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Original Article

Predictors of Long-term Outcomes in the Older Adults with Community-Acquired Pneumonia

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Abstract

Introduction: We aimed to determine the indicators for poor long-term outcome in older adults with community-acquired pneumonia (CAP).
Methodology: Patients with CAP requiring hospitalization were included in this retrospective study. The long-term mortality was defined as all-cause 1-year mortality following hospital admission.
Results: A total of 145 patients with CAP were recorded. The median age was 70 (18-103), of whom 94 (65%) were ≥ 65 years old and 86 (59.5%) were male. Long-term mortality rates following CAP requiring hospitalization were substantially high in both the younger (n = 16, 31.4%) and older adults (n=43, 45.7%). In univariate analysis, the Pneumonia Severity Index (PSI) (p = 0.007), mechanical ventilation (p > 0.001), mental status changes (p = 0.018) as well as the modified Charlson Comorbidity Index (p=0.001), presence of malignancy (p < 0.001) and hospital readmission (p < 0.001) were associated with long-term mortality in the older group. Our results revealed that the need for mechanical ventilation (OR = 47.61 CI = 5.38-500.0, p = 0.001) and hospital readmission (OR = 15.87 CI = 5.26-47.61, p < 0.001) were major independent predictors of 1-year mortality.
Conclusions: Clinicians should consider the lethal possibilities of CAP even after hospital discharge. The need for mechanical ventilation and hospital readmission may predict long-term mortality. Therefore, the patients who have these predictors should be closely monitored.

Key words: community-acquired pneumonia; long-term mortality; intensive care; mechanical ventilation; hospital readmission.

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Introduction

Community-acquired pneumonia (CAP) is a common cause of hospitalization, readmission and mortality particularly among older adults. Aging makes people vulnerable to infections and may cause a longer duration of hospital stay, increased health expenditures and economic burden [1]. Moreover, etiology, prognostic factors and outcomes of CAP in older adults have been changing by vaccinations against bacterial and viral agents [2].

Short-time outcomes are insufficient prognostic measures for studies in older adults with CAP because harmful effects of CAP may not manifest within short-time frame. Despite some efforts to identify predictors for long-term mortality, there are still clinical challenges to predict the long-term effect of CAP in older adults [3-4]. Observed high mortality rates during the long time frame are also crucial for patient and family counseling, as well as clinical management. Advanced knowledge about risk factors for long-term outcomes of patients with CAP would assist in the long-term clinical management. Therefore, the number and proportion of older adults with CAP are increasing all around the world and contemporary studies to identify predictors for poor outcomes are needed.

Limited data exist on post discharge long-term outcomes and its predictors [4-6], although short-term prognostic predictors for CAP were well studied in Turkey [7-10]. In this study, we aimed to determine the indicators for poor short-term and long-term outcomes in older adults with CAP requiring hospitalization. Also, we compared the risk factors, clinical findings, the severity of the course and the treatment responses in patients over and under age 65 with CAP.

Methodology

This retrospective and single-center study includes patients aged ≥18 years who were diagnosed with CAP by the Department of Infectious Diseases and Clinical Microbiology between January and December 2017.

Patients with CAP requiring hospitalization were included in the study. Outpatients, patients with neutropenia, ventilatory-associated or hospital-acquired pneumonia (HAP) were excluded. The diagnosis of CAP was made on the basis of current guidelines [11].

The demographic data, underlying diseases, immunosuppressive conditions, symptoms and physical examination findings, laboratory test results and radiological findings, and outcomes were recorded via a follow-up data sheet. Hospital readmisson for any reason within 3 months of hospital discharge were collected. 1-year mortality was recorded using the National Death Report Database. The cases were divided into two groups according to their ages (< 65 and ≥ 65 years) and comparative analyses were applied.

The modified Charlson comorbidity scores, the CURB-65 (confusion, blood urea nitrogen, respiratory rate, blood pressure, and age ≥ 65 years) and the Pneumonia Severity Index (PSI) were calculated for all the patients [12-14].

Table 1. The demographic characteristics of the patients with community-acquired pneumonia in terms of age groups.

