Usefulness of different prognostic scores for AECOPD: APACHE II, BAP65, 2008, and CAPS scores

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Purpose The purpose of this study was to compare four different scores [Acute Physiology and Chronic Health Evaluation (APACHE II); elevated blood urea nitrogen, altered mental status, pulse >109/min, age >65 years (BAP65); chronic obstructive pulmonary disease (COPD) and Asthma Physiology Score (CAPS); and 2008 score) to test their predictive properties for the need of mechanical ventilation (MV) and short-term mortality in patients with acute exacerbation COPD (AECOPD).

Patients and methods This study enrolled 100 consecutive patients with acute exacerbation COPD, over a 6-month duration, admitted to the Emergency Department in Alexandria Main University Hospitals. The four scores were calculated for each patient, and clinical data and outcome (need for MV and mortality during hospitalization or within a week after discharge) were recorded.

Results Their mean age was 61.1 ± 10.7 years, and 88% were males. Duration of hospital stay was less than or equal to 20 days in 67%. Mortality rate was 4%. Overall, 40% required MV. Blood urea nitrogen, pulse, CO₂, pH, altered consciousness, and white blood cell were significant predictors of mortality in univariate but not multivariate analysis. Previous MV, cyanosis, and paradoxical abdominal movement were significant predictors of need for MV. The highest area under the receiver operating characteristic curve was that of APACHE II score regarding either mortality prediction [area under the curve (AUC), 0.982; P=0.001] or

Introduction

Chronic obstructive pulmonary disease (COPD) is now reported to be the fourth leading cause of death worldwide and expectedly will be the third by 2020 [1–3]. Exacerbations occur in moderate-severe forms, rather than mild COPD [4] The American Thoracic Society and European Respiratory Society define COPD exacerbation [acute exacerbation COPD (AECOPD)] as an acute change in patient's dyspnea, cough, or sputum that is beyond normal variability and that is sufficient to warrant a change in therapy [5]. Scores for mortality prediction in AECOPD could aid in decisions regarding the level of care and allow early hospital discharge, thus reducing morbidity and mortality. The BODE index, which can predict mortality in patients with stable COPD, is not suitable in the setting of acute exacerbation [6]. Other tools for mortality prediction are CURB-65 (confusion, urea, respiratory rate, blood pressure, and 65 years of age or older), BAP65 [elevated blood urea nitrogen (BUN), altered mental status, pulse >109/ min, and age >65 years], and DECAF score (dyspnea, eosinopenia, consolidation, acidaemia, and atrial fibrillation) [7–9].

need for MV (AUC, 0.959; P<0.001), followed by BAP65 score for mortality prediction (AUC, 0.967; P=0.002) and 2008 score for predicting the need for MV (AUC, 0.851; P<0.001).

Conclusion All studied scores correlated significantly with mortality, but only APACHE II and 2008 score correlated significantly with the need for MV. The highest area under the receiver operating characteristic curve was that of APACHE II score regarding either mortality or need for MV prediction. Previous need for MV was the most important predictor for the need for MV. The routine use of these practical scores in triage of patients may direct early interventions to reduce mortality rate.

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The aim of this study was to compare four different scores [Acute Physiology and Chronic Health Evaluation (APACHE II), BAP65, CAPS (COPD and Asthma Physiology Score), and 2008 scores] and test their predictive properties for need of mechanical ventilation (MV) and short-term mortality during hospital admission or within a week after discharge to home in a population of patients hospitalized with AECOPD.

Patients

This study was conducted on 100 consecutive adult patients with AECOPD, over a 6-month duration, admitted to the Emergency Department, Alexandria Main University Hospitals. We included patients older than 40 years, both sexes, smoking history of more than 10 cigarette pack years, primarily diagnosed as having COPD (supported by spirometric evidence

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of airflow obstruction during stable state if present) presenting with acute exacerbation of COPD (an event in the natural course of the disease characterized by a change in the patient's baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations and may have warranted a change in regular medication in a patient with underlying requiring COPD) [3] hospital admission. We excluded patients experiencing lifethreatening comorbidities such as any malignancies, liver failure, or end-stage renal disease; patients with other lung diseases; patients who did not wish to participate; patients with previous inclusion in the study; patients with exacerbation owing to pneumothorax; and patients with primary reason for admission other than AECOPD. Informed consents had been taken from all participants before their inclusion in the study. Approval of Research Ethics committees of the Faculty of Medicine, Alexandria University, had been obtained before the study.

