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Klinik Çalışma

The use of infection probability score and sequential organ failure assessment scoring systems in predicting mechanical ventilation requirement and duration

Mekanik vantilasyon gereksinimi ve süresinin öngörülmesinde enfeksiyon olasılığı skoru ve ardışık organ yetersizliği değerlendirme skoru sistemlerinin kullanılması

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BACKGROUND

This study examines the efficacy of two different scoring systems in predicting mechanical ventilation need (MVN) and duration (DMV) in a surgical intensive care unit (ICU).

METHODS

This prospective observational study included 144 consecutive patients admitted to the ICU for more than 24 hours for whom the Sequential Organ Failure Assessment (SOFA) score and the Infection Probability Score (IPS) were calculated on admission and every 48 hours until discharge or death. Sensitivity and specificity of the two scoring systems were measured by the chi-square method. The Youden index and area under the Receiver Operating Characteristic (ROC) curve were also obtained.

RESULTS

For prediction of MVN, the best cut-off points were 2.5, 3.5, 2.5 for SOFA and 10.5, 10.5, 9.5 for IPS on the day of admission (0) and days 2 and 4, respectively. For the prediction of MVN, SOFA on days 0, 2 and 4 yielded significantly better results in the area under the ROC curve and Youden index than those of IPS ($p<0.05$). Neither of the two scoring systems provided good discrimination in prediction of more than 3 days respiratory support under MV.

CONCLUSION

For prediction of MVN, the SOFA scoring system on days 0, 2 and 4 has better accuracy than IPS.

Key Words: Infection Probability Score; intubation; intensive care unit; mechanical ventilation; Sequential Organ Failure Assessment.

AMAÇ

Cerrahi yoğun bakım ünitesindeki (YBÜ) mekanik ventilasyon gereksinimi (MVN) ve süresinin (DMV) öngörülmesinde iki farklı skorlama sisteminin etkinliği incelendi.

GEREÇ VE YÖNTEM

Bu prospektif gözlemsel çalışmaya, 24 saatten daha uzun süreyle YBÜ'de yatırılan ve kabul edilme sırasında ve taburcu edilene veya ölene kadar her 48 saatte bir ardışık organ yetersizliği değerlendirme (SOFA) skoru ve enfeksiyon olasılığı skoru (IPS) hesaplanan ardışık 144 hasta dahil edildi. Her iki skorlama sisteminin duyarlılığı ve özgüllüğü, ki-kare yöntemi ile ölçüldü. Youden indeksi ve alıcı çalışma karakteristiği (ROC) eğrisi altındaki alan da elde edildi.

BULGULAR

MVN'nin öngörülmesi ile ilgili olarak, sırasıyla hastaneye yatırılma günü (0) ile 2. ve 4. günlerde en iyi kesilme noktaları SOFA için 2,5, 3,5, 2,5 ve IPS için de 10,5, 10,5, 9,5 oldu. MVN'nin öngörülmesi ile ilgili olarak, SOFA, ROC eğrisi altındaki alan ve Youden indeksinde 0., 2. ve 4. günlerde IPS'ninkilere göre anlamlı şekilde daha iyi sonuçlar verdi ($p<0,05$). İki skorlama sisteminin hiçbiri, MV altında üç günden daha uzun süreli respiratuvar desteğin öngörülmesi konusunda iyi bir ayırım sağlayamadı.

SONUÇ

MVN'nin öngörülmesi ile ilgili olarak, SOFA skorlama sistemi, 0., 2. ve 4. günlerde IPS'den daha iyi doğruluğa sahiptir.

Anahtar Sözcükler: Enfeksiyon olasılığı skoru; entübasyon; yoğun bakım ünitesi; mekanik vantilasyon; ardışık organ yetersizliği değerlendirmesi.

