Implication of a Sepsis Protocol in a Respiratory Intensive Care Unit: A 12 Month Experience

Solunumsal Yoğun Bakım Ünitesinde Sepsis Protokolü Uygulaması: Bir Yıllık Deneyim

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Abstract

Aim: Protocol-directed therapy has been shown to improve patient outcome in critical illness. We aimed to evaluate the outcome of patients who were implicated in a sepsis protocol of 12 months duration and the risk factors for mortality in those patients with implicated sepsis protocol at our respiratory intensive care unit (R-ICU).

Material and Methods: This study was designed as a descriptive study. Adult patients admitted to RICU who stayed for >24 h with severe sepsis or septic shock were enrolled into the study within 2006. Demographic and clinic characteristics, treatment features, and outcome were evaluated. Modified sepsis protocol: 1. EGDT: fluid resuscitation (MAP>65mmHg); 2.LTV: Low Tidal Volume (6ml/kg ideal body weight), 3. TGC: Insulin infusion to obtain blood glucose between 80-140mg/L was utilized for all of the patients with hyperglycemia, 4. MDS: Methylprednisolone (20mg 3x/d for 7 d) in case of refractory shock. These were recorded in the first 6 hours of shock. For determination of mortality risk factors in patients with severe sepsis, logistic regression analysis was done.

Results: During the study period, among the 176 patients admitted to RICU, 119 (67.6%) patients with severe sepsis were enrolled into the study. Mean APACHE II score on admission to RICU in patients with severe sepsis was 20.5±6.8. When comparing survivor and non-survivor patients with severe sepsis, non-survivors had a higher APACHE II score, higher rate of invasive mechanical ventilation, vasopressor use, human albumin, insulin infusion, total parenteral nutrition (TPN), and multiple organ failure (MOF). The presence of MOF, TPN and higher APACHE II score (p<0.0001, OR.23.8, CI:7.17-78.85, p<0.020, OR4.5, CI: 1.26- 16.9, p<0.036, OR:1.1, CI: 1.006- 1.19, respectively) were shown as mortality risk factors in severe sepsis patients with implicated sepsis protocol in logistic regression analysis.

Conclusion: We observed a lower mortality rate according to APACHE II score in severe sepsis patients with applied sepsis protocol. MOF, TPN, and higher APACHE II score were found to berisk factors for mortality in those patients. We concluded that lower mortality can be achieved if we recognize and treat severe sepsis patients early and prevent organ failure. (Yoğun Bakım Derg 2010; 2: 35-9)

Key words: Severe Sepsis, septic shock, mortality, early goal directed therapy

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Özet

Giriş: Kritik hastalıklarda protokole dayalı tedavi yaklaşımında hasta prognozlarının daha iyi olduğu gösterilmiştir. Çalışmamızda göğüs hastalıkları yoğun bakım ünitemizde (YBÜ) bir yıllık dönemde sepsis protokolü uygulaması sonuçları ve protokol uygulanan hastalarda mortalite için risk faktörlerini araştırmayı hedefledik.

Gereç ve Yöntemler: Tanımlayıcı klinik çalışma olarak planlandı. 2006 yılında solunumsal YBÜ'ye kabul edilen ve 24 saatten fazla kalan erişkin ciddi sepsis ve septik şoktaki hastalar çalışmaya alındı. Hastaların özellikleri, tedavileri ve prognozları değerlendirildi. Sepsis protokolü olarak ortalama arteryel kan basıncı >65 mmHg olacak şekilde erken hedefe yönelik tedavi, ortalama 6 ml/kg olacak şekilde düşük tidal volüm, kan şekeri 80-140 mg/dl olacak şekilde glisemik kontrol ve tedaviye dirençli şokta günde 3 kez 20 mg metilprednizolon uygulandı. Protokol ugulanan ciddi sepsis hastalarında mortalite için risk faktörleri lojistik regresyon analizi ile değerlendirildi.

