Original Article

Limited Prognostic Utility of a Simplified Vital Sign Based Risk Calculator in Acute Medical Admissions

R Conway, D Byrne, D O'Riordan & B Silke

Abstract

Background: *Accurate efficient prognostication in acute medical admissions remains challenging.***Methods***: We constructed a Vital Sign based Risk Calculator using vital parameters and Major Disease Categories to predict 30-day in-hospital mortality using a multivariable fractional polynomial model.*

Results: *We evaluated 113,807 admissions in 58,126 patients. The Vital Sign based Risk Calculator predicted 30-day in-hospital mortality to increase from 2 points - 3.6% (95%CI 3.4, 3.7) to 12 points - 14.8% (95%CI 14.0, 15.7). AUROC was 0.74 (95%CI 0.72, 0.74). The addition of illness severity and comorbidity data improved AUROC to 0.90 (95%CI 0.89, 0.90).*

Conclusion: *The Vital Sign based Risk Calculator is limited by its simplicity; inclusion of illness severity and comorbidity data improve prediction.*

Keywords

Risk Calculator, Emergency Department, AISS, Comorbidity

Richard Conway
PhD MRCPI

Declan Byrne
MB MSc FRCPI FRCP Edin

Deirdre O'Riordan
MD FRCPI

Bernard Silke
MD DSc FRCPI

MED Directorate, St James's Hospital, Dublin 8, Ireland.

Correspondence
Richard Conway,
Department of Internal Medicine, St James's Hospital, Dublin 8, Ireland
Email: drrichardconway@gmail.com

Introduction

Acute Medicine involves the appropriate specialist management of urgent medical conditions.[1] Clinical outcomes in Acute Medicine have improved over time as shown by reduced 30-day in-hospital mortality.[2-5] These improvements have been attributed to various factors including improved patient flow and operational restructuring.[6,7] The development of Acute Medical Admission Units (AMAUs), structural innovations, and increased consultant involvement are likely to have also contributed.[2-4,8]

Continuing to improve clinical outcomes in Acute Medicine is challenging; focusing limited resources on patients with high illness severity,[9-12] multiple comorbidities[13] or sepsis[14] might be the way forward. A key prerequisite to this is the development of accurate risk calculators to facilitate the identification of at risk patients.[12] The development of these models has been complicated by the apparent need to include key features, such as comorbidity and socioeconomic factors, for which accurate admission may not be available at the time of hospital admission.[15,16] An ideal risk calculator would be simple and readily calculated on admission to hospital; an automated model which could generate a risk score based on existing information from the electronic patient record is one such approach.

A number of prognostic scores have been developed with the goal of identifying those patients who are safe to discharge from the Emergency Department (ED).[17,18] Chang *et al*.[19] recently reported that even minor abnormalities in physiology (vital signs - heart or respiratory rate and blood pressure) at presentation to the ED were predictive of early death, but with considerable overlap to others who did not suffer an early death. Patients with Major Disease Categories (MDCs) of malignant neoplasm, coronary heart disease, chronic obstructive pulmonary disease, congestive heart failure or neurological disease, had a greater likelihood for early death following an ED visit.[19] A risk prediction model based on factors such as those outlined by Chang *et al*. would satisfy the requirements of readily available information and potential automatic input from the electronic medical record but the predictive ability of such a model with regards to the outcome of acute medical admissions is unknown.

In this paper, we utilise our database of acute medical admissions to our institution between 2002 and 2018, to investigate a Vital Sign based Risk Calculator based on the work of Chang *et al*.[19] We tested the ability of this Vital Sign based Risk Calculator to predict 30-day in-hospital mortality in admitted patients.

Methods

Background

Our institution, St. James's Hospital, Dublin, serves as a secondary care centre for emergency admissions in a catchment area with a population of 270,000 adults.

