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Original Article

Klinik Çalışma

The impact of admission hyperglycemia or hypoalbuminemia on need ventilator, time ventilated, mortality, and morbidity in critically ill trauma patients

Kritik hastalarda, başvurudaki hiperglisemi veya hipoalbümineminin vantilatör gereksinimi, vantilasyon süresi, mortalite ve morbidite üzerine etkileri

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BACKGROUND

The aim of this study was to evaluate the value of hypoalbuminemia or hyperglycemia as predictors for need ventilator and for weaning success in critically ill trauma patients.

METHODS

A single center, retrospective trial was done on 600 trauma patients ≥16 years old admitted for three or more days to the intensive care unit. Patients were classified into five different groups according to the reason for respiratory failure. The subsequent parameters were noted: serum albumin and glucose concentration, Acute Physiology and Chronic Health Evaluation III score, need ventilator, ventilator days, and fluid balance.

RESULTS

The initial mean serum glucose concentration was 9.3 (167.4) ± 0.2 (3.6 mg/dl) mmol/L and the initial mean serum albumin concentration was 30.2 (3.02) ± 0.02 (0.2 g/dl) g/L. Even though the circulating albumin concentration was considerably lower and serum glucose concentration was significantly higher in ICU nonsurvivors than in ICU survivors, neither albumin (r=-0.031, p=0.23) nor blood glucose concentration (r=0.050, p=0.11) on ICU admission was a predictor of the duration of mechanical ventilation. The profile of albumin and glucose concentration changes was dissimilar between weaned and mechanical ventilation-dependent patients. An increase of 5 g/L (0.5 g/dl) in serum albumin concentration multiplied the relative success probability by 1.10. Patients with serum albumin concentration less than 30.3 (3.03 g/dl) g/L were 1.2 times more likely to need ventilator than normoalbuminemic patients (relative risk 1.2, 95% confidence interval 1.06-1.31). The risk of need mechanical ventilation did not increase with blood glucose concentration more than 11 mmol/L (200 mg/dl).

CONCLUSION

These results suggest that albumin and blood glucose are possible indexes of the metabolic status of the trauma patient, which could be essential in deciding the need ventilator and weanable status of the patients who are mechanically ventilated for extended periods of time.

Key Words: Blood glucose; critical care; mechanical ventilation; mortality; serum albumin; ventilator weaning.

AMAÇ

Bu çalışmanın amacı, hipoalbüminemi veya hipergliseminin, vantilatör gereksinimi ve vantilatörden ayırma işleminin başarısının göstergeleri olarak değerini saptamaktır.

GEREÇ VE YÖNTEM

Yoğun bakım ünitesine üç gün veya daha uzun süreyle yatırılan ≥16 yaşındaki travmalı 600 hastada tek merkezli ve retrospektif bir çalışma yürütüldü. Hastalar, solunum yetersizliği nedenine göre oluşturulan beş ayrı grupta sınıflandı. Daha sonra şu parametreler kaydedildi: Serum albümin ve glukoz konsantrasyonu, Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi III skoru, vantilatör gereksinimi, vantilatör günü ve sıvı dengesi.

BULGULAR

Başlangıçtaki ortalama serum glukoz konsantrasyonu 9,3 (167,4) ± 0,2 (3,6 mg/dL) mmol/l ve serum albümin konsantrasyonu 30,2 (3,02) ± 0,02 (0,2 g/dL) g/L oldu. Yoğun bakım ünitesinde (YBÜ) sağ kalanlara göre hayatını kaybedenlerde, dolaşımdaki serum albümin konsantrasyonu kayda değer ölçüde düşük ve serum glukoz konsantrasyonu anlamlı şekilde yüksek olmasına karşın, YBÜ'ye yatırılma sırasındaki albümin konsantrasyonu (r=-0,031, p=0,23) ile kan glukoz konsantrasyonu (r=0,050, p=0,11) mekanik vantilasyon süresine ilişkin birer gösterge olmadı. Albümin ve glukoz değişiklikleri, mekanik vantilasyondan ayrılan ve mekanik vantilasyona bağımlı olan hastalar arasında farklılık gösterdi. Serum albümin konsantrasyonunda gerçekleşen 5 g/L (0,5 g/dL) seviyesinde bir artış, görece başarı olasılığını 1,10 oranında artırdı; 30,3 (3,03 g/dL) g/L seviyesinden daha düşük serum albümin konsantrasyonuna sahip olan hastaların normoalbüminemik hastalara göre vantilatöre gereksinim duyma olasılıkları, 1,2 kez daha fazla oldu (göreceli risk 1,2, % 95 güven aralığı 1,06 ile 1,31). Mekanik vantilasyon gereksinimi riski, 11 mmol/l (200 mg/dL) seviyesinden daha yüksek kan glukoz konsantrasyonu ile artmadı.

SONUÇ

Bu sonuçlar, albümin veya kan glukozunun, muhtemelen, travma hastasının metabolik durumuna ilişkin ve aynı zamanda uzayan zaman periyodu boyunca mekanik olarak vantilasyon uygulanan hastaların vantilatör gereksinimine veya ayrılabilirliğine karar vermede temel bir gösterge olacağını göstermektedir.

Anahtar Sözcükler: Kan glukoz; acil bakım; mekanik vantilasyon; mortalite; serum albümin; vantilatörden ayırma.

