An evolution of trauma care evaluation: A thesis on trauma registry and outcome prediction models
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Chapter 6

EXTERNAL VALIDATION OF THE EMERGENCY TRAUMA SCORE FOR EARLY PREDICTION OF MORTALITY IN TRAUMA PATIENTS.

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ABSTRACT

Objective
The Emergency Trauma Score (EMTRAS) is used for early estimation of mortality risk in adult trauma patients with an Injury Severity Score (ISS) of 16 or higher. EMTRAS combines four early predictors from the trauma resuscitation room: age, Glasgow Coma Scale (GCS), base excess, and prothrombin time. The EMTRAS has not been externally validated. Our goal was to validate the EMTRAS in two external cohorts. We also examined the performance of the EMTRAS in patients with an ISS <16, to determine whether EMTRAS is applicable to all adult trauma patients treated in the trauma resuscitation room.

Design
Validation study using data from prospectively collected trauma registries. Calibration and discrimination of the original EMTRAS were assessed within each cohort separately for similar populations as the original EMTRAS population (ISS ≥16), and for patients with an ISS <16.

Setting
Two academic Level I trauma centers.

Patients
Adult patients admitted to the hospital after treatment at the trauma resuscitation room were eligible for inclusion in the cohort.

Measurement and Main Results
A total of 4418 consecutive patients were used for validation of the EMTRAS. The EMTRAS was well calibrated for patients with an ISS ≥16. Discrimination was even slightly better (area under receiver operating curve (AUROC) of 0.9 and 0.89) than the original AUROC of 0.8. The EMTRAS overestimated mortality in patients with an ISS <16, while discrimination remained good for this group of patients.

Conclusions
For patients with an ISS of 16 or higher, the calibration and discrimination of the EMTRAS were excellent. Thus, the EMTRAS is suitable for early mortality risk assessment in this group of patients. The EMTRAS is less suitable for outcome prediction of the entire group of trauma patients treated in the trauma resuscitation room because calibration diminished markedly for patients with an ISS below 16.
INTRODUCTION

A score to quantify the probability of survival of trauma patients shortly after admission to the Emergency Department (ED) enables caregivers to assess the patients’ injury severity to guide clinical decisions and allows for efficient allocation of resources.

In 2009, Raum and colleagues\(^1,2\) introduced the Emergency Trauma Score (EMTRAS) for early estimation of mortality risk in adult trauma patients. EMTRAS combines four early predictors from the emergency room and demonstrated favorable discrimination compared with more complex scores. These early predictors used by EMTRAS are age (years), Glasgow Coma Scale (GCS), base excess (mmol/L), and prothrombin time (%). For each predictor a subscore of 0, 1, 2 or 3 points is assigned, based on the actual value of the predictor. EMTRAS is defined as the sum of these subscores, i.e. the lowest (best) EMTRAS is zero and the highest (worst) is 12. The EMTRAS was developed in a large cohort (n=4808) of trauma patients with an ISS\(^3\) of 16 or higher, derived from the German Trauma Registry (http://www.traumaregister.de). The EMTRAS has been internally validated in a second cohort (n=1292) from a later period within the same database.

The EMTRAS is intended to be an easy-to-compute scoring system for the emergency room based on a limited number of clinical predictors that are commonly and early available. Despite its apparent advantages, the EMTRAS has limitations that have contributed to its relative obscurity. First, generalizability of the EMTRAS has not been established as no validation in an external database has been undertaken yet. Secondly, EMTRAS excludes patients with an ISS below 16. Anatomic injury scales, like the ISS, can only be scored reliably further along the diagnostic or therapeutic process and are usually not available during the initial resuscitation at the ED. Therefore, the ISS criterion forms a limitation to identify patients that are eligible for early outcome prediction using the EMTRAS. Ideally, all potentially severely injured trauma patients should benefit from EMTRAS, including those patients who turn out to have an ISS below 16.

