Ratnayake Hasanka (Orcid ID: 0000-0002-0197-8356)

A laboratory-derived early warning score for the prediction of in-hospital mortality, ICU admission, Medical Emergency Team activation and Cardiac Arrest in general medical wards

Author: Dr Hasanka Ratnayake [1], Dr Douglas Johnson [2], Johan Martensson MD PhD [3], Dr Que Lam [4] and Professor Rinaldo Bellomo [5,6]

Author affiliations

1. Department of Aged Care, Alfred Hospital, Melbourne, Australia
2. Department of General Medicine, Royal Melbourne Hospital, Melbourne, Australia
3. Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden
4. Department of Pathology, Austin Hospital, Melbourne, Australia
5. Data Analytics Research and Evaluation Centre, University of Melbourne and Austin Hospital, Melbourne, Australia
6. Department of Intensive Care, Austin Hospital, Melbourne, Australia

Corresponding Author e-mail: hasanka.ratnayake@gmail.com

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/imj.14613

Abstract

Aim: To assess whether a laboratory based admission score can predict in hospital mortality, ICU admission, Medical Emergency Team (MET) activation or cardiac arrest in a cohort of Australian general medical patients admitted via the emergency department.

Methods: We performed a retrospective observational study of all general medical admissions to hospital via the emergency department in 2015. Admission pathology was used to calculate a risk score. In-patient outcomes of death, ICU transfer, MET Call activation or cardiac arrest were collected from hospital records.

Results: We studied 2942 admissions derived from 2521 patients, with a median age of 81 years. There were 143 in-patient deaths, 82 ICU admissions, 277 MET Calls and 14 cardiac arrest calls. The laboratory-based admission score had an area under the receiver operating characteristic curve (AUC-ROC) of 0.76 (95%CI: 0.72-0.80) for inpatient death, an AUC-ROC of 0.79 (95%CI: 0.66-0.93) for inpatient cardiac arrest, an AUC-ROC of 0.64 (95%CI:0.58-0.70) for ICU transfer and an AUC-ROC of 0.59 (95%CI:0.55-0.62) for MET Call activation. When patients aged over 75 were analysed separately, the AUC-ROC for prediction of in-patient death was 0.74 (95%CI: 0.70-0.78) and increased to 0.86 (95%CI: 0.73-0.98) for the prediction of in-patient cardiac arrest.

Conclusion: A simple laboratory derived score obtained at patient admission is a fair to good predictor of subsequent in-patient death or cardiac arrest in general medical patients

and in the older patient cohort. Prospective interventional studies are required to ascertain the clinical utility of this admission score.

Introduction

General medical wards often admit a varied and undifferentiated cohort of patients from the emergency department who sometimes deteriorate during their hospital stay. Such patients can display clinical abnormalities that may herald their deterioration, and scores derived from various bedside clinical observations may help predict those at risk of *imminent* deterioration [1]. Predicting clinical deterioration allows for timely intervention to prevent harm and/or allow timely goals of care discussion. Accordingly, the Royal College of Physicians in England now advocates the use of a standardized national vital signs-based early warning score (NEWS2) across the NHS [2]. Despite the validation of these clinical bedside observations however, there are still barriers to translating this into appropriate interventions [3] and awaiting vital sign deterioration to risk stratify patients is often a reactive trigger.

Additional routinely available information may also help identify at risk patients much earlier in admission. One such set of information is available in the shape of results from common biochemical and hematological laboratory tests.

There is now a growing body of literature that, similar to vital signs, commonly available laboratory results may also help identify patients at greater risk of death or ICU transfer in both the general medicine and emergency department patient populations [6-12].

One such score is the Laboratory Decision Tree Early Warning Score (LDT-EWS) [10] developed in Britain. Utilizing only commonly available pathology results from admission

blood tests, without the need for patient age, co-morbidities or vital signs input to derive a score; the LDT-EWS appears to provide good discrimination for the prediction of in-hospital death among general medicine patients. These observations, however, may be health care system dependent, were not tested in a context characterized by a mature and effective medical emergency team system, and did not provide information on their ability to predict other important hospital adverse outcomes such as ICU admission, medical emergency team activation, or cardiac arrest.

We also wished to test this score in an older patient cohort aged over 75 years. Clinical experience has shown us that multi-morbid, older patients require nuanced discussions about advanced care planning (ACP). This conversation is often broached for the first time in hospital given the low community uptake of ACP documentation [5]. Though all patients should have advanced care directives discussed and documented at point of admission, a score that highlighted hospital risk could serve as another reminder to have this important discussion.