Methods

This prospective cohort study enrolled 100 patients with COPD exacerbation who attended Emergency Department of Alexandria Main University Hospital and required admission. All patients were subjected to thorough history taking. Assessment of stable-state dyspnea was based on the extended Medical Research Council Dyspnea Score [10]. Cause of AECOPD, previous need for MV (noninvasive or invasive MV), and long-term home oxygen therapy were reported.

Clinical examination included primary survey of airway, breathing, and circulation. Secondary survey consisted of full clinical examination including number of signs of severity (cyanosis, use of accessory muscles, paradoxical inspiratory abdominal movement, asterixis, neurological impairment, and lower limb edema) [11]. ECG, Glasgow coma scale [12] assessment, random blood sugar measurement, complete blood picture, arterial blood gases (ABG), serum urea, BUN and creatinine, and serum sodium, potassium, and albumin were examined. Chest radiograph was done and computed tomography if needed.

The following scores were calculated on admission: APACHE II [13], BAP65 [7], CAPS [14], and 2008 score [15] (Table 1). Patients' prognosis was recorded. Outcome measures included the need for MV, length of hospital stay, and in-hospital mortality. Accordingly, we classified our patients into different groups, as either

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2008 score	Points
Age (years)	
<70	0
≥70	1
MRC (baseline, steady state)	
0–1	0
2–3	1
4–5	2
Number of signs of severity at entry	
0	0
1–2	2
3 and more	3

Signs of severity: cyanosis, use of accessory inspiratory muscles, paradoxical abdominal movement, asterixis, neurological impairment, and lower limb edema. MRC, Medical Research Council.

nonsurvivors or survivors, and the latter group was further classified according to their need for MV. The study was approved by our institutional research ethics committee. Informed consent was obtained from all individual participants included in the study.

Statistical analysis of the data [16]

Data were fed to the computer and analyzed using IBM SPSS software 20.0. (IBM Corp., Armonk, New York, USA) [17] Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, SD, and median. Significance of the obtained results was judged at the 5% level. χ^2 test was used for categorical variables, to compare between different groups. Fisher exact or Monte Carlo correction was used for correction for χ^2 when more than 20% of the cells have expected count less than 5. Student *t* test was used for normally distributed quantitative variables, to compare between two studied groups. Mann-Whitney test was used for abnormally distributed quantitative variables, to compare between two studied groups. Receiver operating characteristic (ROC) curve was plotted, where area under the receiver operating characteristic curve (AUROC) denotes the diagnostic performance of the test. Regression was used to detect the most independent/affecting factor for MV.

Results

Our study enrolled 100 patients. Demographic and clinical data are shown in Table 2. Mean arterial pH, PaCO₂, PaO₂, HCO₃, and O₂ saturation were 7.34 ±0.07, 63.71±18.21 mmHg, 52.67±9.04 mmHg, 32.22 ±6.18 mEq/l, and 80.7±10.11%, respectively. Acidotic