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All emergency medical admissions are admitted from the ED to an AMAU, the operation and outcome of which have been described elsewhere.[3,5,20-22]

Data collection

During hospital admissions core demographics are recorded on the Patient Administration System (PAS), clinical presentation parameters on the ED database, and subsequent post-admission (haematology, biochemical, blood culture or transfusion data) entered into the patient electronic record; these data can then be extracted and collated with the national Hospital In-Patient enquiry (HIPE) scheme dataset.[23,24] In HIPE, International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) has been used for both diagnosis and procedure coding from 1990 to 2005 with ICD-10-CM used since then. The anonymous data on our database consists of the unique hospital identifier, admitting consultant, date of birth, gender, area of residence, principal and up to nine additional secondary diagnoses, principal and up to nine additional secondary procedures, and admission and discharge dates. Additional information cross-linked and automatically uploaded to the database includes physiological, haematological, and biochemical parameters. HIPE data and admission biochemistry and haematological variables are extracted by linkage to the unique hospital number. This study had no interventional component, used anonymised routinely collected data and complied with data protection legislation.

Vital Sign based Risk Calculator

The data of Chang *et al*.[19] was the theoretical basis of our novel Vital Sign based Risk Calculator, based on vital parameters that were strongly associated with mortality within 15 days of an ED visit. These were heart rate >90 beat/min, respiratory rate >20 breaths/min, mean arterial pressure (MAP) <80 mmHg or oxygen saturation <94% on room air. The most frequent MDCs associated with early death were neoplasia, cardiovascular, respiratory or neurological. We entered these vital signs and MDCs into our database of all 113,807 medical admissions between 2002 and 2018, using a multivariable fractional polynomial (MFP) model as previously described.[11,25,26] The parameters were chosen based on those identified by Chang *et al*, we then weighted these parameters based on our MFP analysis to obtain optimum predictive performance of the score. The relative weightings in this model were neoplasm 3.96 (95%CI 3.61, 4.35), cardiovascular 1.45 (95%CI 1.35, 1.55), respiratory 1.61 (95%CI 1.51, 1.71), neurological 1.48 (95%CI 1.37, 1.59) and vital signs outside the described limits – heart rate 1.11 (95%CI 1.04, 1.17), respiratory rate 1.90 (95%CI 1.79, 2.0), MAP 2.2 (95%CI 2.0, 2.4), and oxygen saturation 1.67 (95%CI 1.57, 1.79). The weightings of the individual items involved in the Risk Calculator would require the use of some form of computer or app based calculator, whether automated or otherwise, to facilitate its use.

Comorbidity Score

To construct the Comorbidity Score, ICD codes that captured chronic physical or mental health disorders that limit people in activities that they generally would be expected to be able to perform were grouped according to the following ten systems: (i) cardiovascular, (ii) respiratory, (iii) neurological, (iv) gastrointestinal, (v) diabetes, (vi) renal, (vii) neoplastic disease, (viii) others (including rheumatological disabilities), (ix) ventilatory assistance required and (x) transfusion requirement. In addition, we searched our hospital's other databases for evidence of diabetes (Diamond database),[27] respiratory insufficiency (FEV1 <2L), troponin status (high sensitivity troponin >25 ng/L),[28] low albumin (<35 G/dL) and anaemia (haemoglobin levels <10 G/dL) or chronic renal insufficiency - MDRD <60 mL/min*1.73 m2.[29] Each component of the score was then weighted according to 30-day in-hospital mortality.

Other predictor variables

The Acute Illness Severity Score (AISS) is an age-adjusted aggregrate score derived from admission laboratory parameters; serum sodium, potassium, urea, albumin, red cell distribution width, and white blood cell count.[11,30] We have described full details of the derivation and validation of this score previously.[30,31] The AISS is exponentially related to 30-day in-hospital mortality ranging from 2.5% to 32.1%.[11,32] Sepsis categorisation was based on 1) no blood culture performed, 2) blood culture performed with a negative result, 3) blood culture performed with a positive result.[14] The 30-day in-hospital mortality rates for these categories were 3.1%, 9.6% and 17.8%.

Statistical methods

Descriptive statistics were calculated for background demographic data, including means/standard deviations (SD), medians/inter-quartile ranges (IQR), or percentages. Comparisons between categorical variables and mortality were made using chi-square tests.

