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BURN INDUCED SEQUENTIAL ORGAN DYSFUNCTION, REFLECTED BY SOFA$_{MAX}$ AS A PREDICTOR OF MORTALITY IN BURNS PATIENTS

Plastic Surgery

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ABSTRACT

A prospective study was planned to investigate the temporal relationship between disturbances in hormonal and biochemical profiles in burn patients and their prognostic significance in relation to ABSI and SOFA scoring systems. Fifty patients were divided into four groups depending upon the percentage body surface area involved. The biochemical markers for assessment of organ function were evaluated on day 1, day 4 and weekly thereafter till discharge. The total SOFA score and ABSI were calculated on the specified days and their prognostic significance compared using ROC curves. Results: The mean ± SD TBSA of all the patients was 37.7 ± 19.8 and 68% patients were admitted with inhalation burns. Mean percentage of full thickness burn in the four groups was 4.6 ± 3.9, 12.5 ± 7.9, 24.4 ± 8.2 and 36.2 ± 4.8, respectively. Nine deaths were reported and the per cent mortality increased with increasing TBSA. Significantly higher values of mean scores for SOFA-1, SOFA-4, SOFAmax and ABSI were observed for patients who fail to survive with respective scores of 6.66, 7.88, 11.0 and 11.33 compared to surviving patient with scores of 4.02, 3.26, 6.73 and 7.87 respectively ($p<0.0001$). SOFA max, ABSI, SOFA for day 1 and 4 were good predictors of mortality with SOFA max and ABSI having 100% sensitivity and 95.1% and 82.9% specificity, respectively. Conclusion: SOFAmax was the best predictor of mortality in burns patients. With the increase of 1 unit in SOFA score, the risk of death increases by 21.3%.

KEYWORDS

1.Introduction:

Burns are among the leading causes of disability-adjusted life-years (DALYs) lost and mortality in low- and middle-income South-East Asian countries. In India, over 10,00,000 people are moderately or severely burnt every year[1]. Patients afflicted with a burn injury often suffer hypovolemic shock, sepsis, multiple organ failure, and death despite modern therapeutic advances [2]. The mortality rates remain very high, and correlate with burn severity w.r.t. total body surface area (TBSA). The burns with >20% TBSA require IV fluid resuscitation and may be fatal without treatment. Most deaths occur as the result of sepsis long after the acute phase response is completed. The worldwide estimate for mortality to burns is 265,000 annually and the mortality rates differ by gender, age, region, socio-economic factors and other factors including occupation, poverty, underlying medical conditions, alcohol abuse and smoking, access to chemicals, use of kerosene etc. [1]. Evaluating the risk of death in burn patients is essential for selection and improvement in their overall treatment regimens, and attempts have been made to predict the probability of death from the clinical parameters[3,4].

There are very few composite models for the prediction of mortality in patients with severe burn injury, the four most commonly used are: the Revised Baux score[5], the Belgian Outcome in Burn Injury score[6], Boston score[7], and Abbreviated Burn Severity Index (ABSI)[8]. The use of ABSI, which includes variables such as sex, age, total burned body surface area (TBSA), full-thickness injuries, and burns attributable to inhalation [8,9], has been validated for burn patients. Sepsis-related Organ Failure Assessment, also known as Sequential Organ Failure Assessment (SOFA) score was originally designed to quantitatively describe six organ dysfunction over time and to evaluate morbidity in septic patients; it has also been used to predict mortality [10-13].

The present study was designed to evaluate the predictive ability of SOFA score and compare it with ABSI, in burn patients during their stay in hospital. Our hypothesis was that patients diverge to survival or mortality during their hospital stay due to sequential organ failure that could be assessed using SOFA.

2.Materials and methods:

2.1.Patients and data collection:

This prospective study was conducted in the department of plastic surgery at Christian Medical College and Hospital, Ludhiana. All adult patients admitted to burn unit between 1st May 2014 and 30th April 2015, having total body surface involvement between 10–80% was included in the study.

Data for the physiological and epidemiological variables viz. age, gender, duration of observation, site of injury, burned BSA, thickness of burns and presence of inhalational burns were collected on admission. Inhalation injury was diagnosed clinically by indirect laryngoscopy based on the positive findings of redness, mucosal oedema, ash particles and vascular congestion in addition to evidence of burns to the face, enclosed spaces and nasal vibrissae at the time of admission.

