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RESEARCH PAPER

Factors associated with 30-day mortality in elderly inpatients with community acquired pneumonia during 2 influenza seasons

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ABSTRACT

Community-acquired pneumonia (CAP) refers to pneumonia unrelated to hospitals or extended-care facilities. The aim of this study was to determine factors associated with 30-day mortality in patients with CAP aged ≥ 65 y admitted to 20 hospitals in 7 Spanish regions during the 2013–14 and 2014–15 influenza seasons. Logistic regression was used to identify factors associated with 30-day mortality. The adjusted model included variables selected by backward elimination with a cut off of < 0.02. A total of 1928 CAP cases were recorded; 60.7% were male, 46.67% were aged 75–84 years, and 30-day mortality was 7.6% (n = 146). Pneumococcal vaccination had a significant protective effect (OR 0.68, 95% CI, 0.48–0.96; p = 0.03) and influenza vaccination in any 3 preceding seasons slight protective effect against CAP (OR 0.72, 95% CI, 0.51–1.02;p = 0.06). Factors significantly associated with 30-day mortality were having a degree of dependence (aOR 3.67, 95% CI, 2.34–5.75; p < 0,001); age ≥ 85 y (OR 3.01, 95% CI, 1.71–5.30; p < 0.001), liver impairment (aOR 2.41, 95% CI, 1.10–5.31; p = 0.03); solid organ neoplasm (aOR 2.24, 95% CI, 1.46–3.45; p < 0.001), impaired cognitive function (aOR 1.93, 95% CI, 1.22–3.05; p = 0.005), and ICU admittance (aOR2.56, 95% CI, 1.27–5.16; p = 0.009); length of stay (aOR 1.56, 95% CI, 1.02 – 2.40; p = 0.04) and cardio-respiratory resuscitation (aOR 7.75, 95% CI, 1.20 – 49.98; p = 0.03). No association was observed for other comorbidities such as chronic pulmonary obstructive disease (COPD) or heart conditions in the adjusted model. Offering both pneumococcal and influenza vaccination to the elderly may improve 30-day mortality in patients with CAP.

KEYWORDS
aging; community acquired pneumonia; elderly; mortality

Introduction

Community-acquired pneumonia (CAP), an inflammation or infection of the lungs that impairs respiratory function and is not related to hospitals or extended-care facilities, is a common cause of morbidity and mortality worldwide. It affects 2–13 /1000 community-dwelling persons year with hospitalization rates of 20–60%.[1, 2]

CAP is the most common cause of mortality and disability-adjusted life-years of all respiratory diseases, including chronic obstructive pulmonary disease (COPD).[3] CAP remains a major cause of hospitalization and death in developed countries, especially in people aged ≥ 65 y.[4, 5]

People aged ≥ 65 y account for about one third of all cases of CAP, but are responsible for more than half of all costs.[6] Evaluating the risk of mortality in large groups of older patients will become increasingly important with the aging of populations throughout the industrialized world and CAP is one of the main clinical entities responsible for morbidity and mortality in the elderly. Estimates of the elderly population of Europe in 2030, with consistently low birth rates and higher life expectancy will transform the shape of the EU age pyramid; the most important change will probably be a marked transition toward a much older population structure, and this development is already becoming apparent in several EU Member States.[7]

Prolonged life expectancy in Western countries and medical advances have increased the proportion of patients with CAP who are elderly and/or have multiple comorbidities.[8] Persons aged ≥ 65 y or who have a chronic health condition are considered to be at high risk for pneumonia.[9]

In Spain, the overall adult incidence of CAP ranges between 2 and 10 cases/1,000 persons/year in all ages and between 3.2 and 35/1,000 persons/year in persons aged ≥ 65 y. A Spanish study found incidence rates increased significantly in the elderly according to age (9.9/1,000 in people aged 65–74 y versus 29.4 in people aged ≥ 85 years). Hospitalizations due to CAP increase with age and may reach 67–75.1% in people aged ≥ 65 y.[10]