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In critically ill trauma patients experiencing acute respiratory failure, weaning from ventilatory support is a key survival feature in the intensive care unit (ICU).[1] In spite of the widespread studies in the arena of weaning, clinicians even now are challenged with the problem of the timing for initiating the practice of weaning.[2] Measurements imitating lung mechanics (e.g., tidal volume, lung and chest wall compliance), the power of respiratory muscles (e.g., peak inspiratory pressure), and gas-exchanging ability (e.g., $PaCO_2$) have been suggested to predict the accomplishment of withdrawing mechanical ventilation (MV).[3] Nonetheless, many physiological, respiratory, and mechanical factors also have an effect on weaning, although they are frequently ignored.[4,5] Body protein and fat stores were obviously exhausted in approximately half of the patients with respiratory failure. This information suggests that protein-calorie malnutrition possibly exists in patients with acute respiratory failure.[6] A ventilator-dependent patient who is malnourished can build up infections, pulmonary edema, hypophosphatemia, reduced ventilatory drive, respiratory weakness, and atelectasis (as a result of lesser surfactant production), which enhance the duration of MV.[7] Albumin is a plentiful plasma protein with multiple physiologic functions, and low serum albumin levels have been correlated with increased mortality and poor clinical outcomes in hospitalized patients.[8] Preoperative albumin associated conversely with complications, duration of hospital stay, postoperative stay, ICU stay, mortality, and recommencement of oral intake.[9] Menzies and colleagues[10] demonstrated that in chronic obstructive pulmonary disease patients with acute respiratory failure who required MV, the premorbid serum albumin concentration was related with survival and weaning success. They[10] trusted that this relationship between the albumin concentration and outcome draws attention to the nutritional factors in these patients. Hyperglycemia is frequent in critically ill trauma patients, yet in those with no diabetes mellitus.[11] Hyperglycemia was established to be an independent predictor of mortality and of hospital and ICU duration of stay. Infectious complications, including pneumonia, urinary tract infections, wound infections, and bacteremia, were appreciably increased in patients with raised glucose concentrations.[12] Owing to complications of hyperglycemia, we assumed that hyperglycemic trauma patients are more likely to need ventilatory support and have more ventilator days. There is a scarcity of data appraising serum albumin or blood glucose on admission as a predictor of need ventilator or delayed weaning in trauma patients. To test our assumption, we proposed this study to evaluate the usefulness of hypoalbuminemia or hyperglycemia as predictors for need MV and for weaning success in critically ill trauma patients.

MATERIALS AND METHODS

A single center, retrospective trial was performed on 600 trauma patients ≥16 years old admitted for three or more days to the adult trauma ICU at a university hospital and investigated admission total blood protein, albumin, glucose, PaO_2, hematocrit, the PaO_2/FiO_2 ratio, a diversity of lab tests interrelated with glucose and albumin, need ventilator, duration of MV, hospital/ICU lengths of stay, and universal patient demographics. This study was approved by the University and Hospital Ethics Committees. Patient charts were explored to permit classification into groups, conditional on the impulsive factors most important to respiratory failure. The classification used was analogous to that used by Gillespie et al.[13] in a study on the clinical outcome in respiratory failure. The patients were allocated to one of five groups, derived from the clinical circumstance accountable for the respiratory failure.

Group A: Uncomplicated lung injury

These patients imparted by means of lung injury respiratory failure related with intubation and MV, recent bilateral pulmonary infiltrates on chest roentgenograms, and hypoxemia necessitating an FiO_2 of more than equivalent 0.5, together with positive end-expiratory pressure,[13] which did not cause difficulties during the clinical course of the disease.

Group B: Lung injury complicated by multiple system failure

In this group of patients with lung injury, there was no less than one other system (sepsis, renal, cardiovascular, gastrointestinal, or hematologic) involved. The preponderance of patients in this group encompassed respiratory failure complicated by sepsis or acute renal failure. The description of system failure used was analogous to that used by Gillespie et al.[13] Sepsis was recognized if a minimum of three of the subsequent criteria were present: a) temperature > 39°C; b) white blood cell count of >12,000 cells/mm^3; c) positive blood culture or positive culture from an assumed resource; or d) cardiovascular sign of sepsis (decreased systemic vascular resistance and increased cardiac output). Acute renal failure was characterized as an acute increase in serum creatinine concentration to a concentration of more than 3 mg/dl (more than 265.2 micro mol/L) in patients with formerly normal renal function.

Further organ dysfunctions were identified as: a) cardiovascular complications incorporating myocardial infarction with hemodynamic instability or congestive heart failure, arrhythmia producing diminished cardiac output, and cardiogenic shock; b) gastrointestinal complications comprising hemorrhage necessitating blood substitute, acute puncture or ischemia, prolonged pancreatitis correlated with no less than a twofold increase in serum amylase concentration, liver dysfunction related with an acute twofold or further increase in serum aspartate aminotransferase, alkaline phosphatase concentration, or occurrence of jaundice; c) hematologic complications manifesting as clinically significant bleeding in connection with disseminated intravascular coagulation. The diagnosis of disseminated intravascular coagulation was founded on prolonged prothrombin time or partial thromboplastin time, thrombocytopenia, and increased fibrin split products or decreased fibrinogen concentration.

Group C: Previous lung disease

These patients exhibited preexisting lung disease, as recorded in patient history or observed on physical examination. The greater part of these patients encompassed preexisting chronic obstructive pulmonary disease.