	Survived (<i>N</i> =96) [<i>n</i> (%)]	Nonsurvived (<i>N</i> =4) [<i>n</i> (%)]	Test of significance	Р	Su	rvived	Test of significance	Р
					Mechanically ventilated (<i>N</i> =36) [<i>n</i> (%)]	Nonmechanically ventilated (<i>N</i> =60) [<i>n</i> (%)]		
Sex								
Male	85 (88.5)	3 (75.0)	$\chi^2 = 0.667$	FEP=0.405	30 (83.3)	55 (91.7)	$\chi^2 = 1.540$	FEP=0.321
Female	11 (11.5)	1 (25.0)			6 (16.7)	5 (8.3)		
Age (years)	60.94 ±10.83	65.0±3.56	<i>t</i> =0.745	0.458	58.97±9.49	62.12±11.48	<i>t</i> =1.384	0.170
Comorbidities								
DM	22 (22.9)	1 (25.0)	$\chi^2 = 0.009$	FEP=1.000	6 (16.7)	16 (26.7)	$\chi^2 = 1.274$	0.259
Hypertension	15 (15.6)	1 (25.0)	χ ² =0.251	FEP=0.508	5 (13.9)	10 (16.7)	$\chi^2 = 0.132$	0.717
OSA	4 (4.2)	0 (0.0)	$\chi^2 = 0.174$	FEP=1.000	3 (8.3)	1 (1.7)	$\chi^2 = 2.504$	^{FE} P=0.147
IHD	8 (8.3)	0 (0.0)	$\chi^2 = 0.362$	FEP=1.000	2 (5.6)	6 (10.0)	$\chi^2 = 0.582$	FEP=0.706
AF	6 (6.3)	2 (50.0)	χ ² =9.986*	FEP=0.031*	3 (8.3)	3 (5.0)	$\chi^2 = 0.427$	FEP=0.669
Previous need for MV	28 (29.2)	3 (75.0)	$\chi^2 = 3.771$	^{FE} P=0.087	25 (69.4)	3 (5.0)	χ ² =45.230*	<0.001*
Respiratory rate cycle/min	32.34 ±6.16	34.25±19.12	<i>t</i> =1.999	0.855	33.6±8.89	31.58±3.55	<i>t</i> =1.307	0.198
Heart rate beat/min	89.09 ±14.59	126.25 ±17.97	<i>t</i> =4.953*	<0.001*	90.58±16.80	88.20±13.15	<i>t</i> =0.773	0.441
MAP (mmHg)	95.06 ±14.94	81.68±23.50	<i>t</i> =1.717	0.089	92.46±17.30	96.62±13.23	<i>t</i> =1.327	01.188
Temperature (°C)	37.46 ±0.66	38.23±1.52	<i>t</i> =1.003	0.389	37.49±0.75	37.45±0.60	<i>t</i> =0.303	0.762
GSC	14.58 ±1.04	11.5±1.91	<i>U</i> =7.0*	<0.001*	14.58±1.68	14.98±0.13	<i>U</i> =917.50*	0.006*
Asterixis	6 (6.3)	1 (25.0)	χ ² =2.074	FEP=0.255	5 (13.9)	1 (1.7)	$\chi^2 = 5.736$	FEP=0.027*
Neurological impairment	8 (8.3)	4 (100.0)	χ ² =30.556*	FEP<0.001*	7 (19.4)	1 (1.7)	χ ² =9.309	^{FE} P=0.004*
LL edema	43 (44.8)	3 (75.0)	$\chi^2 = 1.411$	FEP=0.331	24 (66.7)	19 (31.7)	$\chi^2 = 11.146^*$	0.001*
Cyanosis	17 (17.7)	4 (100.0)	$\chi^2 = 15.675^*$	FEP=0.002*	14 (38.9)	3 (5.0)	$\chi^2 = 17.732^*$	< 0.001*
Accessory inspiratory muscle use	45 (46.9)	4 (100.0)	χ ² =4.337	^{FE} P=0.054	21 (58.3)	24 (40.0)	χ ² =3.037	0.081
Paradoxical abdominal movement	33 (34.4)	4 (100.0)	χ ² =7.095*	^{FE} P=0.017*	24 (66.7)	9 (15.0)	χ ² =26.625*	<0.001*

Table 2 Comparison between the different groups according to clinical data

AF, atrial fibrillation; DM, diabetes mellitus; IHD, ischemic heart disease; LL, lower limb; MAP, mean arterial blood pressure; MV, mechanical ventilation; OSA, obstructive sleep apnea. χ^2 : χ^2 test for comparing between the different groups. ^{FE}*P*: *P* value for Fisher's exact for χ^2 test for comparing between different groups. *t*, *P*: *t* and *P* values for Student *t* test for comparing between the different groups. *U*, *P*: *U* and *P* values for Mann–Whitney test for comparing between the two groups. *Statistically significant at *P* less than or equal to 0.05.

exacerbations (pH<7.35) were present in 48 (48%) patients.

For all studied patients, the mean values of the four studied scores on admission were as follows: APACHE II score 14.43±6.40, CAPS 31.62±7.19, BAP65 score 0.89±0.96, and 2008 score 3.11±1.37. Duration of hospital stay ranged from 3 to 48 days, with a mean of 16.92±9.66 days. A total of 67 (67%) patients stayed at hospital for less than or equal to 20 days or less. Moreover, 40 (40%) patients required MV (15 required noninvasive and 25 required invasive MV). Overall mortality rate was 4% (all were on invasive MV). For study analysis and comparison, patients were classified according to clinical outcome into nonsurvivors and survivors, with the latter being further subdivided according to their need for MV.

