Evaluation of severity scoring systems in patients with severe community acquired pneumonia

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Running head: Severity scoring systems in community acquired pneumonia

What is new? What is important?

Evaluation of severity scoring systems in patients with community-acquired pneumonia presents valuable starting point for the general assessment of the disease and hence enabling a better management of the patients, based on an accurately assessed severity of the disease.

ABSTRACT

Background: The aim of this study was to evaluate the ability of severity scoring systems to predict 30-day mortality in patients with severe community-acquired pneumonia.

Methods: The study included 98 patients aged ≥18 years with community acquired pneumonia hospitalized at the Intensive Care Unit of the University Clinic for Infectious Diseases in Skopje, Republic of North Macedonia, during a 3-year period. We recorded demographic, clinical and common biochemical parameters. Five severity scores were calculated at admission: CURB 65 (Confusion, Urea, Respiratory Rate, Blood pressure, Age ≥65 years), SCAP (Severe Community Acquired Pneumonia score), SAPS II (Simplified Acute Physiology Score), SOFA (Sequential Organ Failure Assessment Score) and MPM (Mortality Prediction Model). Primary outcome variable was 30-day in-hospital mortality.

Results: The mean age of the patients was 59.08 ± 15.76 years, predominantly males (68%). The overall 30-day mortality was 52%. Charlson Comorbidity index was increased in non-survivors (3.72 ± 2.33) and was associated with the outcome. All severity indexes had higher values in patients who died, that showed statistical significance between the analysed groups. The areas under curve (AUC) values of the five scores for 30-day mortality were 0.670, 0.732, 0,726, 0.785 and 0.777, respectively.

Conclusion. Widely used severity scores accurately detected patients with pneumonia that had increased risk for poor outcome, but none of them individually demonstrated any advantage over the others.

Key words: community-acquired pneumonia, intensive care, severity scores, prognosis, outcome

INTRODUCTION

Community acquired pneumonia (CAP) is the most common potentially fatal infectious disease and one of the leading causes for hospitalization, high health care costs and death worldwide. Approximately 20 % of all cases are admitted to hospital and 8-36 % among them require treatment in the intensive care unit (ICU) due to disease severity [1,2,3]. Today severe community acquired pneumonia is considered as a separate clinical entity with specific epidemiological characteristics, different distribution of aetiological agents, increased risk of complications such as acute respiratory distress syndrome

(ARDS) and septic shock, as well as a high mortality rate [4,5]. Therefore, accurate assessment of disease severity and early prediction of poor outcome is of crucial importance for successful management [6,7]. Eminent international societies such as Infectious Diseases Society of America (IDSA), American Thoracic Society (ATS), British Thoracic Society (BTS) and European Respiratory Society (ERS) have published guidelines for community acquired pneumonia that recommend a clinical approach based on the assessment of the disease severity [8]. Thus, several severity assessment tools and scoring systems were designed to enable patient stratification based on predicted mortalities. The most frequently used are the Pneumonia severity index (PSI) [9], CURB-65 (Confusion, Urea, Respiration rate, Blood Pressure, Age ≥ 65 years) [10], Severe Community Acquired Pneumonia Score (SCAP) [11] as well the criteria of the American Thoracic Society [12]. The purpose of these scoring models is to guide the clinical decision on the site of care upon the diagnosis and to assess the prognosis of community acquired pneumonia. Patients with the highest score have an increased risk of fatal outcome and should receive an intensive care treatment as severe pneumonia. In addition, in critically ill patients admitted at intensive care units, regardless the diagnosis, assessment of disease severity and mortality prediction is performed by commonly used severity indexes such as SAPS II (Simplified Acute Physiology Score) [13], SOFA (Sequential Organ Failure Assessment score) [14], APACHE II (Acute Physiology and Chronic Health Evaluation II) [15] and MPM (Mortality Prediction Model) [16].

At the ICU Department of the University Clinic for Infectious Diseases and Febrile Conditions, community acquired pneumonia is the second most frequently treated disease and is a leading cause of sepsis and acute respiratory distress syndrome, with a high mortality rate [17]. However, an evaluation of mortality prediction capacities of most commonly used severity indexes for this disease has not been conducted yet.

