Independent Prognostic Indicators in the Elderly with Pneumonia: A Single-Center Prospective Observational Study

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Abstract

Background: The aim of this study was to investigate poor prognostic indicators in the elderly with pneumonia.

Methods: In this prospective observational study, the patients with pneumonia were stratified into younger (18-64 years) and older (≥65 years) groups. The poor prognostic indicators were determined and compared.

Results: There were 184 pneumonia episodes in 155 patients. The median age of the cases was 72 (range, 18-104) of whom 127 (69%) were ≥65 years old and 110 (59.8%) were male. Mental status changes were more common in the elderly group (p=0.04). Multivariate regression analysis determined three variables that could be potential independent risk factors for poor prognosis in the elderly: dyspnea at the onset (OR:5.85, CI:5.18-6.52, p=0.01), previous antibiotic use within the last 3 months (OR:2.97, CI:2.51-3.43, p=0.02), acute renal failure (OR:2.51, CI:2.06-2.96, p=0.04). A receiver operating characteristic (ROC) analysis showed that the area under the curves (AUC) of procalcitonin and C-reactive protein (CRP) as indicators of poor prognosis in the elderly were 0.846 (p<0.001) and 0.650 (p=0.008) respectively. In addition, mental status changes (p<0.001), the confusion, blood urea nitrogen, respiratory rate, blood pressure, and age ≥65 years (CURB-65) score (p<0.001), and the pneumonia severity index (PSI) (p<0.001) were associated with poor prognosis.

Conclusion: Dyspnea at the onset, previous antibiotic use within the last 3 months, acute renal failure, serum CRP and procalcitonin levels along with the PSI and the CURB-65 scores should be carefully evaluated in terms of hospitalization, the need for intensive care unit admission and the initial antimicrobial therapy.

Background

Pneumonia is one of the most common acute infectious conditions causing fatality at any age. Pneumonia treatment is usually commenced empirically based on clinical, radiological and non-specific laboratory findings. Nevertheless definitive microbiological results are rarely achieved before the initial treatment [1 2 3 4].

Pneumonia, including whether community or hospital acquired, leads to more severe outcomes in the elderly than in the young population. This situation causes a significant increase in health expenditures due to prolonged hospitalization and multiple antibiotic uses [5]. As a result, we need to develop new clinical strategies to reduce mortality and morbidity rates in the elderly.

The aim of this prospective study was to investigate the poor prognostic indicators in the elderly with pneumonia. We compared the risk factors, clinical and laboratory findings, the severity of the course and the treatment responses in patients over and under age 65 with pneumonia.

Methods

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

Patients with community-acquired pneumonia (CAP) requiring hospitalization or hospital-acquired pneumonia (HAP) were included in the study. Outpatients, patients with neutropenia, ventilatory-associated or postoperative pneumonia were excluded. The diagnosis of pneumonia was made on the basis of current guidelines [6 7 8 9]. A total of 184 pneumonia episodes in 155 patients were recorded.

A “recurrent episode” was defined as an episode of recurrent pneumonia within at least 30 days following the initial diagnosis of pneumonia during the one-year follow-up period. Each episode of pneumonia was recorded separately, and statistical analyses were made based on the number of episodes.

The demographic data, underlying diseases, immunosuppressive conditions, symptoms and physical examination findings, laboratory test results and radiological findings, the treatments and responses were recorded via a follow-up data sheet. The cases were divided into two groups according to their ages (over or below 65) and comparative analyses were applied.

Modified Charlson comorbidity scores were calculated for all the patients [10]. The CURB–65 (confusion, blood urea nitrogen, respiratory rate, blood pressure, and age ≥65 years) and the Pneumonia Severity Index (PSI) were calculated only for patients with community-acquired pneumonia [11 12].

CRP, procalcitonin, leukocyte, neutrophil, lymphocyte values were recorded on the day of diagnosis of pneumonia, on the 3rd day (+/- 24 hours) and on the 7th day (+/- 24 hours).

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 [13].

A “poor prognosis” was assessed as the development of septic shock associated with infection and/or the need for intensive care and/or death within 30 days.

Quantitative variables were expressed as mean & standard error or median & range if they contain continuous data. If they contain categorical data, they were expressed as percentage (%) and frequency

(n).

The normality of distribution was examined by Kolmogorov-Smirnov and Kurtosis-Skewness Tests. There were no parametric data showing normal distribution.