Table 2 shows the comparison between different groups regarding demographic and clinical data. As for laboratory investigations, comparing survivors with nonsurvivors, ABG analysis showed that both pH and partial pressure of carbon dioxide in arterial blood (PaCO₂) were the only statistically significantly different parameters (P=0.050 and 0.003, respectively). BUN was significantly higher among nonsurvivor group as well (P=0.043). Comparing patients who required MV and those who did not

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	AUC	Р	95% CI	Cut off	Sensitivity	Specificity	PPV	NPV
APACHE II	0.982*	0.001*	0.955-1.008	>22	100.0	95.83	50.0	100.0
BAP65 score	0.967*	0.002*	0.907-1.028	>1	100.0	78.12	16.0	100.0
2008 score	0.948*	0.002*	0.900-0.996	>4	100.0	89.58	28.6	100.0
CAPS	0.896*	0.008*	0.758-1.033	>43	75.0	94.79	37.5	98.9

Table 3 Agreement (sensitivity and specificity) for Acute Physiology and Chronic Health Evaluation II, CAPS, BAP65, and 2008 scores to predict mortality

APACHE, Acute Physiology and Chronic Health Evaluation; AUC, area under the curve; BAP65, elevated blood urea nitrogen, altered mental status, pulse more than 109/min, age more than 65 years; CAPS, chronic obstructive pulmonary disease (COPD) and Asthma Physiology Score; CI, confidence intervals; NPV, negative predictive value; PPV, positive predictive value. *Statistically significant at *P* less than or equal to 0.05.

require, all ABG components showed significant difference (P<0.001). There was no significant difference regarding BUN, but creatinine levels showed significant difference (P=0.002). Serum albumin as well was significantly low among patients who required MV (P=0.002).

Comparison between the different studied groups regarding the four scores revealed that all studied scores were significantly higher among nonsurvivors than survivors: APACHE II score (28.50±4.04 vs. 13.84±5.79, respectively; P<0.00), CAPS score (43.25±7.27 vs. 31.14±6.80, respectively; P<0.00), BAP65 score (3.25±0.96 vs. 0.79±0.83, respectively; P<0.00), and finally, 2008 score (5.0±0.0 vs. 3.03±1.34, respectively; P=0.002). Comparing patients who required MV with patients who did not, only APACHE II and 2008 score were significantly different (19.36±4.28 vs. 10.53±3.66, respectively for APACHE II and 4.0±0.72 vs. 2.45±1.29, respectively, for 2008 score), with P value less than 0.001 for each.

Regarding prediction of mortality, BUN, urea, pulse, CO_2 , pH, altered level of consciousness, and white blood cell (WBC) were all significant in univariate but not in multivariate analysis. Performance of different scores regarding mortality prediction is shown in Table 3 and Fig. 1. APACHE II had the highest area under the curve and highest specificity followed by BAP65, and all showed significant correlations with mortality.

As for predicting the need for MV, multivariate logistic regression showed significant correlations with previous need for MV, cyanosis, paradoxical abdominal movement, $PaCO_2$, HCO_3 , O_2 saturation%, and elevated creatinine levels (P=0.001, 0.018, 0.007, 0.004, 0.013, 0.006, and 0.045, respectively). The most powerful predictor was history of previous MV. Performance of different scores regarding predicting the need for MV is shown in Table 4 and Fig. 2. APACHE II had the





ROC curve for APACHE II, CAPS, BAP65, and 2008 scores to predict mortality. APACHE, Acute Physiology and Chronic Health Evaluation; BAP65, elevated blood urea nitrogen, altered mental status, pulse more than 109/min, age more than 65 years; CAPS, chronic obstructive pulmonary disease (COPD) and Asthma Physiology Score; ROC, receiver operating characteristic.

highest area under the curve followed by 2008 score. Only APACHE II and 2008 score showed significant correlations.