Group D: Head injury or neurologic event

The etiologic factors that necessitated MV in this group were: severe closed-head injury, seizures, hypoxic encephalopathy, paraplegia, and quadriplegia.

Group E: Other medical causes

These patients had need of MV as a consequence of cardiovascular (e.g., rhythm disturbance), gastrointestinal (e.g., hemorrhage, bowel ischemia), pulmonary (e.g., pneumonia), trauma (e.g., multiple fractures of the face), or added reasons (e.g., drug overdose) with no proof of lung injury.

In all categories, only the patients with related disorders associated with the trauma (arrhythmias due to cardiac trauma, seizure due to head injury, etc) were included in the study.

Acute Physiology and Chronic Health Evaluation (APACHE) III (24 h after admission to our respiratory ICU), the cause of respiratory failure, and trigger disease were documented. Those with diabetes mellitus, hypoglycemia, hypokalemia, hypophosphatemia, hypomagnesemia, chest pain or suspected myocardial infarction, coronary bypass surgery, burn injury, addiction and age younger than 16 years old were excluded from data collection. Patients were regarded as hyperglycemic with an admission glucose concentration > 11 mmol/L (>200 mg/dl) and hypoalbuminemic with an admission albumin concentration <30.3 g/L (<3.3 g/dl) on hospital days 1 or 2. Duration of ventilation was identified as the number of days with MV and no effort was made to split into hours. The practice of weaning from MV began when a patient's condition demonstrated obvious improvement or there was a resolution of the primary cause of respiratory failure. To begin the weaning procedure, the subsequent 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, heart rate <140/min, body temperature <38.5°C, hemoglobin >100 g/L, partial arterial oxygen pressure (PaO_2) >60 mm Hg, breathing a fraction of inspired oxygen (FiO_2) <0.4 with a positive end expiratory pressure (PEEP) <5 cm H_2O, no need of vasoactive or inotropic support, PaO_2/FiO_2 ratio >200, and f/Vt ratio <100. The process of weaning began by 5 minutes of spontaneous breathing through a T-tube circuit, with the FiO_2 set at the level employed throughout MV. During the two-hour (2-h) trial, the patient had to meet the following objective criteria: spontaneous respiratory frequency <35/min, arterial blood oxygen saturation (SaO_2) >90% at FiO_2 <0.4, heart rate <140/min or >20% change from the baseline, systolic blood pressure <200 mm Hg or not <80 mm Hg, PaO_2 >60 mm Hg, pH <7.30, and stable clinical condition. The patients who fulfilled these criteria at the end of the 2-h trial were extubated. The weaning procedure was deemed successful if reintubation was not necessary within 48 h of extubation. If any signs of poor procedure tolerance were detected during the 2-h trial, the patient was switched back to assist/control ventilation mode and judged as a patient with difficult initial weaning. In such patients, the same procedure of weaning was repeated after 24 h, or when the patient's clinical condition allowed it. The patients with weaning difficulties through a 2-h spontaneous breathing trial were followed until ICU discharge or death.

Fluid balance (also called water balance) was defined as the discrepancy between the amount of

Table 1. Patient characteristics (mean ± SEM)

	Patient group					
	A	B	C	D	E	All Patients
Number	40	59*	21*	127*	353*	600
Age (yr)	36.4±2.5	34.3±2.5	53.8±3.9*	39.1±1.8	43.0±1.2	41.8±0.9
Gender (M/F)	24/16	35/24	13/8	73/54	202/51	344/256
APACHE III score	28.7±1.8	47.7±2.4*	47.6±2.0*	33.2±2.0	42.7±1.1*	40.3±0.9
Albumin (g/L)	30.3±0.1	30.3±0.1	30.1±0.1	30.3±0.1	30.1±0.04	30.2±0.02
BS (mmol/L)	8.18±0.5	9.6±0.5	10.9±1.1	8.80±0.3	9.4±0.2	9.3±0.2
Need ventilator (%)	70	79.7	85.7	63	74.5	72.7
MV dependency (days)	4.8±0.8	7.2±0.1	6.9±1.2	6.7±0.9	5.8±0.4	6.1±0.3
ICU stay (days)	8.9±1.2	9.1±1.0	9.1±1.1	10.6±0.9	9.3±0.4	9.6±0.4
Hospital stay (days)	15.6±1.7	15.8±1.7	15.9±2.3	16.4±1.2	17.3±0.6	16.9±0.5
ICU mortality rate (%)	10 (n=4)	39 (n=23)	52.4 (n=11)	22 (n=28)	40.2 (n=142)	34.7 (n=208)

A: Patients with lung injury; B: Patients with lung injury with multiple system failure; C: Patients with lung disease; D: Patients with neurologic disease; E: Medical patients; APACHE III: Acute Physiology and Chronic Health Evaluation III; BS: Blood sugar (mmol/L); MV: Mechanical ventilation; ICU: Intensive care unit. *Patient category A, patients with lung injury, is used as reference; p <0.05. To convert albumin from g/L to g/dl, divide the value by 10.

water taken into the body and the amount expelled or lost. The effects of hyperglycemia, hypoalbuminemia, and fluid balance on need ventilator and ventilator days were studied.