Two important dependent variables of the study were “under 65 of age / ≥65 of age” and “good prognosis / poor prognosis”. Three major factors were identified as poor prognosis criteria: “indication of admission to the intensive care unit”, “death within 30 days” and “septic shock”.

Dependent variables were compared with many independent variables such as demographic, clinical, laboratory parameters. Friedman Variance Analysis was used for the analysis of continuous and more than two dependent non-parametric groups. Wilcoxon Signed Ranks Test was used for post-hoc analysis. Afterward, these dependent groups were handled one by one, Receiver operating characteristic (ROC) curves were drawn and “Area Under the Curve (AUC)“, “cut-off values” and “sensitive and specificity of cut-off values” were shown.

Non-parametric groups containing two continuous data were compared, and Mann Whitney U Test was used to determine the significant difference. The significance of the categories of dependent groups and categorical independent groups was examined by Chi-Square Test. There was no situation requiring post-hoc analysis. In cases which the expected numbers may be less than 5, the Cochran Principles were observed. Fisher’s Exact Test was used in cases which “n <20” or “20 <n <40 and at least one expected value was less than 5”. Yates was chosen when “n> 40 and the expected at least one value was less than 5”. In all cases except Pearson Chi-Square Test results were accepted.

The Chi-square test with prognosis dependent variable was found to be significant. Although it was not significant, the partial correlation of the independent variables whose effect on prognosis was examined. The most important and effective variables among the ones at the correlation intersection were subjected to “univariate and multivariate logistic regression”. Univariate logistic regression refers to the regression of one independent variable on one dependent variable.

The results were evaluated in a 95% confidence interval and the statistical significance level was defined as $p < 0.05$. The analyses were performed using IBM SPSS - 21 (Statistical Package for Social Sciences, Chicago, IL, USA).

Results

A total of 184 pneumonia episodes in 155 patients were recorded. Of these episodes, 145 (78.8%) were community-acquired pneumonia (CAP) and 39 (21.2%) were hospital-acquired pneumonia (HAP). Thirteen (7.1%) episodes were directly attributable to in-hospital pulmonary aspiration.

The median age of the cases was 72 (range, 18–104) of whom 127 (69%) were ≥65 years old and 110 (59.8%) were male. Of the 127 cases; 53 (41.7%) were in the 65–74 age group, 44 (34.6%) in the 75–84

age group, and 30 (23.6%) were ≥ 85 years. The demographic characteristics of the cases are given in Table 1.

In 10 (5.4%) cases, no underlying disease was recorded. Of these, only 3/10 (30%) were in the elderly (≥65 years) group (p <0.001). The rates of chronic obstructive pulmonary disease (COPD), diabetes mellitus, hypertension, congestive heart failure, chronic renal failure, coronary artery disease, dementia were significantly higher in the elderly group. HAP occurred significantly more common in this group. Twenty-nine cases (15.8%) were admitted to the intensive care unit. Nineteen (10.3%) patients died.

All of the symptoms, significantly cough (p = 0.02) and hemoptysis (p = 0.004) were more frequent in the younger group. On the contrary, mental status changes were significantly more common in the elderly group (p = 0.04). The distribution of symptoms and findings is given in Table 2.

Microbiological evidence was obtained in 37 (20.1%) cases (26 in sputum culture, 1 in both blood and sputum culture, 4 in respiratory system by multiplex polymerase chain reaction, 2 in bronchoalveolar lavage culture, 2 in endotracheal aspirate, 2 in transtracheal aspirate).

Blood culture was obtained in 114 (62%) cases, and sputum culture was evaluated in 76 (41.3%) cases. Positive blood culture was observed only in 1 case. Of the sputum cultures, the causative microorganisms were isolated in 27 (35.5%) cases.

Pseudomonas spp. (n = 11, 29.7%) was the most common agent, followed by *Streptococcus pneumoniae* (n = 6, 16.2%). Although *Pseudomonas spp.* was more frequent in the elderly compared to the younger group (n = 8 vs. n = 3), there was no significant difference between the two groups (p = 0.54). Other typical bacterial agents were *Haemophilus influenzae* (n = 5, 13.5%), *Acinetobacter spp.* (n = 4, 10.8%) and *Staphylococcus aureus* (n = 4, 10.8%). Of the *Staphylococcus aureus* strains 25% had methicillin resistance. The rate of carbapenem resistance was 45.4% in *Pseudomonas spp.* and 50% in *Acinetobacter spp.*

Regarding atypical agents; *Mycoplasma pneumoniae* was detected in 1 case, *Influenzavirus* in 2 cases, *Metapneumovirus* in 1 case and *Human coronavirus 229E* in one case (coupled with *Streptococcus pneumoniae)* were detected by multiplex PCR in respiratory system.

