

Use of Delta Modified Search Out Severity (Δ M-SOS) Score for Early Detect Clinical Deterioration in Mechanically Ventilated Patients

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Objective: To validate the Delta Modified Search Out Severity (Δ M-SOS) score, the predictive score for clinical deterioration in mechanically ventilated patients.

Materials and Methods: The prospective observational study included respiratory failure patients who were admitted to the respiratory care unit (RCU) of Hatyai Hospital, a tertiary care hospital, between August 2019 and February 2020. The Δ M-SOS score, score change from previous, and maximum M-SOS score were obtained. The main outcomes were clinical deterioration such as need for resuscitation, transfer to ICU, CPR, or dead, and 28-day mortality.

Results: Of the 158 enrolled patients, 54 (34%) patients developed clinical deterioration. The 28-day mortality was 33.5%. The area under the curve of the Δ M-SOS score and M-SOS were 0.78 (95% CI 0.71 to 0.86, $p < 0.001$) and 0.85 (95% CI 0.78 to 0.92, $p < 0.001$), respectively. The Δ M-SOS score at cut off 3 had sensitivity 68.5%, specificity 79.8%, positive predictive value (PPV) 63.8%, and negative predictive value (NPV) 83.0%, while the M-SOS score at a cut off score of 6 exhibited sensitivity 74.1%, specificity 83.6%, PPV 70.2%, NPV 84.1%.

Conclusion: The Δ M-SOS score had a fair to good performance as a predictive score for clinical deterioration in mechanically ventilated patients.

Keywords: Validate, Early warning score, Delta, Detect, Clinical deterioration, Mechanically ventilated patients

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Early detection of clinical deterioration by using the early warning score (EWS) is the main purpose of early intervention to improve outcomes⁽¹⁾. The Modified Search Out Severity (M-SOS) score (Table 1) adapted from the Search Out Severity (SOS) score was developed by the medicine department, Buddhachinaraj Hospital. The M-SOS score is an aggregate weighted scoring system that calculates a score from the derangement of vital signs variable in a weighted manner similar to the Modified Early Warning Score (MEWS)⁽²⁾, or to the National Early Warning Score (NEWS)⁽³⁾. These type of score have good predictive performance in general patients⁽¹⁾.

However, the EWS demonstrated limitation in critically ill patients when hemodynamic and respiratory support may influence the change of vital sign variables⁽⁴⁾. The baseline M-SOS score for a mechanically ventilated patient is 2, with a threshold of 3 a slight change of vital sign may cause a false alarm and potentially result in alarm fatigue. Therefore to improve the accuracy of EWS, the delta change from baseline score may be the key to have a better performance than the usual EWS^(5,6). Nevertheless, the delta change of the score had not been studied for the precision in this group of patients. The objective of the present study was to validate the Delta Modified Search Out Severity (Δ M-SOS) score to detect clinical deterioration in mechanically ventilated patients.

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Materials and Methods

A prospective observational study was performed in the medicine department of Hatyai Hospital, a 700-bed tertiary care hospital. The protocol was approved by the Hatyai Hospital Ethics Committee (Protocol No. 60/2562).

Study population and data collection

All patients admitted to the respiratory care unit

Table 1. The Modified Search Out Severity (M-SOS) score

Score	3	2	1	0	1	2	3
Temperature (°C)		≤35	35.1 to 36	36.1 to 38	38.1 to 38.4	≥38.5	
Pulse rate (beats/minute)	≤40		41 to 50	51 to 100	100 to 120	121 to 139	≥140
Respiratory rate (breath/minute)	≤8	Mechanically ventilated		9 to 20	21 to 25	26 to 35	≥35
Systolic blood pressure (mmHg)	≤80	81 to 90	91 to 100	101 to 180	181 to 199	≥200	Vasoactive agent required
Level of consciousness			Agitate/confuse	Alert	Response to voice	Response to pain	Unconscious

(RCU) between August 2019 and February 2020 were included in the study. Eligible patients were aged 15 years or older with respiratory failure and need for mechanical ventilation and hemodynamic stable at enrollment without vasoactive agents. The exclusion criteria included pregnancy, terminal illness, and post-cardiac arrest.

The following data were collected demographic variable including age, gender, and co-morbidities, diagnosis, indication admit to RCU, type of respiratory failure⁽⁷⁾, laboratory data, duration on mechanical ventilation, complication, length of stay at RCU and hospital, and outcome including the 7-day and 28-day mortality.

Outcomes and definitions

The primary outcome was the clinical deterioration that occurred during the patient on mechanically ventilated and stay in RCU, which defined as one of the following, 1) need for resuscitation with bolus fluid at least 1,000 mL within two hours or required vasoactive agents, 2) transfer to intensive care unit (ICU), 3) cardiac arrest, 4) death. The secondary outcome was the 28-day mortality.