Logistic regression analysis identified potential mortality predictors and then tested those that proved to be significant univariate predictors ($p<0.1$ by Wald test) to ensure that the model included

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all variables with predictive power. We employed a logistic model with robust estimate to allow for clustering; the correlation matrix thereby reflected the average discrete risk attributable to each of these predictor variables.[11] We used the margins command in Stata to estimate and interpret adjusted predictions for sub-groups, while controlling for other variables such as time, using computations of average marginal effects. Margins are statistics calculated from predictions of a previously fitted model at fixed values of some covariates and averaging or otherwise over the remaining covariates. In the multivariable logistic regression model, we adjusted univariate estimates of effect, using the previously described outcome predictor variables including AISS,[11,32] Charlson Index[13] and blood culture results.[14] The model parameters were stored; post-estimation intra-model and cross-model hypotheses could thereby be tested. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated for those predictors that significantly entered the model ($p<0.10$). Statistical significance at $P<0.05$ was assumed throughout. Stata v.15 (Stata Corporation, College Station, Texas) statistical software was used for analysis.

Results

Patient Demographics

There were a total of 113,807 emergency medical admissions in 58,126 patients over the 17 year study period (2002-2018). This included patients admitted directly into the Intensive Care Unit or High Dependency Unit.

We set a cut-point for the Vital Sign based Risk Calculator at >=2.7 points as the median value, (Table 1). Patients with scores >=2.7 were older, median (IQR) 66.2 years (47.6, 78.5) vs. 59.3 years (39.5, 76.8). They had a longer median (IQR) LOS at 5.8 days (2.6, 10.7) vs. 4.2 days (1.8, 8.5). They were more likely to have high AISS (Group >3 82.7% vs. 69.8%), high Comorbidity Scores (> 6 points 60.2% vs. 35.2%), high Charlson Index (Grade 2 33.8% vs. 19.3%) and positive blood cultures (culture positive 4.2% vs. 2.4%).

Vital Sign based Risk Calculator Score and 30-day in-Hospital Mortality

The median (IQR) Vital Sign based Risk Calculator score was 2.7 (1.45, 4.46). The frequency of scores over 4, 6, and 8 points were 20.6%, 6.2% and 0.95%. Over the range 2–12 points, the outcome prediction was near linear; the model predicted 30-day in-hospital mortality per admission increased from 3.6% (95%CI 3.4, 3.7) at 2 points to 5.0% (95%CI 4.8, 5.2) at 4 points , 9.3% (95%CI 8.8, 9.7) at 8 points and 14.8% (95%CI 14.0, 15.7) at 12 points, Figure 1. The AUROC to predict 30-day in-hospital mortality was 0.74 (95%CI 0.72, 0.74). This compared with the full MFP model, that included AISS and Comorbidity Score that achieved an AUROC of 0.90 (95%CI 0.89, 0.90).

Interaction of Vital Sign based Risk Calculator, AISS, and Comorbidity Score

We tested for the presence of a significant interaction between the Vital Sign based Risk Calculator and AISS (Figure 2) or Comorbidity Score (Figure 3) – both interacted significantly. The conditional dependence was of increasing adverse mortality outcomes, at any given Vital Sign based Risk Calculator score. For example, for AISS 30-day in-hospital mortality with a Vital Sign based Risk Calculator of 8 points and AISS Groups of 4, 5, and 6 were 1.8%, 5.3%, and 13.3% respectively. With a Vital Sign based Risk Calculator of 8 points and Comorbidity Scores of 10, 13, and 16 points, 30 day in-hospital mortality was 19%, 32%, and 47% respectively. Therefore, a Vital Sign based Risk Calculator score of 8 estimated 30-day in-hospital mortality of 10.4%, additional information provided by AISS and Comorbidity Score modulate this over a large range between 1.8% and 47%.