Discussion

Predictors of mortality in stable disease do not reflect mortality during AECOPD [18]. Few clinical scores have been tested to assess the prognosis of AECOPD to help clinicians take proper decisions regarding admission and level of care [7,9,19]. In this study, we compared different studied groups regarding individual parameters included in the four scores followed by comparing the performance of the four different scores regarding their ability not only to predict mortality but the need for MV as well. The majority of our patients were males owing to the fact that smoking is more prevalent among males in our

	AUC	Р	95% CI	Cut off	Sensitivity	Specificity	PPV	NPV
APACHE II	0.959*	<0.001*	0.926-0.992	>14	92.50	83.33	78.7	94.3
2008 score	0.851*	<0.001*	0.779-0.923	>3	77.50	76.67	68.9	83.6
CAPS	0.580	0.177	0.457-0.703	>30	55.0	50.0	42.3	62.5
BAP65 score	0.525	0.675	0.407-0.643	>1	27.50	76.67	44.0	61.3

Table 4 Agreement (sensitivity and specificity) for Acute Physiology and Chronic Health Evaluation II, CAPS, BAP65, and 2008 scores to predict mechanical ventilation patients

APACHE, Acute Physiology and Chronic Health Evaluation; AUC, area under the curve; BAP65, elevated blood urea nitrogen, altered mental status, pulse more than 109/min, age more than 65 years; CAPS, chronic obstructive pulmonary disease (COPD) and Asthma Physiology Score; CI, confidence intervals; NPV, negative predictive value; PPV, positive predictive value. *Statistically significant at *P* less than or equal to 0.05.

Figure 2



ROC curve for APACHE II, CAPS, BAP65, and 2008 scores to predict the need for mechanical ventilation. APACHE, Acute Physiology and Chronic Health Evaluation; BAP65, elevated blood urea nitrogen, altered mental status, pulse more than 109/min, age more than 65 years; CAPS, chronic obstructive pulmonary disease (COPD) and Asthma Physiology Score; ROC, receiver operating characteristic.

society. Cardiovascular comorbidities were common in our patients, and half the nonsurvivors experienced atrial fibrillation (AF) versus 6% of survivors, with P=0.031. An Australian study revealed that cardiovascular events contributed to 26% of longterm mortality following the first episode of AECOPD [20]. Others reported that in patients admitted to the hospital for AECOPD, cardiac troponin elevation was an independent predictor of all-cause mortality [21]. Similarly, another study reported that 33.3% of deceased patients had AF, whereas none in the discharged group had AF [22,23]. The common association of AF and COPD may be attributed to blood gases derangements in COPD and can be linked to increased mortality. Thus, it is important to screen patients with AECOPD for concomitant acute cardiac events.

Among all ABG parameters, only academic exacerbations and PaCO₂ were significantly higher in nonsurvivors than survivors, with P=0.05 and 0.003, respectively. Another study matched our results, where PaCO₂ was high and pH was significantly low in the nonsurviving group, whereas other parameters were statistically insignificant, suggesting a poor survival if exacerbation is accompanied by type 2 respiratory failure at the time of admission [24]. WBC, BUN, and urea were also significantly higher in nonsurvivors (P=0.023, 0.043, and 0.042, respectively). High BUN might be attributed to impaired circulation or acute kidney injury leading to poor outcomes. Comparing groups that required MV or not, serum creatinine and albumin differed significantly (P=0.002 for both). Low albumin levels may represent underlying poor nutrition before admission, eventually leading to poor hospital outcomes [25,26].

Patients who required intubation had a mortality rate of 16% (four of 25), which was significantly higher than patients who did not require intubation, as none of them died, P=0.003. This either reflects the severity of the underlying COPD or the sequence of ventilatorassociated complications. Others reported mortality rate of 21.6% among intubated patients, which was significantly higher than nonintubated patients (mortality rate 4.2%) [27,28]. These results highlight the value of noninvasive ventilation; nevertheless, it is important to ensure close monitoring because noninvasive ventilation failure has been linked to high mortality [17].

