Performance of the SCORTEN in Taiwanese patients with Stevens-Johnson syndrome and toxic epidermal necrolysis

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ABSTRACT

Background Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare drug-related skin conditions that are potentially life-threatening with a 20–30% mortality rate. A severity-of-illness score specified for SJS and TEN, SCORTEN, was developed in 2000. Until now, no study of SCORTEN has been conducted in Asian with SJS or TEN. The goal of the present study is to evaluate the performance of SCORTEN in predicting in-hospital mortality in Taiwanese patient with SJS or TEN.

Methods A sample of 51 patients with the diagnosis of SJS or TEN was reviewed from the chart. Performance of the SCORTEN was assessed using logistic regression.

Results The hospital mortality rate predicted by the SCORTEN was similar to the observed mortality rate. The performance of SCORTEN was well on each of the first 5 days of hospitalization, and best on the first day. There were two cases with active tuberculosis and five with diabetes mellitus among our eight deceased patients.

Conclusion The performance of SCORTEN is well in Taiwanese patients with SJS or TEN, especially on the first day of admission. The SCORTEN predicts a relatively accurate in-hospital mortality rate. We suggest that the SCORTEN should always be obtained during the first 24 hours, and can be repeated if the patient’s condition deteriorates quickly in the first 5 days. Pre-existing conditions, such as tuberculosis and pre-existing diabetes, may need more consideration in future studies.

INTRODUCTION

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare drug-related skin conditions with epidermal detachment of the skin and mucosal erosion caused by sudden apoptosis of keratinocytes. They are potentially life-threatening with a mortality rate of 20–30%.¹ SJS and TEN are a spectrum of the same entity. SJS is defined as the total body surface area (BSA) of skin detachment lesser than 10%, while TEN is more than 30%, and in between is called SJS/TEN overlap.²

A severity-of-illness score specified for SJS or TEN, SCORTEN, was developed in 2000 in France. SCORTEN includes seven independent predictive factors, each stand an equal weight in the score, with scores ranging from 0 to 7. The score is used to predict the mortality of a patient with SJS or TEN.¹

SCORTEN was shown to accurately predict mortality in patients with TEN in the United States in 2004.³ It was also used as a mortality evaluating parameter for patients with SJS or TEN using intravenous immunoglobulin (IVIG).⁴ The performance of SCORTEN was also validated in 2006. The result revealed that the SCORTEN performance during the first 5 days of hospitalization was excellent, and best on the third day.⁵

It is important to have a predictable standard for the prognosis of SJS or TEN either for the clinicians or for the
patients and their families. The performance of SCORTEN has yet to be evaluated in Asia. The objective of the present study was to examine the performance of SCORTEN in predicting in-hospital mortality in Taiwanese patients with SJS or TEN. The performance of SCORTEN in the first 5 days of admission was analyzed.

**Materials and methods**

**Patients and data collection**

We included 51 patients with the diagnosis of SJS or TEN admitted to a medical center in Taipei city, from June 2001 to June 2007. We retrospectively reviewed the chart of all patients. Among them, seven cases were ventilated during the first 5 days of admission and none of our patient was treated with IVIG. The outcome was in-hospital mortality.

SCORTEN includes seven independent predictive factors: (1) age greater than or equal to 40 years, (2) presence of malignancy, (3) skin detachment more than or equal to 10% of BSA, (4) heart rate greater than or equal to 120/min, (5) serum glucose level greater than 14.0 mmol/L (252 mg/dL), (6) serum bicarbonate level less than 20 mmol/L (20 mEq/L), and (7) serum urea nitrogen level greater than 9.6 mmol/L (27 mg/dL). Each factor stands an equal weight in the score, thus the score ranges from 0 to 7 (Table 1). We collected the raw data of all the variables. In the original study used to develop SCORTEN, some variables could not be measured in stable patients and were assumed to be within normal range. SCORTEN was calculated once daily on each day of the first 5 days of admission.

**Statistical analysis**

Data were analyzed using SAS 9.1.3 (SAS Institute, Cary, NC, USA) and SPSS 13.0 (SPSS Inc., Chicago, IL, USA) software. Descriptive data are summarized by number (percentages) or mean±standard deviation. Patients who died during hospitalization were compared with those who did not by using Fisher’s exact probability test for nominal variables, and unpaired two-tailed t test for continuous variables. Differences were considered significant at p<0.05.

The expected mortality rate predicted by the SCORTEN was calculated using the formula: P (death) = e^{logit}/1 + e^{logit} where logit = -4.448 + 1.237(SCORTEN).1 The standardized mortality ratio (standardized mortality ratio = \( \frac{\text{observed deaths}}{\text{expected deaths}} \)) was used to determine whether there was a significant difference between observed and expected mortality on the first day.6

The SCORTEN from day 1 to day 5 were analyzed by using Friedman’s test and Dunn’s multiple comparisons test. The statistical performance of the successive SCORTEN from day 1 to 5 was assessed by using logistic regression.