There was no significant difference between the elderly and the younger group in terms of culture positivity. However, the availability of sputum samples was significantly lower in the elderly group (p = 0.04) (Table 3).

In the Friedman analysis, D0 was considered as the first day of the diagnosis and treatment of pneumonia cases. The age-independent analysis showed that the laboratory parameters on day 0, 3 and 7 were significantly different for the five dependent parameters (CRP, procalcitonin, leukocyte, neutrophil, lymphocyte) in at least one consecutive measurement. However, only CRP (p = 0.001) and procalcitonin (p = 0.001) had significant differences in all consecutive measurements. The statistical analysis of these

dependent parameters with mean and median values according to the age groups on day 0, 3 and 7 is summarized in Table 4.

Mean leukocyte, neutrophil and lymphocyte counts on days 0 (D0), 3 (D3) and 7 (D7) were not significantly different between elderly and younger groups. Mean CRP level on D0 and mean procalcitonin level on D7 were significantly different (p = 0.001).

A ROC analysis showed that the AUC of procalcitonin and CRP as indicators of poor prognosis in the elderly were 0.846 (p<0.001) and 0.650 (p = 0.008) respectively (Figure 1). For poor prognosis, the cut-off value of procalcitonin was 0.295 ng/mL in the elderly group, with a sensitivity of 83% and a specificity of 69% (p<0.001). The cut-off value of CRP was 79 mg/L with a sensitivity of 79% and a specificity of 52% (p = 0.008).

Using the Chi-square test, we analyzed the relationship between poor prognosis and age, for the following parameters: gender, epidemiological setting, fever, hypothermia and other symptoms, underlying diseases, acute renal failure and need for dialysis, presence of immunosuppression, presence of hospitalization within the last 1 year, history of antibiotic use within the last 3 months, and history of smoking. The parameters with significant differences are given in Table 5. There was no statistically significant relationship between body temperature and poor prognosis (p = 0.157). In addition, *Pseudomonas spp.* was not associated with poor prognosis (p = 0.573).

Age dependent and independent analyses including univariate and multivariate regression revealed that dyspnea, antibiotic use within the last 3 months, and acute renal failure were associated with poor prognosis. Table 6 shows the odds ratios (OR), confidence intervals (CI) and p values for all ages, and for those 65 years and older.

Discussion

Many studies have demonstrated that increased age is associated with pneumonia-induced mortality [11 12 14 15]. In this prospective observational study, which was the subject of pneumonia in the elderly, the patients with pneumonia were stratified into younger (18 to 64 years) and older (≥65 years) groups. The poor prognostic indicators were determined and compared in both age groups. In our study, we determined three variables that could be potential independent risk factors for poor prognosis in the elderly with pneumonia: previous antibiotic use within the last 3 months (OR:2.97, CI:2.51–3.43, p = 0.02), acute renal failure (OR:2.51, CI:2.06–2.96, p = 0.04) and dyspnea (OR:5.85, CI:5.18–6.52, p = 0.01). Also, we found that serum procalcitonin (p<0.001) and CRP levels (p = 0.008) were valuable indicators of poor prognosis in the elderly. In addition, mental status changes, the CURB–65 score, and the pneumonia severity index (PSI) as well as the independent risk factors were associated with poor prognosis of those that were 65 years and older.

Antibiotic exposure is one of the main reasons for increased pneumonia cases with resistant microorganisms, and leads to a lack of response to empirical antimicrobial therapies. There are several

studies showing that previous antibiotic use is a risk factor for infection with drug-resistant *Streptococcus pneumoniae* [16 17 18]. In our study, the rate of previous antibiotic use within the last 3 months was quite high in the elderly (n = 71, 55.9%) and in the younger group (n = 30, 52.6%). Also, previous antibiotic use within the last 3 months was an independent risk factor for poor prognosis in both age groups.

In our study, the rate of acute renal failure was 52.6% in the elderly with poor prognosis. Acute renal failure was also an independent risk factor for poor prognosis. This finding was consistent with other studies [19 20]. In the study of Murugan et al., acute renal failure was associated increased mortality risk, and also, an increased severity of acute renal failure was correlated with the increased mortality rates [20].