	Total		**Age <65 years**		**Age ≥65 years**		**p**
	n	**%**	**n**	**%**	**n**	**%**	
Number of cases	145	100	51	35.2	94	64.8	
Age							**0.001**
Mean ± se	67.53 ± 16.57		49.82 ± 12.52		77.13 ± 8.69		
Median	70		53		75		
Gender							0.063
Male	86	59.3	25	29.1	61	70.9	
Female	59	40.7	26	44.1	33	55.9	
Underlying disease	135	93.1	44	86.3	91	96.8	**0.034**
COPD	43	29.7	8	15.7	35	37.2	**0.008**
Diabetes mellitus	42	29.0	11	21.6	31	33.0	0.181
Hypertension	73	50.3	17	33.3	56	59.6	**0.003**
Congestive heart failure	26	17.9	4	7.8	22	23.4	**0.023**
Cerebrovascular disease	12	8.3	2	3.9	10	10.6	0.215
Chronic renal failure	45	31	7	13.7	38	40.4	**0.001**
Malignancy	41	28.3	17	33.3	24	25.5	0.339
Asthma	9	6.2	1	2.0	8	8.5	0.160
Coronary artery disease	35	24.1	6	11.8	29	30.9	**0.014**
Dementia	14	9.7	0	0	14	14.9	**0.002**
Immunosuppression	33	22.8	21	41.2	12	12.8	**< 0.001**
Chemotherapy	15	10.3	8	15.7	7	7.4	0.154
Corticosteroids	13	9.0	8	15.7	5	5.3	0.064
Immunosuppressive disease	8	5.5	4	7.8	4	4.3	0.452
Radiotherapy	7	4.8	3	5.9	4	4.3	0.697
History of previous smoking, antibiotic use, and hospitalization							
Smoking	73	72	22	43.1	51	54.3	0.201
Antibiotic use within the last 3 months	69	47.6	24	47.1	45	47.9	0.925
Hospital stay within the last 1 year	65	44.8	26	51.0	39	41.5	0.272
ICU stay within the last 1 year	14	9.7	4	7.8	10	10.6	0.771
Outcomes and implementations							
Septic shock	28	19.3	11	21.6	17	18.1	0.662
Acute renal failure	51	35.2	16	31.4	35	37.2	0.585
Mechanical ventilation	14	9.7	2	3.9	12	12.8	0.139
Acute hemodialysis	4	2.8	2	3.9	2	2.1	0.613
Intensive care admission	18	12.4	4	6.3	14	11.7	0.295
Poor prognosis	38	26.2	13	25.5	25	26.6	1.000
Hospital readmission	51	35.2	17	33.3	34	36.2	0.856
Length of hospital stay (day)							0.270
Mean ± se	12.46 ± 4.35		11.98 ± 3.90		12.71 ± 4.57		
Median	13		12		13		
≤ 7 day	19	13.1	5	9.8	14	14.9	0.450
> 7 day	126	86.9	46	90.2	80	85.1	
Death within 30-day	11	7.6	2	3.9	9	9.6	0.329
Death within 1-year	59	40.7	16	31.4	43	45.7	0.112

Fever was defined as the body temperature measurement ≥ 37.8 °C for patients 65 years and older, ≥ 38 °C for patients under 65 years of age by tympanic membrane measurement. Hypothermia was defined as the body temperature measurement of < 35.6 °C by the same method.

Altered mental status was defined as a Glasgow Coma Scale score less than 15 or as a new-onset disorientation to person, place, or time. Sepsis was defined as life-threatening insufficiency in the organs causing an uncontrolled immune response to infection in the host. Organ failure was assessed according to the "Sequential Organ Failure Assessment (SOFA)" score. Septic shock was defined once a patient had sepsis with hypotension requiring vasopressor support and a serum lactate level> 2 mmol/L despite adequate fluid resuscitation [15].

Our primary outcomes were short-term poor prognosis and all-cause long-term mortality. A "short-term poor prognosis" was defined as a composite endpoint of septic shock and/or the need for intensive care and/or death within 30 days. The long-term mortality was defined as all-cause 1-year mortality following hospital admission.

Frequencies (n) and percentages (%) were used to present the demographic characteristics of the data, while numerical variables were represented through mean ± standard deviation (sd) and median. The Kolmogorov–Smirnov test was used for normal distribution analysis. The Mann–Whitney U test and independent-sample t-test were used to compare the two groups in terms of the continuous variables. Categorical data were compared with Chi-Square test or Fischer's Exact test. To evaluate the factors in short-term poor prognosis and long-term mortality, multivariate logistic regression analysis was performed, incorporating all factors that obtained values of $p < 0.05$ in the univariate analyses. The analyses were performed using IBM SPSS-22 (Statistical Package for Social Sciences, Chicago, IL, USA). A p-value <0.05 was considered as statistically significant.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Declaration of Helsinki and with relevant laws and guidelines. Ethical Committee approval was deemed not to be required and written informed consent was waived, given the retrospective nature of this study.