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Mechanical ventilation (MV) is associated with numerous life-threatening complications.[1] The major factor in successful management of patients under MV is the resolution of the precipitating illness and a stable low requirement for oxygen.[2] The recognition of risk factors that can stratify a population of critically ill patients under ventilatory support into subgroups with different outcome is of great prognostic value for the clinician.[3] The severity of inflammatory response and impairment of organ function are the major determinants of the outcome in critically ill patients.[4-7] Clinical trials and observational studies usually use a scoring system for the assessment of the severity of organ function impairment. One of most popular among them is the Sequential Organ Failure Assessment (SOFA) score.[8] SOFA[9] is composed of scores from six organ systems (respiratory, cardiovascular, hepatic, coagulation, renal, and neurological) graded from 0 to 4 according to the degree of dysfunction/failure (Table 1). The Infection Probability Score (IPS) is a simple score that helps to assess the probability of infection in critically ill patients. The IPS for a patient is calculated as the sum of the points corresponding to the values of the predicting variables for that patient.[10] This score is original in that it includes two additional variables: C-reactive protein (CRP) and the SOFA score. These two scoring systems evaluate the degree of organ dysfunction/failure in six organs that contribute to the management of critically ill patients needing respiratory support. These scoring systems may, as a risk factor for requirement of MV, be useful as prognostic and comparative tools for predicting mechanical ventilation need (MVN) in critically ill patients. Although the predictive criteria for duration of MV (DMV) may help to evaluate the suitability of disconnecting a patient from a ventilator, the role of the SOFA or IPS system in the prediction of DMV needs further evaluation. This was our primary reason for assessing the efficacy of the SOFA and IPS in critically ill patients.

MATERIALS AND METHODS

This prospective observational cohort study was performed in a 28-bed Department of Intensive Care of an academic hospital. During an eight-month period (May 1 to December 31, 2005), all 144 adult patients consecutively admitted to the department for >24 hours were included in the study. Exclusion categories included patients with burn injuries, patients aged under 16 years, deaths within the first hour after admission, patients admitted to the intensive care unit (ICU) either because a separate coronary care or surgical recovery unit did not exist or was not available in the hospital concerned (i.e. they did not require intensive care), patients admitted after cardiac surgery or for exclusion of myocardial infarction, patients with post resuscitation in the emergency room before admission, and patients scheduled for organ donation. This observational study was approved

Table 1. The SOFA scoring system

SOFA score	0	1	2	3	4
Respiration					
PaO_2/FIO_2 (mmHg)	>400	≤400	≤300	≤200 with respiratory support	≤100
Coagulation					
Platelets x $10^3/mm^3$	>150	≤150	≤100	≤50	≤20
Liver					
Bilirubin (mg/dl)	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
(µmol/l)	<20	20-32	33-101	102-204	>204
Cardiovascular					
Hypotension	No hypotension	MAP <70 mmHg	Dopamine ≤5 or dobutamine (any dose)[a]	Dopamine >5 or epinephrine ≤0.1 or norepinephrine ≤0.1[a]	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[a]
Central nervous system					
Glasgow Coma Score	15	13-14	10-12	6-9	<6
Renal					
Creatinine (mg/dl)	<1.2	1.2-1.9	2.0-3.4	3.5-4.9	>5.0
(µmol/l)	<110	110-170	171-299	300-440	>440
or urine output				or <500 ml/day	or <200 ml/day

[a] Adrenergic agents administered for at least 1 h (doses given are in µg/kg per min);
(PaO_2: Arterial oxygen tension; FiO_2: Fractional inspired oxygen; MAP: Mean arterial pressure).

by the hospital ethics committee, which waived the need for informed consent. Demographics (age, gender), admission diagnosis, vital signs, SOFA score, clinical data (temperature, respiratory rate, heart rate [HR], mean arterial pressure, Glasgow Coma Scale [GCS]), laboratory data (white blood cell, platelet count, creatinine, bilirubin, partial arterial oxygen pressure [PAO_2]/fractional inspired oxygen [FiO_2], CRP), need ventilator, and DMV were collected throughout the ICU stay. IPS uses six simple and commonly used variables and ranges from 0 to 26 points (0-2 for temperature, 0-12 for HR, 0-1 for respiratory rate, 0-3 for white blood cell count, 0-6 for CRP, and 0-2 for SOFA score).[10] IPS and SOFA were measured at admission and then every two days until ICU discharge or death. Maximum SOFA score (maximum SOFA score for each patient during ICU stay) was calculated. Intubation criteria were: Immediate: coma (i.e. GCS<8), loss of protective laryngeal reflexes, ineffective respiration (max inspiratory force <25 cm H_2O), ventilatory insufficiency [this was a clinical decision and did not necessarily require blood gas analysis; if blood gas analysis was available, the following results indicated MVN: noncorrectable hypoxemia (pO_2<55 on 100% O_2), hypercapnia (pCO_2>55) with acidosis (pH<7.25)], spontaneous hyperventilation (e.g. $PaCO_2$<25 mmHg (3.5 kPa), airway protection, upper airway obstruction, septic shock, and any other injury requiring ventilation/intubation; Before Transfer: significantly deteriorating consciousness level, bilateral mandibular fracture, any facial injury compromising the airway, copious bleeding into mouth, and seizures.