Data were analyzed using the statistical program SPSS for Windows, Release 11.5. Parametric data consisting of patient demographics of age and weight were analyzed using Student's t test or chi-square test for contingency tables as correct. Differences within groups were subjected to the Wilcoxon signed rank test. Chi-square and Fisher's exact tests were used for categorical variables. Multiple logistic regression analysis was performed to establish the independent risk factors for MV dependency during the ICU stay. Relative risk is given with the 95% confidence interval (CI). Pearson's correlation coefficient and linear regression were used to assess the association concerning ventilator dependency and other variables. A p value of <0.05 was considered statistically significant.

RESULTS

Of a total of 1450 trauma patients, 600 consecutive subjects fulfilled the inclusion criteria. Their characteristics are summarized in Table 1. For the whole sample, the mean ICU stay was 9.6 ± 0.4 days, whereas the length of MV dependency was 6.1 ± 0.3 days. The initial mean serum glucose concentration was 9.3 (167.4) ± 0.2 (3.6 mg/dl) mmol/L and the initial mean serum albumin concentration was 30.2 (3.2) ± 0.02 (0.2 g/dl) g/L, while the APACHE III score on the first day of ICU stay was 40.3 ± 0.9. In general, ICU mortality rate was 34.7%. Mortality rates differed within the five different patient groups. ICU mortality rate varied from 10% (Group A patients) to 52.4% (Group C patients). Even though the circulating albumin concentration was significantly lower and serum glucose concentration and APACHE III score significantly higher in ICU non-survivors than in ICU survivors (Table 2), albumin and blood glucose concentration on ICU admission were not predictors of the duration of MV (Table 3). Moreover, neither patient age, APACHE III score or fluid balance on the first ICU day was related to the duration of MV (Table 3). Length of MV was not correlated with group allocations (Table 4). Not only was the initial albumin concentration different between patients with and without ventilatory support, but the profile of their albumin concentration was different while in the ICU (Fig. 1). Though there was an initial decrease in albumin concentration in

Table 2. Comparison of initial clinical variables between intensive care unit (ICU) survivors and nonsurvivors (mean ±SEM)

	Alive at ICU discharge		
	Yes	No	p[a]
APACHE III	32.13±0.84	55.83±1.43	0.000
Albumin (g/L)	30.30±0.04	20.98±0.05	0.000
Blood glucose (mmol/L)	8.7±0.2	10.2±0.31	0.000
Fluid balance (ml)	1546.63±63.02	1680.8±44.70	0.081
Age (yr)	49.00±10.35	47.69±1.67	0.926

[a]Two-tailed unpaired t-test.
To convert albumin from g/L to g/dl, divide the value by 10.

Table 3. Correlation of initial clinical variables with mechanical ventilation (MV) dependency, intensive care unit (ICU) stay, and hospital stay

	MV Dependency			ICU Stay			Hospital Stay		
	r	Lower 95% CI	Upper 95% CI	r	Lower 95% CI	Upper 95% CI	r	Lower 95% CI	Upper 95% CI
APACHE III	0.089	0.013	0.081	-0.39	-0.32	0.52	-0.139**	-0.100	0.017
Albumin (g/L)	-0.031	-0.836	0.928	-0.012	-1.22	0.84	-0.02	-2.37	0.482
BS (mmol/L)	0.050	-0.006	0.012	-0.015	-0.011	0.010	0.007	-0.005	0.024
FB (ml)	0.052	0.000	0.002	0.146**	0.001	0.003	0.259**	0.003	0.006
Age (yr)	-0.023	-0.005	0.002	0.018	-0.34	0.038	0.008	-0.043	0.056

r: Correlation coefficient; CI: Confidence interval; APACHE III: Acute Physiology and Chronic Health Evaluation III; BS: Blood sugar; FB: Fluid balance. To convert albumin from g/L to g/dl, divide the value by 10. ** Correlation is significant at the 0.01 level (2-tailed).

both groups in the first few ICU days, a continuous decrease was noted in the patients on MV (Figs. 1, 2). This difference in the profile of serum albumin concentration was also detected in patients being weaned from MV (Fig. 2). When patients were successfully weaned, their median albumin concentration was higher than in those patients who continued to be supported on MV (Fig. 2). Is this predicting effect of albumin explained by the fact that its concentration may imitate the severity of illness or fluid balance? We employed a survival prototype to establish whether the predicting effect of albumin concentration continued when we evaluated a patient's weanability, by means of a value that would imitate the severity of illness (APACHE III), a value that would replicate the fluid balance and blood sugar of the patient, and the etiology of respiratory failure. The clinical measurements were held by 1 day to investigate whether success in weaning a patient

Table 4. Multiple regression analysis with mechanical ventilation dependency as outcome (mean±SEM)

Variable	Mechanical dependency value
Patient Category	
B	0.229±0.389
C	0.167±0.364
D	0.503±0.647
E	-0.194±0.238
APACHE III	0.037±0.007*
Score	
Albumin (g/L)	-0.202±0.145
BS (mmol/L)	0.001±0.002
Age (yr)	-0.005±0.005

B: Patients with lung injury with multiple system failure; C: Patients with lung disease; D: Patients with neurologic disease; E: Medical patients; APACHE III: Acute Physiology and Chronic Health Evaluation III; BS: Blood sugar.*Patient category A, patients with lung injury, is used as reference; p<0.05. To convert albumin from g/L to g/dl, divide the value by 10.