Accordingly, we sought to utilize this laboratory derived score in a cohort of Australian general medicine patients, both general and aged over 75 years, admitted from the emergency department in a tertiary hospital to ascertain its performance as a discriminator of not only in hospital mortality but also ICU admission, Medical Emergency Team (MET) activation and cardiac arrest.

Aims

Our primary aim was to ascertain the utility of a simple laboratory based admission score as a predictor of in-patient death, ICU admission, MET Call activation and cardiac arrest **(Table 1).**

Our secondary aim was to ascertain the utility of this score as a predictor of in-patient death, ICU admission, MET Call activation and cardiac arrest in those patients aged over 75 years of age.

Methods

We conducted a retrospective observational study. The study was approved by the Austin Hospital Human Research Ethics Committee. We retrospectively collected all admissions from the Emergency Department (ED) to the General Medicine wards for the 2015 calendar year from our hospital medical records.

Those who had been transferred from another unit or hospital were excluded so as to ascertain the predictive accuracy of the score prior to substantial medical intervention. Patients who were <16 or who were discharged on the same day were also excluded. For each admission, the first full set of pathology required to populate the score, taken within the initial 24 hours of admission, was obtained from the hospital electronic medical record. Multiple laboratory tests taken from within the first 24 hours of admission could be used to populate the score, i.e. if liver function tests were taken later within the first day of admission, those values could be used to populate the score. Patients that did not have the full panel of pathology tests to populate the score from their first 24 hours of admission

blood tests, were listed as having 'no score' in the dataset and excluded from the study. The LDT-EWS was calculated using the original scoring system **(Table 1)** in an excel datasheet for each set of admission pathology sent. The outcomes of interest were acquired from patient and hospital medical records. Data on mortality was obtained from the hospital administrative data set. Intensive Care Unit (ICU) transfers from general medicine were obtained from the ICU admission records. The RiskMan (RiskMan International Pty Ltd, Southbank, Victoria) system was utilized to record all cardiac arrest and MET activation data, as a RiskMan report is always submitted at these emergency calls. Only those emergency ('Code Blue') calls that were described in the RiskMan system as being cardio-respiratory arrest requiring initiation of chest compressions were included as an outcome.

Statistical Analysis

Simple summary statistics (mean, standard deviation or median, interquartile range, or n/N (%)) were used to describe the patient sample. We then assessed the area under the receiver operating characteristic curve (AUC-ROC) to estimate the predictive value of the LDT-EWS for in-patient death, ICU admissions, Code Blue or MET Calls anytime during the patient admission subsequent to pathology collection. Data was analysed using STATA version 11.2 (Stata Corp., College Station, TX)

We utilised a traditional academic point system for evaluating the AUC-ROC score as poor if its value was <0.7, fair if >0.7 but <0.80, good if its value was >0.80 but <0.90, and excellent

if its value was >0.90 [26].

Results

For the 2015 calendar year, after exclusion of 566 admissions due to incomplete day one pathology (in 445 (78%) due to missing albumin data) to populate the score, there were 2942 admissions from the Emergency Department from 2521 patients. The median age of the study patients was 81 years (IQR 71-88) years and 52.5% were female. There were 143 in patient deaths, 82 ICU admissions, 277 MET Calls and 14 cardiac arrest calls.

Prediction of death, ICU admission, MET Call activation and cardiac arrests in all ages

For the prediction of in-patient death in all ages at any time during hospital admission, the LDT-EWS had an AUC-ROC of 0.76 (95%CI: 0.72-0.80) **(Figure 1).** The AUC-ROC for ICU admission was 0.64 (95%CI: 0.58-0.70) **(Figure 2)** and for MET Calls the AUC-ROC was 0.59 (95%CI: 0.55-0.62) **(Figure 3).** The AUC-ROC for in-patient cardiac arrest calls was 0.79 (95%CI: 0.66-0.93) **(Figure 4).** Finally, the AUC-ROC for a composite of these outcomes was 0.66 (95%CI: 0.63-0.69).

Prediction of death, ICU admission, MET Call activation and cardiac arrests older patients

Calculating AUC-ROC values from admissions in those patients over >75years, the AUC-ROC for prediction of in-patient death at any time during patient admission, remained similar at 0.74 (95%CI: 0.70-0.78) but increased for the prediction of cardiac arrest to 0.86 (95%CI: 0.73-0.98). The AUC-ROC for ICU admission in this cohort was 0.61 (95%CI: 0.51-0.71) and for MET Calls the AUC-ROC was 0.55 (95%CI: 0.52-0.60).