The etiology of community-acquired pneumonia in Europe, Latin America, and the United States, and overall, is mainly attributed to *Streptococcus pneumonia*, followed by *Mycoplasma pneumoniae, Chlamydophila pneumoniae, Haemophilus influenza*, and *Legionella pneumophila*. The prevalence of co-infection is high, especially in the winter months, when there is

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greater circulation of respiratory viruses (influenza, respiratory syncytial virus, rhinoviruses, etc.) in the community. [3, 11, 12]

The reported mortality of CAP varies from < 5% in outpatients to approximately 12% in all hospitalized CAP patients, and > 30% in patients admitted to the intensive care unit (ICU). The pneumonia severity index (PSI) was developed to define the risk of mortality, but it has been used to guide site of care decisions, with controversial results, because it may underestimate severe illness in previously healthy individuals and overestimate severity in patients with advanced age and chronic illness. The accuracy of the PSI in predicting outcomes in CAP decreases with advancing age. Severity and the extension of pneumonia, inadequate response to infection, and low functional status are the principal factors associated with mortality in older patients.[13, 14]

In addition, despite improved supportive care and the availability of and widespread adherence to recommended treatment guidelines, the incidence of CAP has not decreased over recent years and remains a frequent problem in clinical practice, particularly in patients requiring hospitalization and/or ICU admission.[15, 16]

The main aim of this multicenter observational study was to determine possible factors associated with CAP outcomes in persons aged ≥ 65 years from 7 Spanish autonomous communities requiring hospitalization in the context of a public health system providing universal free care to the whole population. Outcomes studied were ICU admission, length of hospital stay (LOS), the PSI category and mortality in the first 30 d after admission. We determined associations between 30-day mortality and the clinical presentation, the influenza and pneumococcal vaccination status, comorbidities, the degree of disability and the PSI category.

Results

A total of 1928 CAP cases were recorded during the study period, of which 60.7% were male, and 46.67% were aged 75–84 y. Thirty-day mortality was 7.6% (146 cases), and was highest in patients aged >84 y (44.5%). Pneumococcal vaccination was significantly protective (OR 0.68, (95% CI, 0.48–0.96; p = 0.03) and influenza vaccination in any of the 3 preceding seasons slightly protective (OR 0.72, 95% CI, 0.51–1.02; p = 0.06) against CAP 30 d mortality. (Table 1).

Factors associated with 30 day mortality were a moderate-high degree of dependence (aOR 3.67, 95% CI, 2.34–5.75; p < 0.001); age ≥ 85 y (aOR 3.01, 95% CI, 1.71–5.30; p < 0.001), liver impairment (aOR 2.41, 95% CI, 1.10–5.31; p = 0.03); solid organ neoplasm (aOR 2.24, 95% CI, 1.46–3.45; p < 0.001), impaired cognitive function (aOR 1.93, 95% CI, 1.22–3.05; p = 0.005) and ICU admission (aOR 2.56, 95% CI, 1.27–5.16; p = 0.009);); length of stay (LOS) greater than 15 d (aOR 1.56, 95% CI, 1.02 – 2.40; p = 0.04) and cardiorespiratory resuscitation (CRR) (aOR 7.75, 95% CI, 1.20 – 49.98; p = 0.03). No association was observed for other comorbidities such as COPD or heart condition in the adjusted model (Table 2).

Discussion

The risk of death due to CAP is linked with increasing age. In a Finnish study, the incidence of CAP rose dramatically with age, with a 6-fold increase in incidence between the 30- 44 and ≥ 75 y age groups. In Portugal, case fatality rates were 4.5% for patients aged 18–50 y and 19.4% in those aged ≥ 65 y.[14] Overall observed 30-day mortality in patients aged ≥ 65 y was 7.6%, higher than in a previous Spanish study[17] but lower than in other studies in which 30-day mortality due to CAP in the elderly ranged from 12.5% to 15.5%.[10, 18] Our results show that 30-day mortality in patients aged >84 y was 2.6 times greater, similar to the 3-fold higher rate found in patients aged ≥ 85 y compared with those aged 65–74 y found by Ochoa-Gondar et al. [10] This supports a specific role of age as a predictor of 30-day mortality in patients with CAP, as reflected by the PSI.