In this study, dyspnea was found to be an independent risk factor for poor prognosis. The diagnosis of pneumonia in the elderly is delayed due to the fact that the signs and symptoms are infrequent [1 21 22]. Although dyspnea was seen as less frequent in the elderly, it is vital for the prognostic evaluation. However, due to the weakness of the compensation mechanisms, multiple organ failure and mental status changes develop more easily in the elderly [1]. In our study, mental status changes were found to be more frequent in the elderly (p = 0.035). This finding was consistent with other studies [22 23 24]. That is why mental status changes should be considered one of the most important findings in the early diagnosis of pneumonia in the elderly. Also, an alteration in mental status may be the first clue in the diagnosis of pneumonia in this group.

In our study, fever and hypothermia were less frequent in the elderly group than in the younger group, but no statistically significant difference was found between the two groups. In addition, when the fever and hypothermia were considered together as body temperature changes in the elderly group, there was no statistically significant relationship with poor prognosis (p = 0.157). Also, in the univariate and multivariate regression analysis, there was no relationship between hypothermia and poor prognosis in the elderly group (p = 0.19). Some studies have shown that fever and hypothermia contribute to the diagnostic and prognostic evaluation of pneumonia [25 26 27]. It is known that fever development is less frequent, especially in the elderly population due to the reduced host immune response. In this reduced response, the decrease in the production of endogenous pyrogens such as interleukin–1, interleukin–6 and tumor necrosis factor and the reduced response to these pyrogens has been thought to play a role [28 29 30 31 32 33].In addition, hypothalamic changes occurring with aging, and changes in thermogenic brown fat tissue may also play a role in decreased fever response to infections observed in the elderly [28 29 30].

In our study, sputum culture positivity was 40.4% in the elderly group and 25.8% in the younger group. In the study of Saltoglu et al., microbiological evidence was obtained in 44% of the cases [34]. In Gutierrez's study, the rate was quite high (50.7%) [35]. On the contrary, the microbiological evidence was obtained in 20.1% of the cases in our study. The rate of obtaining the sputum sample in elderly patients was significantly lower than in the younger group (p = 0.037). The low rates in our study can be explained for

a number of reasons such as antibiotic use before inpatient treatment, and sputum production and collection problems in the elderly.

Although the results of microbiological examinations are generally not obtained during diagnosis and empirical treatment, but these results are very important for the reassessment of the initial treatment. Sputum Gram stain and culture and other microbiological examinations including polymerase chain reaction assay in respiratory samples are crucial to providing the most appropriate empirical treatment. Owing to these microbiological evaluations, antimicrobials can properly be tailored. Furthermore, collateral damage including antimicrobial resistance and even mortality can be reduced [1].

In our study, *Pseudomonas spp.* isolated from clinical specimens were significantly higher compared to the other isolates. This may be because of the previous antibiotic use and multiple comorbid diseases. Among cases with *Pseudomonas spp.,* the rate of previous antibiotic use and multiple comorbid diseases (≥ 2 chronic comorbidities) were 81.8% and 63.6% respectively. von Baum et al. reported that age >65 years, congestive heart failure and cerebrovascular disease were indicators for *Enterobacteriaceae (*36).Also*,* chronic respiratory disease and enteral tube feeding were indicators for *Pseudomonas aeruginosa.* However, other studies have demonstrated that increased age is not an indicator for gram negative microorganisms [37 38]. In our study, there was no significant relationship between *Pseudomonas spp.* as a causative agent and poor prognosis (p = 0.573). The rates of carbapenem resistance were also quite high in *Pseudomonas spp.* (45.4%) and in *Acinetobacter spp.* (50%). And 25% of *Staphylococcus aureus* strains were methicillin resistant.

