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ORIGINAL ARTICLE

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Early Mortality in Patients with Community-Acquired Pneumonia: Causes, and Risk Factors

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ABSTRACT

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

METHODS: Prospective observational study of non-immunocompromised adults hospitalized with CAP (1995-2005). Early deaths, defined as death due to any cause ≤48 hours after admission, were compared with all patients who survived > 48 hours. Furthermore, early deaths were compared with late deaths (patients who died > 48 hours) and with survivors.

RESULTS: Of 2,457 patients, 57 died ≤ 48 hours (2.3%). 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 bacteremia, and discordant empiric antibiotic therapy.

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

INTRODUCTION

Community-acquired pneumonia (CAP) continues to be a major health problem worldwide [1-3]. Despite more accurate etiologic 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% to 50% of hospitalized patients and overall mortality rates that range from around 10% for patients treated in a hospital setting to more than 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 on.

In this setting, information regarding the causes and factors related to mortality within the first 48 hours of pneumonia are scarce, and there is no clear consensus on whether or not this very early mortality is modifiable by medical intervention [8-10].

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

MATERIAL AND METHODS

Study subjects and study design

The study was carried out in a 900-bed university hospital for adults in Barcelona, Spain. The hospital serves an area of 1,100,000 inhabitants and admits approximately 24,000 patients per year. All non-immunocompromised patients with CAP who were admitted to the hospital from February 1995 through December 2005 were prospectively recruited and followed up. Patients with neutropenia, HIV infection or transplantation were not included. For the purposes of this study, patients were divided into two groups: those who died due to any cause $\leq$ 48 hours after admission (early deaths), and those who survived the first 48 hours after admission. Additionally this group was divided in two: patients who died > 48 hours after admission (late deaths) and survivors. This prospective, longitudinal and observational study was approved by the Ethical Committee of our Institution.

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 hematology 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

Community-acquired pneumonia was defined as the presence of a new infiltrate on chest radiography plus at least 1 of the following: fever (temperature $\geq$ 38.0ºC) or hypothermia (temperature $\leq$ 35.0ºC), new cough with or without sputum production, pleuritic chest pain, dyspnea, or altered breath sounds on

auscultation. The diagnosis of septic shock was based on a systolic blood pressure of less than 90 mmHg and peripheral hypoperfusion with clinical or bacteriologic evidence of uncontrolled infection. Complications were defined as any untoward circumstance occurring during hospitalization, with the exception of the side effects of the medication. Antibiotic therapy was administered according to the hospital guidelines, which recommended the administration of a ß-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 allowed for selected cases. Concordance of antibiotic therapy was examined for all cases with an etiologic diagnosis according to susceptibility test criteria for classic respiratory pathogens. Early death was defined as death due to any cause $\leq$ 48 hours of hospitalization, late death was defined as a death due to any cause > 48 hours of hospitalization and within 30 days of hospitalization. Overall mortality was defined as death due to any cause within 30 days of hospitalization. The severity of illness at presentation was quantified using the validated PORT prediction rule for 30-day mortality and medical complications in CAP [4].

Microbiologic studies

The etiologic diagnosis of community-acquired pneumonia was established as described elsewhere [11]. Isolation of *Legionella* was attempted in sputum and other respiratory samples by using selective media (BCYE-α). Detection of *L. pneumophila* serogroup I antigen in urine was performed by an immunoenzymatic commercial method (*Legionella* Urinary Antigen, Binax, Portland, Maine). Detection of the *S. pneumoniae* antigen in urine was performed by a rapid immunochromatographic assay (Now™, Binax, Portland, Maine). 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 CDC criteria [12] were used for *C. 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, by using a commercial microdilution panel (STRHAEl, Sensititre; Trek Diagnostic Systems Ltd, West Sussex, England) in accordance with the National Committee for Clinical Laboratory Standards guidelines [13]. We used the National Committee for Clinical Laboratory Standards 2001 criteria to define susceptibility of pneumococcal isolates) [14].