Bulgular: Çalışma dönemindeki 176 hastanın 119 (67.6%)'unda ciddi sepsis kriterleri bulundu ve çalışmaya dahil edildi. Ciddi sepsis hastalarının YBÜ'ye kabuldeki APACHE II değeri ortalama 20.5±6.8 idi. Yaşayan ve ölen ciddi sepsisli hastalar karşılaştırıldığında yüksek APACHE II değeri; invaziv mekanik ventilasyon, vazopressör, insulin, albumin, total parenteral beslenme (TPB) uygulamaları; çoklu organ yetmezliği (ÇOY) varlığı ölenlerde anlamlı olarak fazla bulundu. Lojistik resresyon analizinde ÇOY varlığı, TPB uygulaması ve yüksek APACHE II değeri mortalite için risk faktörleri olarak bulundu (sırasıyla OR 23.8 (7.17-78.85), p=0.0001; OR 4.5 (1.26- 16.9), p=0.020; OR 1.1 (1.006- 1.19), p=0.036). APACHE II skoruna göre beklenen mortalite %35.5 iken, gözlenen mortalite %24.4 (n=29) idi.

Sonuç: Sepsis protokolü uygulanan hastalarımızda APACHE II ye göre beklenenden düşük mortalite gözlendi. Mortalite için ÇOY, TPB ve yüksek APACHE II değeri risk faktörü olarak bulundu. (Yoğun Bakım Derg 2010; 2: 35-9)

Anahtar sözcükler: Ciddi sepsis, septik şok, mortalite, erken hedefe yönelik tedavi

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Introduction

Sepsis and septic shock as a result of an invasive infection are challenging problems in critically ill patients and frequently end in acute organ dysfunction. Current estimates suggest that some 750,000 cases of severe sepsis occur annually in the United States, with a mortality rate of around 29% (1). The recent Sepsis Occurrence in Acutely Ill Patients (SOAP) study across Europe reported that more than 35% of intensive care unit patients had sepsis at some point during their stay, with a mortality rate of 27% (2). International organizations developed management guidelines for severe sepsis and septic shock that would be of practical use for the bedside clinician, under the auspices of the

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Surviving Sepsis Campaign, an international effort to increase awareness and improve outcome in severe sepsis (3). With the introduction of the Surviving Sepsis Campaign guidelines, the campaign leaders aimed to reduce mortality from severe sepsis, but adherence to these recommendations is a first and crucial step in obtaining these goals. A comprehensive evaluation of both, adherence to a sepsis program and whether this results in better outcomes for patients, is therefore essential to guide informed decision-making regarding the implementation of such an evidence-based protocol. Surviving Sepsis Campaign guidelines for patients with septic shock, suggesting that early goal-directed therapy (EGDT) described by Rivers et al. (4), is a sepsis cardiovascular support protocol aimed at early hemodynamic optimization. The protocol is initiated as soon as sepsis induced hypoperfusion is identified and targets end points of resuscitation derived from hemodynamic monitoring (central venous pressure [CVP], mean arterial pressure [MAP], and central venous oxygen saturation [$ScvO_2$]). Administering physiologic doses of hydrocortisone favorably influences mortality (240-300 mg/day, over 5-7 days) (5, 6). A famous landmark study was published by the Leuven 1 investigators reporting intensive insulin therapy in a population of surgical intensive care unit (ICU) patients, targeting 80 to 110 mg/dl in the interventional arm, and this prospective, controlled, randomized trial spurred clinicians in ICUs around the world to adopt tight glycemic control (TGC) (7). In patients with acute lung injury and the acute respiratory distress syndrome, mechanical ventilation with a lower tidal volume (6 ml/ ideal body weight in kg) than is traditionally used results in decreased mortality and increases the number of days without ventilator use (8). Although the impact of the individual evidence-based interventions has been well described, the overall impact of multiple evidence-based protocols on outcome has not been well studied. Thus, we implemented multiple, evidence-based sepsis protocols and analyzed the results in our respiratory intensive care unit in a 12 month period. In addition, we looked for predictors of mortality in our patient group.

Patients and Methods

Study design and patients

A 12 month prospective cohort study (Jan. 2006-Dec. 2006) was conducted in a 10-bed respiratory intensive care unit (RICU) of Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital in Istanbul. All patients' treatment decisions were directly given by pulmonary specialists (day time, five and at night, one). All pulmonary specialists were well trained about sepsis guidelines. Among the patients admitted to the RICU due to acute respiratory failure and who stayed at least 24 hours in the RICU, those having severe sepsis or septic shock (9) were enrolled in the study. The patients were examined for the presence of concomitant diseases and severity of illness as measured by the Acute Physiology and Chronic Health Evaluation II score (APACHE II), and the mortality rate was assessed (10). Definitions of sepsis syndromes and multi organ failure were used according to previous studies (9, 11). The protocol implemented for study patients is summarized as follows:

EGDT protocol (4): Intravenous fluids are given targeting CVP of 8-12 mm Hg and MAP of > 65 mmHg. If the MAP target cannot be reached by fluids despite appropriate CVP, vasopressors (doputamin, dopamine) are initiated. Packed red blood cells are given if hemoglobin <7 g/dl or if hemoglobin < 10 g/dl for patients with cardiac diseases (3).