A series of blood samples were taken from the patients on days 1, 4 and 7 of hospital admission and then once a week until discharge. Samples were taken once a day for the analysis of the biochemical parameters, viz. serum urea, creatinine, electrolytes and liver function tests. Haematological parameters such as coagulation of platelets ($10^3/mm^3$), bilirubin (mg/dL) and renal creatinine (mg/dL) were observed for the calculation of SOFA score ranging from 0–4.

During the patient's evaluation, the total SOFA score with its components were recorded from the first day (SOFA-1) to the fourth day (SOFA-4) and subsequently every week till discharge or death. The maximum value of SOFA on any day for a patient, during hospitalization was recorded as SOFA$_{max}$. The clinical outcomes collected were the length of hospital stay, and burn unit and hospital mortality.

Total burn scores ranging from 2 to 13 were also calculated using five-variable ABSI scale consisting of patient's sex, age, presence of inhalation injury, body surface area burned.

2.2.Statistical analyses:

Kruskal Wallis test was used to tabulate and analyze total body surface area percentage of burns (quantitative variables). Chi-Square test was used to analyze the associated co-morbidity, type of burns, inhalational burns and mortality (qualitative variables). SOFA$_{max}$, ABSI, SOFA-1 and SOFA-4 was analyzed using Mann Whitney test. Data analysis

was performed by using statistical software SPSS version 21.0. Sensitivity and specificity of two scales to predict mortality was evaluated by using of area under receiver operating characteristic (ROC) curve and cut off values.

3.Results:

3.1.Distribution of patients:

The study included 50 out of 54 patients, four were excluded due to insufficient data. In total, there were 15 (30%) females and 35 (70%) males with mean age of 33.44(range 18–60) years, patients were distributed into four groups depending on their percentage of TBSA burned. Group I (n=19) consisted of patients who sustained 10–30% of TBSA burned, Group II (n=19) patients sustained 31–50% of TBSA burns, Group III (n=8) patients sustained burn in 51–65% TBSA and in Group IV (n=4) patients 66–80% of TBSA was affected.

3.2.Types of burn injuries:

A wide range of extent and types of burn injuries were observed in the study population. The mean total percentages of burns across the group I-IV were 16.7, 41.3, 60.6and 73.8 respectively (Table 1). Blast injury was reported in 6 (31.6%) group I, 1 (5.3%) in group II and 1 (12.5%) patient in group III, whereas in group IV no patients attained blast injury. Chemical burns were seen in one patient (5.3%) each of group I and group II. Electrical burns were reported in 6 (31.6%), 3 (15.8%), 3 (37.5%) and 1 (25%) patients in group I, II, III and IV respectively. Only 1 (5.3%) patient in group I and 2 (10.5%) patients in group II had scald injuries. Although the groups were divided according to the percent body surface area, they did not differ from each other in the type of burns ($p>0.05$).

Presence of inhalational burns were noticed in a total of 34 (68%) patients. Within groups, 15 (78.9%) in group I, 10 (52.6%) in group II, 5 (62.5%) in group III and all 4 (100%) patients in group IV were affected with inhalation burns. As expected, the degree of thickness of burns increased with the increasing %TBSA. The mean percentage of full thickness burn in group I, II, III and IV was 4.6 ± 3.9, 12.5 ± 7.9, 24.4 ± 8.2 and 36.2 ± 4.8, respectively (Table 1) with statistically significant difference in between the groups ($p<0.05$).

Characteristic	Group I (n = 19)	Group II (n = 19)	Group III (n = 8)	Group IV (n = 4)	Total (n = 50)	P-value
Age (years)	30.2 ± 9.2	37.0 ± 12.4	32.5 ± 11.2	34.0 ± 8.7	33.4 ± 10.8	0.252
Male n (%)	16 (84.2)	12 (63.2)	6 (75.0)	1 (25.0)	35 (70.0)	0.102
Duration of observation (days)	21.2 ± 13.5	30.2 ± 20.2	18.5 ± 15.9	17.0 ± 13.5	23.8 ± 16.9	0.292
Total percentage of burns	16.7 ± 6.9	41.3 ± 5.7	60.6 ± 5.0	73.8 ± 4.8	37.7 ± 19.8	<0.0005
Percentage full thickness burns	4.6 ± 3.9	12.5 ± 7.9	24.4 ± 8.2	36.2 ± 4.8	13.3 ± 11.1	<0.0001

3.3.Prediction of mortality:

Out of 50 patients, 9 (18%) deaths were reported in hospital. Statistically significant differences was found in number of death in study groups with 0 (0%), 2 (10.5%), 4 (50.0%) and 3 (75%) deaths in group I, II, III and IV respectively. The mortality caused in females with the age range between 24-60 years is 4 (8%), whereas for males it is 5 (10%) with age range between 23-45 years, as shown in Table 2. Two females died as compared to one male in group IV having severe burns.