The objective of this study is to validate the EMTRAS in two external cohorts. The secondary aim is to examine the performance of the EMTRAS in patients with an ISS below 16, and thus determine whether the applicability of the EMTRAS can be extended to all adult trauma patients.

PATIENTS AND METHODS

The EMTRAS was externally validated in two separate cohorts of trauma patients treated at the trauma room in an urban Level I trauma center A and a rural Level I trauma center B center in the Netherlands. Data were derived from the prospectively collected trauma registries of both trauma centers. The first cohort consisted of consecutive patients who were admitted during the period from 2004 to 2010 (center A). The second cohort consisted of consecutive patients who were admitted during the period from 2006 to 2011 (center B). In both centers, patients treated at the trauma resuscitation room were judged potentially severe trauma patients and eligible for inclusion in the cohort. The decision for a patient to be transported to a Level I trauma center is based on the triage and expertise of the prehospital Emergency Medical Services personnel, following national and international protocols. Triage criteria include vital parameters and mechanism of injury. The initial evaluation and resuscitation of trauma...
patients was performed following ATLS guidelines. All patients admitted to the hospital, patients who died in the ED, or patients referred immediately after trauma, were included. Patients declared dead on arrival, patients discharged home directly from the ED and children (aged younger than 16 years) were excluded.

**EMTRAS Calculation**

Four predictors for mortality are included in the EMTRAS: age in years, Glasgow Coma Scale (GCS), base excess (mmol/L) and prothrombin time (%). Each predictor value is scored into 4 categories ranging from zero to three. EMTRAS is defined as the sum of these subscores, i.e. the lowest (best) EMTRAS is zero and the highest (worst) is 12. Subscores for the predictors (Table 1) and coefficients for calculation of predicted mortality were taken from the original publication. The GCS was recorded on admission at the emergency department. In intubated patients, the most recent GCS before intubation was recorded. Laboratory tests were obtained directly on, or shortly after admission at the emergency department. Prothrombin time was expressed as percent of the reference value. Outcome in the two validation cohorts was inhospital mortality, as it was in the original EMTRAS study.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Category</th>
<th>Subscore</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>&lt;40</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>40-60</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>61-75</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>&gt;75</td>
<td>3</td>
</tr>
<tr>
<td>Glasgow Coma Scale</td>
<td>13-15</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>10-12</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>6-9</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>3-5</td>
<td>3</td>
</tr>
<tr>
<td>Base excess (mmol/L)</td>
<td>&gt;-1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>-1 to -5</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>-5.1 to -10</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>&lt;10</td>
<td>3</td>
</tr>
<tr>
<td>Prothrombin time (%)</td>
<td>&gt;80</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>80-50</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>49-20</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>&lt;20</td>
<td>3</td>
</tr>
</tbody>
</table>

| Table 1 | Emergency trauma score subscores |

**Statistical Analysis**

Multiple imputation methods (10 rounds) were used to impute missing values on the EMTRAS predictors in the validation cohort. Imputation was done on the original continuous measurement scale of the predictors based on multivariate normal distributions. Values for age (center A and B) and GCS (center B) were complete, so no imputation was needed. Other available variables deemed valuable for imputation of EMTRAS predictors were: sex, ISS, outcome, heart rate, systolic blood pressure, oxygen saturation, respiratory rate, serum lactate, hemoglobin, platelet count and activated partial thromboplastin time. For analysis involving imputed data, the results of \( m=10 \) imputed datasets were combined to obtain final estimates.
External validation of the EMTRAS

Performance of the EMTRAS was studied by determining calibration and discrimination within both cohorts after imputation. Calibration and discrimination were analyzed within each cohort separately for a similar population as the original EMTRAS population (ISS ≥16), and for patients with an ISS <16.

Calibration plots were used to visualize predicted and actual mortality. Discrimination was measured by calculating the area under receiver operating curve (AUROC) with 95% confidence intervals. In the calibration and discrimination analysis the EMTRAS was applied as it was presented in the original paper, i.e. a twelve-point scale based on recorded predictors.