Duration of MV was defined as number of days with MV; no attempt was made to subdivide into hours. The procedure of weaning from MV began when a patient's condition showed visible improvement or there was a resolution of the underlying cause of respiratory failure. To start the weaning procedure, the following criteria had to be met: spontaneous respiration rate (f) <35/min, spontaneous respiratory volume (Vt) >5 ml/kg body weight, maximum spontaneous inspiratory effort (Pi max) >25 cm H_2O, HR <140/min, body temperature <38.5°C, hemoglobin >100 g/L, PaO_2 >60 mm Hg, breathing a FiO_2 <0.4 with a PEEP <5 cm H_2O, no need for vasoactive or inotropic support, PaO_2/FiO_2 ratio >200, and f/Vt ratio <100. The procedure of weaning started with 5 minutes of spontaneous breathing through a T-tube circuit, with the FiO_2 set at the level used during MV. Patients who did not meet these criteria when first tested were reevaluated on a daily basis. The primary physician terminated the trial if the patient had any of the following signs of poor tolerance: a respiratory frequency of more than 35 breaths/min, SaO_2 below 90%, HR above 140 beats/min or a sustained increase or decrease in the HR of more than 20%, systolic blood pressure above 200 mmHg or below 80 mmHg, and agitation, diaphoresis, or anxiety.[11] A trial was considered to have been successful when the patient could breathe without MV for two hours.[12] If a patient had any of the signs of poor tolerance at any time during the trial, MV was reinstituted. From this point forward, the methods for MV and/or weaning were freely chosen by the primary physician, and neither was specified by protocol. A patient who had no signs of poor tolerance at the end of the trial was immediately extubated and received supplemental oxygen by face mask. A successful outcome is almost invariably defined as the toleration of extubation for 24 hours or longer. Unsuccessful weaning attempts are usually defined as the development of significant distress when ventilator support is withdrawn, or as the need for reintubation within a fixed period following extubation.

Data Analysis

The sensitivity, specificity and correct prediction of outcome for each cut-off point were calculated from the two-by-two table in SPSS for Windows (Microsoft) for SOFA and IPS. The best cut-off point in each scoring system is determined when the point yields the best specificity and sensitivity in the two-by-two table. The best Youden index also determines the best cut-off point. The Youden index is used to compare the proportion of cases correctly classified. The higher the Youden index,[13] the more accurate is the prediction (higher true positive and true negatives and fewer false positive and false negatives) at the cut-off point. Descriptive statistics were expressed as mean ± SD unless otherwise stated. A Receiver Operating Characteristic (ROC) curve[14] depicts the relation between true positive and false positive for each scoring system. This method compares scores without fixing arbitrary cut-off points. The ROC curve was calculated by the Medcal® software programs (MedCalc® version 9.0.1.1). The area under the ROC curve was evaluated. Such an area represents the probability that a randomly chosen diseased subject is more correctly rated or ranked than a randomly chosen non-diseased subject.[14] A value of 0.5 under the ROC curve indicates that the variable performs no better than chance and a value of 1.0 indicates perfect discrimination.

Table 2. Demographic characteristics of 144 patients

Variable	Cases	%	Mean±SD	Range	p
Sex					
Male (needed MV)	98 (66)	68.1 (67.3)			0.204[a]
Female (needed MV)	46 (27)	31.9 (58.7)			
Age					
All patients			45.2±16.7	17-89	
Needed MV			45.0±17.4	17–89	0.892*
No need for MV			45.4±15.4	17-84	
Type of injury					
Head	31 (21.4)				
Torso	34 (23.6)				
Limb	79 (55.0)				
Initial SOFA					
All patients			4.1±2.8	0 -17	
Needed MV			5.1±2.8	0-17	0.000*
No need for MV			2.2±1.4	0-6	
Initial IPS					
All patients			9.9±4.9	0-21	
Needed MV			10.9±4.8	0-21	0.001*
No need for MV			8.0 ±4.4	0-17	
Maximum SOFA					
All patients			5.5±3.2	0-17	
Needed MV			6.9±3.0	2-17	0.000*
No need for MV			3.0±2.0	0-10	
Maximum IPS					
All patients			11.8±4.8	0-21	
Needed MV			13.4±4.2	3-21	0.000*
No need for MV			9.0±4.5	0-18	

MV: Mechanical ventilation; [a] Chi-square test, * *t*-test.