Low tidal volume: In our unit, if there is no contraindication, non invasive mechanical ventilation is the first choice of ventilatory support for all types of respiratory failure. The protocol was based on providing tidal volume not greater than 6 ml/kg per ideal body weight. During mechanical ventilation the sedation protocol is applied. Richmond sedation scale (12) is used to titrate sedation, infusion and assessment of daily need for sedation. Daily interruption of sedation is also used.

Moderate dose steroids: Stress-dose steroid therapy is given only in septic shock after blood pressure is identified to be poorly responsive to fluid and vasopressor therapy, without obtaining basal cortisol or a ACTH stimulation test since these tests are not available in our hospital. Because of the absence of hydrocortisone in our country, methyl prednisolone is used at a dose of 20 mg tid for 7 days (3). Stress-dose steroid therapy is not given to patients with septic shock who have active gastro intestinal bleeding, fungemia (positive blood culture specimen for fungi) or endobronchial evidence of fungal infection by observing endobronchial whitish plaque lesions with fiber optic bronchoscopy.

Glucose Control protocol: If blood glucose is over 150 mg/dl, continuous intravenous insulin infusion is titrated to maintain blood glucose levels between 80 and 140 mg/dl (3).

The following variables were obtained: Patients'characteristics, co-morbid diseases (i.e, diabetes, cardiovascular diseases, chronic renal diseases, chronic respiratory diseases), APACHE II score, non-invasive (NIV) and invasive mechanical ventilation (IMV) and duration of IMV, central venous catheterizations (CVC), sedation (midazolam) doses and duration, use of TPN, human albumin, vasopressor drugs, steroid, insulin, presence of ventilator associated pneumonia (VAP) (13), catheter related infections, empiric antibiotherapy, culture results, presence of organ failure, length of stay (LOS) in ICU and mortality in ICU.

Statistical analysis

Descriptive analysis was performed to define the demographics of the study population. Data are presented as mean±SD or numbers and percentages when appropriate. Continuous variables are summarized using mean and standard deviation for normally-distributed variables and median for non-normally distributed variables. Categorical variables are summarized with percentages in each category. For the comparison of the categorical variables the Chi-square test and Fisher's test (if n=<5) were performed. Survivor and non-survivor group differences for continuous variables are evaluated using Student -t test for normally distributed variables, or Mann-Whitney U test for non-normally distributed variables. The final analysis is utilized by logistic regression analysis to evaluate risk factors for mortality. Presence of multiple organ failure; use of total parenteral nutrition, vasopressors, human albumin, insulin, NIV, IMV and APACHE II score on admission were included in the regression model. Statistical analysis was performed using SPSS version 12.0 and the results were considered statistically significant at a level of $p<0.05$.

Results

Among 176 patients admitted to RICU during the study period, 119 (67.6%) patients who met the inclusion criteria for severe sepsis were enrolled in the study. The characteristics of the 119 severe sepsis patients, implications of sepsis protocols and ICU outcomes were summarized in Table 1. Also in Table 1, patient characteristics and ICU parameters were compared between survivors and non-survivors. The majority of the patient population was male (74.8%), median age was 66. Sex, age, body mass index were similar in survivors and non survivors. Mean APACHE II score was 20.5±6.8 and predicted mortality rate was 34.5%. Non-survivors had significantly higher APACHE II scores on admission than survivors (24.2±6.8 vs 19.2±6.9, p=0.001). Chronic respiratory diseases were observed mostly (n=70, 58.8%) (52 chronic obstructive pulmonary diseases, 4 asthma, 6 obesity hypoventilation, 5 bronchiectasis, 3 kyphoscoliosis) as concomitant diseases. Survivors had more chronic respiratory diseases than non-survivors (62% vs %48, p=0.026). All patients received mechanical ventilation as NIV, IMV or