### Table 1 SCORTEN: Seven independent prognostic factors of Stevens-Johnson syndrome/toxic epidermal necrolysis.*

<table>
<thead>
<tr>
<th>Prognostic factor</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr) ≥40</td>
<td>1</td>
</tr>
<tr>
<td>Malignancy</td>
<td>1</td>
</tr>
<tr>
<td>Body surface area of skin detachment &gt;10%</td>
<td>1</td>
</tr>
<tr>
<td>Heart rate ≥120/min</td>
<td>1</td>
</tr>
<tr>
<td>Serum glucose &gt;14 mmol/L (252 mg/dL)</td>
<td>1</td>
</tr>
<tr>
<td>Serum bicarbonate &lt;20 mmol/L (20 mEq/L)</td>
<td>1</td>
</tr>
<tr>
<td>Serum urea nitrogen &gt;9.6 mmol/L (27 mg/dL)</td>
<td>1</td>
</tr>
</tbody>
</table>

*SCORTEN represents the summary of abnormal variables each with a weight of one among the seven independent prognostic factors.

To evaluate model calibration, the correspondence between the predicted probabilities of mortality produced by the model and the actual in-hospital mortality was evaluated by Hosmer-Lemeshow statistic. To evaluate model discrimination, we used c statistics, which represents the area under the receiver-operating characteristic (ROC) curve. The c statistic values range from 0.5 (no greater predictive power than chance) to 1.0 (perfect prediction).7,8

### RESULT

**Patients**

The database included 51 cases and 29 (56.86%) were males. Thirty-seven patients had SJS (72.55%), eight overlap SJS/TEN (15.69%), and six TEN (11.76%). The mean age was 62.71±18.90 years. The mean admission delay was 6.75±7.62 days (range 0–30). There were eight deaths at discharge with a 16% mortality rate. The mortality rate in patients with SJS, overlap SJS/TEN, and TEN were 8.11%, 37.5%, and 33.33%, respectively (Table 2). We used the same method as the original study in developing SCORTEN, if a variable was not measured for a stable patient, it was assumed to be within normal range.1 Every patient had a SCORTEN value. Among the 51 patients, there were 12 patients actually available for all seven SCORTEN factors (SJS 6/37, overlap SJS/TEN 4/8, and TEN 2/6).

**Mortality estimated by SCORTEN on the first day**

Predicted mortality numbers were calculated by using the formula (P (death) = e^{logit}/1 + e^{logit} [logit = -4.448 +1.237 (SCORTEN)]) on the first day of hospitalization; the observed mortality are presented in Table 3 and Figure 1. The observed mortality of our patients was not significantly different from the predicted mortality by using standardized mortality ratio analysis (standard mortality ratio, 1.12; 95% confidence interval, 0.48–2.21).6 There are 8 deaths among
In order to find the differences of risk factors for death between Caucasian and Asian, we tried to identify other possible risk factors other than the seven factors in SCORTEN. In our data, the admission delay and the age of the patient showed significant difference between the patients who were alive and dead. Thus, we also analyzed the admission delay and attempted to determine a new cutting value of the age. However, these two variables became non-significant while using logistic regression.

Evolution of SCORTEN during admission

We also examined the evolution of SCORTEN over time with Friedman’s test and Dunn’s multiple comparisons test. However, there was no statistical difference between the SCORTEN through day 1 to day 5.

**DISCUSSION**

In our study, the mortality rate of patients diagnosed with SJS or TEN is 16%, which is lower than the 20–30% mortality rate reported in France and the United States. This may be because that the most of our cases were diagnosed with 51 reviewed cases. Their clinical information is listed in Table 4.

**The performance of SCORTEN**

The successive SCORTEN values of the first 5 days of hospitalization are demonstrated in Table 5. Calibration and discrimination of the SCORTEN were evaluated by logistic regression. Calibration of the SCORTEN evaluated by Hosmer-Lemeshow statistic indicated an excellent agreement between the expected and observed numbers of deaths. Moreover, calibration was best on the first day of admission (p = 0.88). Discrimination of the SCORTEN was excellent and all c statistics were above 80% (Table 5).

**Reanalysis of variables used to develop SCORTEN in our data**

We collected all variables used to develop SCORTEN. We obtained a formula predicting the mortality with logistic regression with our own patient: 

\[
P(\text{death}) = \frac{e^{\text{logit}}}{1 + e^{\text{logit}}} \]

where logit = –4.448 + 1.237(SCORTEN). The result revealed similar findings between the predicted number of death calculated by our formula and the original SCORTEN formula.
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SJS(T37/51), which has lesser skin detachment and lower mortality rate (<10%) compared with the mortality rate (30 to 50%) of SJS/TEN overlap and TEN.