In this study, we found that serum procalcitonin and CRP levels were valuable indicators of poor prognosis in the elderly. There are various studies showing the contribution of complete blood count, CRP and procalcitonin used in the diagnosis and follow-up of pneumonia. However, there are fewer studies evaluating elderly patients with pneumonia in terms of these parameters [39 40 41 42]. In our study, the mean CRP value on D0 was 181.68 ± 15.86 mg/L in the younger group and 118.11 ± 8.34 mg/L in the elderly (p = 0.001). This difference between the elderly group and the younger group showed that the initial CRP values on D0 may be lower in the elderly group than in the younger group. If the cut-off value is evaluated independent of age, it should be considered that CRP value may be less sensitive in the diagnostic and prognostic evaluation of the elderly group. In order to evaluate poor prognosis, the optimal cut-off value of CRP on D0 was 91.5 mg/L in the age-independent group, and 79 mg/L in the elderly group. In the study of 70 patients by Zhang et al., most of them were with pneumonia, examined the relationship of leukocyte, CRP and procalcitonin with sepsis/septic shock [41]. They showed that CRP can predict poor prognosis at least as accurately as procalcitonin. They found that the cut-off value for CRP was 74.2 mg/L, sensitivity and specificity were 78% and 75% respectively.

In our study, procalcitonin was found to be the best prognostic indicator in the ROC curve in both the age-independent and the elderly group. For poor prognosis, the cut-off value was 0.295 ng/mL in the elderly group, with a sensitivity of 83% and a specificity of 69% (p<0.001). The cut-off value was 0.265 ng/mL in age-independent analysis, with a sensitivity of 77% and a specificity of 65% (p <0.001). In the meta-

analysis of Liu et al., the prognostic cut-off value of procalcitonin was less than 0.5 ng/mL in only two studies [43]. However, our study was consistent with the studies showing that procalcitonin is a reliable prognostic indicator [40 44 45 46 47 48 49 50 51]. On the other hand, in a total of 667 cases evaluated by Akagi et al., including 436 pneumonia cases aged 75 years and over, procalcitonin was not an independent predictor of mortality in the elderly and in the young group, but was associated with the severity of pneumonia [39]. In Zhang's study, when the cut-off value of procalcitonin was 0.250 ng/ml, the sensitivity and specificity were 88% and 65%, respectively [41]. This finding was consistent with our study.

In the elderly, the immune response to infections is decreased due to immunosenescence, and a chronic, low-grade systemic inflammation occurs. In addition, subclinical inflammation caused by exposure to various antigens in elderly patients manifests with relatively lower CRP and procalcitonin release in response to exogenic antigens. However, decreased procalcitonin levels in elderly patients can also be due to various etiologies of pneumonia with varying cytokine release patterns [39 52].

The modified Charlson comorbidity score was not correlated with poor prognosis in both age

groups. These findings suggest that the CURB–65 and the PSI are still consistent pneumonia cases and are superior to the modified Charlson comorbidity classification to accurately predict the prognosis.

Various studies have demonstrated that mortality rates are high in the elderly population [39 53 54]. In our study, the 30-day mortality rates were found to be higher in the elderly group (11.8%) compared to the younger group (7%), but no statistically significant (p = 0.435). In the study of Saltoglu et al., the mortality rate of 130 patients with CAP was 3% and the mean age was 40±13.6 years [34]. The high mortality rate in our study may be because of the high mean age of the patients (69.27±1.23) and the inclusion of HAP with severe infection. This may be due to the relatively high (49.63±1.68) mean age of our younger group.

Our study has several limitations. First, it was conducted in a single-center. Second, the rate of microbiologically confirmed cases was low, and we did not consider the causative pathogens other than *Pseudomonas spp.* as a risk factor. This study has also several strengths. First, it is a prospective study. Second, multiple comorbidities and different types of variables were included in the multivariate regression analysis. Also, this study has good generalizability because the results are broadly applicable to many different types of people and situations.

Conclusion

In conclusion, CRP and procalcitonin should be included in the diagnostic and prognostic work-up of elderly patients since the classical symptoms and signs of pneumonia are less common in this group. Dyspnea and acute renal failure at the onset should be taken into consideration along with the PSI and the CURB–65 scores to evaluate the need for hospitalization and intensive care unit admission. In addition, previous antibiotic use within the last 3 months and current resistance rates of common

causative microorganisms should be evaluated to determine the most effective initial antimicrobial therapy.

Abbreviations

ROC: Receiver operating characteristic

AUC: Area under the curves

CRP: C-reactive protein

CURB–65: Confusion, blood urea nitrogen, respiratory rate, blood pressure, and age ≥65 years,

PSI: Pneumonia severity index

CAP: Community-acquired pneumonia

HAP: Hospital-acquired pneumonia

SOFA: Sequential Organ Failure Assessment

Declarations

Ethics approval and consent to participate: The investigation was carried out in compliance with relevant laws and guidelines, in accordance with the ethical standards of the Declaration of Helsinki. The study was approved by the Clinical Research Ethics Committee of Istanbul University Cerrahpasa Medical Faculty (approval number: 83045809–604.01.02–52675). All patients gave written informed consent to be included in the study.

