original article

Factors associated with mortality in younger and older (≥75 years) hospitalized patients with community-acquired pneumonia

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BACKGROUND: Pneumonia is among the most serious infections in the elderly. The evaluation of prognosis and predicting the outcome is essential in managing the treatment of patients with pneumonia.

OBJECTIVES: Evaluate factors that might affect the mortality of elderly patients hospitalized for community-acquired pneumonia (CAP) in two age groups.

DESIGN: Medical record review.

SETTING: Tertiary care hospital.

PATIENTS AND METHODS: The study included CAP patients who were hospitalized during the period from January 2017 and December 2019. The CURB-65 scale was chosen to assess the severity of pneumonia on admission. Multivariate analyses were conducted separately for patients younger than 75 years and 75 years or older.

MAIN OUTCOME MEASURES: 30-day mortality, factors associated with mortality.

SAMPLE SIZE AND CHARACTERISTICS: 1603 patients with a median age of 74, including 918 women (57%).

RESULTS: The 30-day mortality rate was 6.5%. Patients with carbapenem-resistant gram-negative bacteria had lower survival rates ($P<.0001$). In the multivariate analysis, age, lung cancer, CURB-65, carbapenem resistance, and duration of hospital stay were associated with mortality in patients aged 75 years or older. Lung cancer, malignant disease, carbapenem resistance, duration of hospital stay and procalcitonin level were associated with mortality under the age of 75. Of 640 sputum cultures tested, *P aeruginosa* (42%) was the most common pathogen.

CONCLUSION: The risk factors that affected mortality differed among patients aged 75 years or older versus younger patients. Our findings are important in determining factors associated with mortality in managing the treatment and follow up of hospitalized CAP patients younger or 75 years of age or older.

LIMITATION: Single-center, retrospective.

CONFLICT OF INTEREST: None

Pneumonia is among the most serious infections in the elderly. Pneumonia with influenza is the fifth leading cause of death among people aged 65 years and older.[1] Despite widespread availability of antibiotic therapies, community-acquired pneumonia (CAP) continues to be a leading cause of death worldwide. The 30-day mortality rate of pneumonia in elderly patients ranges from less than 1% to 25%, depending on the severity of pneumonia and comorbid conditions.[2-4] Morbidity and mortality increases with age due to decreased efficiency of the adaptive and innate immune systems and increased susceptibility to infectious diseases in the elderly.[5] Additionally such immunological changes limit the response to vaccines in the elderly.[6]

The frequency of comorbid illness rises with age. Chronic obstructive pulmonary disease (COPD) and malignant diseases are often accompanied by complications and are related to poor prognosis. Physicians commonly use several severity scoring systems to make decisions on the site of care and to assess the prognosis of CAP. CURB-65 is one of the preferred scoring systems for predicting short-term mortality in CAP.[7] Elevations of infection biomarkers such as serum procalcitonin and C-reactive protein (CRP) are associated with pneumonia. The microbiological etiology of pneumonia is related to the severity of the disease,[8] and antibiotic-resistant pathogens are associated with increased mortality rates in hospitalized patients with pneumonia.[9] Accurate evaluation of prognosis and prediction of outcome is essential in managing treatment. In this study we separately investigated the factors that might affect mortality in two groups of elderly patients hospitalized for CAP – the group younger than 75 years, and the group 75 years or older.