The aim of this study is to evaluate the ability of severity scoring systems to predict 30-day mortality in patients with severe community-acquired pneumonia.

MATERIAL AND METHODS

The study included 98 patients aged ≥18 years with community acquired pneumonia consecutively admitted at the Intensive Care Unit of University Clinic for Infectious Diseases in Skopje, Republic of North Macedonia. It was a retrospective, observational and group comparison study that took place from January 2016 to December 2018. The hospital ethical committee approved the research. Community acquired pneumonia was defined in accordance with IDSA/ATS guidelines as presence of at least one of the clinical symptoms of cough, sputum, fever, dyspnea, and pleural chest pain, plus at least more than one finding of coarse crackles on auscultation or elevated inflammatory biomarkers, in addition

to a new infiltrate on chest radiography. Exclusion criteria were: age <18 years, acquired immune deficiency syndrome, hospital-acquired pneumonia or nursing home residency. Outcome was defined as survival or death during the 30 days of hospital treatment. For the purpose of this analysis, patients were divided into two groups according to the outcome: survivors and non-survivors. For all patients the demographic data, comorbidities, clinical findings and most common laboratory tests were recorded. Severity indexes such as CURB-65, SCAP, SAPS II, MPM and SOFA score were calculated during the first 24 hours of admission. Charlson Comorbidity Index was calculated to predict the 10-year survival. The set of analysed clinical parameters included: mental status (assessed with Glasgow Coma Scale), body temperature, respiratory rate, blood pressure, heart rate, and signs of shock (defined as mean arterial pressure <65 mmHg regardless of the adequate therapy with intravenous fluids). Biochemical parameters that were measured upon admission were: blood count, fasting glucose levels, serum urea, creatinine, electrolytes, lactate-dehydrogenase, bilirubin level, hepatic transaminases, serum albumin, C-reactive protein, procalcitonin and gas analyses. All laboratory tests were performed by standard methods in the biochemical laboratory at the hospital. Patients received treatment in accordance with the national CAP guidelines and for the purpose of this study they were monitored up to 30 days of hospitalization.

Statistical analysis

Continuous variables were expressed as mean and standard deviation (SD), whereas categorical variables were expressed as frequency (percentage), as appropriate. Continuous variables were analysed by Student's t-test and categorical variables were assessed with the Chi-square test. Univariate analysis was performed for predicting 30-day mortality. Multivariate analysis using stepwise logistic regression analysis was conducted for all variables that were found to have a P value of ≤0.1 on univariate analysis. To assess the usefulness of existing pneumonia severity scores for predicting the prognosis of CAP, we performed Receiver Operating Characteristic (ROC) curve analysis with application of the Bonferroni correction for two-way comparisons of the AUCs of pneumonia severity scores. All statistical tests were two-tailed and value of $P < 0.05$ was considered as significant. Data were analysed with SPSS 23.0 software (SPSS, Chicago, IL).

RESULTS

A total of 98 patients were enrolled in the study. The mean age was 59.08 ± 15.76 years and 68% of the patients were males. The overall 30-day mortality rate was 52 %. Charlson Comorbidity Index in non-survivors was 3.72 ± 2.33 that showed significant association with the outcome. Patient who died had shorter duration of ICU stay, in average of 11 days. The highest frequency of patients was registered in

winter and spring, 42 % and 25 %, respectively. The baseline characteristics of the study population, stratified by the outcome, are presented in Table 1.

Clinical findings observed at admission in ICU such as mental status, body temperature, respiratory rate, heart rate and signs of shock are provided in Table 2. Septic shock and encephalopathy were clinical parameters that significantly associated with the outcome.

Table 3 presents the biochemical parameters analysed in the study population, stratified into two groups according to the outcome. Non-survivors had higher leukocyte count, elevated serum levels of urea, glucose, aminotransferases, LDH and lactates. Both survivors and non-survivors had increased values of inflammatory markers such as C-reactive protein and procalcitonin at admission, but their values were not significantly associated with the outcome. Blood gas analyses showed that the deceased patients had lower pH value and low PaO_2/FiO_2 ratio, presenting worse respiratory function in this group of critically ill patients.