Results

A total of 145 patients with CAP were recorded. The median age was 70 years (range, 18-103). Of whom, 94 (65%) were ≥ 65 years old and 86 (59.5%) were male. Of the 94 cases; 43 (46 %) were in the 65-74 age group, 33 (35 %) in the 75-84 age group, and 18 (19%) were ≥ 85 years. In 10 (6.9%) cases, no underlying diseases were recorded. Of these, only 3/10 (30%) were in the elderly (≥ 65 years) group ($p <$ 0.034). The rates of chronic obstructive pulmonary disease, hypertension, congestive heart failure, chronic renal failure, coronary artery disease, and dementia were significantly higher in the elderly group. Fourteen cases (9.7%) were admitted to the intensive care unit. The 30-day and 1-year mortality rates were 7.6% (n = 11) and 40.7% (n = 59) respectively. The demographic characteristics of the cases are given in Table 1. Risk classifications of the cases in terms of age groups are given in Table 2.

Microbiological evidence was obtained in 30 (20.7%) cases (22 in sputum culture, 4 in respiratory system by multiplex polymerase chain reaction (PCR), 2 in bronchoalveolar lavage culture, 2 in endotracheal aspirate). Blood culture was obtained in 84 (57.9%) cases, and sputum culture was evaluated in 62 (42.8%)

Table 2. Risk classifications of the patients with community-acquired pneumonia in terms of age groups.

	Total		Age < 65 years		Age ≥ 65 years		p
	n	%	n	%	n	%	
Modified Charlson							**< 0.001**
Class 1	38	26.2	28	54.9	10	10.6	
Class 2	34	23.4	13	25.5	21	22.3	
Class 3	36	24.8	6	11.8	30	31.9	
Class 4	37	25.5	4	7.8	33	35.1	
CURB-65							**< 0.001**
Class 1	64	44.1	37	72.5	27	28.7	
Class 2	51	35.2	11	21.6	40	42.6	
Class 3	30	20.7	3	5.9	27	28.7	
PSI							**< 0.001**
Class 1-2-3	38	26.2	27	52.9	11	11.7	
Class 4	63	43.4	18	35.3	45	47.9	
Class 5	44	30.3	6	11.8	38	40.4	

cases. Positive blood culture was not observed. Of the sputum cultures, the causative microorganisms were isolated in 22 (35.5%) cases.

Pseudomonas spp. (n = 8, 26.6%) was the most common agent, followed by *Streptococcus pneumoniae* (n = 7, 23.3%). Although *Pseudomonas spp.* was more frequent in the older group compared to the younger group (n = 6 vs. n = 2), there was no significant difference between the two groups (p = 0.713). Other typical bacterial agents were *Staphylococcus aureus* (n = 4, 13.3%), *Haemophilus influenzae* (n = 3, 10.0%) and *Acinetobacter spp.* (n = 3, 10.0%). Of the *Staphylococcus aureus* strains 25% had methicillin resistance. The rate of carbapenem resistance was 50.0% in *Pseudomonas spp.* and 33.3% in *Acinetobacter spp*. Regarding atypical agents; *Mycoplasma pneumoniae* was detected in 1 case, *Influenzavirus* in 1 case, *Metapneumovirus* in 1 case and *Human Coronavirus 229E* in 1 case (coupled with *Streptococcus pneumoniae*) were detected by multiplex PCR in respiratory system.

In univariate analysis, the CURB-65 ($p = 0.011$) and the PSI ($p = 0.014$) scores were associated with short-term poor prognosis in the younger group, whereas need for mechanical ventilation ($p < 0.001$), mental status changes ($p = 0.001$) and history of intensive care unit (ICU) stay within the last 1 year ($p = 0.020$) as well as the CURB-65 ($p < 0.001$) and the PSI scores ($p < 0.001$) were associated with short-term poor prognosis in the older group. The parameters with significant differences are given in Table 3. Also, multivariate regression analysis revealed that history of ICU stay within the last 1 year (OR = 10.20 CI = 2.25-45.25, $p = 0.003$) was associated with short-term poor prognosis in the older adults.