Discussion

Statement of key findings

We conducted a retrospective study to test the hypothesis that, in a tertiary hospital with a mature MET system, the performance of a pathology based risk score validated in a UK context would perform similarly as a predictor of in-hospital mortality. We found that this score was a fair predictor of in-patient mortality (AUC-ROC 0.76) and cardiac arrest calls (AUC-ROC 0.79) but a poor predictor of MET Calls or ICU transfer. Our AUC-ROC was comparable for in-patient mortality as found in the study that developed the score.

Comparison to other studies

The LDT-EWS was chosen for its requirement of readily available pathology and its predictive utility for the entirety of a patient admission, despite being derived from admission bloods alone. Not requiring patient age, comorbidities or vital signs means the LDT-EWS could be generated automatically by a hospital computer system without the burden of manual calculation, which would increase its acceptability to staff. Studies by

Loekito et al [7] and Asadollahi et al [8] used biochemical variables alongside age to predict in-hospital mortality with an AUC-ROC of 0.872 (95% CI: 0.85–0.89) and AUC-ROC of 0.848 respectively. The addition of age in these models improved their power to discriminate mortality [26]. However, our focus was on laboratory tests as predictors of outcome independent of other factors. Established vital signs-based warning scores such NEWS2, APACHE II or SOFA, have robust ability to predict hospital mortality in a broad range of patients. However, these scores serve a different purpose to the LDT-EWS and in the case of APACHE II and SOFA, are applied to ICU patients who are in the ICU. Our score, is designed to use admission pathology alone, on undifferentiated patients, and predict risk for the patient's entire hospital admission. Having this risk highlighted early, instead of awaiting overt deterioration to trigger concern, would allow greater time for treating teams to plan management appropriate and acceptable to patients and their families.

Strengths and Limitations

Our study is the first to our knowledge to utilize this risk score in an Australian cohort, and the first to extend this score to analyze other outcomes such as cardio-respiratory arrest, MET Call activation and ICU transfer. Such additional assessment widens the potential utility of the score and allows a broader approach to risk stratification. Moreover, our study is also the first to assess an admission laboratory score as a predictive tool for in-patient death and cardio-respiratory arrest in the elderly (age over 75), who are a growing population in medical wards of Australian hospitals. As such, it may act as a catalyst for

important discussions around advanced care planning given its relevance to older patients. We also identified a fair or good predictive value from our score for the outcomes of in-hospital death and cardio respiratory arrest calls despite these being relatively low in occurrence. This observation signals a degree of clinical utility for this approach to prediction and risk stratification.

Our study has several limitations. First, this is a retrospective observational study with all the inherent limitations of such investigations. However, the laboratory data were available electronically and were objective and not open to interpretation and the outcomes in question are easily verifiable and were prospectively collected as part of hospital quality assurance activities. As such they are essentially free of both selection bias and ascertainment bias. Second, this is not an interventional study. Thus, we cannot make any claim that the identification of higher risk patients has therapeutic utility. However, identification of a higher risk population is a crucial preliminary step in the development of targeted therapeutic interventions. We chose a specific cut-off point of 75 years of age to define an older cohort with sufficient numbers to provide robust estimates of performance. The number of events was limited thus affecting the robustness of our findings. However, the ability to predict such events, even when uncommon, provides indirect support for their utility We acknowledge that this is partly arbitrary and only exploratory in nature. We only studied patients admitted to the medical wards from the ED, thus our findings may not apply to the full population of medical ward patients. However, it is typically in patients

admitted via the ED that acute prognostication is most important. Finally, we did not document the proportion of patients who had limitations of medical treatment documented on admission, which would have influenced our data as it pertains to MET Call, Code Blue or ICU admission.

Conclusion

We applied a routine pathology derived score to the assessment of a large cohort of medical admissions from the emergency department and found it to be a fair to good predictor of in-patient death and cardio-respiratory arrests in general medical ward patients and in the older medical patient cohort. Our findings support the view that a score based on routine pathology collected at admission could serve as a useful clinical tool to risk stratify patients very early in their hospital stay. This would allow treating teams time to implement monitoring and management appropriate to the patient, as well as to clarify goals of care. Further study is now warranted to establish clinical utility cut-off scores as well as prospective interventional studies to ascertain if implementation of this pathology score translates into better clinical care and outcomes.

