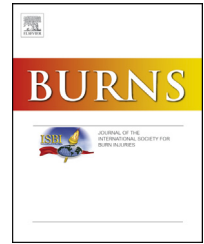


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# Do standard burn mortality formulae work on a population of severely burned children and adults?

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## ABSTRACT

Accurate prediction of mortality following burns is useful as an audit tool, and for providing treatment plan and resource allocation criteria. Common burn formulae (Ryan Score, Abbreviated Burn Severity Index (ABSI), classic and revised Baux) have not been compared with the standard Acute Physiology and Chronic Health Evaluation II (APACHEII) or re-validated in a severely ( $\geq 20\%$  total burn surface area) burned population. Furthermore, the revised Baux (R-Baux) has been externally validated thoroughly only once and the pediatric Baux (P-Baux) has yet to be. Using 522 severely burned patients, we show that burn formulae (ABSI, Baux, revised Baux) outperform APACHEII among adults (AUROC increase  $p < 0.001$  adults;  $p > 0.5$  children). The Ryan Score performs well especially among the most at-risk populations (estimated mortality [90% CI] original versus current study: 33% [26–41%] versus 30.18% [24.25–36.86%] for Ryan Score 2; 87% [78–93%] versus 66.48% [51.31–78.87%] for Ryan Score 3). The R-Baux shows accurate discrimination (AUROC 0.908 [0.869–0.947]) and is well-calibrated. However, the ABSI and P-Baux, although showing high measures of discrimination (AUROC 0.826 [0.737–0.916] and 0.848 [0.758–0.938]) in children, exceedingly overestimates mortality, indicating poor calibration. We highlight challenges in designing and employing scores that are applicable to a wide range of populations.

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## 1. Background

Burn is a significant global public health concern and is one of the major causes of trauma-related mortality worldwide [1].

The prediction of mortality following burn is advantageous to evaluate processes of care, to analyze and standardize populations for research purposes, and for its potential to provide criteria for triage and information to clinicians, patients and their families considering care plans. For the

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latter uses, accuracy and statistical validity of the formulae are crucial, particularly when applied to populations most at risk for death, namely those with severe burns. In addition to the Acute Physiology and Chronic Health Evaluation (APACHE II) severity score or the DENVER2 score for multiple organ failure (MOF) developed for the general ICU population, there are several commonly used burn patient-specific formulae. These burn-specific severity scores include the Ryan Score, Abbreviated Burn Severity Index (ABSI) and the classic and revised Baux Scores. It is necessary to evaluate whether or not specialized burn scores indeed provide a more accurate prediction than generalized scores, among critically ill burn patients.

The Ryan study, which included adult and pediatric patients admitted between 1990 and 1994, identified burn size >40% TBSA, age >60 years and inhalation injury status as the three major risk factors for mortality [2]. These grouped variable categories, as established by the Ryan Score, have been studied in various populations [3–5], but not specifically in a severely burned setting. The classic Baux Score, formulated in 1961 [6,7] and the ABSI described in 1982 [8] have been validated in various studies [3,9–14]. However, some have proposed that updated scoring systems reflecting treatment improvements and demographic changes may be advantageous [10,11,15]. A recent study found that mortality among patients with extensive burns have significantly reduced since the 1960s [16], thus further suggesting that the Baux Score developed prior to these improvements may require modifications. The revised-Baux (R-Baux) Score for adults, which differs from its predecessor by the inclusion of the presence of inhalation injury in the cumulative score was described in 2010 [17] and externally validated thoroughly in a large independent cohort [18]. It was also assessed in a study using a limited number of patients [4]. The pediatric-Baux (P-Baux) Score [19] was subsequently devised in 2013 and is yet to be externally validated.

These scoring formulae were developed using non-homogenous populations including patients with all kind of burn sizes (ranging in TBSA minimum category range 0–10% to maximum category range 90–100%) and none of them have been externally validated in a population of extensively ( $\geq 20\%$  TBSA) burned adult and children. Considering that burn size is one of the most important predictors of death, error is potentially introduced when the formula used was developed based on a general population of burn patients among which the vast majority of subjects have smaller burns. Especially since severe burns would likely lead to disproportionately increased mortality, inclusion of data points of small burns may influence the coefficient estimates of the fitted logistic regression models and subsequently may result in under or overestimation of mortality probability among a unique population of extensively burned patients. Furthermore, the recently developed R-Baux has been re-validated vigorously only once in a population of less severe burns (TBSA 6% median 3–12% interquartile range) [18] and the P-Baux has yet to be externally validated. Lastly, despite various studies investigating mortality scores, one evaluating the different scores simultaneously and examining both the adult and pediatric patients from the same study base has never been conducted. We therefore compared the various burn-specific scores to the generalized APACHEII and re-validated them

using severely thermally injured patients with at least 20% TBSA. Our findings contribute to the on-going discourse on the performance and validity of different mortality prediction scoring systems in burn patients.

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## 2. Methods

### 2.1. Study design/patient and definition outcome

This study was performed by means of the secondary use of 573 patient clinical data from the Inflammation and the Host Response to Injury Study (“Glue Grant”), a prospective, longitudinal study which enrolled burn patients with minimum 20% total burn surface area (TBSA) at six US institutions between 2003 and 2009. Permission for this secondary use of the de-identified data was obtained from the Massachusetts General Hospital Institutional Review Board. Among a total of 573 patients, 522 patients with early arrival ( $\leq 96$  h), having complete clinical data and spent at least one day in the ICU were included in the analysis. Fifty-one patients were excluded for one or more of the following reasons: 2 patients had arrival hour since injury >96 h, 6 patients had days in ICU < 1, 3 patients suffered from electrical burns, thus TBSA values were considered to be not representative of the severity of their burn, 42 patients had missing data (40 patients in the field of APACHEII and 2 patients had missing height information) (Supplementary Figure 1). The 42 patients with missing data appeared to be at random, with TBSA range 28–92 and age 0–78, 55% suffered from inhalation injury, 70% were males and reported mortality was 16.5% death, therefore we considered them as not affecting the analyses. Participating institutions followed the guidelines outlined by the GLUE Grant Consortium for the diagnosis of inhalation injury – physical examination, followed by bronchoscopy, where possible [20]. Where bronchoscopy was not performed, the following clinical criteria were considered: burns of the head and neck, burn occurring in a closed space vicinity, carboxyhemoglobin >15 if obtained in a timely manner after burn, carbonaceous sputum, and burns and/or soot in the oropharynx. Bronchoscopy was conducted in patients with these clinical criteria among intubated patients, where possible. For bronchoscopic confirmation, the minimal criteria for diagnosis was observation of either patchy areas of erythema or carbonaceous deposits in the proximal and/or distal bronchi. A total of 77 patients were considered to have experienced death due to burn trauma in our study if they had recorded death days before discharge (69 patients); or death recorded after discharged to another acute care facility (3 patients) or inpatient rehabilitation facility (2 patients); or when death were recorded after discharge to a nursing home from primary causes related to burn including sepsis, multiple organ failure, pneumonia (1 patient), hypoxia (1 patient) and respiratory failure (1 patient). One patient with recorded death 119 days after discharge at home from liver infection was classified as a survivor, thus making the total number of non-survivors to 77 and survivors to 445 (Supplementary Figure 2).

For assigning age- and sex-adjusted BMI categories (underweight, healthy, overweight, obese), patients were classified according to the Centers for Disease Control and

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