The M-SOS score (Table 1) was calculated by a well-trained nurse, which consisted of body temperature, pulse rate, respiratory rate, systolic blood pressure, and level of consciousness for every four hours interval as a usual vital sign record. Scores range from 0 to 14 with a cut-point at 3. The Δ M-SOS score was derived from the difference between the present and the previous 4-hour M-SOS score. Time to an event defined as the time from maximum M-SOS score to clinical deterioration.

Statistical analysis

The sample size was calculated on the basis of previous data, the prevalence of clinical deterioration in the authors' RCU patients was estimated to be 26%. To get the desired precision of 15% and 95% confidence interval (CI), the minimum sample size was 150 mechanically ventilated patients.

The continuous variables expressed with a mean \pm standard deviation (SD) in parametric distribution and median, in interquartile range [IQR] for non-parametric distribution. Categorical variables presented with percent. Differences between the clinical deterioration and the control groups analyzed with the Student t-test or Mann-Whitney U test, depending on the distribution of continuous data. Chi-square tests used for comparing categorical variables. The predictive performance that included sensitivity, specificity, positive and negative predictive value (PPV and NPV) of M-SOS and Δ M-SOS were calculated and constructed a receiver operating characteristic (ROC) curve with calculated area under the ROC curve (AUROC). The optimum cut-point value was selected by a maximizing of the Youden index⁽⁸⁾. Statistical significance defined as a p-value of less than 0.05. Stata Statistical Software, version 16.1 (StataCorp LLC, College Station, TX, USA) was used for statistical analyses in the present study.

Results

One hundred fifty-eight patients were enrolled, 55.1% were male, and the median (IQR) age was 68.5 (56, 79) years. Fifty-four patients (34%) developed clinical deterioration. The baseline characteristic are summarized in Table 2. Most of the patients (89%) had at least one co-morbid disease, which had no significant difference between the clinical deterioration and the control group. Pneumonia (47.5%) was the majority diagnosis for all participants, followed by chronic obstructive pulmonary disease (COPD) or asthma (31%), acute heart failure (29%), septicemia (15%), tuberculosis (TB) (14%), and acute respiratory distress syndrome (ARDS) (0.6%), respectively. Only COPD or asthma was significant higher in the control group (37.5% versus 18.5%, $p=0.01$). Hypoxic (88.9%) was the most common type of respiratory failure. There was a larger proportion of patients, who needed respiratory support as an indication for RCU admission in the clinical deterioration group (40.7% versus 15.4%, $p<0.001$), whereas the control group

Table 2. Baseline characteristic of mechanically ventilated patient in the clinical deterioration and control group

Characteristic	All (n=158); n (%)	Clinical deterioration (n=54); n (%)	Control (n=104); n (%)	p-value
Age (year); median (IQR)	68.5 (56, 79)	70.5 (59, 82)	67 (52.5, 77.5)	0.11
Sex: male	87 (55.1)	31 (57.4)	56 (53.8)	0.67
Underlying disease				
Hypertension	75 (47.5)	31 (57.4)	44 (42.3)	0.07
COPD/asthma	59 (37.3)	16 (29.6)	43 (41.3)	0.15
Diabetes mellitus	44 (27.8)	17 (31.5)	27 (26.0)	0.46
Dyslipidemia	34 (21.5)	11 (20.4)	23 (22.1)	0.80
Previous Stroke	23 (14.6)	12 (22.2)	11 (10.6)	0.05
Congestive heart failure	21 (13.3)	6 (11.1)	15 (14.4)	0.56
Chronic kidney disease	17 (10.8)	6 (11.1)	11 (10.6)	0.92
Ischemic heart disease	15 (9.5)	8 (14.8)	7 (6.7)	0.10
Malignancy	14 (8.9)	6 (11.1)	8 (7.7)	0.47
HIV	13 (8.2)	6 (11.1)	7 (6.7)	0.34
Diagnosis				
Pneumonia	75 (47.5)	29 (53.7)	46 (44.2)	0.26
COPD/asthma	49 (31.0)	10 (18.5)	39 (37.5)	0.01
Acute Heart failure	29 (18.4)	13 (24.1)	16 (15.4)	0.18
Septicemia	15 (9.5)	5 (9.3)	10 (9.6)	0.94
TB	14 (8.9)	5 (9.3)	9 (8.7)	0.90
ARDS	1 (0.6)	1 (1.9)	0 (0.0)	0.16
Baseline laboratory value; median (IQR)				
Blood urea nitrogen (mg/dL)	23.0 (13, 41)	40.0 (19, 70)	18.5 (11, 30)	<0.001
Creatinine (mg/dL)	0.9 (0.7, 1.5)	1.2 (0.7, 2.2)	0.9 (0.6, 1.3)	0.01
Albumin (g/dL); mean±SD	3.3±0.7	2.9±0.6	3.5±0.6	<0.001
Lactate (mmol/L)	2.3 (1.6, 3.5)	2.3 (1.7, 3.2)	2.1(1.5, 3.7)	0.82
pH	7.5 (7.4, 7.5)	7.4 (7.3, 7.5)	7.5 (7.4, 7.5)	0.28
PaO ₂ (mmHg)	135.9 (88.1, 185.0)	136.1 (86.6, 166.8)	135.9 (92.0, 200.8)	0.31
PaCO ₂ (mmHg)	30.1 (23.8, 38.5)	30.2 (23.6, 36.5)	29.9 (24.7, 40.1)	0.42
PaO ₂ /FiO ₂ (mmHg)	325 (215.7, 435.0)	297.5 (155.0, 411.2)	352.4 (257.3, 467.0)	0.02

