

## **The diagnostic value of procalcitonin, WBC, and CRP in diagnosis of lower respiratory tract infections in elderly patients.**

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### **Abstract**

**Objective:** Lower Respiratory Tract Infections (LRTI) in elderly patients hospitalized in Intensive Care Units (ICU) cause high morbidity and mortality. In this study; the prognostic value of CRP, WBC, and procalcitonin in respiratory infections were evaluated in elderly patients hospitalized in intensive care units.

**Methods:** Study population was included of 62 patients hospitalized in intensive care unit. All patients were intubated and received mechanic ventilation for more than ten days. Cultures and Gram stain of 62 bronchial aspiration samples of the patients sent to the Microbiology laboratory were evaluated. CRP, procalcitonin and WBC were measured. The diagnostic value of WBC, procalcitonin, and CRP were evaluated according to diagnostic standard. Clinical information and laboratory data were obtained from hospital medical records and evaluated retrospectively. **Results:** On Gram stain of 30 samples, bacteria and >25 Polymorphonuclear Leukocytes (PMNs) were seen in every field. Also, samples were positive in quantitative culture with >100.000 cfu/ml. These samples were considered as purulent. The sensitivity, specificity, PPV and NPV for CRP were 100%, 3.1%, 49.1% and 100%, respectively. The sensitivity, specificity, PPD and NPV for procalcitonin were 73.3%, 31.2%, 50% and 55.5%, respectively. The sensitivity, specificity, PPD and NPV for WBC were 56%, 40%, 52% and 61.9% respectively. T-test was used in order to determine if the parameters vary in patients with purulent and not-purulent samples. According to t-test; CRP did not differ in two groups ( $p=0.346>0.05$ ). Procalcitonin was not found useful for determining the purulence ( $p=0.772>0.05$ ). No statistically significant difference was detected for WBC in two groups ( $p=0.559>0.05$ ).

**Keywords:** Lower respiratory tract infections, Procalcitonin, WBC, CRP, Culture.

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### **Introduction**

Lower Respiratory Tract Infections (LRTI) in elderly patients hospitalized in Intensive Care Units (ICU) cause high morbidity and mortality [1]. By age; the prevalence of chronic diseases increase [2]. Also, epithelial barriers of the systems are affected worse, body defense decreases and individual becomes susceptible to various infections and the frequency and severity of infections increase [1,3,4] The length of stay in the Intensive Care Unit (ICU) is an important factor for respiratory infection. Also, elderly patients hospitalized in ICU generally have multiple comorbidities with the disease leading to admission. Delay in treatment would cause exacerbations of the infections. So the early determination of bacterial infection is essential. The first problem is the accurate diagnosis in LRTI [5]. Especially in immunocompromised patients; lung involvement may be due to several reasons, and it is important to determine if an infection present and is there a requirement for antimicrobial therapy [6]. Especially the diagnosis of

ventilator-related pneumonia is difficult as it may be confused with many diseases [6].

According to Guidelines of American Thoracic Society for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia; the aim of diagnostic tests are to determine the presence of pneumonia and if present, to determine the etiologic agent [7]. Such as the presence of fever, leukocytosis, purulent sputum or tracheal aspirate and growth in culture suggest tracheobronchitis [7]. It is hard to determine the accurate diagnosis in LRTI hospitalized patients in ICU. The risk of LRTI in patients with mechanical ventilation is higher than others [6]. And increases day by day [3]. For diagnosis of respiratory infections; culture and Gram stain of bronchial aspirate, sputum, bronchial brushing, and biopsy samples are mostly used [3]. On Gram stain; the presence of >25 PMNs and growth in culture are the indicator of purulence so a sign of infection [8]. In the case of no growth in culture especially if antibiotic wasn't used or changed excludes pneumonia [6]. Although culture is useful; it

takes a long time. For planning the therapy; it is important to decide the presence of bacterial infection. Today; C-reactive protein (CRP), procalcitonin, and leukocyte counts are frequently used in the diagnosis of LRTI. In this study; the prognostic value of CRP, WBC, and procalcitonin in respiratory infections were evaluated in elderly patients hospitalized in intensive care units.