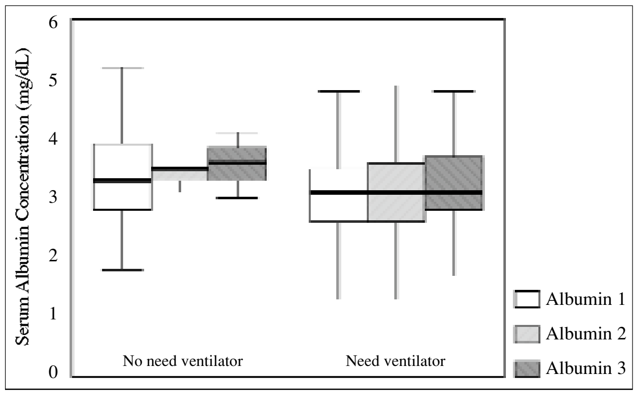

Fig. 1. Box plot of serum albumin concentration in intensive care unit (ICU) patients with and without ventilatory support during the first two days of ICU stay (albumin 1) , days of beginning ventilatory support (albumin 2) and the days of being weaned from mechanical ventilation (albumin 3). Serum albumin concentration in ICU patients with ventilator support was lower during the days of ICU stay, whereas it was relatively higher in patients without ventilator support.

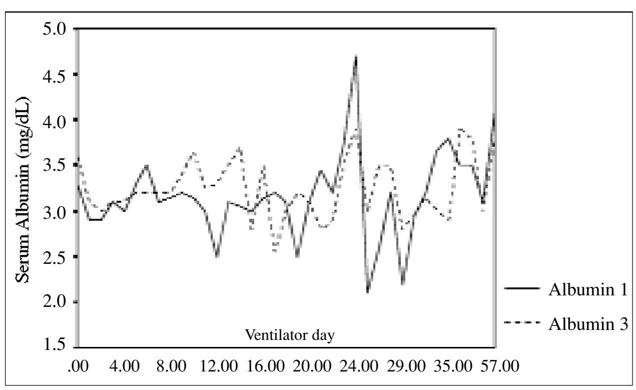

Fig. 2. Serum albumin concentration profiles of patients during mechanical ventilation (MV) (albumin 1) and on the day they were successfully weaned from MV (albumin 3). In patients supported by MV, median serum albumin is represented by the solid line. In successfully weaned patients, serum albumin concentration on that day is represented by the dashed line. On the day when patients were successfully weaned from the ventilator, the median albumin concentration was higher than in those patients who continued to be supported by MV.

Table 5. Fitted model for weaning success

Variable	Changes in variable	Relative success of weaning	Lower 95% CI	Upper 95% CI
Patients category[a]				
B	1	3.50	3.15	6.45
C	1	5.43	4.40	9.32
D	1	5.40	5.02	8.41
E	1	5.20	5.05	6.49
Albumin (g/L)	5	0.81	0.76	0.90
Blood sugar (mmol/lL)	5	7.25	6.18	11.66
APACHE III	5	3.90	1.34	6.20
Fluid balance (ml)	500	3.30	2.52	6.88

CI: Confidence interval; B: Patients with lung injury with multiple system failure; C: Patients with lung disease; D: Patients with neurologic disease; E: Medical patients; APACHE III: Acute Physiology and Chronic Health Evaluation III; a: Patient category A, patients with lung injury, is used as reference; p<0.05. To convert albumin from g/L to g/dl, divide the value by 10.

from MV could be predicted from the preceding-day values. The best, most appropriate and economical prototype encompassed APACHE III score, serum albumin concentration, fluid balance, and patient category. These variables (APACHE III, albumin concentration, fluid balance, and patient category) were equally significant at p <.0001 (Table 5), and each of these individual parameters had a significant effect on the predictability of weaning. When patients were successfully weaned, their mean serum glucose concentration was lower than in those patients who continued to be supported by MV (Fig. 3). On day 1, of the 600 patients admitted to the ICU, 436 (72.7%) received MV and comprised the study group for determining consequent duration of ventilation. Of the day 1 ventilated patients, 192 (31%) experienced ventilation for 7 or more days. Overall

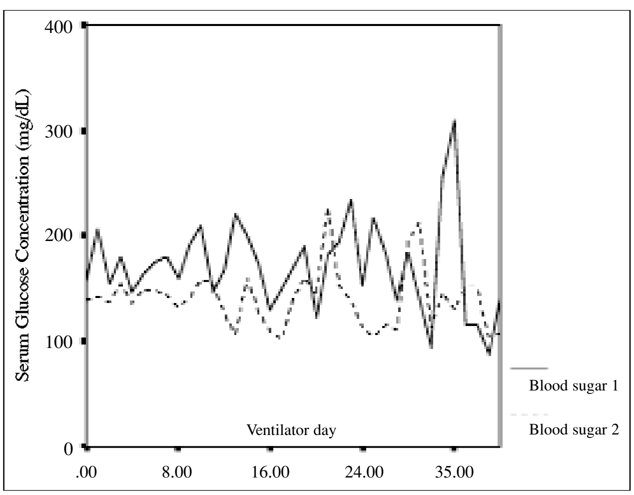

Fig. 3. Serum glucose concentration profiles of patients during mechanical ventilation (MV) (blood sugar 1) and on the day they were successfully weaned from MV (blood sugar 3). In patients supported by MV, mean serum glucose is represented by the solid line. In successfully weaned patients, serum glucose concentration on that day is represented by the dashed line. On the day when patients were successfully weaned from the ventilator, the mean glucose concentration was lower than in those patients who continued to be supported by MV.