both. Non-survivors received less NIV and more IMV than survivors (p=0.024 for both). Significantly more numbers of non-survivors had catheters; TPN, albumin, vasopressors, insulin infusion than survivors (p=0.003, p=0.0001, p=0.001, p=0.0001, p=0.036 respectively). Emprical antibiotics were given to 102 patients (85.7%), the remaining 17 patients received previously started antibiotherapy and newly added antifungal therapy. Among empirical antibiotherapy receiving patients, half of them (54.4%) had pathogens sensitive to the given treatment. Microorganims were isolated in 86 (72.3%) patients. Major pathogens were *P auriginosa* (n=32), *Candida spp* (n=28), *methicilline resistant S aureus* (n=7), *Klebsiella spp* (n=7). Survivors and non-survivors had similar pathogens, although Candida spp and bacteria were isolated twice more frequently from non-survivors than from survivors. Multi organ failure (MOF) was observed in 24.4 % of all patients with severe sepsis, and significantly more non-survivors had MOF than survivors (72.4% vs 8.8%, p<0.0001). Median length of stay (LOS) in ICU was 12 days and survivors and non-survivors had similar ICU LOS. Overall mortality rate was 24.4% and this was less than the APACHE II predicted mortality rate (35.5%).

For determining risk factors for mortality, we used the binary logistic regression model. We included variables that were found to be statistically significant after comparing survivors and non-survivors as seen in Table 1 in the logistic regression model: APACHE II score, TPN, NIV, IMV, vasopressor, insulin, human albumin use, multiple organ failure. The result of the logistic regression analysis is summarized in Table 2. Presence of MOF, TPN and higher APACHE II score on admission were factors affecting mortality in patients with severe sepsis who were treated with sepsis protocol.

Discussion

We conducted a study on patients with severe sepsis or septic shock presenting to the RICU of a teaching hospital in Istanbul, Turkey. In these patients who were treated with a protocol, the overall mortality rate was found to be 24.4%.

Protocol-directed therapy has been shown to improve patient outcome in critical illness. In a protocol-directed therapy, a protocol to guide therapy is applied to achieve a predetermined target. The end points used for achieving the desired therapeutic targets should be safe and attainable, and associated with improved outcomes. Early goal-directed therapy, drotrecogin alpha, low-dose steroid therapy, tight glucose control, and low-tidal volume ventilation have been demonstrated to reduce mortality in large randomized, controlled trials (4, 14, 6-8) Rivers et al. (4) demonstrated a 16% decrease in absolute 28-day mortality by implementing an emergency department-based resuscitation protocol during the first 6 h of severe sepsis.

Van den Berghe et al. (7, 15) reported that aiming a target of 80 to 110 mg/dl blood sugar level by intensive insulin therapy demonstrated a 3.7% absolute mortality reduction in a surgical intensive care unit. However, recently, a meta-analysis (16) which included 29 randomized controlled trials with a total of 8432 patients, indicated that hospital mortality did not differ between patients who received tight glucose control and patients who received the usual care (21.6% vs 23.3%, respectively; relative risk 0.93; 95% confidence interval [CI], 0.85-1.03). Very recently, the NICE-SUGAR study (17) demonstrated that intensive glucose control (81-108 mg/dl) increased mortality rate compared to conventional glucose control (< 180 mg/dl). Our study was carried out before the NICE-SUGAR study, and in addition, we did not perform very tight glucose control, instead we targeted blood sugar level of 80 to 140 mg/dl.

Patients with severe sepsis often require mechanical ventilation (8), and sepsis and acute lung injury frequently co-exist (18). In the present study, we applied the tidal volume 6 ml/kg ideal body weight. A lung-protective ventilatory strategy, based on tidal volumes of 6 mL/kg of predicted body weight led to significantly fewer organ failures and reduced mortality in patients with acute respiratory distress syndrome (8).