PATIENTS AND METHODS

In this retrospective study, we analysed CAP patients who were hospitalized between January 2017 and December 2019 in the chest clinic ward at Sultan Abdulhamid Han Research and Training Hospital, a 500-bed tertiary care teaching hospital in Istanbul, Turkey. CAP diagnoses were based on the Infectious Diseases Society of America/American Thoracic Society (IDSA/ATS) guidelines.[10] The diagnoses were categorized according to International Statistical Classification of Diseases and Related Health Problems-10 (ICD-10). Patients younger than the age of 18 years, patients infected with HIV or patients with hospital-acquired pneumonia (HAP) were excluded. The ethics committee of The Health Sciences University of Turkey approved this study (Ref. no: B.10.1.THK.4.34.H.GP.0.01/318, 8 October 2020). The data was collected from the medical records by means of a structured electronic format excluding the patient identities. The CURB-65 scale was chosen to assess the severity of pneumonia on admission. The 'CURB 65' score is a simple well-validated tool for the assessment of severity in CAP. One point is awarded for each of the following: Confusion, Urea >7 mmol/L, Respiratory rate ≥30 breaths per minute, low Blood pressure (systolic <90 mmHg or diastolic ≤60 mmHg), and age ≥65 years. The risk of death at 30 days increases as the score increases. Patients with pneumonia and a score of 0 have a low risk of death (<5%), patients with scores of 1 or 2 score have a risk of death up to 10% and patients with a score of 3 or more have a higher risk of death.[11] The 30-day mortality and factors associated with survival were the primary outcome measures (age, the sex, the vital signs, the test results and the comorbidities). The comorbidities included chronic heart disease, COPD, diabetes mellitus, malignant disease and chronic kidney disease. We also assessed the effect of the seasons on mortality and the presence of clinically significant microorganisms based on CDC criteria.[12] The identification and the minimum inhibitory concentrations of the microorganisms were measured by an automated system (VITEK 2, Biomerieux, Marcy l'Etoile, France). Microorganisms were identified and antibiotic resistance determined by the Clinical and Laboratory Standards Institute (CLSI) guideline.[13]

IBM SPSS for Windows version 21.0 was used for the analysis of data. The categorical variables are presented with frequencies and percentages. Mean, standard deviation, or median and range are given as descriptive values for continuous data. The Mann Whitney U-Test was used for statistical comparisons of nonuniform data. The Kruskal Wallis H-Test for comparisons of more than two groups. Categorical variables were analysed with the chi square test. Logistic regression analysis was used to examine factors that might affect survival. Factors with $P<.05$ in univariate analyses were included in the multivariate analysis. A P value less than .05 was considered statistically significant.

RESULTS

Of 1603 patients with CAP, the median age and range was 74 (18-104) years and 914 (57.1%) were women. There were 884 (52.7) patients younger than 74 years old and 759 (47.3%) 75 years of age or older. The 30-day mortality rate was 6.5% (105/1603). ICU admission was required in 160 patients. The most common comorbidity was COPD (50%), followed by diabetes (26%), chronic heart disease (21%), chronic kidney disease (9%), lung cancer (7%) and malignant disease

(8%). Older age, lung cancer and malignant disease were significantly higher among the non-surviving patients (**Table 1**). The CURB-65 score was higher in the non-surviving patients. CRP and procalcitonin levels were significantly higher in non-surviving patients. Non-surviving patients had a longer length of hospital stay compared to surviving patients. There was no significant difference based on the season among surviving and non-surviving patients.

Of 640 sputum cultures tested, 194 (30%) were positive. The most common pathogen was *P aeruginosa* (42%), followed by *A baumannii* (22%), *K pneumoniae* (13%), *E coli* (8%), *S aureus* (5%), *S pneumonia* (5%), *Stenotrophomonas spp.* (4%) and *Enterobacter spp.* (3%) (**Figure 1**). Upper respiratory tract flora was detected in 24% of the culture positive sputum samples. There were no significant differences in the types of pathogens between surviving and non-surviving patients. Patients with carbapenem-resistant gram-negative bacteria had lower survival rates (*P*<.0001). All factors associated with mortality in the univariate analyses were statistically significant in the multivariate analyses (**Tables 2 and 3**).

DISCUSSION

In this study, we analysed the data of 1603 hospitalised patients with CAP. Patients of older age, lung cancer and malignant disease, high levels of CRP, high levels of procalcitonin, high CURB-65 scores and carbapenem resistance had lower survival rates. We investigated the predictors of mortality among patients younger than 74 years and separately among patients 75 years or older.

In both groups lung cancer, pneumonia with carbapenem-resistant gram-negative bacteria and longer hospital durations were associated with greater mortality. Patients aged 75 years or older had additional risk factors for mortality–age and high CURB-65 scores, while patients aged 74 years or younger had additional

Table 1. Clinical and demographic characteristics of patients with community-acquired pneumonia.