A larger area under the ROC curve represents more reliability[15,16] and good discrimination of the scoring system. For the computation of the odds ratios and interactions associated with each component of the system, we fitted a logistic regression model with MVN in the ICU as the dependent variable. Logistic regression analysis was used to evaluate the relationship between SOFA score and MVN. Linear regression analysis was used to evaluate the correlation between mean SOFA and MVN in the ICU.

Statistical Significance

Continuous variables were expressed as means ± SD unless stated otherwise. Comparisons between groups were performed with unpaired Student's t-test, one-way ANOVA, Mann Whitney U or Kruskal Wallis *H*-tests for continuous variables according to data distribution. Post-hoc multiple comparisons were performed with the Bonferroni test. Chi-square tests were used to carry out comparisons between categorical variables. The correlation coefficient (r) or the Spearman rank correlation (r_s) was used to determine the relationship between two variables, according to the characteristics of the variables, i.e., numerical or ordinal. The significance level was set as $p<0.05$. The data of correct prediction outcome were analyzed by McNemar test and statistical significance was indicated if p was less than 0.05.

RESULTS

One hundred forty-four critically ill patients were admitted into our ICU in an eight-month period. Their ages ranged from 17 to 89 years (mean: 45.2 years). There were 98 males and 46 females (Table 2). Of all trauma patients enrolled in the study, blunt trauma accounted for 78.4% of the admissions. The patients were also grouped according to region injured: 1) head (skull, face, and neck); 2) torso (chest, abdomen, and pelvic content); and 3) limbs including pelvic girdle. One-hundred seventeen (81.3%) patients were intubated in the ICU. On the 1st, 2nd, 3rd, 4th, 5th and 6th days of admission, 23 (19.6%), 55 (47%), 28 (24%), 8 (6.8%), 2 (1.7%), and 1 (0.8%) patients were intubated, respectively.

Table 3. Comparison of the assessment scores in mechanical ventilation need

	Cut-off point	Sensitivity (%)	Specificity (%)	Correct prediction outcome (%)	Youden index	ROC area
SOFA 0	2.5	87.0	64.5	80.6	0.52#	0.82±0.04*
SOFA 2	3.5	70.0	87.1	77.6	0.57#	0.84±0.04*
SOFA 4	2.5	83.1	67.7	79.1	0.51#	0.83±0.04*
IPS 0	10.5	56.5	72.0	64.6	0.28	0.64±0.05
IPS 2	10.5	57.6	87.5	70.1	0.45	0.74±0.05
IPS 4	9.5	61.2	71.9	72.6	0.33	0.75±0.05

SOFA, IPS 0, 2, 4: Sequential Organ Failure Assessment and Infection Probability Score on the first, second, fourth days of admission to the intensive care unit; ROC: Receiver operating characteristic. * SOFA 0, 2, 4 vs. IPS 0, 2, 4: p= 0.000. # SOFA 0, 2, 4 vs. IPS 0, 2, 4: p<0.05.

Ninety-three (64.5%) patients needed MV. Mean DMV and ICU stay were 6.2±3.4 and 7.4±4.4 days, respectively. Thirty-one patients died in the hospital; the hospital mortality in this study was 21.5%. Among the deceased patients, 24 (78%) died of malfunction of the central nervous system, among whom 19 (80%) died before the 16th day after admission. Seven patients died from other organ failures, among whom eight patients (81%) died after the 15th day from admission.