## Methods

Study population was included of 63 patients hospitalized in intensive care unit of Konya Numune Hospital during 2015. All patients were intubated and received mechanic ventilation for more than ten days. All patients had fever and findings in chest radiography. Cultures and Gram stain of 63 bronchial aspiration samples of the patients sent to the Microbiology laboratory were evaluated. VITEK 2 Compact system (bioMérieux, France) was used for identification of the strains. CRP was measured with an immunonephelometric assay on BN system (Siemens Healthcare Diagnostic Inc, Newark, USA) and the diagnostic cut-off value for CRP was accepted 5 mg/L. Procalcitonin was measured with ADVIA Centaur (Siemens Healthcare Diagnostic Inc., Newark, USA) and the diagnostic cut-off value for procalcitonin was accepted as 0.5 ng/mL. For WBC (White Blood Cell) count; XT 2000i (Roche Diagnostic) system was used, and  $>11000/\text{mm}^3$  values were accepted as a sign of infection. The diagnostic standard was taken as Gram stain with  $>25$  Polymorphonuclear Leukocytes (PMNs) in every field and quantitative culture with  $>100.000$  CFU/ml in bronchial aspirate samples. WBC, procalcitonin, and CRP were measured on the same day with culture taking time. The diagnostic value of WBC, procalcitonin, and CRP were evaluated according to diagnostic standard. The study was approved by the Ethics Committee of Konya Numune Hospital. Informed consent was not considered as necessary. Clinical information and laboratory data were obtained from hospital medical records and evaluated retrospectively.

Statistical analysis included sensitivity, specificity, positive predictive value, negative predictive value, and test validation. For comparison the mean of WBC, procalcitonin, and CRP independent samples t-test was used. Statistical significance was considered at  $p<0.05$ . The statistical analysis of our data was performed with the program SPSS, version 15.0.0 [9].

## Results

This hospital has 90 ICU beds. A total of 63 patients were included in this study. All patients were intubated and received mechanic ventilation. The mean age was 74.33. All patients had radiographic findings and fever. On Gram stain of 30 samples, bacteria and  $>25$  Polymorphonuclear Leukocytes (PMNs) were seen in every field. Also, samples were positive in quantitative culture with  $>100.000$  cfu/ml. These samples were considered as purulent. Of the patients with purulent bronchial aspirate samples; 18 were male, and 12 were female. All test values are shown in Table 1. Of the bronchial aspirate cultures; *A. baumannii* strains were isolated in 22 (73.3%), *E. coli* in 1 (3.3%), *Klebsiella pneumoniae* in 3 (10 %), *Pseudomonas aeruginosa* in 3 (10 %), and *S. aureus* in 1 (3.3%), patients. Results are shown in Table 2. There was no growth in culture and leukocyte on Gram stain of other 33 samples. The sensitivity, specificity, PPV and NPV for CRP were 100%, 3.1%, % 49.1 and 100%, respectively. The sensitivity, specificity, PPD and NPV for procalcitonin were 73.3%, 31.2%, 50% and 55.5%, respectively. The sensitivity, specificity, PPD and NPV for WBC were 56%, 40%, 52% and 61.9% respectively. Results are shown in Table 3. T-test was used in order to determine if the parameters vary in patients with purulent and not-purulent samples. According to t-test; CRP did not differ in two groups ( $p=0.346>0.05$ ). Procalcitonin was not found useful for determining the purulence ( $p=0.772>0.05$ ). No statistically significant difference was detected for WBC in two groups ( $p=0.559>0.05$ ).

**Table 1.** The distribution of test values in samples with purulence and bacteria in gram stain with positive bacterial cultures ( $>100.000$  cfu/ml)\* and samples with no purulence and bacteria in gram stain and no growth in culture\*\*.

	CRP (n)		Procalcitonin (n)		White Blood Cell (n)	
	$>5$ mg/L	$<5$ mg/L	$>0.5$ ng/mL	$<0.5$ ng/mL	$>11000/\text{mm}^3$	$<11000/\text{mm}^3$
With purulence and positive bacterial culture	30	0	21	9	19	11
Without purulence and no growth in culture	32	1	22	11	19	14

n=number of samples

**Table 2.** Bacteriological results of purulent samples.

Isolated bacterial agents	Number of samples
<i>A. baumannii</i>	22
<i>Klebsiella pneumoniae</i>	3
<i>Pseudomonas aeruginosa</i>	3