Overall mortality was 4% in our study. Shorr *et al.* [7] reported similar mortality rate (4%). The 2008 UK National COPD Audit showed mortality rate of 7.7% [29]. Steer *et al.* [9] reported higher mortality rates of 10.4%, which may be because they enrolled patients older than our study population. The mortality rate ranged from 4 to 14% in the Asia-Pacific region based on different cohorts and was as high as 25% for patients requiring ICU admission [30–33]. On

the contrary, others reported lower mortality rates, where the in-hospital mortality rate was 2% [34]. This difference may reflect the variation in threshold for hospital admission among different countries and variation in mean age of population enrolled; in addition, some studies enrolled only patients requiring ICU admission. Finally, this variation may be attributed to difference in severity of COPD and quality of care. Roche et al. [15] found that age is an independent risk factor for inhospital mortality. Similarly, a Japanese study found a higher mortality in patients with older age [30]. Yousif and El Wahsh [35] found that the nonsurvivors had a statistically significant higher age, with P=0.012. In the present study, we found no correlation between age and mortality; moreover, on comparing between survivors and nonsurvivors, there was no significant difference regarding age, with P=0.458. We attribute our findings to the relatively small sample size.

Limsuwat *et al.* [27] using multivariate analysis demonstrated that the mortality rate was significantly associated with a low mean arterial blood pressure [odds ratio (OR) 0.91, 95% confidence interval (CI)]s, an intubation event (OR 6.12, 95% CI), and an elevated BUN (OR 1.06, 95% CI) (P<0.05 each). In the current study, BUN, urea, pulse, CO₂, pH, altered level of consciousness, and WBC were all significant in univariate but not multivariate analysis.

On the contrary, regarding prediction of need for MV, multivariate analysis revealed that history of previous need for MV was a powerful predictor (OR 43.59, 95% CI, as well as cyanosis OR 19.23, 95% CI) and paradoxical abdominal movement (OR 20.02, 95% CI). We excluded the four studied scores from multiregression analysis to eliminate the possibility that a composite score would obscure the contribution of individual items.

We tried to compare the four studied scores. The BAP65 score was developed by Shorr *et al.* [7] who stated that it had AUROC of 0.77 and correlated well with both in-hospital mortality and the need for MV. It also showed consistent results between two completely different populations (American and Lebanese) [36]. Another study showed that both DECAF and BAP65 scores were good predictors of both mortality and the need for ventilation [22]. We totally agree with and confirm the previous findings regarding mortality prediction. In the current study, BAP65 score correlated well with mortality, with a

sensitivity of 100% and specificity of 78%, with AUROC of 0.967. This could be explained by the following: elevated BUN, tachycardia, and altered consciousness were significantly more common among nonsurvivors, and elevated BUN and tachycardia reflect intravascular volume depletion [34,37]. Altered mental status is also a better of indicator of hypercapnia than the PaCO₂, which can be chronically elevated without manifesting clinical disturbance [34]. Nevertheless, we disagree regarding its sensitivity for prediction of need for MV, as in the current study, BAP65 score did not show significant correlation with the need for MV where sensitivity was 27% and specificity was 76%, AUROC=0.525. Yousif and El Wahsh [35] compared among DECAF, modified DECAF, 2008, and BAP65 scores to predict mortality and found that the highest AUROC curve was that of the BAP65 score (0.861). Our study revealed higher AUROC curve for BAP65 but agreed regarding the fact that BAP65 was superior to 2008 score in mortality prediction. In agreement with Steer et al. [9], we found that APACHE II score was also superior to and CAPS score regarding mortality BAP65 prediction, with AUROC=0.982.

This is not a retrospective study. It did not rely on already available medical records. It focused on readily available parameters on admission. Patients younger than 40 years old were excluded to avoid bronchial asthma misdiagnosis. As for limitations, we relied on previous diagnosis of COPD. The relation between FEV1 and AECOPD outcomes was not determined. Finally, frequency of last year exacerbations, details of drug treatment, and sputum bacteriology were also missing.

Conclusion

In conclusion, all studied scores correlated significantly with mortality, but only APACHE II and 2008 scores correlated significantly with the need for MV. Previous need for MV, presence of cyanosis, and paradoxical abdominal movement can predict the need for MV. APACHE II score proved to be the most powerful score, as it not only predicted mortality but also the need for MV. BAP65 score follows for mortality prediction and 2008 follows for predicting the need for MV. BAP65 score has the advantages of being simple and objective. The four scores are practical and not time consuming. We recommend larger studies to confirm our results and the routine use of these scores in triage of patients; nevertheless, individualization must be done based on clinical judgment.

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Conflicts of interest

There are no conflcits of interest.

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