The performance of SCORTEN on the first day of admission as demonstrated in Table 3 revealed good correspondence between the observed and predicted mortality, meaning that the SCORTEN is suited in predicting the mortality of SJS and TEN in Taiwanese. We also analyzed the performance of SCORTEN in the first 5 days of admission. The highest correlation was on the first day of admission. A previous study showed an excellent agreement between the observed and expected numbers of death during the first 5 days of admission, with the highest agreement on the third day. Their data suggested that SCORTEN might evolve over time since the disease did progress significantly in the first few days. The SCORTEN score might underestimate the mortality on day 1 and day 2 and overestimate the mortality on day 4 and day 5. However, our data showed high p value of the Hosmer-Lemeshow statistic on each of the first 5 days of admission, especially on the first day. In our opinion, the original SCORTEN model was established by using data obtained on the first day. As a result, it should have the best agreement on the first day. We suggested that, in Taiwanese patients with SJS or TEN, SCORTEN should always be obtained during the first 24 hours, and could be repeated if the patient's condition deteriorated quickly in the first 5 days.

We also obtained our formula for predicting the mortality with logistic regression within our patient. We compared the predicted mortality with the mortality calculated by the original SCORTEN formula. The result revealed similar findings between the observed number of deaths and predicted number of deaths calculated by the original formula and our formula. The above results indicated that there is no difference in the SCORTEN-predicted mortality between Caucasian and Taiwanese.

The SCORTEN could be used to evaluate the effectiveness of new therapeutic agents. The predicted mortality rate could also be modified when effective treatment becomes available. The performance of the SCORTEN has been examined at a burn center in Canada, with results suggesting SCORTEN as an accurate scoring system. In another study in the United States, only 24 cases of TEN were included. The difference between the actual and predicted mortality found in that study was not statistically significant. The same author had used SCORTEN to evaluate the mortality of 16 patients treated with IVIG. The result revealed that the mortality of patients treated with IVIG significantly decreased in comparison with the SCORTEN-predicted mortality rate. Another study in 2006 claimed that SCORTEN overestimates mortality. In that study, 109 patients diagnosed with TEN were enrolled. They were admitted to the burn intensive care unit and thus received higher standardized treatment than did the ordinary ward, including routine IVIG administration. The lower mortality rate in this study

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Clinical information of deceased patients.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis at admission/clinical condition and possible cause of SJS/TEN disease (in 24 hrs)</td>
<td>Serum bicarbonate (mmol/L)</td>
</tr>
<tr>
<td>Underlying disease</td>
<td>Serum glucose (mmol/L)</td>
</tr>
<tr>
<td>C1</td>
<td>84M</td>
</tr>
<tr>
<td>C2</td>
<td>78M</td>
</tr>
<tr>
<td>C3</td>
<td>83M</td>
</tr>
<tr>
<td>C4</td>
<td>56F</td>
</tr>
<tr>
<td>C5</td>
<td>81M</td>
</tr>
<tr>
<td>C6</td>
<td>81M</td>
</tr>
<tr>
<td>C7</td>
<td>71M</td>
</tr>
<tr>
<td>C8</td>
<td>71M</td>
</tr>
</tbody>
</table>

SJS = Stevens-Johnson syndrome; TEN = toxic epidermal necrolysis; M = male; F = female; TBSA = total body surface area; DM = diabetes mellitus; TB = tuberculosis; ICG = intracranial hemorrhage; SLE = systemic lupus erythematosus; HTN = hypertension; COPD = chronic obstructive pulmonary disease; CVA = cerebrovascular accident; TCC = transitional cell carcinoma; Tx = treatment; ND = not done.
may be attributed to the standardized protocol, including routine administration of IVIG. However, it remains controversial whether IVIG was an effective treatment of SJS or TEN.4,11–16

There are several severity-of-illness score being used to evaluate the mortality rate for critically ill patients but none are developed specifically for the patients of SJS and TEN. Acute Physiology and Chronic Health Evaluation II (APACHE II) score, one of the most commonly used score, has been used in patients with TEN for evaluating the therapeutic interventions. Research was only able to show that higher APACHE II score correlated with increasing mortality without validating its discriminatory power in predicting mortality.17,18 The risk factors of scores proposed for burns are usually related to inhalation injury in addition to age and burn area.19 With respect to Simplified Acute Physiology Score II (SAPS II), the original development sample excluded burns patients and TEN patients.1 In fact, the discriminatory powers of SAPS II and the burn score proposed by Ryan et al19 were not satisfactory given that the area under the ROC curve was 0.72 in the former and 0.75 in the latter.