Consent for publication: Not applicable.

Availability of data and material: The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: SS contributed to the study conception and design, acquisition/analysis/interpretation of data, drafting and critical review of the article. IIB, OFB, RKA, BM, GC, FT and NS contributed to study conception and design, analysis/interpretation of data, critical revision, and supervision. All authors have contributed to and approved the final manuscript.

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Tables

Table 1. The demographic characteristics of the cases in terms of age groups

	In total		<65 years		≥65 years		p
	n	%	n	%	n	%	
Number of cases	184	100	57	44.9	127	55.1	**<0,001**
Mean age ±se	69.27 ±1.23		49.63 ±1.68		78.09 ±0.81		**<0.001**
Median age	72		53		76		
Male	110	59.8	28	49.1	82	64.6	**0.048**
Female	74	40.2	29	50.9	45	35.4	
CAP	145	78.8	51	89.5	94	74.3	0.561
HAP	39	21.2	6	10.5	33	26	**0.019**
Aspiration associated pneumonia	13	7.1	4	7	9	7.1	1.000
Underlying disease	174	94.6	50	87.7	124	97.6	**0.011**
COPD	58	31.5	8	14.0	50	39.4	**0.001**
Diabetes mellitus	61	33.2	12	21.1	49	38.6	**0.020**
Hypertension	99	53.8	19	33.3	80	63.0	**0.000**
Congestive heart failure	36	19.6	5	8.8	31	24.4	**0.015**
Cerebrovascular disease	16	8.7	2	3.5	14	11.0	0.155
Chronic renal failure	64	34.8	9	15.8	55	43.3	**<0.001**
Malignancy	51	27.7	20	35.1	31	34.4	0.135
Cystic fibrosis	1	0.5	1	1.8	0	0	-
Asthma	10	5.4	1	1.8	9	7.1	0.178
Bronchiectasis	4	2.2	4	7.0	0	0	-
Coronary artery disease	52	28.3	7	12.3	45	35.4	**0.001**
Dementia	22	12.0	0	0	22	17.3	**<0.001**
Immunosuppression	36	19.6	21	36.8	15	11.8	**<0.001**
Chemotherapy	16	8.7	8	14.0	8	6.3	0.096
Steroid	14	7.6	8	14.0	6	4.7	**0.037**
Immunosuppressive disease	9	4.9	4	7.0	5	3.9	0.462
Radiotherapy	8	4.3	3	5.3	5	3.9	0.705
History of previous tuberculosis	10	5.4	7	12.3	3	2.4	**0.011**
Smoking history	94	51.1	24	42.1	70	55.1	0.103
Previous antibiotic use within the last 3 months	101	54.9	30	52.6	71	55.9	0.412
Hospital stay within the last 1 year	95	51.6	32	56.1	63	49.6	0.638
ICU stay within the last 1 year	24	13.0	6	10.5	18	14.2	0.638
Sepsis / septic shock	**41**	**22.3**	**14**	**24.6**	**27**	**21.3**	**0.702**
Acute renal failure	63	34.2	18	31.6	45	35.4	0.737
Mechanical ventilation	25	13.6	5	8.8	20	15.7	0.249
Dialysis	5	2.7	2	3.5	3	2.4	-
Intensive care need	29	15.8	7	12.3	22	17.3	0.512
Poor prognosis	55	29.9	17	29.8	38	29.9	1.000
Death	19	10.3	4	7	15	11.8	0.435

Table 2. The distribution of symptoms and findings in terms of age groups

	In total		<65 years		≥65 years		p
	n	%	n	%	n	%	
Cough	145	78.8	51	89.5	84	74.0	**0.019**
Sputum	121	65.8	42	73.7	79	62.2	0.135
Dyspnea	141	76.6	48	84.2	93	73.2	0.132
Mental disorder	25	13.6	3	5.3	22	17.3	**0.035**
Fever	83	45.1	29	50.9	54	42.5	0.292
Hypothermia	15	8.2	6	10.5	9	7.1	0.561
Hemoptysis	13	7.1	9	15.8	4	3.1	**0.004**