Analysis

To assess factors associated with early mortality, we compared early deaths with the remaining patients. To discern more accurately among risk factors for early mortality and late mortality, we compared early deaths with late deaths. To detect significant differences between groups we used the chi-square test with continuity correction for categorical variables, and the Student's t-test for continuous variables. To identify independent factors associated with early mortality we performed two multivariate analyses with the groups described above. We included all significant variables detected in the univariate analysis and considered clinically relevant. The analyses were performed with the step-wise logistic-regression model of the SPSS software package (SPSS, Chicago). In all analyses, we considered P values less than 0.05 to be statistically significant. All reported P values are two-tailed.

RESULTS

A total of 2457 hospitalized patients with CAP were included in the study. Of these, 57 (2.3%) were early deaths (≤48 hours), 131 (5.4%) were late deaths, and 2269 (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 as 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 bacteriemic pneumonia was more frequent in early deaths.

Causes of early mortality are shown in Table 2. Acute respiratory failure secondary to pneumonia and multiorgan failure associated to 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. Bacteremic pneumococcal pneumonia was significantly more frequent in early and late deaths. Of 324 *S. pneumoniae* strains isolated from the 718 patients with pneumococcal pneumonia, we found no significant differences in the rates of antibiotic resistance between groups (early deaths, late deaths, survivors, and all [late deaths and survivors]): penicillin (MIC≥ 4 μg/mL; 20.0% vs. 8.7% [p=.738], vs. 8.1% [p=.448], and vs. 8.3% [p=.521]), cefotaxime/ceftriaxone (MIC ≥ 2 μg/mL; 0% vs. 0% [p=1], vs. 6.3% [p=.563], and vs. 6.4% [p=.586], erythromycin (MIC ≥ 1 μg/mL; 37.5% vs. 15.8% [p=.464], vs. 13.7% [p=.058]), and vs. 13.4 [p=.088], and ciprofloxacin (MIC ≥ 4 μg/mL; 0% vs. 0% [p=1], vs. 1.9% [p=1], and vs. 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 *P. aeruginosa* pneumonia. No significant differences were observed regarding the frequency of *P. aeruginosa* between nursing home residents and the remaining patients (1.9% vs. 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 of 57 early deaths, 85 of 131 late deaths, and 1223 of 2269 survivors. Overall, early deaths received discordant antibiotic therapy

more frequently than all the others. Discordant empirical antibiotic therapy in early deaths was mainly due to lack of coverage against *P. aeruginosa* infection (5/6 patients, 83%). All these 5 patients were older than 70 years and were classified into the PSI risk class of V; 3 of them had bacteremia and septic shock and 2 had 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 ($\leq$48 hours) were increased age, altered mental status, multilobar pneumonia, shock at admission, pneumococcal bacteremia, and discordant empiric antibiotic therapy. No significant differences were found in these factors associated with death, when analyzing 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 (OR 2.683 [95% CI 1.014-7.097]), whereas chronic heart disease was associated with late deaths (OR 0.382 [CI 95% 0.153-0.956]).

DISCUSSION

It is widely recognized that the evolution of patients with CAP within the first 48 hours 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, we analyzed the causes and factors associated with early failure in hospitalized patients with CAP [11]. In our definition of early failure as "lack of response or worsening of clinical or radiological status at 48 to 72 hours requiring changes in antibiotic therapy or invasive procedures", we specifically excluded those patients who had died within the first 48 hours of admission. 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 this series of patients admitted according to predefined criteria [18], which exclude the severe immunosuppressed population, the early mortality rate was 2.3%, that is, one third of the total of patients with CAP who died during hospital admission. This figure, though relatively low in our view, is difficult to compare with others obtained in previous series due to differences in definitions and study populations.

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

The most frequent causes of early deaths were respiratory failure and shock/multiorgan failure. Indeed, a large proportion of them had bacteremia, 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.