Regression coefficients using the EMTRAS predictors in their continuous form were re-estimated in each validation cohort and compared to the coefficients of the original generating cohort (Table 3 in Raum and personal communication). A risk score was calculated based on the original coefficients following the formula: 0.4035 + 0.0397*Age - 0.1722*GCS - 0.0639*base excess - 0.0334*prothrombin time. Coefficients were re-estimated for the EMTRAS predictors in the two validation cohorts using logistic regression with the risk score used as offset. In this way, the difference between the original and newly estimated coefficient could be tested for statistical significance. Significance was attributed to a p-value of 0.05.

All analysis was performed using the Statistical Package for Social Sciences version 18.0 (IBM, 2010, USA).

RESULTS

During the years 2004 to 2010, a total of 3001 patients were admitted to center A after presentation at the trauma resuscitation room. Two hundred patients died in hospital (overall mortality 6.7%). Of the 1417 patients who were admitted to center B after presentation at the trauma resuscitation room during the period 2006 - 2011, a total of 203 patients died in hospital (overall mortality 14.3%).

Table 2 shows demographic data and prognostic variables in both validation cohorts. The original population in which the EMTRAS has been developed (‘EMTRAS’ population), is included for comparison.

Both validation cohorts for patients with an ISS ≥16 were comparable for sex and injury mechanism with the original EMTRAS population. For patients with an ISS ≥16 mortality was 17.1% in center A and 25.2% in center B. The mean ISS was lower in center A (25.5) and almost equal in center B (29.9) compared to the original EMTRAS population in which overall mortality was 21.9%. The distribution of the EMTRAS predictor values was comparable between the validation cohorts and the original EMTRAS population. Age and GCS for both validation cohorts were similar to the original EMTRAS population. Base excess was slightly lower for both validation cohorts, while prothrombin time was slightly shorter.

The validation cohorts for patients with an ISS <16 showed small differences for sex (more females in center A) and injury mechanism (more penetrating in both centers) with the EMTRAS population. Age in both cohorts was comparable with the EMTRAS population. As expected, the distribution of predictor values were more favourable in patients with an
ISS <16; including a higher GCS, a higher base excess and a shorter prothrombin time than in the original EMTRAS population. These findings correlate with a less severely injured population with a mean ISS of 6.3 and 7 for center A and center B respectively. Mortality in both validation cohorts for patients with an ISS <16 was 1.4%. Physiologic parameters, except GCS, were not available for center B.

Predictors for EMTRAS calculation were complete for 2353 patients (78.4%) in the center A, and for 1096 patients (77.3%) in the center B. Calibration and discrimination analysis were performed on the imputed datasets.

![Graph 1](image1.png)

Figure 1. Calibration of the Emergency Trauma Score in trauma center A (continuous line) and B (dashed line) for patients with an ISS ≥ 16. Each dot represents patients with similar EMTRAS scores (ie EMTRAS 0, EMTRAS 1 etc). Higher EMTRAS scores are represented with a single dot due to smaller patient numbers. The diagonal line indicates perfect calibration.

![Graph 2](image2.png)

Figure 2. Calibration of the Emergency Trauma Score in trauma center A (continuous line) and B (dashed line) for patients with an ISS < 16. Each dot represents patients with similar EMTRAS scores (ie EMTRAS 0, EMTRAS 1 etc). Higher EMTRAS scores are represented with a single dot due to smaller patient numbers. The diagonal line indicates perfect calibration.
## External validation of the EMTRAS