Hydrocortisone is widely used in patients with septic shock even though survival benefit has been reported only in patients who remained hypotensive after fluid and vasopressor resuscitation and whose plasma cortisol levels did not rise appropriately after the administration of corticotropin (19). A recent meta-analysis (20) demonstrated that 28-day mortality was unaffected by hydrocortisone, however, the time to shock reversal was significantly reduced. They concluded that steroids had no effect on mortality but shorten the time to shock reversal, therefore they had a limited role in septic shock patients. In the present study a greater percentage of patients received steroids due to chronic respiratory diseases at home or in the ward, and 34.5% of them continued to receive steroids in the ICU, and 18 patients received steroids for sepsis. Non-survivors received steroids more than survivors but the difference was not statistically significant (24% of non-survivors vs 12% of survivors, p=0.11). Because of our study design, we cannot claim that steroids decrease mortality. Steroids were not used in severe sepsis patients with fungemia or tracheobronchial fungal infection (34.8%).Very recently, another study, called the CORTICUS study, (21) was done, which concluded that hydrocortisone did not improve survival or reverse shock in patients with septic shock. Russell JA and co-workers (22) studied whether vasopressin treatment interacted with corticosteroid treatment in septic shock nonresponsive to fluid resuscitation and norepinephrine infusion. They found that a combination of low-dose vasopressin and corticosteroids was associated with decreased mortality and organ dysfunction compared to norepinephrine and corticosteroids.

Few studies about the effect of protocol combinations on patient outcome have been performed. Nguyen et al. (23) described their experience with early goal-directed therapy, corticosteroid administration, and recombinant human activated protein C administration in patients with severe sepsis or septic shock in the emergency department, and reported an in-hospital mortality rate of 25%. In another study (24), 116 patients, 79 of whom had septic shock, were treated using Multiple Urgent Sepsis Therapies (MUST) protocol and the mortality rate was reported to be 18%. In a recent study comparing the mortality rate of intensive care unit patients with septic shock treated with a modified goal-directed protocol and non-goal therapy, the in-hospital mortality rate was found to be 53.7% vs 71.6 % respectively (25). Thus, the authors suggested that implementation of a goal-directed protocol improves survival and clinical outcome in intensive care unit patients with septic shock.

There are a few limitations in our study. First, we had no control group. Therefore, we could not claim that this protocol reduced mortality. However, the mortality rate of our patients was lower than that of predicted mortality. Second, we initiated steroid treatment without performing the ACTH stimulation test or obtaining a basal cortisol level because of lack of availability in our hospital. Third, glucose control in this study, although not very tight, might still be tight according to the NICESUGAR study (17). Fourth, we did not have enough information about whether targets were reached all the time. Brunkhorst and co-workers (26) designed a one day cross-sectional study, in order to simultaneously determine perceived vs. practiced adherence to recommended interventions for the treatment of severe sepsis or septic shock in 214 ICUs in Germany. They found that the current therapy of severe sepsis in German intensive care units complies poorly with practice recommendations (26).

Drotrecogin alfa (activated, APC) reduced mortality in the PROWESS study, in patients with severe sepsis at high risk of death (14) but it is not available in our center and it is very difficult to obtain APC in a short time and therefore we could not use it. And lastly, although we applied

Table 1. Severe sepsis patients' characteristics and ICU outcomes and comparison of survivors and non-survivors with those parameters

