Research Article



Early detection of nonneurologic organ failure in patients with severe traumatic brain injury: Multiple organ Wysfunction f core or f equential brgan failure assessment?

Sara Ramtinfar, Shahrokh Yousefzadeh Chabok, Aliakbar Jafari Chari, Zoheir Reihanian, Ehsan Kazemnezhad Leili, Arsalan Alizadeh

Abstrac

Objective: The aim of this study is to compare the discriminant function of multiple organ dysfunction score (MODS) and sequential organ failure assessment (SOFA) components in predicting the Intensive Care Unit (ICU) mortality and neurologic outcome. Materials and Methods: A descriptive-analytic study was conducted at a level I trauma center. Data were collected from patients with severe traumatic brain injury admitted to the neurosurgical ICU. Basic demographic data, SOFA and MOD scores were recorded daily for all patients. Odd's ratios (ORs) were calculated to determine the relationship of each component score to mortality, and area under receiver operating characteristic (AUROC) curve was used to compare the discriminative ability of two tools with respect to ICU mortality. Results: The most common organ failure observed was respiratory detected by SOFA of 26% and MODS of 13%, and the second common was cardiovascular detected by SOFA of 18% and MODS of 13%. No hepatic or renal failure occurred, and coagulation failure reported as 2.5% by SOFA and MODS. Cardiovascular failure defined by both tools had a correlation to ICU mortality and it was more significant for SOFA (OR = 6.9, CI = 3.6–13.3, P < 0.05 for SOFA; OR = 5, CI = 3-8.3, P < 0.05 for MODS; AUROC = 0.82 for SOFA; AUROC = 0.73 for MODS). The relationship of cardiovascular failure to dichotomized neurologic outcome was not significant statistically. ICU mortality was not associated with respiratory or coagulation failure. Conclusion: Cardiovascular failure defined by either tool significantly related to ICU mortality. Compared to MODS, SOFA-defined cardiovascular failure was a stronger predictor of death. ICU mortality was not affected by respiratory or coagulation failures.

Keywords: Multiple organ dysfunction syndrome, organ failure, sequential organ failure assessment, traumatic brain injury

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Introduction

Multiple organ dysfunction syndrome (MODS) is the most common cause of death in patients admitted to Intensive Care Unit (ICU) settings.^[1,2]

From:

Department of Neurosurgery, Poursina Hospital, Guilan University of Medical Science, Guilan, Iran

Correspondence:

Dr. Sara Ramtinfar, Department of Neurosurgery, Poursina Hospital, Guilan University of Medical Science, Guilan, Iran. E-mail: dr.ramtinfar@yahoo.com

The development of MODS among patients with severe traumatic brain injury (TBI) is of significant

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importance. MODS could occur in this subtype of patients independent of any inflammation or infection. In addition to neurogenic injury which results in nonneurologic organ dysfunction, the procedure of treatment itself can lead to multiple organ damage. Catecholamine release following TBI might result in cardiopulmonary dysfunction.^[3]

Neurocortical care involves using barbiturates and hypothermia to manage cerebral hypertension. This type of treatment affects the immune system and may cause different types of infection including pneumonia.^[4,5]

SOFA and MODS are two of the most commonly used MOD scoring systems in ICU settings. Both predicting tools include six components, evaluating cardiovascular, renal, hepatic, respiratory, hematologic, and neurologic systems. The main difference between two tools is the cardiovascular part which is calculated based on pressure-adjusted heart rate in MODS and thus is independent of treatment. Cardiovascular section of SOFA is based on mean arterial pressure and dosage of inotrope used. Parameters applied to evaluate organ damages other than cardiovascular system are almost the same for both tools, differing in the range of parameter which classifies the score into dysfunction or failure. [6]

The aim of our study was to describe the scores of all five sections and to compare them component by component, and to determine the relationship of death and unfavorable neurologic outcome to each component score.

Materials and Methods

This descriptive-analytic study was conducted at a level I trauma center. All patients with severe TBI who admitted to neurosurgery ICU from November 2012 to December 2013 were enrolled. Severe TBI was defined as a TBI causing at least one of the followings: An initial resuscitated Glasgow Coma Scale (GCS) of 8 or less at admission; a postresuscitation GCS at presentation to the trauma center of 8 or less in the absence of any type of sedation; indication for intracranial pressure monitoring; or the presence of a clinical herniation syndrome as verified by a neurosurgeon.^[7] Patients who were excluded from the study were patients with concomitant chest, abdominal and pelvic trauma resulted in vital organ damage, patients with previous history of vital organ involvement, and patients with unknown past medical history. APACHE II score was calculated for all patients during the first 24 h of admission. SOFA and MOD scores were collected every day for all patients based on original guidelines.[8,9]

For data analysis, we used SPSS for windows, Version 22.0 (Armonk, Ny:IBM Corp). Odd's ratio (OR) and Fisher's exact test were used. For both tools, the frequency of each component score was defined, and the relationship of each component score to outcome was calculated using OR. Contradictory results were reported. Glasgow outcome scale (GOS) was dichotomized into favorable (GOS: 4, 5) and unfavorable (GOS: 1, 2, 3). Areas under receiver operating characteristic curve (AUROC) were used to define the discriminant function of component scores in predicting the ICU mortality. All tests were two-sided, and P < 0.05 considered statistically significant.