### Original cohort

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Number of patients</th>
<th>ISS ≥ 16</th>
<th>ISS &lt; 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>11533</td>
<td>1013</td>
<td>770</td>
</tr>
<tr>
<td>Male (%)</td>
<td>73.4</td>
<td>100/100</td>
<td>73.1</td>
</tr>
<tr>
<td>ISS</td>
<td>30.1 (±12.5)</td>
<td>100/100</td>
<td>25.5 (±10.7)</td>
</tr>
<tr>
<td>Blunt (%)</td>
<td>96.3</td>
<td>100/100</td>
<td>92.1</td>
</tr>
</tbody>
</table>

### EMTRAS predictors

- **Age (years)**: 42.3 (±19.2)
- **GCS**: 10 (±4.9)
- **BE (mmol/L)**: -3.3 (±5.4)
- **PT (%)**: 73.9 (±2.6)
- **complete (n)**: 4808

### Physiologic

- **SBP (mmHg)**: 119 (±32)
- **HR (per minute)**: 91 (±24)
- **O₂ Sat. (%)**: 97 (±6)
- **RR (per minute)**: 14.9 (±5.4)
- **Intubation (%)**: 94.0

### Laboratory test

- **Hb (g/dL)**: 11.0 (±3.2)
- **PC (10E9/L)**: 190 (±58)
- **APTT (s)**: 38.8 (±24.1)
- **Lact. (mmol/L)**: 5.3 (±8.6)
- **INR**: 19.90

### Outcome

| Mortality (%) | 21.9 | 100/100 | 17.1 | 25.2 | 100/100 | 1.4 | 1.4 |


Table 2 | Characteristics of potentially severe trauma patients who were admitted to trauma center A and trauma center B. The original generating population of the Emergency Trauma Score is shown in the second column.
The EMTRAS was well calibrated in both validation cohorts when selecting patients with an ISS ≥ 16 (Figure 1). In patients with an ISS < 16, the EMTRAS overestimated mortality in both validation cohorts, as is shown in Figure 2.

The EMTRAS demonstrated good discrimination for both validation cohorts for patients with an ISS ≥ 16, as well as patients with an ISS < 16. Discrimination was even slightly better than the AUROC of 0.81 for the original EMTRAS population. AUROC’s together with confidence intervals are presented in Table 3.

Re-estimation of the logistic regression coefficients using the EMTRAS predictors in their continuous form in the validation cohort resulted in significant changes for several predictors compared to the original coefficients (Table 4). For patients with an ISS ≥ 16 the coefficient for GCS changed significantly in both validation cohorts, while the coefficient for the prothrombin time changed significantly only for center A. For patients with an ISS < 16 the coefficient for GCS changed significantly for center A. The direction of change indicated to a stronger association between the predictor and mortality, which corresponds with the increase in AUROC’s found in both validation cohorts.

### Table 3

| Validation cohorts | 
|-------------------|---|---|---|---|---|---|---|---|
| ISS ≥ 16          | Original cohort | center A | center B | center A | center B | center A | center B | center A | center B |  |
| Number of patients | 4808 | 1013 | 770 | 1988 | 647 |  |
| AUROC (95%CI)     | 0.81 (0.80 – 0.83) | 0.90 (0.88 – 0.92) | 0.89 (0.87 – 0.92) | 0.94 (0.90 – 0.98) | 0.82 (0.65 – 0.99) |  |

**Table 3** Discrimination of the Emergency Trauma Score in the original and the two validation cohorts stratified by ISS. Discrimination is expressed by the area under the receiver operating curve (AUROC).

### Table 4

| Validation cohorts | 
|-------------------|---|---|---|---|---|---|---|---|
| ISS ≥ 16          | Original cohort | center A | center B | center A | center B | center A | center B | center A | center B |  |
| Predictor         | p-value | p-value | p-value | p-value | p-value | p-value | p-value | p-value | p-value |  |
| Age               | 0.0397 | 0.040 | 0.94 | 0.048 | 0.16 | 0.034 | 0.66 | 0.077 | 0.13 |  |
| Glasgow Coma Scale| -0.1722 | -0.242 | 0.01 | -0.312* | 0.00 | -0.306* | 0.02 | -0.291 | 0.15 |  |
| Base excess       | -0.0639 | -0.083 | 0.32 | -0.072 | 0.74 | -0.130 | 0.08 | -0.027 | 0.74 |  |
| Prothrombin       | -0.0334 | -0.047* | 0.02 | -0.039 | 0.41 | -0.039 | 0.58 | -0.017 | 0.34 |  |

**Table 4** Original coefficients and re-estimated coefficients for Emergency Trauma Score predictors in the two validation cohorts stratified by ISS. P-values indicate to the difference between the original coefficient and the re-estimated coefficient in the validation cohort.