The values of severity scoring systems SAPS II, SOFA, MPM, CURB 65 and SCAP for both survived and non-survivors are shown in Table 4. All evaluated indexes are significantly different between the groups, i.e. the deceased patients had higher values in every score. ROC analysis was performed to compare the predictive values of the severity indexes and curves are presented on Figure 1. Due to the small number of patients in which SCAP score was calculated, a ROC curve was not calculated for this score and was excluded from the analysis. The analysis showed that all indexes have area under the curve (AUC) above 0.5 presenting that they all have good predicting ability. The highest value of AUC was measured for MRM0 score and the lowest was obtained for CURB-65 (Table 5).

DISCUSSION

Community acquired pneumonia remains one the leading causes of death worldwide, thus a successful management requires an accurate assessment of disease severity. A primary goal of this study was to evaluate the predictive ability of the most commonly used severity scoring systems in patients with severe community acquired pneumonia. SAPS II, MPM0, MPM24, SOFA, SCAP and CURB-65 were analysed in the first 24 hours of patient's hospital admission. The key finding of the analysis was that the tested severity indexes adequately identified patients with pneumonia who have a high risk of poor outcome, they all have a similar predictive capacity, but none of them showed superiority over the others regarding mortality prediction.

In our study, 30-day mortality was 52 %, which is high, but it is still within the range of published data [18,19,20]. This high mortality rate can be explained with the fact that the study analysed a relatively

small number of patients from only one centre in a tertiary health institution, and additionaly the study was conducted at the only intensive care unit in the country for patients with the most severe infectious diseases, including patients with complications such as septic shock and ARDS, patients who need mechanical ventilation, haemodialysis etc.

The mean age of the patients was 59.08 ± 15.76 years and males were predominant with 68 %. However, gender and age did not show association with the outcome, unlike many studies which report advanced age as an independent risk factor [19,21]. The reason for this discrepancy in the results could be the design of the analysed sample, meaning that the age was not a limiting factor in this study, but it included all patients above the age of 18. Similar to the findings of our study, Brancarti and associates noted that even after a two-year observation, age has shown no correlation with the mortality rate of patients with community acquired pneumonia [22].

The severity of the comorbidities and prediction of 10-year survival were assessed by Charlson comorbidity index, which showed a higher value in patients that died and correlated with an increased risk of poor outcome. This result corresponds with the studies that confirm the predictive value of Charlson comorbidity index in patients with pneumonia [23,24]. Clinical parameters which showed statistically significant difference between the deceased and the survived patients were encephalopathy and septic shock. These findings are in agreement with published data which suggest that patients with multiple organ dysfunction, sepsis/septic shock, respiratory failure and decompensated comorbidity have a higher risk for death [25-27]. Biochemical parameters that showed a significant association with the mortality were platelets count, serum lactates and pH value as markers of acidosis, a result which has also been confirmed in several studies [28,29]. Biomarkers such as leukocytes, procalcitonin and C-reactive protein were not significantly associated with the mortality in our study, although there was a difference in the values registered between the deceased and the survived patients. There are variable data regarding the significance of these biomarkers as outcome predictors. Most studies suggest that procalcitonin is more sensitive than the C-reactive protein in differentiating the bacterial etiology of pneumonia, but that both have little correlation with the severity and the outcome of the disease [30-32].