Results

Of all patients, 83 patients were eligible to enter the study. The mean age of participants was 33 years and 78 of them were males. The mean ICU length of stay was 12 days. During the study, 23 patients (27.7%) died. Demographic data are shown in Table 1.

The proportion of patients who had any type of nonneurologic organ failure based on SOFA and MOD scoring system is presented in Table 2. The percentage of patients who had cardiovascular and respiratory failure based on SOFA was more than that of MOD scoring system. In terms of detecting other organ failures, their performance was the same. Based on both tools, none of our patients had renal or hepatic failure. Table 3 demonstrates the relationship of ICU mortality to nonneurologic organ failure/dysfunction defined by component scores of SOFA and MODS. Of 83 patients, 85.5% had SOFA-based abnormal cardiovascular system, 78.8% known to have

Table 1: Basic characteristic features of the study population

	Study population (n=83)
Age (years)	33±18
Gender	
Female	5
Male	78
Length of stay (days)	12
APACHE II	14±3
Mortality	23 (27.71)

APACHE: Acute Physiology And Chronic Health Evaluation

Table 2: Frequency of organ failure detected by multiple organ dysfunction syndrome and sequential organ failure assessment

Component score	SOFA (failure %)	MODS (failure %)	
Cardiovascular	18.1	13.3	
Respiratory	26.1	13	
Coagulation	2.5	2.5	
Renal	0	0	
Hepatic	0	0	

MODS: Multiple organ dysfunction score; SOFA: Sequential organ failure assessment

Table 3: The relationship of organ dysfunction and failure defined by sequential organ failure assessment and multiple organ dysfunction syndrome with mortality

	Survivors, n (%)	Nonsurvivors, n (%)	Total (n)
SOFA			
Hepatic			
Dysfunction	42 (71)	17 (28)	59
Failure	-	-	-
Coagulation			
Dysfunction	45 (66.2)	23 (33.8)	68
Failure	2 (0)	2 (100)	2
Renal			
Dysfunction	48 (67.6)	23 (32.4)	71
Failure	-	-	-
Respiratory			
Dysfunction	27 (64.3)	15 (35.7)	42
Failure	II (64.7)	6 (35.3)	17
Cardiovascular			
Dysfunction	48 (85.7)	8 (14.3)	56
Failure	O	15 (100)	15
MODS			
Hepatic			
Dysfunction	42 (71.2)	17 (28.8)	59
Failure	-	-	-
Coagulation			
Dysfunction	45 (66.2)	23 (33.8)	68
Failure	2 (100)	0	2
Renal			
Dysfunction	48 (67.6)	23 (32.4)	71
Failure	-	-	-
Respiratory			
Dysfunction	32 (6.27)	19 (37.7)	51
Failure	6 (75)	2 (25)	8
Cardiovascular			
Dysfunction	48 (80)	12 (20)	60
Failure	0	11 (100)	11

 ${\sf MODS:}\ {\sf Multiple}\ {\sf organ}\ {\sf dysfunction}\ {\sf score};\ {\sf SOFA:}\ {\sf Sequential}\ {\sf organ}\ {\sf failure}\ {\sf assessment}$

cardiovascular dysfunction and 21.1% categorized as patients with cardiovascular failure. All of those who had SOFA-based cardiovascular failure and 14.3% of those with SOFA-defined cardiovascular dysfunction have died. Similar results show the relationship between the MOD-defined cardiovascular failure and ICU mortality. The cardiovascular failure defined by both tools was significantly related to mortality (SOFA: OR = 6.9, 95% CI = 3.6–13.3, P < 0.05, MODS: OR = 5, 95% CI = 3.01-8.3, P < 0.05) and is presented in Figure 1, that relation is more significant about SOFA than MODS (AUROC curve 0.82 vs. 0.73). The cardiovascular failure defined by both tools presented as good predictors of mortality (discriminant function for SOFA = 32.6% and for MODS: 23/9%). There was no significant relation between other organ failures defined by tools to mortality.