Table 6. Characteristics of patients ventilated on first ICU day and those not ventilated on first ICU day

N	Ventilated (n=436)[1]	Not ventilated (n=164)
Age (yr)	42.7 (1.05)*	39.3 (1.50)
APACHE III	43.9 (1.02)*	31.0 (1.43)
Albumin (g/L)	30.1 (0.06)*	30.3 (0.06)
Blood sugar (mmol/L)	9.49 (4.85) **	8.67 (4.85)
Mean ICU LOS, d	11.4 (0.45)*	5.1 (0.31)
Mean Hospital LOS, d	18.8 (0.62)*	12.1 (0.62)
Death rate in ICU, %	44 (0.02)*	9 (0.02)

LOS: Length of stay; [1]Standard errors of means in parentheses.
*All variables significant at p=0.0001 level; ** All variables significant at p=0.01 level.

Table 7. Duration of mechanical ventilation based on initial variable

Variable	Duration of mechanical ventilation (day)*
Albumin (g/L)	
<30.3	6.3 (0.37)
>30.3	5.7 (0.53)
Blood sugar (mmol/L)	
< 11	6.1 (0.37)
> 11	6.1 (0.54)
BS <11 + Albumin >30.3	5.7 (0.63)
BS >11 + Albumin <30.3	6.1 (0.63)

BS: Blood sugar; *No variables significant at p<0.05.

Table 8. Application of the model for weaning success

	Patient B		Patient C	
	Value	Relative Success of Weaning	Value	Relative Success of Weaning
Patient category	B	1	C	1.07
Albumin (g/L)	25	1	30	4.60
Blood glucose (mmol/L)	8.25	1	100	5.80
APACHE III Score	20	1	25	0.79
Fluid balance (ml)	1000	1	1500	0.04
Cumulative relative success of weaning	1		0.90	

C: Patients with lung disease; APACHE III: Acute Physiology and Chronic Health Evaluation III. Patient category B, patients with lung disease with multiple system failure, is used as reference. To convert albumin from g/L to g/dl, divide the value by 10.

hospital mortality for 436 patients ventilated on day 1 was 44.5% and increased to 48% for patients ventilated on day 2 and to 86% for patients ventilated 7 days or longer. Table 6 summarizes the most significant differences between ventilated and nonventilated patients admitted to the ICU. Generally, ventilated patients were somewhat older and had lower initial serum albumin concentration and higher initial blood glucose concentration, higher APACHE III scores, longer ICU and hospital stays, and higher ICU mortality. Table 7 summarizes duration of MV in hypoalbuminemic (albumin <30.3 g/L, <3.03 g/dl) and/or hyperglycemic (blood glucose >11 mmol/L, >200 mg/dl) patients admitted to the ICU. On the whole, ventilator days were a little longer in hypoalbuminemic or hyperglycemic patients. Receiver operating characteristic (ROC) analysis for admission blood glucose and albumin concentration was done. By comparison of the areas under the ROC curve (AUC), blood glucose (AUC=0.562; standard error, 0.026; 95% CI, 0.51-0.61) was found to have the closer correlation to the need ventilator and had significantly higher (p=0.019) discriminatory power than albumin (AUC=0.418; standard error, 0.027; 95% CI, 0.36-0.47). Patients in Group C, as compared with patients in Group B, increased their relative chances of weaning by a factor of 1.07 (Table 8). An increase of 5 in the APACHE III score decreased the relative probability of weaning by a factor of 0.79. An increase of 5 g/L (0.5 g/dl) in serum albumin concentration increased the relative probability by a factor of 4.60. A decrease of 2.75 mmol/L (50 mg/dl) in serum glucose concentration increased the relative probability by a factor of 5.80. Lastly, an increase in fluid balance of 500 ml decreased the relative probability of weaning by 0.04. The model employed entails that these factors can be merged multiplicatively in order that they modify the relative probability of weaning by 0.90 (1.07 x 4.60 x 5.80 x 0.79 x 0.04).

DISCUSSION

The purpose of this study was to determine if the serum albumin or blood glucose concentration could be a predictor of need ventilator or weaning success in critically ill trauma patients. We revealed that the serum albumin or blood glucose concentration on the day of ICU admission did not predict the duration of MV. Conversely, the serum albumin or blood glucose profile for the period of MV was a determinant of weaning success. This effect of albumin or blood glucose was unrelated to the severity of illness (APACHE III), fluid balance, or the cause of respiratory failure.

Even though others have revealed that albumin is a good predictor of the weaning[14] or survival[15] of ICU patients, our study is distinctive in that we were able to reveal that its predictive role is not necessarily as reliant for its individual value as it is for the profile of its changes in concentration. Even if the circulating albumin concentration was significantly lower and serum glucose concentration was significantly higher in ICU nonsurvivors than in ICU survivors, there was no correlation between initial albumin or blood glucose concentration and the length of MV.