Both bacteremic 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 bacteremic pneumococcal pneumonia that did not show differences in mortality between those with susceptible and those with non-susceptible pneumococci when controlling for age, underlying disease,

severity of illness on presentation, and appropriate treatment [19,20]. In fact, all patients with early deaths and pneumococcal infection were given concordant antibiotic therapy from the beginning. 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 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, randomized clinical trials addressing the potential role of steroids as adjunctive therapy in severe CAP are needed.

On the other hand, it has been shown that polysaccharide pneumococcal vaccination may prevent invasive pneumococcal disease in adults and improve outcomes [24,25]. In our study, less than 10% of patients who died had received pneumococcal vaccination despite more than 75% had underlying disease. Our finding concurs with other studies showing that current vaccination rates among target persons remain low [26,27]. We believe that a wider use of the pneumococcal polysaccharide vaccine may help to preventing bacteremic pneumococcal pneumonia and conceivably for lowering the rates of early deaths in CAP.

On the other hand, our data suggest a possible relationship between early deaths and discordant therapy in cases of *P. aeruginosa* pneumonia, since 5 of 6 patients with early deaths while receiving discordant therapy had this diagnosis. None of these patients had 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 metal status, multilobar pneumonia and shock, have also been recognized in previous studies as factors associated with overall mortality and with mortality occurring within the first 5 days of admission [4, 5,6,7,28]. This factor would be expected to influence early evolution if present at admission. In addition, our 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. In addition, our study identified discordant therapy as an independent risk factor for early mortality. Nevertheless, our finding is supported almost exclusively by the cases of patients with *P. aeruginosa* pneumonia, as discussed above, 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 in future research.

As conclusions, current early mortality is relatively low, representing around one third of deaths of patients with CAP who died during hospital admission. It occurs mainly in elderly patients or patients presenting with altered mental status and septic shock. . Pneumococcal bacteremia and discordant antibiotic therapy mainly due to lack of coverage against *P. 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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Table 1. Main demographic and clinical characteristics of 2457 patients hospitalized for community-acquired pneumonia[a].

Characteristic	Early deaths (≤ 48 hours)		Early survivors (> 48 hours)								
			Late deaths		P value[b]	Survivors at 30 days		P value[c]	All		P value[d]
	n =57	%	n =131	%		n =2269	%		n = 2400	%	
Demographics											
Age, years (mean, SD)	71.74 +/- 16.79		73.01+/-13.19		.564	64.69 +/- 16.95		.001	65.23 +/- 16.86		.004
≥ 70 years	40	70.2	92	46.1	.994	1048	70.2	<.001	1140	47.8	.001
Male, sex	45	78.9	95	72.5	.352	1579	69.6	.169	1674	70.2	.396
Current smoker	10	19.6	22	16.8	.899	636	28.0	.208	658	27.7	.267
Heavy drinking	8	15.4	19	14.5	.887	420	18.5	.591	439	18.5	.718
Vaccination status											
Influenza vaccine (season)	24	42.4	65	49.6	.342	934	41.2	.886	999	45.5	.861
Pneumococcal vaccination[e]	4	11.1	10	7.6	882	267	11.8	1	277	12.6	1
Underlying disease	43	78.2	115	87.7	.033	1721	75.8	.932	1836	77.0	1
COPD[f]	12	22.2	41	31.3	.112	616	27.1	. 382	657	28.0	.361