The CURB-65 ($p = 0.011$), the modified Charlson Comorbidity Index ($p = 0.020$), presence of malignancy ($p = 0.027$) and hospital readmission ($p<0.001$) were associated with long-term mortality in the younger group, whereas the PSI (p=0.007), mechanical ventilation ($p > 0.001$), mental status changes ($p = 0.018$) as well as the modified Charlson Comorbidity Index ($p = 0.001$), presence of malignancy ($p < 0.001$) and hospital readmission ($p < 0.001$) were associated with long-term mortality in the older group. The parameters with significant differences are given in Table 4. Also, multivariate regression revealed that mechanical ventilation (OR = 47.61 CI = 5.38-500.0, $p = 0.001$) and hospital readmission (OR =15.87 CI=5.26-47.61, $p < 0.001$) were associated with long-term mortality in the older adults.

Discussion

In this study, we determined the indicators for poor outcomes in short-term and long-term in the older adults with CAP requiring hospitalization. This study demonstrated that long term mortality rates following CAP requiring hospitalization were substantially high in both the younger (n=16, 31.4 %) and older adults (n = 43, 45.7 %). Our results revealed that a history of ICU stay within the last 1 year (OR=10.20 CI=2.25-45.25, $p = 0.003$) was the independent predictor of short-term poor prognosis, while the need for mechanical ventilation (OR=47.61 CI = 5.38-500.0, $p = 0.001$) and hospital readmission (OR = 15.87 CI = 5.26-47.61, $p < 0.001$) were major independent predictors of 1-year mortality. The 30-day mortality rate was higher (n = 9,

Table 3. Predictors for short-term poor prognosis in patients with community-acquired pneumonia.

	Age < 65 years					**Age ≥ 65 years**				
	Good prognosis		**Poor prognosis**			**Good prognosis**		**Poor prognosis**		
	n	**%**	**n**	**%**	**p**	**n**	**%**	**n**	**%**	**p**
Total	38	74.5	13	25.5		69	73.4	25	26.6	
Gender					1.000					0.468
Male	19	50.0	6	46.2		43	62.3	18	72.0	
Female	19	50.0	7	53.8		26	37.7	7	28.0	
CURB-65					**0.011**					**< 0.001**
Class 1	30	78.9	7	53.8		26	37.7	1	4.0	
Class 2	8	21.1	3	21.1		33	47.8	7	28.0	
Class 3	0	0	3	23.1		10	14.5	17	68.0	
PSI					**0.014**					**< 0.001**
Class 1-2-3	24	63.2	3	23.1		11	15.9	0	0	
Class 4	11	28.9	7	53.8		38	55.1	7	28.0	
Class 5	3	7.9	3	23.1		20	29.0	18	72.0	
Mechanical ventilation	0	0	2	15.4	0.061	0	0	12	48.0	**< 0.001**
Mental disorder	2	5.3	0	0	1.000	4	5.8	9	36.0	**0.001**
History of ICU stay within the last 1 year	2	5.3	2	15.4	0.266	4	5.8	6	24.0	**0.020**

9.6%) in the older group compared to the younger group (n = 2, 3.9%). However, there was no significant difference between the younger and older adults in terms of short-term and long-term mortality, outcomes such as development of septic shock, acute renal failure, length of hospital stay, hospital readmission, and implementations such as need for mechanical ventilation, acute dialysis, intensive care.

In the present study, the baseline characteristics of CAP and short term mortality rates were consistent with previous studies on CAP in Turkey [5-7]. However, in a multicenter retrospective study, Erdem *et al.* reported that 30-day mortality rate was %31.2 (n=129/413) in patients with severe CAP [10]. In some studies, 1-year mortality rates have been previously reported between 17% and 59.6% [16-19]. In a recent study [20], 1-year mortality rate was quite low (14%) compared to the previous studies. In the study of Tokgoz *et al.*, they showed that 5-year mortality was 74.8%, while 1-year mortality was 29.9% [4]. One study of 259 adult CAP patients showed a low 1-year mortality rate of 8.9% but only survival patients during admission had been included in the long-term analysis [21]. These variable mortality rates may partly be explained by the differences of the study populations. Kaplan *et al.* [22] reported that hospital mortality and 1-year mortality rates for the 65 years or older hospitalized with CAP were 11.0% and 40.9% respectively. One-year mortality rate in hospital survivors of the CAP was 33.6%. The poor long-term outcomes may be related to chronic inflammaging which triggers aging and early mortality. CAP has caused an inflammatory storm, and persistent systemic inflammation after a clinical resolution of CAP has been resulted in poor outcomes [23-24]. Therefore, CAP may be considered like some chronic diseases such as chronic obstructive pulmonary disease or chronic renal failure.