Discussion

We developed the Vital Sign based Risk Calculator as an assessment tool in order to investigate the utility of such an instrument as a prognostic tool in acute medical admissions. We have demonstrated in this study that while the use of composite vital parameter assessment tools such as the Vital Sign based Risk Calculator does afford some predictive ability, this is inherently limited with an AUROC of 0.74 to predict 30-day in-hospital mortality. Prognostication is significantly improved by incorporating other measures of illness severity such as the AISS, and even further by the consideration of comorbidity. Our final MFP model including these attributes had a greatly improved AUROC of 0.90.

The data of Chang *et al*.[19] was the theoretical basis on which we based the Vital Sign based Risk Calculator Score - they demonstrated that an early death within 15 days was more likely in patients with abnormal vital signs outside certain limits. This paper led to an intriguing accompanying Editorial 'that every heart beat counts'[33] – as the original article summary indicated that every additional heart beat increased conferred additional risk.[19] Depending on ones' mood or theoretical viewpoint, one can argue that this is correct or plain wrong. Any deviation from the normal distribution of a vital parameter is likely to confer additional risk, as is the presence

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Table 1. Characteristics of Emergency Medical Admissions by Vital Sign based Risk Calculator Score

	ED Score <2.7 (N = 48,598)	ED Score >=2.7 (N = 53,886)	p-value
Age (years)			
Mean (SD)	57.8 (21.3)	62.33 (19.8)	<0.001
Median (Q1, Q3)	59.3 (39.5, 76.8)	66.2 (47.6, 78.5)	
Length of Stay (days)			
Mean (SD)	6.3 (6.1)	7.7 (6.7)	<0.001
Median (Q1, Q3)	4.2 (1.8, 8.5)	5.8 (2.6, 10.7)	
Gender			
Male	23634 (48.6%)	26512 (49.2%)	<0.07
Female	24964 (51.4%)	27374 (50.8%)	
30-day in-Hospital Mortality			
Alive	47681 (98.1%)	50226 (93.2%)	<0.001
Dead	917 (1.9%)	3660 (6.8%)	
Acute Illness Severity Score			
1	2059 (4.9%)	1009 (2.1%)	<0.001
2	4234 (10.0%)	2506 (5.2%)	
3	6440 (15.3%)	4816 (10.0%)	
4	7803 (18.5%)	7251 (15.1%)	
5	8181 (19.4%)	9380 (19.5%)	
6	13509 (32.0%)	23032 (48.0%)	
Comorbidity Score			
< 6	31481 (64.8%)	21420 (39.8%)	<0.001
6	14277 (29.4%)	23041 (42.8%)	
10	2406 (5.0%)	7081 (13.2%)	
13	341 (0.7%)	1646 (3.1%)	
16	90 (0.2%)	654 (1.2%)	
Charlson Index			
0	25709 (57.3%)	18277 (36.0%)	<0.001
1	10544 (23.5%)	15347 (30.2%)	
2	8650 (19.3%)	17157 (33.8%)	
Sepsis Group			
1	39877 (82.1%)	38810 (72.0%)	<0.001
2	7569 (15.6%)	12814 (23.8%)	
3	1152 (2.4%)	2262 (4.2%)	

of any disease, in principle. If these are markedly influential then they can be incorporated into a predictive algorithm – but that does not necessarily mean that they will be clinically useful.[34]

The AISS identifies six risk group with progressively increasing 30 day in-hospital mortality rates of 0.3%, 0.1%, 0.8%, 1.8%, 5.0% and 27.6%; indeed the AISS had the highest predictive OR of any factor in the multivariable logistic regression model of 4.4 (95%CI 3.5, 5.5). The AISS is based on the concept that the underlying physiological substrate counterregulatory and will attempt to restore homeostatic balance; the extent of deviation of a panel of admission laboratory data from normality may be predictive. The use of admission laboratory data to construct illness severity scores and order to predict outcomes. has been well research with a number of predictive models described.[10,35,36] In our experience, abnormality in laboratory data is relatively common in emergency medical admissions with >67% of episodes falling within the top three risk groups with model predicted episode 30-day in-