Significantly higher values of mean scores for SOFA-1, SOFA-4, $SOFA_{max}$ and ABSI were observed for patients who fail to survive with respective scores of 6.66, 7.88, 11.0 and 11.33 compared to surviving patient with scores of 4.02, 3.26, 6.73 and 7.87 respectively ($p<0.0001$) (fig 1).

Table 2: Mortality rates for SOFA and ABSI scales

Scales used*	No Mortality (n=41)	Mortality (n=9)	P value
SOFA-1	4.0 ± 1.7	6.7 ± 2.2	0.001
SOFA-4	3.3 ± 1.9	7.9 ± 2.8	<0.0005
$SOFA_{max}$	6.7 ± 1.9	11.0 ± 2.9	<0.0005
ABSI	7.9 ± 1.8	11.3 ± 1.3	<0.0005

*** All values in mean ± SD**

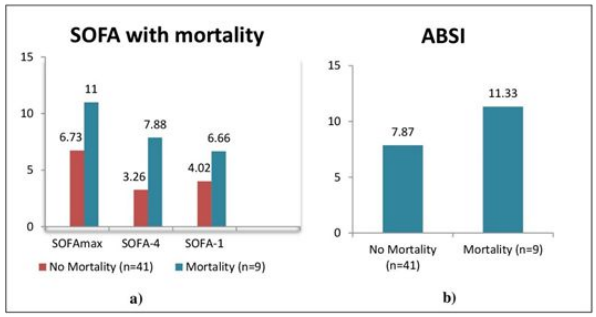

Figure1: Comparison between mortality and patients who survived using a) SOFA score and b) ABSI score

3.4.Sensitivity and specificity w.r.t. mortality :

Sensitivity of $SOFA_{max}$ and ABSI was 100%. Lower specificity was observed for $SOFA_{max}$ than ABSI (27% vs. 82.9%). The sensitivity and specificity of SOFA-1 were 88.89% and 65.85% and for SOFA-4 sensitivity and specificity were 88.90% and 51.20%. We thus inferred that $SOFA_{max}$ showed the good response for predicting the mortality in burned patients with area under the ROC curve 0.991 as compared to SOFA-1, SOFA-4 and ABSI (fig 2).

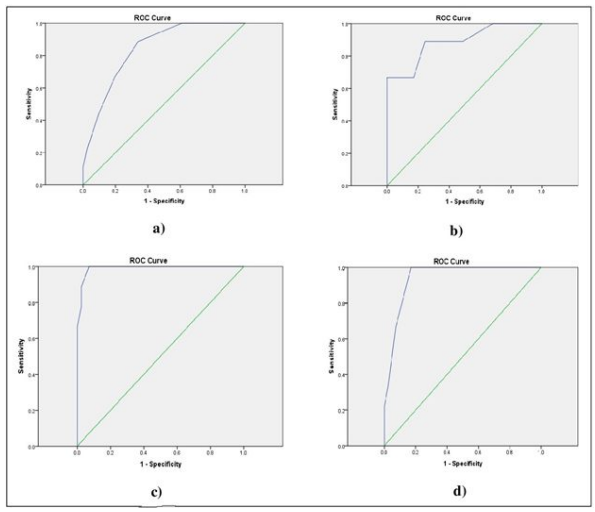

Figure 2: Receiver operating characteristics curve a) SOFA-1; b) SOFA-4; c) $SOFA_{max}$ and d) ABSI

In Binary logistic regression analyses, adjusted odds ratios (ORs) of organ dysfunction measurements for mortality for SOFA max, ABSI, SOFA-1 and SOFA-4 were 1.213, 1.134, 1.262 and 1.507 respectively ($p<0.05$). Thus, we inferred that $SOFA_{max}$ is the best predictor of mortality in burns patients, as shown in Table 3. With the increase of 1 unit in SOFA score, the risk of death increases by 21.3%.