Diabetes mellitus	13	23.6	32	24.4	.810	391	17.2	.357	423	18.8	.383
Cancer	10	18.2	19	14.5	.595	183	8.0	.0.20	202	9.0	.031
Cerebrovascular disease	3	5.5	9	6.8	.678	95	4.1	.737	104	4.7	.783
Chronic heart disease	11	20.0	49	37.4	. 014	579	25.5	. 283	628	27.8	. 225
Chronic renal disease	1	1.8	16	12.2	.043	89	3.9	.384	105	4.5	.313
Chronic liver disease	4	7.3	7	5.3	.653	126	5.5	.570	133	6.0	.686
Dementia	3	5.5	12	9.1	.539	77	3.4	.483	89	4.0	.588
Others	17	29.8	40	30.5	.922	625	27.5	.817	665	27.7	.765
High severity risk PSI class (IV-V)	52	91.2	119	90.8	.848	1174	51.7	<.001	1293	54.1	<.001
Clinical features											
Altered mental status on admission	23	41.1	45	34.4	.431	246	10.8	<.001	291	12.2	<.001
Renal failure (Cr > 150 mmol/L)	17	42.5	48	36.6	.366	267	11.7	<.001	315	13.3	<.001
Heart rate (mean;+/-SD)	107.82 +/- 22.89		104.09 +/-24.01		.402	98.37+/-19.49		.003	98.71 +/- 19.83		.005
Respiratory rate (mean;+/-SD)	34.88 +/-7.54		33.89+/-8.123		.441	28.12+/-7.53		<.001	28.51 +/- 33.1		<.001
Fever (mean;+/-SD)	37.64 +/-1.37		37.7+/-1.06		.779	38.1+/-1.01		.001	38.1+/-1.02		.021
Leucocytes (mean;+/-SD)	6 140 +/-3380.4		6320 +/- 3420.4		.396	12 060+/-5145.5		.397	12 158+/-5213		.395
PO2/fiO2[f] < 300	44	88.8	111	84.7	.211	1210	53.3	<.001	1321	67.2	<.002

Multilobar infiltrates	31	56.4	70	53.4	.904	713	31.4	<.001	783	32.1	<.001
Shock at admission	16	29.1	19	14.5	.028	66	2.9	<.001	85	3.5	<.001
Pleural effusion	11	20.0	27	20.6	.836	402	17.7	.894	429	18.0	.722
Bacteremia	21	40.4	28	21.4	.026	258	11.4	<.001	286	12.4	<.001

[a] Data are given as number (percentage)except where otherwise indicated.

[b] Comparasion of early deaths and late deaths.

[c] Comparison of early deaths and survivors.

[d] Comparison of early deaths and all the others.

[e] Pneumoccocal vaccination (< 5 years).

[f] Abbreviations: COPD, Chronic obstructive pulmonary disease; fiO2, fraction of inspired oxyge

Table 2. Causes of early and late death in patients hospitalized with community-acquired pneumonia

Cause of death	Early deaths n= 57 (%)	Late deaths n= 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)

Table 3. Etiology of community-acquired pneumonia of 2457 patients hospitalized for community- acquired pneumonia.

Etiology	Early deaths (≤ 48 hours)		Early survivors (> 48 hours)								
			Late deaths		P value[a]	Survivors at 30 days		P value[b]	All		P value[c]
	n =57	%	n=131	%		n=2269	%		n=2400		
Streptococcus pneumoniae	16	28.1	39	29.7	.813	663	29.2	.967	702	29.3	1
Bacteremic pneumococcal pneumonia	13	22.8	21	16	.257	210	9.2	.001	231	7.6	.003
Legionella pneumophila	4	7.0	6	4.5	.740	162	7.1	.965	168	7.0	1
Haemophilus influenzae	1	1.8	11	8.4	.165	140	6.2	.169	151	6.3	.259
Bacteremic *H. influenzae* pneumonia	-	-	1	0.8	1	18	0.8	1	19	0.8	1
Aspiration pneumonia	5	8.8	20	15.3	.331	122	5.4	.228	142	5.9	.387
Atypical agents	-	-	3	2.2	.604	122	5.4	.112	125	5.2	.116
Gram negative bacilli	7	12.3	11	8.3	.405	20	0.1	<.001	31	5.3	<.001
Bacteremic gram negative bacilli	5	8.7	6	4.6	.736	6	0.3	<.001	12	0.5	.003
Pseudomonas aeruginosa	6	10.5	5	3.8	.143	11	0.1	<.001	16	0.7	<.001
Bacteremic *P. aeruginosa* pneumonia	4	7	3	2.3	.415	2	0.04	<.001	5	0.2	.002
Other etiologies	4	7.1	7	5.3	.911	63	2.8	.085	70	2.9	.086
Unknown etiology	19	33.3	43	32.8	.945	1050	46.3	.071	1093	45.5	.080

[a] Comparasion of early mortality and late deaths.
[b] Comparison of early deaths and survivors.
[c] Comparison of early deaths and all the others.