	Total (n=1603)	Surviving patients (n=1498)	Non-surviving patients (n=105)	*P* value
Age	74 (18-104)	73 (18-102)	81 (42-104)	**<.0001**
Gender (male)	914 (57.0)	855 (57.1)	59 (56.2)	.919
Chronic obstructive pulmonary disease	794 (49.5)	746 (49.8)	48 (45.7)	.422
Diabetes mellitus	412 (25.7)	387 (25.8)	25 (23.8)	.729
Chronic heart disease	335 (20.9)	305 (20.4)	30 (28.6)	.061
Chronic kidney disease	143 (8.9)	129 (8.6)	14 (13.3)	.110
Lung cancer	116 (7.2)	99 (6.6)	17 (16.2)	**.001**
Malignant disease	123 (7.7)	107 (7.1)	16 (15.2)	**.007**
CURB-65 score (mean, SD)	1.76 (1.00)	1.72 (0.977)	2.3 (1.153)	**<.0001**
Season				
Autumn	317 (19.8)	299 (20.0)	18 (17.1)	.497
Winter	582 (36.3)	538 (35.9)	44 (41.9)	
Spring	428 (26.7)	399 (26.6)	29 (27.6)	
Summer	276 (17.2)	262 (17.5)	14 (13.3)	
Positive sputum culture	195 (12.2)	177 (11.8)	18 (17.5)	.214
Carbapenem resistance	63 (4.0)	46 (3.1)	17 (16.8)	**<.0001**
Duration of hospital stay (days)	6 (0-183)	6 (0-117)	9 (0-183)	**<.0001**
C-reactive protein	92.45 (0.02-475.0)	90.0 (0.02-475.0)	120.0 (2.0-335.0)	**.004**
Procalcitonin	0.16 (0.0-77.52)	0.13 (0.0-77.52)	0.36 (0.0-76.90)	**.002**

Data are number (%) or median (interquartile range) unless otherwise noted.

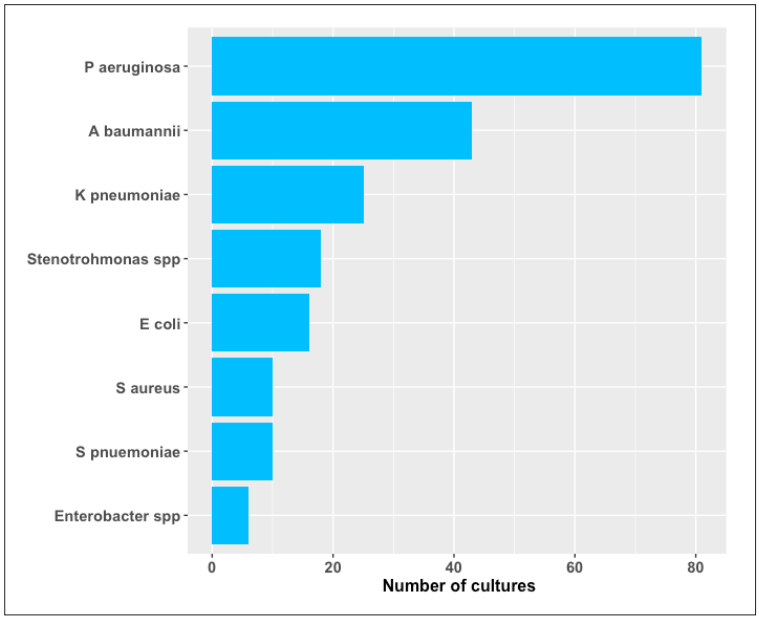

Figure 1. Distribution of the microorganisms causing pneumonia in 194 positive sputum samples.

risk factors for mortality—elevated levels of procalcitonin and malignant disease.