Table 3: Comparison of predictive efficacy for SOFA and ABSI scales

Scales used	AUC (95%CI)	P value	Cut off	Sensitivity	Specificity	Odds Ratio (95% CI)
SOFA-1	0.840 (0.709 to 0.928)	<0.0001	4.5	88.89%	65.85%	1.262 (1.052-1.514)
SOFA-4	0.889 (0.765 to 1.00)	<0.0001	3.5	88.90%	51.20%	1.507 (1.077-2.109)
$SOFA_{max}$	0.991 (0.971 to 1.00)	<0.0001	7.50	100%	95.12%	1.213 (1.074-1.370)
ABSI	0.942 (0.880 to 1.00)	<0.0001	9.50	100%	82.9%	1.134 (1.037-1.241)

AUC, area under the ROC curve

4.Discussion:

There are some studies concluding that no system is valid for prediction of death rate in surgical ICU patients. This leads to the question that what are the prudent characteristics of mortality-predictors and how to solve the uncertainty that exists between elucidating the calculated probability of mortality and anticipating whether a patient will survive or die [14-16]. Mortality due to burns in our study was 9 out of the 50 patients, which limits statistical power. In this work, a decision was made to measure overall organ dysfunction in terms of the SOFA score, and use this as a proxy measure. The SOFA score was originally designed to quantitatively describe organ dysfunction over time in patients with sepsis [11]. There was statistically significant difference in the total percentage of burns and percentage of full thickness burn between the groups which suggested group IV had major burns with increased TBSA and percentage full thickness involvement as compared to groups III, II and I. This may be attributed to the increasing severity of burns with increase in total body surface involvement.

Our study correlates with the observations made by Palmieri *et al.* [17] who found that the maximum SOFA score was an independent risk factor for mortality. Lorente *et al.* [12] also concluded that SOFA score is useful to assess organ dysfunction in burn patients. Burn induced organ dysfunction (early and late), as well as the change in organ dysfunction, is independently associated with mortality. They observed that the SOFA scores at days 1 and 4 were independent predictors of mortality, but as compared to our study it shows that $SOFA_{max}$ with cut off >7.50 is the one to predict mortality more precisely than SOFA-1 and SOFA-4 with cut off >4.5 and >3.5 respectively. SOFA is one of the subjective score which is set up by the panel of experts assigned to select the variables and gives weightage to each variable based on their opinion [18].

There was significant increase in the percentage of patients dying as the TBSA increased. While group I had no mortality, group II, III and IV had 2 (10.53%), 4 (50%) and 3 (75%) number of patients dying as a result of burn injury sustained respectively. Burn size was one of the main risk factor of death observed in a study conducted by Fazeli *et al.* [19]. A prospective study done by Bale *et al*. [20] determined that mean and maximum SOFA scores are remarkably useful predictors of the outcome being independent of starting score and maximum SOFA score at 48 hr predicts an rise in mortality rate of presentation. Ferreira *et al*. [21] studied that, regardless of the starting score, the increase in SOFA score within the first 48 hr in the ICU estimated a mortality rate of not less than 50%. In a study by Vosylius *et al*. [22] determined that cumulative SOFA score are better in distinguishing the outcome in comparison with a single organ dysfunction score. A prospective multicenter study including 1685 ICU patients by Timsit *et al*. [23] inferred that daily SOFA scores is the good predictor showing accuracy and internal consistency, and can be used to alter the severity for events during the ICU stay.

In our study, all of the severity scores were found significantly associated with mortality ($p < 0.05$). As discovered in studies by Alan E. Jones *et. al.* [24] and J. A. Lorente [12], our survivors had significantly lower mean scores for all scoring systems compared to mortality. SOFA score with maximum value i.e. $SOFA_{max}$ obtained during the hospital course is the best predictor of mortality in burns patients. With the increase of 1 unit in SOFA score, the risk of death increases by 21.3%.

5.Conclusions:

Predicting mortality in burns is challenging and has always been an area of interest for clinicians and scientists. The prognostic scoring systems for immediate post-traumatic patient evaluation, classification and outcome prediction have gained increasing acceptance during the past three decades. The clinical outcome of burn patients is directly associated with TBSA and percent of full thickness burns.

The ABSI is a good tool to predict mortality, however results from the present study establish SOFA score as a promising candidate with very good sensitivity and specificity. $SOFA_{max}$ has an edge over SOFAday1 or SOFAday4 for prediction of mortality in burn patients admitted in hospital. However, larger studies and meta-analysis of controlled trials would be required before the universal acceptance of the tool in this indication.

6.Author's contribution:

All authors have made substantial contributions to all of the following:

(1) The concept and design of the study, or acquisition of data, or analysis and interpretation of data.
(2) biochemical analysis, protocol development and supervision of the study, drafting the article or revising it critically for important in intellectual content.
(3) Data analysis, writing and final approval of the manuscript for submission.

7.Conflict of interest statement:

None of the authors have any conflicts of interest to disclose.

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