Although 100% of patients with cardiovascular failure defined by SOFA or MODS died, surprisingly there was no correlation between cardiovascular or respiratory failure and neurologic outcome [Table 4].

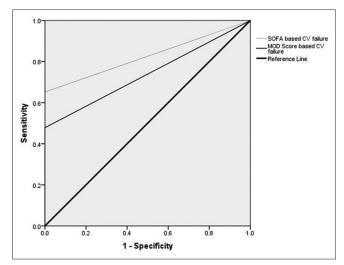


Figure 1: The relationship of cardiovascular score defined by multiple organ dysfunction score and sequential organ failure assessment to Intensive Care Unit mortality

Discussion

Neurologic injury, as a pro-inflammatory state, could result in multiple organ failure. Organ failure deteriorates the neurologic outcome and increases the mortality independently. ^[10] Organ failure had a very high incidence among patients with brain injury and reported in literature up to 80%–90% of cases. ^[11]

In this study, 46.7% of patients developed a failure at least in one organ. None of the patients developed renal or hepatic failure and the incidence of hematologic failure was as low as 2.5%. The most common organ failure reported was cardiovascular and respiratory. The incidence of SOFA-defined respiratory failure was twice higher of the same component presented by MODS.

SOFA-based cardiovascular component, comparing to MODS, showed a stronger predictability of ICU death.

Zygun *et al.* described a population of 209 severe TBI patients with a single organ failure incidence of 35%. The most common reported was respiratory (23%), followed by cardiovascular (18%), coagulation (8%), and one case of renal failure with no cases of hepatic failure.^[5]

A cohort study done by Ulvik *et al.* reported 28% of single organ failure in trauma patients admitted to ICU. The most common was respiratory failure (57%), followed by cardiovascular (3%), renal (2%), and hepatic failure (1%), defined by SOFA.^[12]

Zygun *et al.* conducted a trial on patients with severe head trauma or SAH to define the proportion of patients

Table 4: The relationship between organ dysfunction and failure defined by sequential organ failure assessment and multiple organ dysfunction syndrome with neurologic outcome

	Good outcome, n (%)	Poor outcome, n (%)	Total (n)
SOFA			
Hepatic			
Dysfunction	4 (6.8)	55 (93.2)	59
Failure	-	-	0
Coagulation			
Dysfunction	5 (7.4)	63 (92.6)	68
Failure	0	2 (100)	2
Renal			
Dysfunction	5 (7)	66 (93)	71
Failure	-	-	0
Respiratory			
Dysfunction	3 (7.1)	39 (92.9)	42
Failure	0	17 (100)	17
Cardiovascular			
Dysfunction	5 (8.9)	51 (91.1)	56
Failure	0	15 (100)	15
MODS			
Hepatic			
Dysfunction	4 (6.8)	55 (93.2)	59
Failure	-	-	0
Coagulation			
Dysfunction	5 (7.4)	63 (92.6)	68
Failure	0	2 (100)	2
Renal			
Dysfunction	5 (7)	66 (93)	71
Failure	-	-	0
Respiratory			
Dysfunction	3 (5.9)	48 (94.1)	51
Failure	0	8 (100)	8
Cardiovascular			
Dysfunction	5 (8.3)	55 (91.7)	60
Failure	0	11 (100)	П

MODS: Multiple organ dysfunction syndrome; SOFA: Sequential organ failure assessment

with subsequent nonneurologic organ failure. SOFA was calculated retrospectively for 55 patients with severe TBI. They reported 82% and 80% of cardiac and respiratory failure, respectively. No renal or hepatic failure developed and three cases defined as having hematologic failure. [13]

Based on Zygun *et al.*'s trial, study on patients with severe TBI revealed nonsignificant incidence of hepatic, renal, or hematologic failure, but 56% and 18% of SOFA and MODS defined cardiovascular failure.^[7] They reported 43% of respiratory failure detected by SOFA and 23% by MODS.^[9]

As SOFA cardiovascular score rises due to more inotrope use, the component score is going toward to be classified as failure. Inotrope use in patients with severe TBI has different indications. Ordering sedatives in ICU setting is very common for the management of intracranial hypertension and mechanical ventilation. [14,15] All types of sedatives may cause the patients to get

hemodynamically unstable and for maintaining blood pressure inotropes are used. In this subtype of patients, as well as management of intracranial hypertension, trying to maintain the cerebral perfusion pressure above 60 mmHg is consequential. Treatment of vasospasms and prevention of secondary ischemia are achieved by inotropes, vasopressors, and volume expanders.