Severity scoring models SAPS II, SOFA, MPM0, MPM24, SCAP and CURB-65 score were evaluated in our study. With logistic regression all indexes proved to have a significant association with the mortality and all were identified as independent outcome predictors. Many studies analyse and compare these scores in order to determine the superior one for mortality prediction but they report different results regarding their specificity, sensitivity and predictive values. Some suggest that the PSI score better identifies low mortality rate in young patients without comorbidities, whereas the CURB score is more useful in elderly and more severe patients [33-35]. On the other hand, the ATS criteria and

SCAP show better prediction of hospitalization at intensive care units [36,37,38]. In order to compare the predictive values of the severity indexes analyzed in this study, we conducted a ROC analysis and found area under a curve for each index individually as follows: 0,670 for CURB–65, 0.732 for SAPS II, 0.726 for SOFA, 0.785 for MPM0, and 0.777 for MPM24 score. This result corresponds with the data from the studies that confirm the similarity between these indexes in their ability to predict the mortality in patients with severe community acquired pneumonia [39-42].

CONCLUSION

Severity scoring systems commonly used to predict mortality in patients with community acquired pneumonia were found to be equally effective for the purpose of this study. These indexes provide more objective assessment of disease severity and contribute in clinical practice for early and accurate identification of patients with increased risk of poor outcome.

Introducere: Scopul studiului a fost de evalua capacitatea predictivă a scorurilor de severitate ale pneumoniei pentru mortalitatea la 30 zile

Metode: Au fost incluşi 98 de pacienţi cu vârste peste 18 ani diagnosticaţi cu pneumonie comunitară şi spitalizaţi pe parcursul a trei ani în secţia de terapie intensivă a Spitalului Clinic de Boli Infecţioase din Skopje. Au fost înregistrate date demografice, clinice şi biochimice. Au fost calculate cinci scoruri de severitate la internare CURB 65 (Confusion, Urea, Respiratory Rate, Blood pressure, Age ≥65 years), SCAP (Severe Community Acquired Pneumonia score), SAPS II (Simplified Acute Physiology Score), SOFA (Sequential Organ Failure Assessment Score) şi MPM (Mortality Prediction Model). Efectul primar căutat a fost mortalitatea la 30 zile de la internare.

Rezultate: Pacienţii au avut vârstă medie de 59.08 ± 15.76 şi au fost preponderent bărbaţi (68%). Mortalitatea la 30 de zile a fost de 52%. Indexul de comorbiditate Charlson era mai mare la pacienţii non-supravieţuitori (3.72 ± 2.33). Toate scorurile de severitate au fost mai mari la pacienţii care au decedat. AUC pentru mortalitatea la 30 de zile pentru scoruri a fost de 0.670, 0.732, 0,726, 0.785 şi respectiv 0.777.

Concluzii: Scorurile de severitate au detectat pacienţii cu pneumonie ce au avut risc de a dezvolta complicaţii severe însă niciunul nu a fost superior.

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Table 1. Baseline characteristics of study population stratified by the outcome

	Survivors n=47	Non-survivors n=51	P -value
Age (years; mean ±SD[a])	56.43 ± 13.25	61.53 ± 17.54	0.10
Male (n, %)	33 (70)	34 (67)	0.82
Female (n, %)	14 (30)	17 (33)	
Charlson Comorbidity Index (value; mean ± SD)	2.53 ± 2.00	3.72 ± 2.33	0.02
ICU[b] stay (days; mean ± SD)	15.89 ± 11.31	10.65 ± 8.56	0.01
Season of hospitalization (n, %)			
Spring	14 (56)	11 (44)	
Summer	10 (59)	7 (41)	
Autumn	9 (60)	6 (40)	
Winter	14 (34)	27 (66)	
Overall 30-day mortality (n, %)	47 (48)	51 (52)	

[a]SD: standard deviation; [b]ICU: intensive care unit

Table 2. Clinical findings in patients with severe community-acquired pneumonia by the outcome

	Survivors n=47	Non-survivors n=51	P-value
Body temperature (°C; mean ± SD[a])	37.79 ± 0.98	37.35 ± 0.86	0.47
Heart rate (beats/min; mean ± SD)	107.74 ± 21.09	110.39 ± 23.53	0.56
Respiratory rate (breaths/min; mean ± SD)	32.11 ± 11.11	30.67 ± 6.84	0.43
Signs of shock -with shock (n, %) -without shock (n, %)	5 (23) 42 (55)	17 (77) 34 (45)	0.01
Mental status -altered (n, %) -normal (n, %)	9 (26) 38 (59)	25 (74) 26 (41)	0.01