A degree of dependence was significantly associated with 30-day mortality. The aging trend of the population of industrialized countries and increased life expectancy means there will be a greater proportion of dependent elderly persons. In agreement with previous studies, the functional status was a predictor of mortality. Patients who died had greater immobility and multivariate analysis confirmed this diagnosis as an independent factor associated with mortality. Similar results were reported by another study of 353 elderly patients which found that functional impairment at admission correlated strongly with death.[19,20] Factors that contribute to mortality in the elderly correlate to functional and cognitive impairment, functional decline, disease severity, comorbidity scores, older age and male gender.[21] In our study related comorbidities were not associated with 30-day mortality. This might be explained by the quality of health care and follow up in the context of healthy aging initiatives. In epidemiologic studies of the elderly, modified diagnosis-based scores using empirically-derived weighting such as the Charlston index, might lead to improved adjustments for comorbidity and enhance the validity of findings.[22] However, greater access to controls and follow up of underlying conditions, vaccination, nutrition and healthy lifestyle in the elderly are still the most plausible reasons for this outcome.

Vaccination remains the primary preventive strategy in the elderly against *Streptococcus pneumoniae* and influenza infections. The effectiveness of this strategy in preventing pneumonia has been in doubt despite the increase in vaccination coverage in the elderly. Pneumococcal vaccination was significantly protective and influenza vaccination in the 3 preceding seasons slightly protective against CAP. Although in the adjusted model both variables did not result statistically significant, probably because of the small number of deaths registered within 30 d of CAP hospital admission. Other reports have found that pneumococcal and influenza vaccination were associated with reductions in mortality and hospitalizations in patients with CAP.[23-25] Offering both pneumococcal and influenza vaccination to the elderly can improve 30-day mortality in patients with CAP. The severity and extension of pneumonia, an inadequate response to infection, and low functional status were the main factors associated with mortality in elderly patients with CAP. Increased understanding of long-term CAP mortality (> 3 months) is needed to better determine risk factors and their importance in clinical management and preventive strategies to improve CAP mortality in the elderly.

Methods

Study design and setting

A multicenter study was conducted in patients aged ≥ 65 y recruited in the context of a case-control study to assess the

Table 1. 30-day mortality in hospitalized CAP cases during the 2013–2014 and 2014–2015 influenza seasons according to independent factors studied.