Inotrope use is also recommended by the current guidelines for short-term management of cardiac decompensation.^[16] Myocardial dysfunction is a known result of neurologic insult. Different neurogenic pathways such as sympathetic overactivity hypothesized to play a role.^[17,18]

The score of SOFA cardiovascular component presents the state of cardiac failure with the use of inotropes, but without considering the indication. Thus, differentiating between a case with low cardiac ejection fraction and a case with normal cardiac ejection fraction but low cerebral perfusion pressure or cerebral vasospasm who is also in need of inotropes is not possible. Based on using pressure-adjusted heart rate, a treatment independent indicator by MODS, it seems to be advantageous over SOFA cardiovascular component. [6,20]

Because SOFA takes into account not only patients with cardiac failure but also patients with cerebrovascular indications for inotrope use, it is expected to detect more patients than MODS as having cardiovascular failure. As presented in Table 2, in this study, 18% of patients were detected by SOFA as having cardiovascular failure and 15% were detected by MODS. Similar to other studies, respiratory failure reported by SOFA is about twice of that reported by MODS. It is consistent with other studies and could be explained by various cutoff values used by SOFA and MODS. [9]

In this trial, cardiovascular component score of both tools represented as significant predictors of death. Patients with SOFA- and MODS-defined cardiovascular failure had a 6.9- and 5-fold increase in mortality, respectively. In comparison between two tools, AUROC curve gave a good discrimination ability for SOFA but just acceptable for MODS (0.82 vs. 0.73). Unexpectedly, the relation of cardiovascular failure with neurologic outcome was out of any statistical significance.

Although we found differences in proportion of patients with respiratory failure defined by SOFA and MODS, no statistically significant correlation was found between respiratory failure and mortality, neither between respiratory failure and neurologic outcome.

Zygun *et al.* found no correlation between mortality of patients with head injury or SAH and organ dysfunction on admission or during the days of ICU stay. They studied population of 55 patients with closed head injury or SAH, evaluated by modified SOFA for organ dysfunction. This was the first work of this group.^[20]

Peres Bota *et al.* found no differences between MODS and SOFA in the prediction of mortality of ICU patient and both tools were introduced as reliable predictors of mortality. Cardiovascular component of SOFA has shown to be superior in terms of discriminating the mortality (AUROC = 0.82 for SOFA, AUROC = 75 for MODS).^[1]

Holland *et al.* conducted a prospective 4-year study on patients with head trauma. Acute lung injury developed in 31% of patients with severe TBI. Thirty-eight percent of those with ALI and 15% of those without ALI died. The correlation between developing ALI and mortality was significant. ALI presented as an independent risk factor for mortality and long-term neurologic outcome.^[21] Gonzalvo *et al.* reported similar results.^[19]

Corral *et al.* enrolled 224 patients in a cohort trial to study the impact of nonneurologic complications on mortality. They reported 44% of hypotension, 41% of respiratory failure, and 8% of AKI. Independent of neurologic status, a 2-fold increase in mortality was observed in patients with AKI. Hypotension had an effect only on mortality of patients with initial GCS of 3–5. Similar to our results, they reported no association between respiratory failure and mortality.^[22]

As well as treatment-related side effects, neurogenic insult is the main cause of the development of nonneurologic organ dysfunction.

Hypothermia used in neurocortical care for decreasing the ICP and prevention of secondary brain injury improves neurological outcome and decreases the mortality rate.[15] Many trials have shown hypothermia to associate with increased rates of infection and pneumonia. [23] Barbiturates applied for prevention of posttraumatic seizures, a common and potentially fatal complication of head injury, increase the rate of pneumonia by immunosuppression.^[24] Although the pathophysiology was unclear, recent trials proposed interaction mechanisms that could explain neurogenic induced organ failure.[22] Respiratory failure followed by severe TBI is not only the result of sympathetic hyperactivity and increased vasoconstriction and permeability but also neuroinflammatory cascades leading by cytokines and neutrophil aggregation and dysregulated endothelial function, also known to play a part in the development of cardiopulmonary failure. [25] Myocardial dysfunction, neurogenic pulmonary edema, and DIC are also introduced as a consequence of high levels of catecholamine release and the toxic adrenergic effect following neurogenic insult. [26,27] In this study, only cardiovascular failure defined by SOFA and MODS elucidated a significant relation to mortality. Sample size of study population and patient selection only from an ICU of one center is a limitation of this study.

Conclusion

High incidence of nonneurologic organ failure in patients with head injury necessitates application of prognostic scoring systems with good discrimination and calibration with all components. Routine use of these systems helps clinicians to guide their treatment based on prognosis and most importantly can provide guidance for prevention, and in equivocal cases serve as a guide to limit the implementation of life support services. [28]

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Conflicts of interest

There are no conflicts of interest.

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