Table 3. Distribution of blood and sputum culture characteristics

	In total		<65 years		≥65 years		p
	n	%	n	%	n	%	
Presence of blood culture	114	62	36	63.2	78	61.4	0.822
Blood culture positivity	1	0.9	0	0	1	1.3	-
Presence of sputum culture	76	41.3	30	52.6	46	36.2	**0.037**
Sputum culture positivity	27	4.6	8	25.8	19	40.4	0.228

Table 4. The analysis of five dependent laboratory parameters on D0, D3 and D7

		D0		D3		D7	
Age		<65	≥65	<65	≥65	<65	≥65
WBC*	Mean ± se	12,761.40 ±845.07	11,971.65 ±527.41	9,575.80 ±617.70	10,215.49 ±506.77	10,209.80 ±660.69	10,297.98 ±634.44
	Median	11900	11900	9295	9200	10000	9050
	p	0.460		0.755		0.587	
Friedman p<0.001		The day which is made a significant difference was D0.					
CRP*	Mean ± se	181.68 ±15.86	118.11 ±8.34	79.47 ±11.13	79.24 ±6.85	35.51 ±6.42	47.68 ±5.40
	Median	179	92	51	56	19	31
	p	**0.001**		0.755		0.119	
Friedman p<0.001		All the days were made a significant difference.					
PRC*	Mean ± se	2,.05 ±0.81	1.99 ±0.88	2.36 ±1.79	1.16 ±0.45	0.20 ±0.09	0.32 ±0.07
	Median	0.24	0.25	0.16	0.18	0.07	0.16
	p	0.758		0.703		**0.002**	
Friedman p<0.001		All the days were made a significant difference.					
NEU*	Mean ± se	11,017.54 ±896.59	9,399.68 ± 472.05	7,176.40 ±573.02	7,513.06 ±396.74	7,655.00 ±662.25	7,345.31 ±402.12
	Median	9,300	8,600	6,350	6,800	6,300	6,400
	p	0.173		0.702		0.792	
Friedman p<0.001		The day which is made a significant difference was D0.					
LYMP*	Mean ± se	1142,10±88.04	1,560.48 ±226.04	1,498 ±133.11	1,641.65 ±332.71	1,757.31 ±161.53	1,943.77 ±465.30
	Median	1000	1,200	1,350	1,200	1,600	1,400
	p	0.072		0.354		0.235	
Friedman p<0.001		The day which is made a significant difference was D7.					

*WBC: Leukocyte CRP:C-reactive protein PRC: Procalcitonin NEU: Neutrophile LYMP: Lymphocyte

Table 5. Chi-square test for poor prognosis

	Age-independent			≥65 years		
	n	%	p	n	%	p
Number of cases	184	100		127	55.1	
Cases with poor prognosis	55/184	29.9		38/127	29.9	
Gender			0.772			1.000
Male	32	58.2		25	65.8	
Female	23	41.8		13	34.2	
Dyspnea	52	94.5	**<0.001**	35	92.1	**0.002**
Mental status changes	18	32.7	**<0.001**	17	44.7	**<0.001**
Mechanical ventilation need	25	45.5	**<0.001**	20	52.6	**<0.001**
CURB-65 class			**<0.001**			**<0.001**
Class 1	8	21.1		1	4.0	
Class 2	10	26.3		7	28.0	
Class 3	20	52.6		17	68.0	
PSI class			**<0.001**			**<0.001**
Class 1	3	7.9		0	0	
Class 2	14	36.8		7	28.0	
Class 3	21	55.3		18	72.0	
Acute renal failure	28	50.9	**0.002**	20	52.6	**0.014**
Previous antibiotic use within the last 3 months	39	70.9	**0.006**	27	71.1	**0.032**
ICU stay within the last 1 year	12	21.8	**0.03**	9	23.7	0.055
Malignancy	22	40.0	**0.015**	12	31.6	0.261
Hospital-acquired pneumonia	17	30.9	**0.048**	13	34.2	0.189