Using a survival prototype, we were capable of showing that an increase of 5 g/L (0.5 g/dl) in serum albumin concentration increased the relative success possibility by 1.10 (Table 5). Decrease of 5 mmol/L (90 mg/dl) in blood glucose concentration increased the success likelihood by 0.25 (Table 5). As a result, the probability of successfully weaning a patient the next day was 10% higher compared with the probability in an individual whose albumin concentration was unchanging. Each 5.5 mmol/L (100 mg/dl) of blood glucose quantified on admission was correlated with an increase in the time ventilated in the ICU of 0.3 days.

Based on the preliminary measure, a decrease in serum albumin concentration of 5 g/L (0.5 g/dl) throughout the first 48 hours in the ICU extended the duration of MV a minimum of one hour. The possibility of need ventilator increased with hypoalbuminemia. Patients with serum albumin concentration <30.3 g/L (3.03 g/dl) were 1.2 times more likely to need ventilator than normoalbuminemic patients (relative risk 1.2, 95% CI 1.06-1.31).

The possibility of need ventilator did not increase with blood glucose concentration more than 11 mmol/L (200 mg/dl). To ascertain if the alteration in albumin or blood glucose concentration could merely imitate adjustments in fluid balance or the severity of illness, we considered the APACHE III score, fluid balance, and the cause of respiratory failure as likely predictors of weaning success. The findings indicated that these three factors did have predictive significance. Each factor, nevertheless, had an exclusive effect on the prototype.

The reality that the cause of respiratory failure, APACHE III score, and fluid balance are essential predictors of weaning success is not wholly unexpected because they are well-known important prognostic factors for patients with respiratory failure.[15,16]

Why would albumin be a good predictor of weaning success? Metabolic and nutritional status has been revealed to impact weaning potential.[5] Albumin has been used by many investigators as an indicator of the nutritional and metabolic status of patients.[14,15] Murray and colleagues,[14] investigating 111 ICU patients, established that serum albumin, determined on the third day of ICU stay, was associated with the number of ICU days and hospital days. It is, however, the best frequently applied measurement of nutritional status.[14]

In recent times, albumin was additionally used as an indicator of nutritional status in a large multicenter investigation[17] assessing the possibility of death in hemodialysis patients. Low albumin concentrations in patients might be a result of their nutritional status, hepatocellular dysfunction or stressful stimuli such as sepsis or surgery. In acute disease, injury, surgery, or sepsis, the metabolic reaction modifies to create great amounts of acute phase proteins.[18]

Since albumin is not an acute-phase protein, its synthesis possibly will reduce.[19] This reaction is believed to be mediated by the release of cytokines such as tumor necrosis factors and interleukin-1.[19,20] The reduced synthesis of albumin is most likely correlated to a decrease in the amount of cells that synthesize it.[21]

The mechanism of reduced albumin synthesis in these acute conditions is probably enhanced vascular permeability, which would encourage a larger shift of albumin from the vascular to the interstitial space.[19,20,22] Ultimately, in protracted stress, albumin deprivation could be partly accountable for its reduced concentration. This course of action is likely because in protracted stress, albumin may possibly add to the amino acid pool.[19,23] Albumin, consequently, may be an excellent predictor of weaning since it is a trustworthy marker of the physiologic reaction to stress.

The failure to raise the serum albumin concentration most likely indicates that the acute inflammatory reaction is not sufficiently managed, making need ventilator and weaning more complicated. Our findings are comparable to the initial descriptions[24,25] proposing that an increase in albumin concentration has a predictive role in weaning ventilated patients. Scheinhorn[24] proposed that an increase of 2 g/L (0.2 g/dl) in albumin raises weaning success by a factor of 5.

Our findings additionally showed that by maintaining patients' blood glucose levels in normal range, ICU mortality and need ventilator could be considerably diminished. Duration of MV was less in patients with normal blood glucose. The risk of need ventilator increased with hypoalbuminemia but not with blood glucose concentration more than 11 mmol/L (200 mg/dl).

By comparison of the AUC, blood glucose was found to possess the closer association to need ventilator and had significantly higher discriminatory power than albumin. Furthermore, the ROC curve analysis demonstrated that the blood glucose level of 4.57 mmol/L (83 mg/dl) had higher sensitivity (87%) and specificity (53%) to distinguish five ventilator days. In other words, in patients in whom the initial mean blood glucose levels were greater than 4.57 mmol/L (83 mg/dl), the possibility of more than five days ventilatory support was higher than in the group of patients in whom blood glucose control was maintained <4.57 mmol/L (83 mg/dl).

Why would blood glucose be a good predictor of need ventilator or weaning success? Van den Berghe et al.[26] described that tight control of blood sugar decreased mortality. Moreover, the patients treated with the intensive insulin regimen had fewer episodes of sepsis, shorter length of stay in the ICU, less need for prolonged MV and renal replacement therapy, and a lower incidence of polyneuropathy, a frequent complication in ICU patients.[26]

Belgian investigators prospectively studied 1,548 mechanically ventilated adults admitted to the ICU over a one-year period.[26] They found that by maintaining patients' blood glucose levels in the normal range (4.4- 6.05 mmol/L, 80 to 110 mg/dl) with intensive insulin treatment, morbidity and mortality could be considerably decreased.[26] Intensive treatment reduced in-hospital mortality by 34%, and it lowered the frequency of bloodstream infections, critical-illness polyneuropathy, and acute renal failure by 46%, 44%, and 41%, respectively. Intensive insulin treatment also significantly decreased the need for prolonged antibiotic therapy, the amount of red-cell transfusions administered, and the duration of MV and ICU care.[26]

In conclusion, the findings presented in this article showed that the initial serum albumin or blood glucose concentration does not predict weaning success in critically ill trauma patients. Conversely, profile of serum albumin or blood glucose concentrations evaluated on the ICU days of admission is essential in determining the relative chance of being successfully weaned from the ventilator. In light of the above results, we recommend that the weaning index should comprise not only factors that verify the mechanical and gas exchange status of the lung but also those that indicate the metabolic state of the patient. Serum albumin or blood glucose could be one of these factors.