<i>E. coli</i>	1
<i>S. aureus</i>	1

**Table 3.** Sensitivity, specificity, positive predictive value and negative predictive values of tests.

	CRP (%)	Procalcitonin (%)	White Blood Cell (%)
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Sensitivity	100	73.3	56
Specificity	3.1	31.2	40
Negative predictive value	49.1	50	52
Positive predictive value	100	55.5	61.9

## Discussion

C-reactive protein is an acute-phase protein and present in plasma in normal level. In case of inflammation, tissue damage and other stimuli; it is synthesized by the liver and elevated in hours [10-12]. Several factors may cause an increase in CRP. In our study no statistically significant difference was detected for CRP in patients with purulent and not-purulent samples. The sensitivity of CRP was 100%, but specificity was very low. Procalcitonin is a prohormone of calcitonin secreted by thyroid C cells as a response to hypercalcemia. It is defined as an indicator of bacterial infection [10]. In literature, it is reported as valuable in patients admitted to hospital [11]. For bacterial blood stream infections; procalcitonin has been reported as a very important marker but nevertheless medical history, examination, and other laboratory tests are recommended by authors [13]. In this study; procalcitonin was found as less sensitive and more specific than CRP. It is reported as more accurate for differentiating bacterial infections from noninfective inflammation and viral infections [14]. In our study; WBC showed a low sensitivity and specificity. None of the tests had a statistical value for discriminating purulent and not-purulent samples. In fact, in literature, there are several about this topic. Hatherill et al. reported procalcitonin as a better diagnostic marker for determining the infection than WBC and CRP [15]. All patients included in this study were hospitalized in ICU. As it is known; increased hospital stay is a risk factor for lower respiratory tract infection, especially in elderly patients. In our study; the mean age was 73.3 years, and all patients were intubated and had hospitalization time for more than ten days with comorbidities such as trauma, chronic obstructive pulmonary disease cardiac arrest and others. In this group of patients; it is hard to determine if the patient is pneumonia or not. In this case, true diagnosis of respiratory infection and accurate treatment is essential and can reduce the mortality rate [7,16]. American Thoracic Society (ATS) suggests obtaining Low Respiratory Tract (LRT) samples for culture and microscopy before therapy [7]. Semi quantitative or quantitative cultures would help to select the appropriate antimicrobial [7]. Gram stain also could be directive in deciding for therapy. ATS suggests detecting another source of fever in negative Gram stain of tracheal aspirate in patients with fever as it is important to determine whether the patient needs an antibiotic therapy. Antimicrobial resistance is a very important global problem today. In the long-term hospitalization; it is more likely to isolate MDR pathogens in cultures. In this study of 30 samples; in 22 *A. baumannii* strains were isolated. Duration of endotracheal intubation is related with respiratory infections [8]. It is very important to separate colonizing from the respiratory infection. So the use of

unnecessary antimicrobial may decrease [8]. Gram stain is essential for determining the infectious origin [8]. Several studies evaluated the value of these tests in prognosis and diagnosis of respiratory infections. Nouvenne et al. reported that in their study; procalcitonin showed insufficient accuracy while crp over 61 mg/L was useful for diagnosis of respiratory infections in elderly patients [17]. Agarwal et al. compared the prognostic value of PCT, CRP and total leukocyte count with clinical risk scores and PCT was reported more associated with positive bacterial culture than CRP and total leukocyte count [18]. Another study from China; the relationship of PCT, and sputum culture were investigated and it was seen that procalcitonin did not increase in all cases with bacterial pneumonia [19]. Procalcitonin is commonly used in the diagnosis of respiratory infections but may not be sufficient alone for the diagnosis of bacterial respiratory infection [19]. Especially in intensive care units; there can be several factors that cause an increase of CRP, procalcitonin, and WBC. Or; especially in immunocompromised patients; the parameters could be affected. In anergic patients; WBC count may remain normal even in systemic inflammatory response syndrome [1]. Zhu et al. reported PCT as valuable in early diagnosis of respiratory infections, but procalcitonin exhibited a lower specificity [19]. To administer the patients in ICU are very hard. Thiem et al. research the prognostic value of CRP and WBC in LRTI in elderly patients and reported that these parameters are not valuable in predicting the prognosis of LRTI [20]. Generally patients hospitalized in intensive care units have multimorbidities. So for diagnosis probably more than one parameter would be required. Further prospective studies would be useful for determining the value of these tests for diagnosis of LRTI of patients in ICU.

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