While we had a 6.6% 30-day mortality rate, other researchers reported the mortality rates of elderly patients with CAP ranging from 6.4% to 33%.[14-17] Other studies have shown a mortality rate of 6% in those under 65 years of age, and a mortality rate of 47% in those aged over 85 years and a gradual increase in between.[18] We found that the increased age in elderly patients 75 years of age or beyond to be a major prediction of mortality, while age factor was not significant for patients aged under 74 years of age. The predictors of mortality among the elderly other than increased age are underlying comorbidities or the severity of the illness in patients with CAP.[19] Patients having lung cancer or malignant disease had a higher rate of mortality in our study. Besides, we found that lung cancer was a significant risk factor for mortality regardless of age. All pneumonia patients with underlying lung cancer should be carefully managed as it is an independent risk factor for mortality.

Table 2. Risk factors for mortality in hospitalized patients with pneumonia <74 years of age.

Characteristics	Univariate model OR (95% CI)					Multivariate model OR (95% CI)				
	Coefficient β	SE	Wald	OR (95% CI)	*P* value	Coefficient β	SE	Wald	OR (95% CI)	*P* value
Age	0.01	0.01	0.24	1.01 (0.98-1.03)	.624					
Lung cancer	1.49	0.38	15.0	4.42 (2.09-9.37)	**<.0001**	1.37	0.27	13.2	2.73 (1.13-6.61)	**.026**
Malignant disease	1.24	0.41	9.27	3.44 (1.55-7.61)	**.002**	1.15	0.37	7.56	2.47 (0.98-6.24)	**.046**
CURB-65 score	0.19	0.17	1.31	1.22 (0.87-1.69)	.252	-	-	-	-	-
Carbapenem resistance	1.43	0.62	5.37	4.20 (1.25-14.11)	**.020**	1.32	0.54	4.57	3.41 (0.89-13.04)	**.044**
Duration of hospital stay	0.05	0.01	11.4	1.05 (1.02-1.08)	**<.001**	0.04	0.02	2.13	1.05 (1.02-1.08)	**<.0001**
C-reactive protein	0.01	0.01	3.59	1.004 (1.000-1.007)	.058	-	-	-	-	-
Procalcitonin	0.07	0.03	7.00	1.08 (1.02-1.13)	**.006**	0.06	0.03	5.33	1.06 (1.01-1.12)	**.028**

Model summary measures: Nagelkerke R2: .144, Hosmer-Lemeshow test: >0.05

The severity scoring system CURB-65 for pneumonia has been in wide use. However, CURB-65 may not perform well in elderly patients. Their atypical clinical presentations may provide unreliable cut-off values for the scoring system.[20] Therefore, the validity of such scores in the elderly population is questionable. Higher CURB-65 scores were found in non-surviving patients in our study. CURB-65 was therefore of considerable help to us in predicting mortality in patients 75 years or older. Prolonged duration of hospitalisation is also known to be a predictor for mortality.[21] Factors such as disease severity, admission to an intensive care unit and multi-lobar pneumonia were associated with poor prognosis resulting in prolonged hospital stays.[21] In our study the duration of the hospital stay was a significant predictor of mortality regardless of age. Faster and shorter-term treatments should be on the agenda for pneumonia.

CRP values are a direct indicator of the severity of the inflammation. A high CRP is considered an independent risk factor for the 30-day mortality rate in patients with CAP.[22] CRP and procalcitonin are useful in the diagnosis and prognosis of pneumonia, but data on biomarkers of infections in elderly patients with pneumonia are limited. High levels of procalcitonin indicate a poor prognosis in elderly patients.[23] In our study, patients with increased CRP and procalcitonin levels had lower survival rates. The procalcitonin levels were associated with mortality in patients younger than 74 years of age, while this was not a risk factor for patients older than 75 years of age.

Out of the 1603 patients only 640 sputum samples were taken for culture; 194 were positive. The relationship between the microorganisms and mortality could not be calculated due to the small sample size. Microorganisms that cause CAP may differ by region. In a study including European countries, researchers found that *S pneumoniae, M pneumoniae, C pneumoniae, L pneumophila* and *H influenzae* were the most common bacterial causes of CAP. In another study involving Asian countries, Leon et al detected gram-negative bacteria, *S aureus* and *M tuberculosis* in higher proportions among patients with CAP.[24] In a recently published article, the top five pathogens of pneumonia

Table 3. Risk factors for mortality in hospitalized patients with pneumonia ≥75 years of age.