REFERENCES

1. Balk R, Bone RC. Classification of acute respiratory failure. Med Clin North Am 1983;67:551-6.
2. Sporn PH, Morganroth ML. Discontinuation of mechanical ventilation. Clin Chest Med 1988;9:113-26.
3. Jabour ER, Rabil DM, Truwit JD, Rochester DF. Evaluation of a new weaning index based on ventilatory endurance and the efficiency of gas exchange. Am Rev Respir Dis 1991;144(3 Pt 1):531-7.
4. Todorova L, Temelkov A. Weaning from long-term mechanical ventilation: a nonpulmonary weaning index. J Clin Monit Comput 2004;18:275-81.
5. Benotti PN, Bistrian B. Metabolic and nutritional aspects of weaning from mechanical ventilation. Crit Care Med 1989;17:181-5.
6. Driver AG, McAlevy MT, Smith JL. Nutritional assessment of patients with chronic obstructive pulmonary disease and acute respiratory failure. Chest 1982;82:568-71.
7. Spector N. Nutritional support of the ventilator-dependent patient. Nurs Clin North Am 1989;24:407-14.
8. Yukl RL, Bar-Or D, Harris L, Shapiro H, Winkler JV. Low albumin level in the emergency department: a potential independent predictor of delayed mortality in blunt trauma. J Emerg Med 2003;25:1-6.
9. Kudsk KA, Tolley EA, DeWitt RC, Janu PG, Blackwell AP, Yeary S, et al. Preoperative albumin and surgical site identify surgical risk for major postoperative complications. JPEN J Parenter Enteral Nutr 2003;27:1-9.
10. Menzies R, Gibbons W, Goldberg P. Determinants of weaning and survival among patients with COPD who require mechanical ventilation for acute respiratory failure. Chest 1989;95:398-405.
11. Finney SJ, Zekveld C, Elia A, Evans TW. Glucose control and mortality in critically ill patients. JAMA 2003;290:2041-7.
12. Laird AM, Miller PR, Kilgo PD, Meredith JW, Chang MC. Relationship of early hyperglycemia to mortality in trauma patients. J Trauma 2004;56:1058-62.
13. Gillespie DJ, Marsh HM, Divertie MB, Meadows JA 3rd. Clinical outcome of respiratory failure in patients requiring prolonged (greater than 24 hours) mechanical ventilation. Chest 1986;90:364-9.
14. Murray MJ, Marsh HM, Wochos DN, Moxness KE, Offord KP, Callaway CW. Nutritional assessment of intensive-care unit patients. Mayo Clin Proc 1988;63:1106-15.
15. Apelgren KN, Rombeau JL, Twomey PL, Miller RA. Comparison of nutritional indices and outcome in critically ill patients. Crit Care Med 1982;10:305-7.
16. Mitchell JP, Schuller D, Calandrino FS, Schuster DP. Improved outcome based on fluid management in critically ill patients requiring pulmonary artery catheterization. Am Rev Respir Dis 1992;145:990-8.
17. Owen WF Jr, Lew NL, Liu Y, Lowrie EG, Lazarus JM. The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. N Engl J Med 1993;329:1001-6.
18. Cengiz O, Kocer B, Sürmeli S, Santicky MJ, Soran A. Are pretreatment serum albumin and cholesterol levels prognostic tools in patients with colorectal carcinoma? Med Sci Monit 2006;12:CR240-7.
19. Doweiko JP, Nompleggi DJ. The role of albumin in human physiology and pathophysiology, Part III: Albumin and disease states. JPEN J Parenter Enteral Nutr 1991;15:476-83.
20. Rothschild MA, Oratz M, Schreiber SS. Serum albumin. Hepatology 1988;8:385-401.
21. Michaelson J. The significance of cell death in apoptosis: The molecular basis of cell death. In: Tomei LD, Cope FO, editors. Current Communications in Cell and Molecular Biology. New York: Cold Spring Harbour Laboratory Press;

1991. p. 31-46.
22. Bone RC. Sepsis syndrome. New insights into its pathogenesis and treatment. Infect Dis Clin North Am 1991;5:793-805.
23. Rodoman GV, Shalaeva TI, Dobretsov GE, Naumov EK, Obolenski VN. Serum albumin in systemic inflammatory reaction syndrome. Anesteziol Reanimatol 2006;(2):62-4. [Abstract]
24. Hurford WE, Favorito F, Wilson D: Serum albumin concentrations during the weaning of mechanical ventilator-dependent patients. Am Rev Respir Dis 1991;143:A685. [Abstract]
25. Scheinhorn DJ: Increase in serum albumin and decrease in body weight correlate with weaning from prolonged mechanical ventilation. Am Rev Respir Dis 1992; 145:A522.
26. Van den Berghe G et al: Intensive insulin therapy in the critically ill patients. N Engl J Med 2001;345:1359-67.