IQR=interquartile range; COPD=chronic obstructive pulmonary disease; ARDS=acute respiratory distress syndrome; TB=tuberculosis; SD=standard deviation

wanted weaning (89.4% versus 61.1%, $p<0.001$). The four laboratory tests found statistically significant difference in the clinical deterioration group versus the control group, including blood urea nitrogen (40.0 versus 18.5, $p<0.001$), creatinine (1.2 versus 0.9, $p<0.01$), albumin (2.9 versus 3.5, $p<0.001$), and PaO₂/FiO₂ (297.5 versus 352.4, $p=0.02$). Sixteen patients (10%) died during RCU stay, and 53 (33%) died within 28 days. The clinical deterioration group had higher hospital complications, duration on mechanical ventilation, and mortality (Table 3). Whereas there had no significant difference in the length of RCU (9.5 versus 6.0 days, $p=0.15$) and in hospital (19 versus 14 days, $p=0.12$) stay. In multivariate analysis, age and

maximum M-SOS were the independent risk factors related to 28-day mortality (Table 4).

Predictive performance

The median M-SOS score at enrollment was 3, which was the same in both groups ($p=0.09$). The AUROC of Δ M-SOS and M-SOS score for prediction of clinical deterioration were 0.78 (95% CI 0.71 to 0.86, $p<0.001$) and 0.85 (95% CI 0.78 to 0.92, $p<0.001$), respectively, as shown in Figure 1. The delta changes at 3 for Δ M-SOS score had a sensitivity of 68.5%, a specificity of 79.8%, a PPV of 63.8%, and an NPV of 83%. The optimum cut-point value for M-SOS was 6, which exhibited sensitivity 74.1%,

Table 3. Complications and outcomes in the clinical deterioration and control group

Characteristic	All (n=158); n (%)	Clinical deterioration (n=54); n (%)	Control (n=104); n (%)	p-value
Duration of mechanical ventilator; median (IQR)	9.5 (5.0, 19.0)	16.5 (7.0, 30.0)	7.5 (5.0, 16.5)	0.002
Complication				
Organ failure	76 (48.1)	43 (79.6)	33 (31.7)	<0.001
Hospital acquired infection	63 (39.9)	31 (57.4)	32 (30.8)	0.001
Cardiac complication	26 (16.5)	14 (25.9)	12 (11.5)	0.02
Shock	40 (25.3)	40 (74.1)	0 (0.0)	<0.001
Cardiopulmonary resuscitation	10 (6.3)	10 (18.5)	0 (0.0)	<0.001
Length of RCU stay; median (IQR)	7.0 (4.0, 17.0)	9.5 (4.0, 24.0)	6.0 (4.0, 12.0)	0.15
Length of hospital stay; median (IQR)	15.0 (9.0, 28.0)	19.0 (9.0, 34.0)	14.0 (8.0, 23.5)	0.12
Dead during RCU stay	16 (10.0)	16 (10.0)	0 (0.0)	<0.001
Dead at 7 day	20 (12.7)	20 (37.0)	0 (0.0)	<0.001
Dead at 28 day	53 (33.5)	43 (79.6)	10 (9.6)	<0.001

IQR=interquartile range; RCU=respiratory care unit

Table 4. Multivariate analysis of factors associated 28-day mortality

Variable	Odds ratio	95% CI
Maximum M-SOS score	2.616	1.93 to 3.54
Age category <55	1.00	
Age category 55 and <70	10.257	2.18 to 48.19
Age category >70	10.62	2.47 to 45.75

M-SOS=Modified Search Out Severity; CI=confidence interval

specificity 83.7%, PPV 70.2%, and NPV 89.1%. Time median (IQR) from maximum M-SOS to a clinical deterioration event was 120 (60 to 352) minutes.