Table 4. Antibiotic therapy of 2457 patients hospitalized for community- acquired pneumonia.

Therapy	Early deaths (≤ 48 hours) n =57 (%)	Early survivors (> 48 hours)					
		Late deaths n=131 (%)	P value[a]	Survivors at 30 days n=2269 (%)	P value[b]	All n = 2400 (%)	P value[c]
Initial antibiotic therapy							
Monotherapy	36 (63.2%)	91 (69.5%)	.402	1755 (77.3%)	.018	1846 (76.9%)	.025
Beta-Lactams	32	80	.879	1284	.027	1364	.027
Macrolides	2	3	.987	159	.766	162	.379
Quinolones	-	6	.233	255	.007	261	.004
Other	2	2	.752	57	.235	59	.735
Combination therapy	21 (36.8%)	40 (30.5%)	.402	514 (22.7%)	.018	554 (23.1%)	.025
Beta-lactams + macrolides	12	20	.331	197	.093	201	.003
Beta-lactams + quinolones	7	19	.860	278	.099	297	.146
Other combinations	2	1	.454	55	.849	56	.642
Initial antibiotic therapy in high-severity risk population[d]	**n =52**	**n = 119**		**n = 1174**		**n =1293**	
Monotherapy	33 (63)	89 (74.8)	.4.83	862 (73.4)	.146	951 (73.5)	.113
Beta-Lactams	31	76	.735	735	.210	811	.124

Macrolides	-	3	.553	41	.395	44	.394
Quinolones	-	9	.312	60	.160	69	.086
Other	2	1	.177	26	.276	27	.583
Combination therapy	19 (36.5)	30 (25.2)	.483	312 (26.6)	.146	342 (26.5)	.113
Beta-lactams + macrolides	11	14	.636	110	.046	124	.010
Beta-lactams + quinolones	7	16	.404	190	.396	206	.846
Other combinations	1	0	.400	12	.815	12	.815
Initial antibiotic therapy in pneumoccocal pneumonia	**n = 16**	**n =39**		**N=663**		**n = 702**	
Combination therapy	4 (25)	13 (33.3)	.749	140 (21.1)	.757	153 (21.8)	.763
Beta-lactams + macrolides	1	3	1	28	3 122	31	.525
Beta-lactams + quinolones	3	10	1	112	1	122	1
Other combinations	0	0	-	3	1	3	1
Discordant initial therapy[d]	6/38 (15.8)	5/85(5.9)	.092	18/1223(1.5)	<.001	23/1308 (1.7)	<.001

[a] Comparasion of early mortality and late deaths.
[b] Comparison of early deaths and survivors.
[c]Comparison of early deaths and all the others.
[d] Concordance of antibiotic therapy was examined in 1346 patients with an etiologic diagnosis, 38 patients in early deaths and 1308 patients in all the others.

Table 5. Risk factors associated with early deaths in 2457 patients hospitalized with community-acquired pneumonia by mulitvariate analysis.

	Odds Ratio (95% CI)
Risk factor	**Multivariate analysis**
Male sex	0.538 (0.254-1.140)
Age $\geq$ 70 years	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 (pO2/FiO2<300)	2.073 (0.848-5.067)
Multilobar pneumonia	1.979 (1.042-3.758)*
Discordant antibiotic therapy	11.281 (3.497-36.387)*
Bacteremic pneumococcal pneumonia	2.373 (1.083-5.200)*

*Significant values of multivariate analysis.