*significant change.
DISCUSSION

The results of this study show that the EMTRAS for early prediction of mortality performs well in two external validation cohorts. For patients with an ISS of at least 16 the EMTRAS discriminates even slightly better between those who will survive and who will not than in the original study. The EMTRAS is well calibrated for this group of patients, as predicted mortality is in close agreement with observed mortality across the full range of the EMTRAS score. The EMTRAS can also be used to discriminate between survivors and non-survivors in patients with an ISS below 16, but the EMTRAS is poorly calibrated in these patients. EMTRAS is a feasible tool to estimate mortality risk at an early stage in potentially severe trauma patients, as approximately 80% of the patients has complete data to calculate EMTRAS.

The strength of the EMTRAS can be explained by the fact that each predictor alone is strongly related to mortality and that the model was developed in a large cohort producing robust estimates. Age represents an independent predictor of mortality in trauma patients. 

Age classified in five categories improved predictive performance over age as a continuous linear variable. The age categories in that study (15-44, 45-54, 55-69, 70-79, 80+) included an extra category for septuagenarian but were otherwise much comparable to the EMTRAS age categories.

Initially described as an assessment tool for head injured patients, the GCS has become an essential component of trauma severity systems. In the Revised Trauma Score the GCS carries the most weight compared to the respiratory rate and systolic blood pressure. It has been suggested that physiologic data, like GCS, are often missing. In our study data for GCS were missing in approximately 10% of the cases for center A, while there were no missings for center B. The GCS cannot be obtained reliably in intubated or obtunded patients. Using the motor component of the GCS, only partly eliminates this problem as most intubated patients are sedated as well. In this study we used the last GCS obtained before intubation.

The base excess and prothrombin time both reflect the life-threatening condition called the ‘lethal triad’. Base excess reliably reflects physiologic disturbances in trauma patients. An outcome prediction model for trauma patients incorporating base excess outperformed existing models in trauma patients admitted to the intensive care. Improved discrimination of models incorporating base excess was confirmed in a Dutch trauma population. Most early trauma deaths are related to uncontrolled hemorrhage. Coagulopathy is invariable related to hemorrhagic shock and is an independent predictor of mortality. Both laboratory parameters were available in the majority of trauma patients, also in those who were less severely injured (approximately 90%). However, there are two disadvantages that make prothrombin time less suitable for an early prediction model. It is not sensitive for acute traumatic coagulopathy and it may take 45-60 minutes for the result to become available, although modern analyzers can report prothrombin time within 30 minutes.

The strength of this study is that it addresses some of the shortfalls of the original EMTRAS publication as were noted by Esposito in his fine commentary. As suggested, the performance of EMTRAS in patients with an ISS < 16 is investigated. Missing values in prognostic models lead to a reduction in statistical power and may lead to biased results. In our study, multiple imputation was applied on predictors necessary for EMTRAS calculation and therefore no cases were lost for analysis. This study is the first validation of the EMTRAS in an external database.
How should the poor calibration for patients with an ISS below 16 be explained? Either there is a structural overestimation of mortality, or an under registration of deceased patients. The possibility of under- or incorrect registration of mortality could be excluded since the relevant administrative procedure is strictly monitored. Therefore, we sought to find explanations in our data that contribute to a high EMTRAS but that are not related to an increased mortality risk due to trauma. A few cases of epileptic insult combined with minor injuries have been identified that can explain a low GCS but this usually does not result in adverse outcome. Other causes of impaired consciousness not caused by trauma are alcohol intoxication and hypothermia. Inevitably, some patients will have been sedated and intubated because of dangerous agitation and have been assigned a GCS of 3. Finally, oral anticoagulant therapy was not evaluated in this study. In some cases the prothrombin time may have been prolonged due to anticoagulant therapy and not related to traumatic hemorrhage or tissue injury.