Discussion

The Δ M-SOS had a fair to good accuracy for predicting clinical deterioration in the mechanically ventilated patient. Whereas the M-SOS performed a good predictive performance. The previous study used the aggregated weight EWS in general medical patients to predict similar composite outcomes and found a higher AUROC of 0.87 (0.87 to 0.88)⁽⁹⁾. In contrast to a systematic review, which reported mixed results in the predictive ability of EWS for cardiac arrest, ICU admission, and death within 48 hours⁽¹⁰⁾. Variation in the study populations and setting such as the medical ward, surgical ward, emergency department, and pre-hospital, made it difficult to assess the effect of EWS across the studies.

The patients with baseline physiology abnormality decrease the accuracy of the EWS, as shown in the hypercapnic respiratory failure⁽¹¹⁾, brain

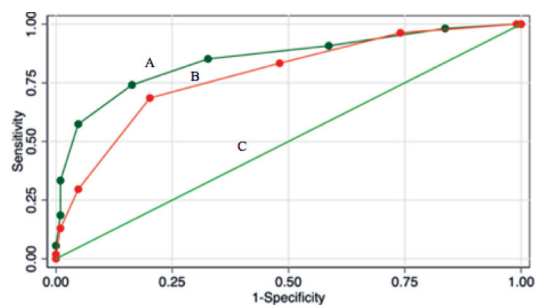


Figure 1. Receiver operating characteristic curve for the ability of M-SOS and Δ M-SOS scores to predict clinical deterioration in mechanically ventilated patients. Line A represents M-SOS score [area under the receiver operator curve (AUROC) 0.85 (95% CI 0.78 to 0.92, $p < 0.001$)], and line B Δ M-SOS score [AUROC 0.78 (95% CI 0.71 to 0.86, $p < 0.001$)]. The diagonal line C represents an AUROC=0.5.

injury⁽¹²⁾, and end of life care⁽¹³⁾. This limitation was also found in critically ill patients⁽³⁾ in which the possible explanations could be in two ways. First, the false positive or false alarm, begins with a score of 2 for a mechanically ventilated patient. A slight change of physiology variables affected the score to be oversensitive. The second was the false negative, which treatment or intervention received in ICU blunt the sympathetic activity, such as sedative or analgesic or neuromuscular blocking agent, antipyretic drug, and cooling methods. Adjusting for a new higher cut-off point at M-SOS of 6 or higher as compared to the currently used of 3, demonstrated a better predictive performance with sensitivity of 74.1% and specificity of 83.7% versus sensitivity of 98.2% and specificity of 16.4%. These findings were

similar to the other studies in a particular population, that accuracy improved by modifying the score threshold^(3,14).

According to the delta of a score, the previous studies reported the usefulness of the change of SOFA score to predict the outcomes^(5,15,16). To the authors' knowledge, this is the first study exploring the change of EWS for early detection of clinical deterioration in mechanically ventilated patients. The potential utility for the clinical use was, when the serial monitor for M-SOS scores was changed to 3 or greater, it warned about the progression and consequence with the critical events.

The median (IQR) time from maximum M-SOS to the event was 120 minutes (60, 352). Most of the previous studies predicted clinical deterioration within the range of 24 to 48 hours^(10,17), which seemed to be long. The advantage for reporting at a median time was more practical and it can be used to activate the early intervention or rapid response team. Several studies showed that abnormal vital signs were identified at an average of six to eight hours before a serious adverse event occurred⁽¹⁸⁻²⁰⁾. This difference maybe because of the higher level of the patient that already had a respiratory organ failure, which could promptly deteriorate.

There were some limitations of the present study. Firstly, the study population was only the medical patient, therefore, there had no type III, perioperative respiratory failure participant. Secondly, the present study was performed in the RCU, which might have a selection bias due to the authors' institute, the severe cases such as ARDS, pulmonary hemorrhage, and multi-organ failure, which are mostly admitted at ICU. Thirdly, the present study was a cross-sectional study that might confound the data, which might not represent the entire year, and some disease prevalence could be influenced by seasoning. Further investigation with a varied group of respiratory failure patients and setting such as medical ward, surgical ward, and ICU, need to validate the score.

Conclusion

Implement of the EWS in the specific population required score validation. The Δ M-SOS at the cut-point of 3 had a fair to good performance to predict the clinical deterioration in mechanically ventilated patients. The M-SOS showed an excellent ability, and the adjustment of trigger threshold made M-SOS perform better. However, it never replaces the physical examination skills, clinical experience, and judgment in management for the critical patient.

What is already known on this topic?

The aggregated weight, early warning score had good predictive value for general patients. Whereas for some other specific populations, more information and validation of the score before implementation is essential.

What this study adds?

For mechanically ventilated patients, Δ M-SOS scores have a fair to good predictive ability for early detection of clinical deterioration.

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Conflicts of interest

The authors declare no conflict of interest.

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