	30-day mortality (n = 146) Cases (%)	30-day survival (n = 1782) Cases (%)	OR (95%CI)	p value
Age group				
65–74 years	27 (18.5%)	571 (32.0%)	1	
75–84 years	54 (37.0%)	845 (47.4%)	1.35 (0.84 – 2.17)	0.21
≥ 85 years	65 (44.5%)	366 (20.5%)	3.76 (2.35 – 5.99)	<0.001
Barthel index				
Moderate to high degree of dependency	108 (74.0%)	668 (37.5%)	4.74 (3.23 – 6.94)	<0.001
Little or no dependency	38 (26.0%)	1114 (62.5%)	1	
Smoking status				
Non smoker	71 (48.6%)	779 (43.7%)	1	
Smoker	15 (10.3%)	153 (8.6%)	1.08 (0.60 – 1.93)	0.81
Ex-smoker	60 (41.1%)	850 (47.7%)	0.77 (0.54 – 1.11)	0.16
Alcohol consumption				
No	125 (85.6%)	1428 (80.1%)	1	
Yes	21 (14.4%)	354 (19.9%)	0.68 (0.42 – 1.09)	0.11
Solid neoplasm				
Yes	40 (27.6%)	298 (16.7%)	1.89 (1.29 – 2.78)	0.001
No	105 (72.4%)	1482 (83.3%)	1	
Immunosuppressive treatment				
Yes	10 (6.8%)	66 (3.7%)	1.91 (0.96 – 3.79)	0.07
No	136 (93.2%)	1712 (96.3%)	1	
Kidney impairment				
Yes	39 (26.7%)	310 (17.4%)	1.73 (1.17 – 2.55)	0.005
No	107 (73.3%)	1471 (82.6%)	1	
Chronic obstructive pulmonary disease (COPD)				
Yes	34 (23.6%)	553 (31.2%)	0.68 (0.46 – 1.01)	0.06
No	110 (76.4%)	1218 (68.8%)	1	
Cardiovascular disease				
Yes	55 (38.2%)	479 (26.9%)	1.68 (1.18 – 2.39)	0.004
No	89 (61.8%)	1303 (73.1%)	1	
Disabling neurological disease				
Yes	23 (15.9%)	135 (7.6%)	2.30 (1.42 – 3.71)	0.001
No	122 (84.1%)	1646 (92.4%)	1	
Liver impairment				
Yes	9 (6.2%)	66 (3.7%)	1.72 (0.84 – 3.52)	0.14
No	136 (93.8%)	1714 (96.3%)	1	
Anemia or altered hemoglobin				
Yes	29 (20.0%)	276 (15.5%)	1.36 (0.89 – 2.09)	0.16
No	116 (80.0%)	1504 (84.5%)	1	
Cognitive impairment				
Yes	41 (28.1%)	190 (10.7%)	3.27 (2.21 – 4.83)	<0.001
No	105 (71.9%)	1590 (89.3%)	1	
Intensive care unit (ICU) admission				
Yes	14 (9.7%)	68 (3.8%)	2.68 (1.47 – 4.89)	0.001
No	131 (90.3%)	1703 (96.2%)	1	
Mechanical ventilation				
Yes	36 (24.7%)	297 (16.7%)	1.63 (1.10 – 2.42)	0.02
No	110 (75.3%)	1480 (83.3%)	1	
Vasopressor treatment				
Yes	23 (16.1%)	117 (6.7%)	2.68 (1.65 – 4.35)	<0.001
No	120 (83.9%)	1636 (93.3%)	1	
Cardiorespiratory resuscitation (CRR)				
Yes	2 (1.4%)	5 (0.3%)	4.98 (0.96 – 25.9)	0.06
No	141 (98.6%)	1754 (99.7%)	1	
Readmission at 30- days				
Yes	26 (17.9%)	239 (13.4%)	1.41 (0.90 – 2.20)	0.13
No	119 (82.1%)	1542 (86.6%)	1	
Length of hospital stay (LOS)				
1–14 days	107 (73.3%)	1464 (82.2%)	1	
≥ 15 days	39 (26.7%)	318 (17.8%)	1.68 (1.14 – 2.47)	0.01
Pneumonia severity index (PSI)				
I-III	33 (22.6%)	717 (40.5%)	1	
IV-V	113 (77.4%)	1055 (59.5%)	2.33 (1.56 – 3.47)	<0.001
Influenza vaccination in any of the 3 previous seasons				
Yes	91 (62.3%)	1243 (69.8%)	0.72 (0.51 – 1.02)	0.06
No	55 (37.7%)	539 (30.2%)	1	
Pneumococcal vaccination				
Yes	62 (42.5%)	935 (52.5%)	0.68 (0.48 – 0.96)	0.03
No	84 (57.5%)	847 (47.5%)	1	

effectiveness of 23-valent polysaccharide pneumococcal vaccine and seasonal influenza vaccine in the prevention of hospitalizations due to pneumonia and influenza. Patients hospitalized due to CAP through the emergency departments of 20 public hospitals in 7 Spanish regions (Andalusia, Castile and Leon, Catalonia, Madrid, Navarra, the Basque Country, Community

Table 2. Factors associated with 30-day mortality in CAP cases. 2013–2014 and 2014–2015 influenza seasons.