Initial SOFA score and IPS (0-24 hours) were significantly higher in patients needing MV. There was also significant difference in maximum SOFA or IPS between patients with probability of MVN (Table 2). Maximum SOFA score was higher in patients needing MV more than three days, and the difference was statistically significant (7.25±2.9 vs. 5.67±2.61, p=0.027). Maximum IPS was greater in patients needing more than three days MV, but the difference was not significant. The trend of the mean SOFA score or IPS for the first 20 days of ICU stay and probability of MVN and DMV derived from each scoring system are shown in Figures 1 and 2. SOFA score on days 1-16 and IPS on days 1-6 were also significantly higher in patients needing MV (p<0.05). The SOFA score was significantly higher in patients with more than three days MV on ICU days 1-6 (p<0.05). The sensitivity, specificity, correct prediction outcome, Youden index and area of

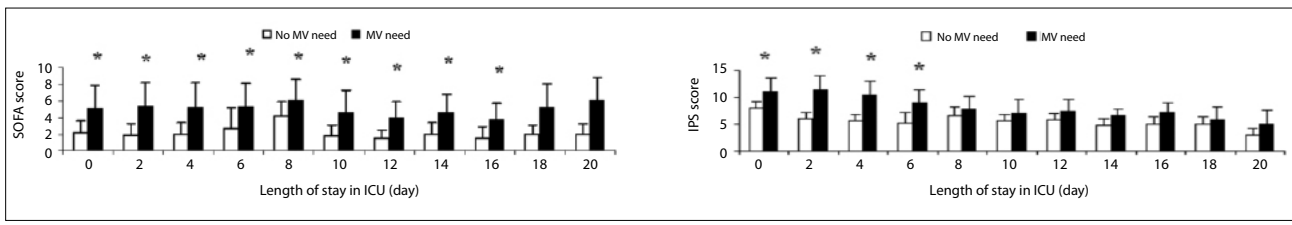

Fig. 1. Sequential Organ Failure Assessment (SOFA) score and Infection Probability Score (IPS) as the determinants of mechanical ventilation need (MVN) in the study patients. The trends in daily SOFA or IPS have been shown for critically ill patients over the first 20 days in the intensive care unit (ICU). The patients were divided in two groups according to MVN status. MVN was higher in patients with higher SOFA or IPS. The SOFA or IPS was significantly higher in patients with MVN on days 0-16 for SOFA and on days 0-6 for IPS (*p<0.05). Data are presented as mean ± SD.

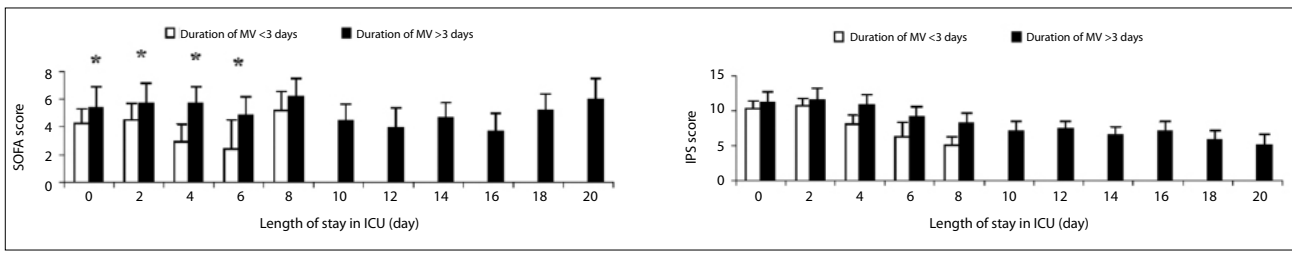

Fig. 2. Sequential Organ Failure Assessment (SOFA) score and Infection Probability Score (IPS) as the determinants of duration of mechanical ventilation (DMV) in the study patients. The trends in daily SOFA or IPS scores have been shown for critically ill patients over the first 20 days in the intensive care unit (ICU). The patients were divided in two groups according to DMV. DMV was higher in patients with higher SOFA or IPS. The SOFA score was significantly higher in patients with more than three days MV on ICU days 0-6 (*p<0.05). Data are presented as mean ± SD.

the ROC curve at the best cut-off point for MVN are presented in Table 3. There were statistical differences in Youden index and area under the ROC curve between SOFA score on days 0, 2, 4 and IPS for MVN. The ROC curves for MVN are shown in Figure 3. In MVN, the SOFA score on days 0, 2, 4 provided good results, as shown in Table 3. By contrast, IPS yielded poor results. Therefore, only SOFA score on days 0, 2, and 4 plays a crucial role in the prediction of MVN. Neither of the two scoring systems provided good discrimination in prediction of more than three days respiratory support under MV during ICU stay (AUC <0.5). In order to evaluate the relative contribution to MVN of the SOFA score or IPS present at ICU admission and that developing during first four days of ICU stay, a non-stepwise logistic regression equation was developed. Results demonstrated that SOFA score on days 0-4 was more important for predicting MVN than IPS (Table 4). The associated odds ratios for a one-point change in the scores are shown in Table 4.