[a]SD: standard deviation

Table 3. Biochemical parameters of patients with severe community-acquired pneumonia by the outcome

Parameter	Survivors n=47	Non-survivors n=51	P-value
Leucocyte count (x10^9/L; mean±SD[a])	12.96 ± 7.08	14.98 ± 10.72	0.27
Platelets (x10^9/L; mean±SD)	242.70 ± 133.75	192.65 ± 95.53	0.03
Glucose (mmol/L; mean±SD)	8.26 ± 3.84	9.51 ± 4.95	0.16
Urea (mmol/L; mean±SD)	11.18 ± 8.17	13.95 ± 8.66	0.10
Creatinine (mmol/L; mean±SD)	111.60 ± 80.29	137.22 ± 110.49	0.19
ALT[b](IU/L; mean±SD)	60.70 ± 61.23	104.62 ± 222.09	0.19
AST[c] (IU/L; mean±SD)	67.24 ± 53.78	165.84 ± 398.91	0.09
Albumin (gr/L; mean±SD)	28.57 ± 5.32	28.41 ± 6.05	0.90
LDH[d] (IU/L; mean±SD)	1320.63 ± 795.74	2153.04 ± 3282.19	0.10
CRP[e] (mg/L; mean±SD)	255.28 ± 152.45	227.42 ± 154.92	0.37
PCT[f] (ng/mL; mean±SD)	14.46 ± 23.75	26.36 ± 58.17	0.42

Lactates (mmol/L;mean±SD)	2.45 ± 1.22	3.31 ± 2.62	0.04
pH (value; mean±SD)	7.41 ± 0.10	7.36 ± 0.13	0.04
PaO_2/FiO_2 ratio (value; mean ± SD)	142.91 ± 93.15	121.60 ± 73.64	0.21

[a]SD: standard deviation, [b]ALT: alanine transferase, [c]AST: asparat transferase, [d]LDH: lactate dehydrogenase, [e]CRP: C-reactive protein, [f]PCT: procalcitonin

Table 4. Severity indexes in patients with severe community-acquired pneumonia stratified by the outcome

Index	Survivors n=47	Non-survivors n=51	P -value
SAPS II[a] (value; mean±SD[b])	35.95 ± 14.33	48.68 ± 12.96	0.001
SOFA[c] (value; mean±SD)	5.0 ± 2.59	7.82 ± 3.69	0.001
MPM0[d] (value; mean±SD)	18.61 ± 17.32	33.10 ± 20.77	0.001
MPM24[e] (value; mean±SD)	21.57 ± 20.05	40.43 ± 24.37	0.001
CURB-65[f] (value; mean±SD)	2.03 ± 1.16	2.65 ± 0.95	0.024
SCAP[g](value; mean±SD)	10.80 ± 10.69	27.86 ± 11.06	0.001

[a]SAPS II (Simplified Acute Physiology Score); [b]SD: standard deviation; [c]SOFA (Sequential Organ Failure Assessment); [d] MPM0 (Mortality Prediction Model at admission), [e]MPM24 (Mortality Prediction Model after 24 hours); [f]CURB-65 (Confusion, Urea, Respiration rate, Blood Pressure, Age ≥ 65 years); [g]Severe Community-Acquired Pneumonia Score (SCAP)

Table 5. Areas Under Curves of severity indexes in patients with severe community acquired pneumonia

Variable	Area	Std. Error[a]	Asymptotic Sig.[b]	95% Confidence Interval
SAPS II	0.73	0.06	0.002	0.60 - 0.85
MPMII0	0.78	0.05	0.001	0.67 - 0.89
MPMII24	0.77	0.06	0.001	0.66 - 0.89
SOFA	0.72	0.06	0.002	0.60 - 0.85
CURB-65	0.67	0.06	0.021	0.53 - 0.80

a. Under the nonparametric assumption
b. Null hypothesis: true area = 0.5

Figure 1. ROC analyses of severity indexes in patients with severe community acquired pneumonia