	aOR (95% CI)	p value
Gender- Male	1.54 (0.88 – 2.68)	0.13
Age group		
65–74 years	1	
75–84 years	1.20 (0.70 – 2.06)	0.50
>84 years	3.01 (1.71 – 5.30)	<0.001
Barthel score		
Any degree of disability	3.67 (2.34 – 5.75)	<0.001
Solid neoplasm	2.24 (1.46 – 3.45)	<0.001
Pneumonia in 2 previous years	1.36 (0.87–2.14)	0.18
COPD	0.68 (0.42 – 1.09)	0.11
Heart condition	1.31 (0.89 – 1.93)	0.17
Liver impairment	2.41 (1.10 – 5.31)	0.03
Cognitive impairment	1.93 (1.22 – 3.05)	0.005
ICU admission	2.56 (1.27 – 5.16)	0.009
CRR	7.75 (1.20 – 49.98)	0.03
Length of hospital stay (> 15d)	1.56 (1.02 – 2.40)	0.04

of Valencia) during the 2013–2014 and 2014–2015 influenza seasons.

Exclusion criteria were institutionalized patients, patients with nosocomial pneumonia (onset ≥ 2 d after hospital admission) and patients whose initial diagnosis of CAP was not confirmed during the hospital stay.

A case of pneumonia was defined as a patient with a chest X-ray showing pulmonary infiltrate compatible with pneumonia and ≥ 1 of the following symptoms or signs of acute infection of the lower respiratory tract: cough, pleural chest pain, dyspnea, fever >38°C, hypothermia < 35°C and abnormal auscultator respiratory sounds unexplained by other causes. The study was approved by the ethics committee of each participating hospital.

Data collection and follow-up

At the initial visit and before initiation of empirical antibiotic therapy, patients underwent a complete clinical history and physical examination. A follow-up appointment was made one month after hospital discharge.

Patient information was obtained through 2 sources:

a) Review of written hospital medical records and b) Interview of the patient or close relatives (spouse or offspring) to collect data on occupation, educational level, family situation, municipality or district of residence, and smoking status, using a questionnaire completed by qualified staff. In all participating hospitals, data were collected by trained staff according to an identical protocol prepared by the working group.

Data measurements

The primary outcomes studied were length of stay, ICU admission and overall mortality in the first 30 d after hospital admission. LOS was measured in days and calculated as the time from the date of hospital admission to the date of discharge.

Other variables analyzed

For each patient, information was obtained on age, sex, Barthel dependency index,[26] smoking status (current smoker, ex-smoker, non smoker), alcohol consumption (> 40 g/day in men, > 20 g/day in women) and the presence or absence of underlying diseases: solid or hematologic neoplasm with activity in the past year, radiotherapy in the previous 3 months, immunosuppressive therapy or treatment with corticosteroids ≥ 20 mg/day in the preceding month, influenza immunization in any of the 3 previous seasons, pneumococcal immunization status, autoimmune disease, chronic renal failure on dialysis, disabling neurological disease (neurological disease impeding daily activities), diabetes mellitus, heart failure, chronic obstructive pulmonary disease (COPD) and liver disease. Severity of illness at presentation was quantified in 5 risk classes using the PSI at admission.[13]

Statistical Methods

A bivariate analysis was made to compare 30-day mortality and 30-day survival according to sociodemographic variables and risk medical conditions.

Multivariate logistic regression with backward selection procedure of variables, with cut-off point of $p < 0.2$ was used to calculate the crude and adjusted odds ratios (OR) and their corresponding 95% confidence intervals (CI). All statistical tests were 2-tailed and statistical significance was established as p value <0.05. The statistical analysis was made using the SPSS v.23 statistical program.

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Abbreviations

CAP	Community acquired pneumonia
COPD	Chronic obstructive pulmonary disease
LOS	Length of stay
ICU	Intensive care unit
OR	Odds ratio
aOR	adjusted Odds ratio
CI	Confidence interval
CRR	Cardio-respiratory resuscitation
EU	European Union
PSI	Pneumonia Severity Index

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No potential conflicts of interest were disclosed.

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