Table 6. Univariate and multivariate analysis for poor prognosis

	Age-independent univariate analysis			≥ 65 years univariate analysis			Age-independent multivariate analysis			≥ 65 years multivariate analysis		
	OR	CI	p	OR	CI	p	OR	CI	p	OR	CI	p
Dyspnea	7.80	7.18-8.42	**<0.01**	8.97	8.32-9.62	**<0.01**	6.24	5.60-6.88	**<0.01**	5.85	5.18-6.52	**<0.01**
Hypothermia	2.21	1.66-2.76	0.15	3.23	2.57-3.89	0.07	1.98	1.28-2.68	0.33	2.97	2.13-3.81	0.19
Previous antibiotic use within the last 3 months	2.63	2.28-2.98	**<0.01**	2.95	2.57-3.33	**<0.01**	2.51	2.09-2.93	**0.03**	2.97	2.51-3.43	**0.02**
Acute renal failure	2.79	2.45-3.13	**<0.01**	3.07	2.69-3.45	**0.01**	2.84	2.44-3.24	**<0.01**	2.51	2.06-2.96	**0.04**
Modified Charlson class 1	1.30	0.78-1.82	0.95	0.84	0.29-1.39	0.79	2.00	1.11-2.89	0.44	2.08	1.14-3.02	0.43
Modified Charlson class 2	1.29	0.81-1.77	0.59	1.45	0.93-1.97	0.48	1.69	0.84-2.54	0.54	2.45	1.55-3.35	0.53
Modified Charlson class 3	1.94	1.48-2.04	0.15	1.88	1.36-2.40	0.22	2.40	1.56-3.24	0.30	2.45	1.45-3.35	0.32

Figures

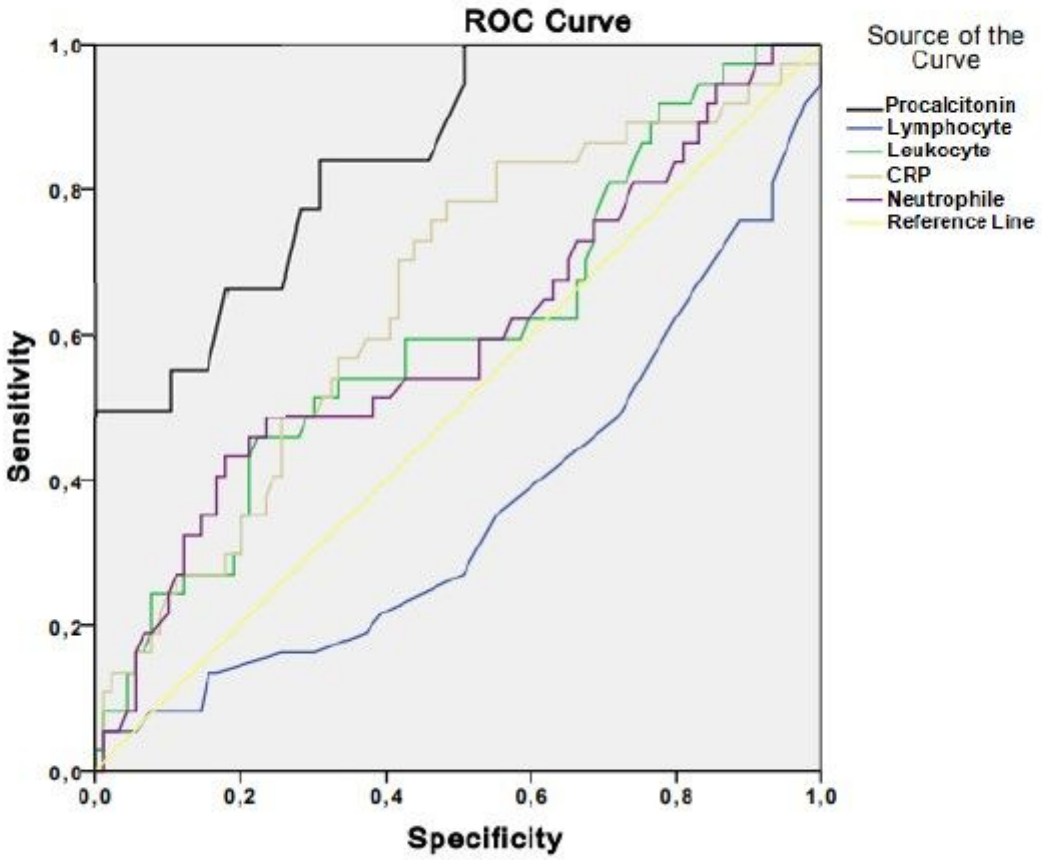

Figure 1

Receiver operating characteristic curve of procalcitonin, CRP levels, leukocyte, neutrophile and lymphocyte counts for prediction of poor prognosis of elderly with pneumonia

Supplementary Files

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