Previous studies evaluating long-term prognostic factors in patients with CAP have shown that older age and some comorbidities increase mortality. Tokgöz *et al.* reported that increased age, the absence of fever, an increased Charlson Comorbidity Index, a higher blood urea nitrogen/albumin ratio and a decreased alanine aminotransferase levels were associated with increased 1-year mortality [4]. In the study of Holter *et al.*, age, cardiovascular disease, chronic obstructive pulmonary disease, immunocompromisation and low serum albumin level at admission associated with 1-year mortality [21]. Adamuz *et al.* reported that chronic obstructive pulmonary disease, diabetes mellitus, malignity, dementia, rehospitalization and nursing home residence were predictors for long-term mortality [25]. Wesemann *et al.* [26] reported that age, nursing home residency, hemiplegia, dementia and congestive heart failure were associated with mortality in univariate analysis. Neither CURB-65 nor the Charlson Comorbidity Index were excellent predictors.

In the present study, while CURB-65 classified into the risk groups for short-term poor prognosis, the modified Charlson Comorbidity Index classified into

Table 4. Predictors for long-term (1-year) mortality in patients with community-acquired pneumonia.

	Age < 65 years					**Age ≥ 65 years**				
	Survive		**Non-survive**			**Survive**		**Non-survive**		
	n	**%**	**n**	**%**	**p**	**n**	**%**	**n**	**%**	**p**
Total	35	68.6	16	31.4		51	54.2	43	45.8	
Gender					1.000					0.087
Male	17	48.6	8	50.0		29	56.9	32	74.4	
Female	18	51.4	8	50.0		22	43.1	11	25.6	
CURB-65					**0.011**					0.103
Class 1	28	80.0	9	56.3		16	31.4	11	25.6	
Class 2	5	14.3	6	37.5		25	49.0	15	34.9	
Class 3	2	5.7	1	6.3		10	19.6	17	39.5	
PSI					0.121					**0.007**
Class 1-2-3	22	62.9	5	31.3		9	17.6	2	4.7	
Class 4	9	25.7	9	56.3		27	52.9	18	41.9	
Class 5	4	11.4	2	12.5		15	29.4	23	53.5	
Modified Charlson					**0.020**					**0.001**
Class 1	23	65.7	5	31.3		10	19.6	0	0	
Class 2	8	22.9	5	31.3		12	23.5	9	20.9	
Class 3	2	5.7	4	25.0		17	33.3	13	30.2	
Class 4	2	5.7	2	12.5		12	23.5	21	48.8	
Mechanical ventilation	1	2.9	1	6.3	0.533	1	2.0	11	25.6	**0.001**
Mental disorder	2	5.7	0	0	1.000	3	5.9	10	23.3	**0.018**
Malignancy	8	22.9	9	56.3	**0.027**	5	9.8	19	44.2	**< 0.001**
Hospital readmission	5	14.3	12	75.0	**< 0.001**	8	15.7	26	60.5	**< 0.001**

the risk groups for long-term mortality in the older adults. Altough there are some conflicting results regarding severity scoring systems [3-4, 17, 21, 26, 27], this result is not unexpected as the CURB-65 reflects acute instability. However, the PSI surprisingly classified into the risk groups for both short-term poor prognosis and long-term mortality in the older adults. Johnstone *et al.* also reported that as well as older age and male sex, the PSI was associated with increased long-term mortality [28]. The predictive value of modified Charlson Comorbidity Index and the PSI for long-term mortality can be explained by their prediction rules include comorbid conditions such as malignancy as confirmed by this study. Nevertheles, the scoring systems were not found to be independent risk factors in our study.

Our results justify the need for preventive strategies after discharge. Immunization programs, such as pneumococcal and influenza vaccinations, and reducing environmental risk factors by supporting lifestyle modification such as regular physical activity and balanced diet may improve long-term outcomes [29]. Also, better understanding the causal association between CAP and long-term mortality is vital for improving outcomes in the older adults with CAP.

The strength of this study is that multiple comorbidities and different types of variables were included in the multivariate regression analysis. However, our study has several limitations. First, it was conducted in a single-center. Second, this study had a small sample size and a control group did not included. Therefore, the generalizability of our results may limited. Third, causes of death were not determined in the study. Fourth, the rate of microbiologically confirmed cases was low, and we did not consider the causative pathogens as risk factors.

Conclusions

As a result, CAP is still a significant threat to both older and younger adults. Patients hospitalized with CAP are at high risk for readmission. Also, clinicians should consider the lethal possibilities of CAP even after hospital discharge. The need for mechanical ventilation and hospital readmission may predict long-term mortality. Therefore, the patients who have these predictors should be closely monitored.

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