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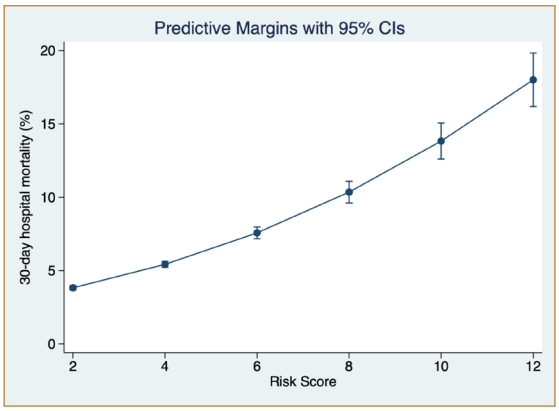


Figure 1. Prediction of the 30-day in-hospital mortality per admission by Vital Sign based Risk Calculator

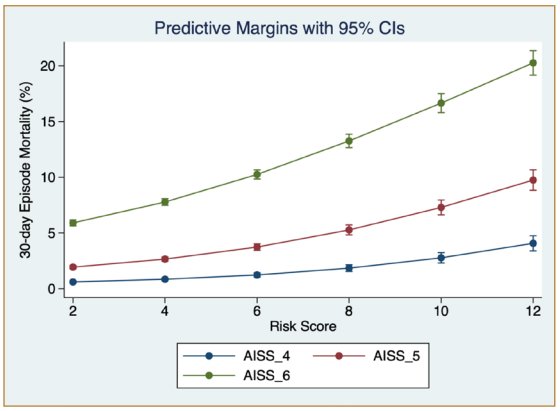


Figure 2. 30-day in-hospital mortality per admission by Vital Sign based Risk Calculator Score and Acute Illness Severity Score (AISS).

hospital mortality ranging between 0.8% and 6.9%. This is however, on average, and as Figure 1 shows at any given Vital Sign based Risk Calculator scores the range of predicted mortalities could be considerably greater; a Vital Sign based Risk Calculator score of 8 for the AISS IV, V and VI Grades predicted episodes mortality rates were 1.8%, 5.3% and 13.3% respectively. The reductionist model, developed to simplify prediction calculations, cannot accurately compute the complexity that exists within the domain of illness severity.

In contrast a high existing burden of disease, as represented by Comorbidity Score, is relatively less common with only 15.3% of patients having a Comorbidity Score >=10 points. However, high Comorbidity Score weighs the scales even more adversely; a Vital Sign based Risk Calculator score of 8 points would at Comorbidity Score of 10, 13 and 16 points predict 30-days episode mortality rates of 19%, 32% and 47%. The interesting point to debate would be as to whether an experienced clinician would intuitively distinguish between high from low risk individual – it is obvious from the above consideration that the Vital Sign based Risk Calculator, although having many attractive features,

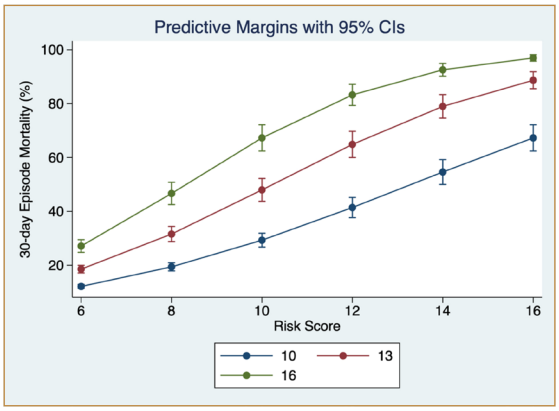


Figure 3. 30-day in-hospital mortality per admission by Vital Sign based Risk Calculator Score and Comorbidity Score.

would not rise to that challenge. The average Vital Sign based Risk Calculator prediction, could on the data analysed cover a 26 fold difference (Vital Sign based Risk Calculator 8 points predicted mortality 10.4% - highest and lowest of AISS/Comorbidity subsets of 1.8% and 47% respectively).