There were eight deaths in our study and seven of them developed SJS or TEN after admission. They were all complicated with sepsis and antibiotics were suspected as the causative agents of SJS and TEN. If there was no other suitable antibiotic that could treat the infection without exacerbating the skin condition, the patient would have less chance to survive.

There were two cases with active tuberculosis and five with diabetes mellitus in our deceased patients. It has been proposed that tuberculosis and pre-existing diabetes should be taken into account.20 Since pre-existing tuberculosis could be considered as a kind of pulmonary condition that could be reflected on serum bicarbonate, and pre-existing diabetes could be reflected on serum glucose level, these pre-existing conditions may require more consideration in future studies.

Investigators have proposed that SCORTEN might not reflect the effect of respiratory involvement such as bronchial necrosis21 since it did not include ventilated patients in the first 5 days of admission in the original study.1 In our opinion, the factor serum bicarbonate level could be taken as a predicting factor for poor oxygenation. In our study, there were seven cases ventilated during the first 5 days of admission. The good performance of predicted mortality rate was not affected.

It has been argued that SCORTEN should be modified, and that BSA involvement and age should be weighted more in calculations.20 The main problem is related to the statistical method. We tried to analyze our patient data with Cox’s regression model and tried to grade the value of each variable. However, we also encountered similar problems discussed in the original article proposing the SCORTEN, which enrolled 165 patients.1 Another study suggesting modification of SCORTEN only enrolled 10 patients.20 Logistic regression might not be the best method in this type of study, but it is a relatively acceptable and feasible way for providing useful information. Thus, we applied logistic regression to examine our variables.

The admission delay and the age of the patient showed significant differences between the survivors and the deceased in our raw data analysis. However after analyzing the admission delay using the logistic regression model, no significant differences emerged. In a previous study,5 the admission delay was not different between deceased patients and survivors; this result was probably attributed to earlier

### Table 5

<table>
<thead>
<tr>
<th>SCORTEN, mean±SD</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximal value</td>
<td>6</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>SCORTEN (%)</td>
<td>0</td>
<td>2 (3.92)</td>
<td>2 (3.92)</td>
<td>3 (5.88)</td>
<td>3 (5.88)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>24 (47.06)</td>
<td>23 (45.10)</td>
<td>20 (39.22)</td>
<td>20 (39.22)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>17 (33.33)</td>
<td>17 (33.33)</td>
<td>15 (29.41)</td>
<td>14 (27.45)</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>4 (7.84)</td>
<td>5 (9.80)</td>
<td>6 (11.76)</td>
<td>7 (13.73)</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>3 (5.88)</td>
<td>3 (5.88)</td>
<td>6 (11.76)</td>
<td>5 (9.80)</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>1 (1.96)</td>
<td>1 (1.96)</td>
<td>1 (1.96)</td>
<td>1 (1.96)</td>
</tr>
<tr>
<td>SCORTEN, OR (95% CI)</td>
<td>3.36 (1.42–7.96)</td>
<td>5.16 (1.82–14.63)</td>
<td>4.94 (1.86–13.08)</td>
<td>4.67 (1.75–12.52)</td>
<td>5.89 (1.98–17.52)</td>
</tr>
<tr>
<td>ρ (calibration)*</td>
<td>0.88</td>
<td>0.73</td>
<td>0.52</td>
<td>0.65</td>
<td>0.79</td>
</tr>
<tr>
<td>c statistic†</td>
<td>0.808</td>
<td>0.887</td>
<td>0.910</td>
<td>0.904</td>
<td>0.922</td>
</tr>
</tbody>
</table>

*As determined by Hosmer-Lemeshow statistic in logistic regression, it indicates the correspondence between the predicted and the actual in-hospital deaths; †c statistic represents the area under the receiver-operating characteristic curve, which ranges from 0.5 (no greater predictive power than chance) to 1.0 (perfect prediction).
admission of the severe cases.\textsuperscript{5} We tried to determine a cutting value for age, which had been a factor in SCORTEN, in our study population. However, due to the small sample size and possible selection bias for being a veteran hospital, where the patient group was older than the general population of patients from other hospitals, the factor ‘age’ revealed no statistic significance using logistic regression. A larger sample size is needed to collect more usable information for the variables. At present, we believe that SCORTEN is a better scoring system than other severity evaluating system for patients of SJS or TEN.

In conclusion, SCORTEN performed well in Taiwanese patients with SJS or TEN, especially for the first day of admission. The SCORTEN predicts a relatively accurate mortality. We suggest that SCORTEN should always be obtained during the first 24 hours, and could be repeated if the patient’s condition deteriorated quickly in the first 5 days.

REFERENCES