DISCUSSION

The purpose of intensive care medicine is to diagnose and treat patients with acute life-threatening illness, and to restore them to their previous health and quality of life. The latter is more meaningful, because the functional results are as important as the mortality prediction.[17] The appropriate allocation of the limited resources available should be considered in decision-making.

In comparing the SOFA score and IPS, we found the accuracy of the SOFA score to be significantly better than that of IPS for prediction of MVN. The SOFA and IPS scoring systems include some major respiratory-related modifications, such as taking into account patients' respiratory rate, the partial pressure of oxygen in arterial blood, and fraction of inspired oxygen, which contribute to the management of critically ill patients in decision-making regarding MVN and predicting DMV.[8,9] The SOFA score provides more information on determining factors, such as age, underlying diseases, special respiratory parameters, and acute physiological conditions than IPS, which are crucial for MVN and DMV.[8]

The SOFA score is not much better than the IPS in the prediction of DMV, because many biases are found in the use of these two systems. First, treatment error is not predictable, especially in surgical

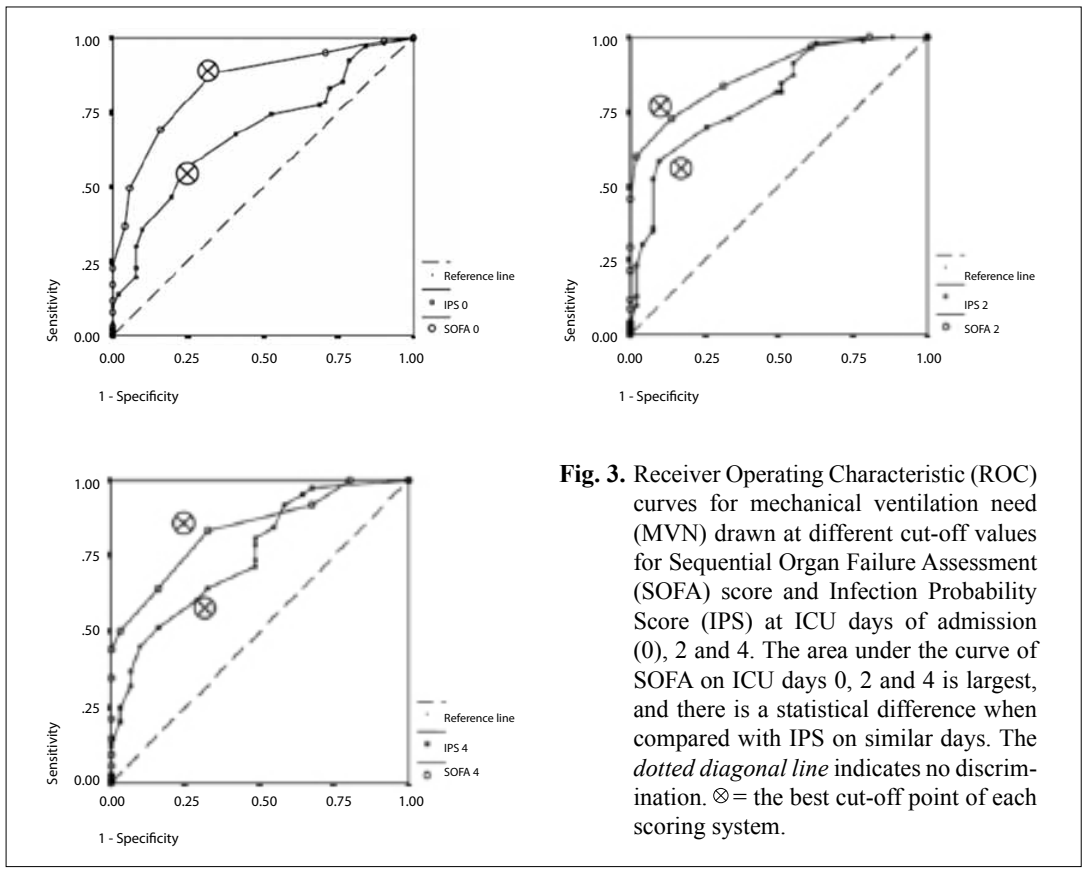

Fig. 3. Receiver Operating Characteristic (ROC) curves for mechanical ventilation need (MVN) drawn at different cut-off values for Sequential Organ Failure Assessment (SOFA) score and Infection Probability Score (IPS) at ICU days of admission (0), 2 and 4. The area under the curve of SOFA on ICU days 0, 2 and 4 is largest, and there is a statistical difference when compared with IPS on similar days. The *dotted diagonal line* indicates no discrimination. ⊗ = the best cut-off point of each scoring system.