It is stating the obvious that a tool with such discrepancies cannot be the basis for life and death decisions. Brabrand *et al.* cite the results of the SUPPORT trial that showed that providing the physicians with objective outcome predictions did not significantly change physician's attitudes and behaviour when treating their patients.[34] These authors were of the opinion that most scoring systems "had been developed for use on groups of patients and not on an individual level"; we would argue that the latter reflects the reality that score systems have been found to be intrinsically unreliable at the individual patient level rather than an intrinsic wish for a group overview on distinct subsets of patients. Furthermore, Brabrand *et al.* conclude it would be agreed by most clinicians that should scoring systems be able to identify patients at risk that might be overlooked by the medical staff and thereby improve the therapy and outcomes this alone would justify their existence. A systematic review recently considered data from 14,768 citations of prediction models from which 78 papers were selected and 17 studied in detail.[37] Model performance varied considerably from an AUROC 0.63 to 0.93.

When dealing with the realm of prediction one has to consider the fundamentals of Bayes' theorem, that if an event is unlikely before a prediction, then it is unlikely after the prediction whatever the prediction may be. Mortality for patients admitted to hospital has fallen over time and 30-day in-hospital mortality is now <5%.[38,39] Therefore, one can take this pre-test likelihood of a fatal outcome and use a diagnostic calculator to estimate the likelihood that our predictions might prove correct; for example

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for a death to occur within 24 hours following a NEWS Score of >5 (sensitivity 91%, specificity 58%)[40] would yield a post-test probability of 10% or at higher NEWS cut-off of >7 (sensitivity 74%, specificity 89%) a post-test probability of 25%. In other words, the large majority of positive tests would be false – for this example 90% or 75% of adverse mortality predictions are incorrect. Therefore, as the likelihood of the event decreases, the reliability of the prediction deceases as the pre and post-test probability are linked by Bayes' theorem. One can pre-select a high-risk subgroup thereby increase the pre-test and consequent post-test probability. For example, we could decide to employ a Vital Sign based Risk Calculator as a screening tool and to apply discharge decision making to those scored >75% centile, this would reduce the population of interest to 18.8% with a mortality risk of 9.6% (95%CI 9.1%, 10.0%). This higher pre-test probability would increase the accuracy of the prediction with a post-test probability of 27% (at hypothetical sensitivity 75%, specificity 80%). This is as good as one is likely to achieve with a reductionist model; the Vital Sign based Risk Calculator deliberately restricts the input parameters to four vital signs and four MDCs.

Better modelling of outcomes that are dependent on complex factors inevitably requires more information – this reality appears to be little acknowledged as evidenced by the plethora of papers with the expectation that some new combination of predictors will yield a major breakthrough. Additional information, supporting physiological parameters could include a standard laboratory panel on patients of interest (with automated computation of AISS) and a screen for Comorbidity using MDCs by system. Taking for example the top two AISS groups/individuals with Comorbidity Scores >10 would restrict the populations of interest to 1.1% and 0.5% respectively with predicted episode mortalities of 19% and 30.5% respectively. Were the sensitivity and specificity at a similar level (sensitivity 75%, specificity 80%), then the post-test probability could be estimated at 47% and 66%. This subset might be too restrictive and there would need to be trial to establish what was practical, in terms of data collection within the time available, the manpower resource constraints, and overall utility. However, devising new risk prediction score systems, ignoring the constraints imposed by a low pre-test probability and reductionist models that at best appear to have post-test prediction in the range 10% or so, does not appear a useful way forward.

There are a number of limitations to the current work. We have shown the prognostic ability of certain vital parameters, laboratory results, and comorbidity; it does not necessarily follow that targeted intervention has the potential to improve outcomes. Indeed, well-intentioned interventions can frequently have unexpected negative consequences.[41] This study examined outcomes in acute medical admissions, the results are not necessarily transferable to other disciplines such as cardiology or surgery.

In conclusion we have demonstrated that while the use of vital sign parameters in prognostication has some clinical utility this is significantly limited in the absence of additional measures of illness severity and comorbidity.

Conflict of interests

The authors declare that they have no conflict of interest regarding this publication.

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