Characteristics	Univariate model OR (95% CI)					Multivariate model OR (95% CI)				
	Coefficient β	SE	Wald	OR (95% CI)	*P* value	Coefficient β	SE	Wald	OR (95% CI)	*P* value
Age	0.09	0.02	15.4	1.10 (1.05-1.14)	**<.0001**	0.08	0.03	8.83	1.08 (1.02-1.13)	**.004**
Lung cancer	1.00	0.48	4.39	2.71 (1.07-6.91)	**.036**	1.24	0.54	5.31	3.27 (1.18-9.06)	**.023**
Malignant disease	0.79	0.43	3.30	2.21 (0.94-5.20)	**.069**	-	-	-	-	-
CURB-65 score	1.10	0.45	3.44	2.10 (1.58-2.80)	<.0001	0.81	0.35	2.49	1.65 (1.19-2.29)	**.003**
Carbapenem resistance	1.91	0.43	20.2	6.79 (2.95-15.66)	**<.0001**	1.56	0.49	10.2	3.89 (1.55-9.75)	**.004**
Duration of hospital stay	0.04	0.01	14.2	1.05 (1.02-1.07)	**<.0001**	0.02	0.01	3.40	1.02 (1.00-1.05)	**.040**
C-reactive protein	0.00	0.00	3.31	1.003 (1.000-1.006)	.069	-	-	-	-	-
Procalcitonin	0.03	0.05	0.42	1.03 (0.93-1.15)	.444	-	-	-	-	**-**

Model summary measures: Nagelkerke R2=.044, Hosmer Lemeshow test <0.05

were identified as *Acinetobacter* (32%), *Pseudomonas* (18%), *Klebsiella* (17%), *E coli* (5%) and *Staphylococcus* (4%).[25] Increased rates of *Pseudomonas* infections of hospital-associated pneumonia were detected in a multicenter study in Turkey between 2015 and 2018.[26] Our findings were consistent with that study. The predominant pathogen was *P aeruginosa* (42%), followed by *A baumannii* (22%), *K pneumoniae* (13%), *E coli* (8%), *S aureus* (5%). Infections with gram-negative bacteria are often related to comorbid illnesses. Also chronically ill elderly patients from the community who fail to improve on standard therapy could be contaminated with these bacteria. *S pneumonia*, which is the most common pathogen in CAP, was isolated in only 5% of our patients. In a recent multicenter study researchers in Turkey determined similar rates for gram-negative bacteria and *S pneumoniae* in the sputum cultures of the patients with CAP.[27] The wide use of pneumococcal vaccination among the elderly, and empirical antibiotic treatments prior to admission of the patients may be two of the reasons behind the low rates of *S pneumonia* detected in our study.

Carbapenem-resistant bacterial pneumonia was a major factor associated with mortality among our hospitalized patients. Antibiotic-resistance among gram-negative bacterial infections is associated with a particularly high mortality rate.[27] The increasing trend of carbapenem resistance in gram-negative bacteria is a major issue in pneumonia patients.[26] Treatment options for these infections are extremely limited. Seasonal variations were not a risk factor for mortality from pneumonia in our study.

Limitations of our study were that antibiotic use in the last 48 hours prior to admission and pneumococcal vaccination status was not considered. Moreover, the role of atypical pathogens and viral agents in CAP was not evaluated. This was a single-center medical record review study. Our findings are important in indicating factors associated with mortality more specifically by age group. We observed a difference in risk factors in those older and younger than 75 years of age. Namely, procalcitonin levels and malignant disease were separately effective until the age of 75 and lost their significance beyond that age. Procalcitonin values may not be reliable in patients over the age of 75; hence this factor should be carefully evaluated in the decision-making process for the treatment of the CAP patients. Older age and high CURB-65 scores were statistically significant risk factors beyond the age of 75 years. We advise that high CURB-65 scores in the elderly patients should be interpreted carefully for the management of the disease.

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