Table 4. Relative contributions for mechanical ventilation need of SOFA and IPS

Variable	β	SE	Wald S	P	R	Odds ratio (95% CI)
MV need						
SOFA 0	0.814	0.153	28.120	0.000	0.497	2.256 (1.670-3.047)
SOFA 2	0.936	0.166	31.950	0.000	0.579	2.551 (1.843-3.529)
SOFA 4	0.739	0.170	18.851	0.000	0.481	2.094 (1.500-2.923)
MV need						
IPS 0	0.130	0.040	10.765	0.001	0.283	1.139 (1.054-1.231)
IPS 2	0.231	0.044	27.665	0.000	0.484	1.260 (1.156-1.373)
IPS 4	0.175	0.045	15.428	0.000	0.388	1.192 (1.092-1.301)

MV: Mechanical ventilation; SOFA, IPS 0, 2, 4: Sequential Organ Failure Assessment and Infection Probability Score on the first, second, fourth days of admission to the intensive care unit; β: Coefficient; SE: Standard error; CI: Confidence intervals; Wald S: Wald statistic; R: Partial correlation. Odds-ratios are presented for a one-point change in the scores for each organ.

patients.[18] Second, the data collected on the day of admission or during the ICU stay may not completely reflect the unforeseen events that may be major determinants of outcome.[19] Recently, in the evaluation of the SOFA score, Ferreira et al.[20] suggested that a sequential record of the SOFA scores may yield greater accuracy. Third, the co-morbidity condition[21] is not taken into account sufficiently in these scoring systems.

The admission SOFA or IPS reflects the degree of failure already present when the patient enters the ICU. This measurement (admission SOFA score)[22] can be used to stratify patients according to severity of illness, for example, for inclusion in clinical trials. The daily SOFA or IPS measures the progress of the patient during the ICU stay and is potentially influenced by therapy.

The fact that SOFA was a good prognostic indicator after controlling for admission SOFA score or IPS suggests that strategies directed at the prevention and/or limitation of further organ dysfunction will have a significant impact on prognosis, independent of the condition of the patient on admission to the ICU. This certainly needs further research.

The quantification of the total insult suffered by the patient during the ICU stay (maximum SOFA or IPS) was a very important prognostic indicator. This suggests that it can be used to quantify the impact of therapeutic interventions on overall or organ-specific morbidity.

However, SOFA and IPS are not recommended for routine use in clinical decision-making. Whether to withhold or withdraw intensive life support is a difficult decision and requires the consideration of predicted survival and projected quality of life.[17] Although SOFA yielded more sensitivity for MVN, this still does not justify its application to individual patients for prediction of outcome in order to change our decision-making. However, decision-making, in terms of transferring patients from the ICU, the reinforcement of medical treatment or surgical intervention, may be changed if we make sequential records of the scoring system for individual patients.

Our study presents some limitations that must be acknowledged. First, we only evaluated the relationship of SOFA or IPS with MVN and DMV in the ICU and not with hospital or 30-day mortality. Thus, more research should be undertaken to examine whether a link exists between organ dysfunction/failure or infection during the ICU stay and short-term (ICU) and long-term mortality. For that purpose, patients must be followed after ICU discharge and monitored for the development of further complications. Second, SOFA and IPS, similar to all the published organ failure scores, uses the GCS for neurological evaluation,[23] and this computation can be very difficult or impossible in sedated patients and is very prone to errors in data collection. Certainly we need to develop better ways to assess neurological dysfunction in the critically ill, non-trauma patient. Third, our study was performed in an academic referral hospital; therefore, our results may not be applicable to institutions with different patient populations.

In conclusion, for the prediction of MVN, SOFA is better than IPS. In the meantime, instruments like the SOFA score and their derived measures should be used for evaluation and risk stratification in clinical trials including critically ill patients.

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