expected to influence early evolution if present at admission. Additionally, the present study identified discordant therapy as an independent risk factor for early mortality. Nevertheless, this finding is supported almost exclusively by the aforementioned cases of patients with *P. aeruginosa* pneumonia, and the issue requires further study. The question of whether the use of appropriate antibiotics has a clear impact on survival in the first hours after admission remains unanswered, and should be addressed by future research.

In conclusion, current early mortality is relatively low, representing around one third of deaths in patients with community-acquired pneumonia who died during hospital admission. It occurs mainly in elderly patients or patients presenting with altered mental status and septic shock. Pneumococcal bacteraemia and discordant antibiotic therapy, mainly due to lack of coverage against *Pseudomonas aeruginosa*, are also significant risk factors. The major causes of early death are pneumonia related, such as respiratory failure and shock in the setting of an inadequate host response.

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