We rejected the possibility of taking both patient groups with an ISS ≥ 16 and ISS < 16 together and determine EMTRAS performance in the complete group. Despite better overall calibration, the poor calibration in the ISS < 16 would have been obscured by the good calibration in the ISS ≥ 16.

Several limitations need to be taken into account when interpreting the results of this study. Our primary aim was to validate the EMTRAS in an external dataset. About one-third of the patients included in this study were treated in center B. The same center also contributes patients to the German Trauma Registry. The EMTRAS was originally developed in a cohort of the German Trauma Registry during the period 1993 until 2003. Therefore, theoretically we conducted a partly temporal validation of the EMTRAS. However, the contribution of center B to the original EMTRAS population was approximately 1%, so we consider this study to be a truly external validation.

Inclusion criteria for patients judged as potentially severe trauma patients were not identical for both institutions. In center A all patients presented at the trauma resuscitation room were included, while for center B only ‘code red’ patients were included. For patients not classified as ‘code red’ no full trauma team was activated and no extensive laboratory tests were routinely performed. Therefore, these patients were not eligible for EMTRAS calculation. This resulted in the inclusion of relatively more severe injured patients for center B. The ratio of ISS ≥16 versus ISS <16 was approximately 1:2 for center A and 1:1 for center B. This also demonstrates that even in the presence of a national ambulance protocol that states criteria for Level I trauma center referral, in-hospital triage criteria vary between institutions around the country. Determining criteria for potential severe trauma patients eligible for early outcome prediction using the EMTRAS that coincide with field triage criteria proves to be difficult. In particular when these criteria will be applied to emergency medical systems in various countries with different pre-hospital triage protocols and in-hospital trauma team activation protocols. Early outcome prediction using the EMTRAS of a broader range of trauma patients, e.g. including those with normal physiologic parameters, would increase missing data for a selected group of patients. Presumably, many institutions will not routinely perform laboratory tests like base-excess and prothrombin time on hemodynamically stable trauma patients.

For the above mentioned reasons, and due to the poor calibration of the EMTRAS in patients with an ISS < 16, this study has failed to identify patients eligible for early outcome prediction.
External validation of the EMTRAS

using the EMTRAS on other criteria than the ISS. For practical reasons, inclusion criteria for those amenable for EMTRAS outcome prediction should coincide with (field) triage criteria or trauma team activation criteria.

The clinical value of the EMTRAS has not been established with this study. Discrimination and calibration for patients with an ISS ≥ 16 is good, so the EMTRAS seems to be suitable for prognostication of this group of patients. The practical value of the EMTRAS as a tool for clinical decision making needs to be determined in further studies. The potential of the EMTRAS lies in the selection of patients who may benefit of damage control surgery, who need admission to a monitored setting or in counseling patient and family.

CONCLUSION

The present study validates the EMTRAS for early outcome prediction of trauma patients in two external cohorts. For patients with an ISS of 16 or higher the performance of the EMTRAS, examined by discrimination and calibration, was excellent. The EMTRAS tended to overestimate mortality risk in patients with an ISS below 16.

Eligibility criteria for early outcome prediction with the EMTRAS based on the ISS is undesirable, as the anatomic nature of the ISS prevents early calculation during the resuscitation process.
REFERENCES

5. American College of Surgeons Committee on Trauma. Advanced Trauma Life Support for Doctors. Chicago, IL: American College of Surgeons; 2008.
External validation of the EMTRAS