	All patients n=119	Survivors n=90	Non-survivors n=29	p*
Age, median (range)	66.0±14.5 (18-88)	66.0±14.1	68.1±15.2	0.80
Gender, female/male	30/89	23/67	7/22	0.87
Body mass index, kg/m^2, mean (range)	23.8±5.4 (10-50)	23.4±6.2	23.2±3.4	0.26
APACHE II score mean	20.5±6.8	19.2±6.9	24.2±6.8	0.001
Concomitant diseases				
Chronic respiratory diseases, n (%)	70 (58.8)	56 (62.2)	14 (48.3)	0.026
Diabetes mellitus, n (%)	19 (16)	17 (18.8)	2 (6.8)	0.12
Renal Diseases, n (%)	9 (7.6)	5 (5.5)	4 (13.8)	0.14
Cardiovascular diseases, n (%)	30 (25.2)	24 (26.7)	6 (20.7)	0.51
Mechanical ventilation				
NIV, n (%)	78 (65.5)	64 (71.1)	14 (48.3)	0.024
IMV, n (%)	79 (66.4)	55 (61.1)	24 (82.8)	0.024
IMV, hours, median (range)	144±545 (1-2688)	144±537	162±576	0.70
Central venous catheter, case n (%)	42 (35.3)	25 (27.8)	17 (58.6)	0.003
Catheter related infections, n (%)	11 (26.2)	6 (6.6)	5 (17.2)	0.09
Total parenteral nutrition, n (%)	55 (46.2)	32 (35.5)	23 (79.3)	0.0001
Albumin infusion, n (%)	30 (25.2)	16 (17.7)	14 (48.3)	0.001
Vasopressor, n (%)	36 (30.3)	17 (18.8)	19 (65.5)	0.0001
Steroid for septic shock, n (%)	18 (15.1)	11 (12.2)	7 (24.1)	0.11
for chronic respiratory disease, n (%)	41 (34.5)	39 (43.3)	12 (41.4)	0.78
Insulin infusion, n (%)	28 (23.5)	17 (18.8)	11 (37.9)	0.036
Midazolam infusion, n (%)	51 (42.9)	34 (37.7)	17 (58.6)	0.26
Total doses, mg, median	380±1144	323±92	503±1437	0.31
Total durations, hour, median	72±116	72±136	94±142	0.64
Ventilator assosciated pneumonia, n (%)	23 (29.1)	15 (16.6)	8 (27.6)	0.20
Emprical antibiotics, n (%)				0.23
Appropriate (sensitive pathogen)	65 (54.6)	54 (60)	11 (37.9)	
Partially appropriate (intermediate)	15 (12.6)	11 (12.2)	5 (17.2)	
Inappropriate (resistant pathogen)	22 (18.5)	13 (14.4)	9 (31.0)	
Microorganisms, n (%)				0.35
Pseudomonas spp.	32 (37.2)	28 (31.1)	4 (13.7)	
Candida spp & bacteria	23 (26.7)	14 (15.5)	9 (31.0)	
Methicilline resistan S aureus	7 (8.1)	6 (6.6)	1 (3.4)	
Klebsiella spp.	7 (8.1)	6 (6.6)	1(3.4)	
Candida spp.	5 (5.8)	4 (4.4)	1 (3.4)	
Enterobacteriacea spp.	4 (4.7)	4 (4.4)	0 (0)	
Escherichia coli	4 (4.7)	3 (3.3)	1 (3.4)	
A. baumanni	3 (2.5)	3 (3.3)	0 (0)	
S pneumonia & M. catarallis	1 (1)	1 (1.1)	0 (0)	
Multi organ failure, n (%)	29 (24.4)	8 (8.8)	21 (72.4)	0.0001
LOS in ICU, median day (range)	12.0±26.0 (1-165)	11.0±24.1	15.0±31.2	0.44
Mortality, n (%)	29 (24.4)	-	29 (100)	-
APACHE II adjusted mortality rate	%35.5			

NIV: non-invasive mechanical ventilation, IMV: invasive mechanical ventilation. ICU: intensive care unit, APACHE II: an ICU severity scoring system, for acute physiologic and chronic health evaluation II. LOS: Length of stay. *p values related with the comparison of survivor and non-survivors. Mean values ± Standard deviation, p< 0.05 statistically significant

Table 2. Logistic regression models of mortality risk factors in patients with severe sepsis

Variables	Odd Ratio	95% C.I. for OR		p values
		lower	upper	
Presence of multiple organ failure	23.784	7.174	78.854	0.0001
Total parenteral nutrition	4.527	1.266	16.191	0.020
APACHE II on ICU admission	1.096	1.006	1.194	0.036

C.I.: confidence intervals, O.R.: odd ratio. APACHE II: acute physiologic and chronic health evaluation II , ICU: intensive care unit

although we applied, we did not involve other protocols such as those developed for nutrition support, de-escalation antibiotic therapy, preventing ventilator associated pneumonia, intermittent sedation and analgesia, weaning, prophylaxis which might decrease the mortality rate in critically ill patients (27).

In conclusion, this study might deserve attention so that standardized protocols might have an impact on prognosis of septic patients. The findings of the present study demonstrated that protocol based management of the critically ill patients is applicable in real life, paying attention to whether they are strictly adhered to. Although we could not claim that this protocol reduced the mortality rate, our patients did have a lower rate of mortality than the predicted mortality rate according to the APACHE II score. MOF, TPN, and higher APACHE II scores were found to be risk factors for mortality in severe sepsis patients who received a sepsis protocol. We can also speculate that it can be possible to reduce mortality further with early recognition and treatment of severe sepsis patients to prevent organ failure.

Conflict of Interest

No conflict of interest is declared by authors.

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