Tables

Table 1: Laboratory data decision tree EWS (LDT-EWS) for male and female patients

	3	2	1	0	1	2	3
Males							
Hb		≤11.1	11.2-12.8	≥12.9			
WCC				≤9.3	9.4-16.6	≥16.7	
Urea				≤9.4	9.5-13.7		≥13.8
Cr				≤114	115-179	≥180	
Na		≤132		133-140	≥141		
K			≤3.7	3.8-4.4	4.5-4.7	≥4.8	
Alb		≤30	31-34	≥35			
Females							
Hb			≤12.0	12.1-14.8	≥14.9		
WCC				≤12.6	12.7-14.8	≥14.9	
Urea				≤8.4	8.5-13.8		≥13.9
Cr				≤91	92-157	≥158	
Na			≤134	135-140	≥141		
K			≤3.3	3.4-4.5	≥4.6		
Alb		≤28	29-34	≥35			

Hb, haemoglobin; WCC, white cell count; Alb, serum albumin; Cr, serum creatinine; Na, serum sodium; K, serum potassium.

Figures

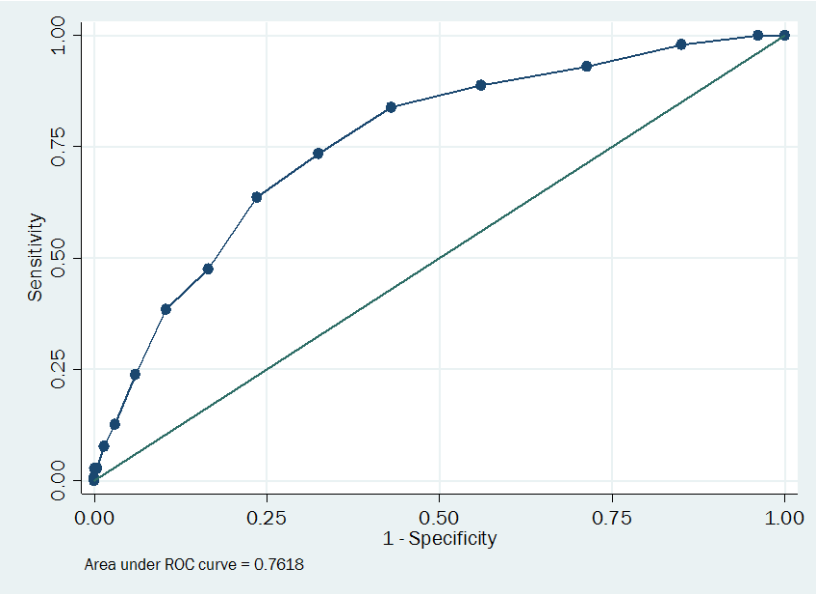

Figure 1: AUC-ROC for in-patient death at any time during hospital admission 0.76 (95%CI: 0.72-0.80)

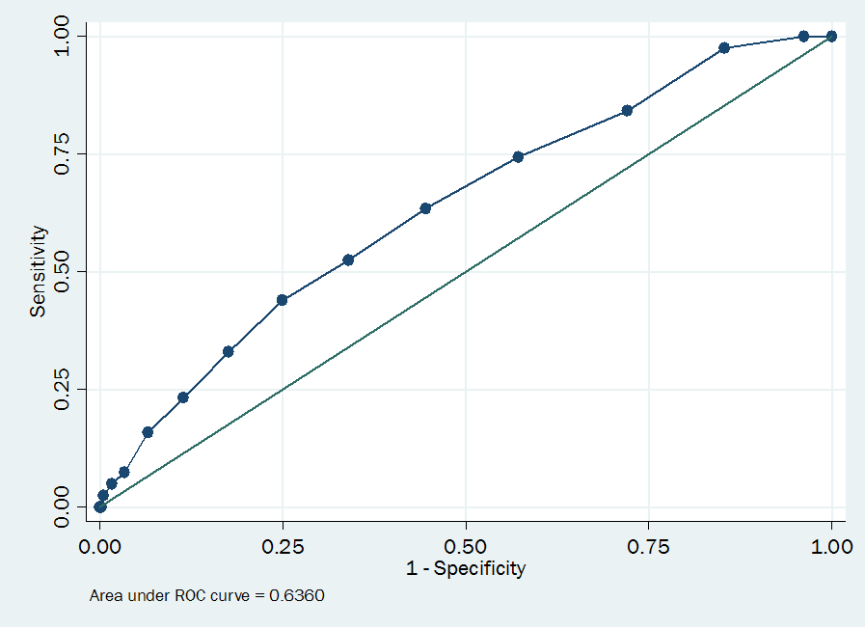

Figure 2: AUC-ROC for in-patient ICU Admission at any time during hospital admission 0.64 (95%CI: 0.58-0.70)

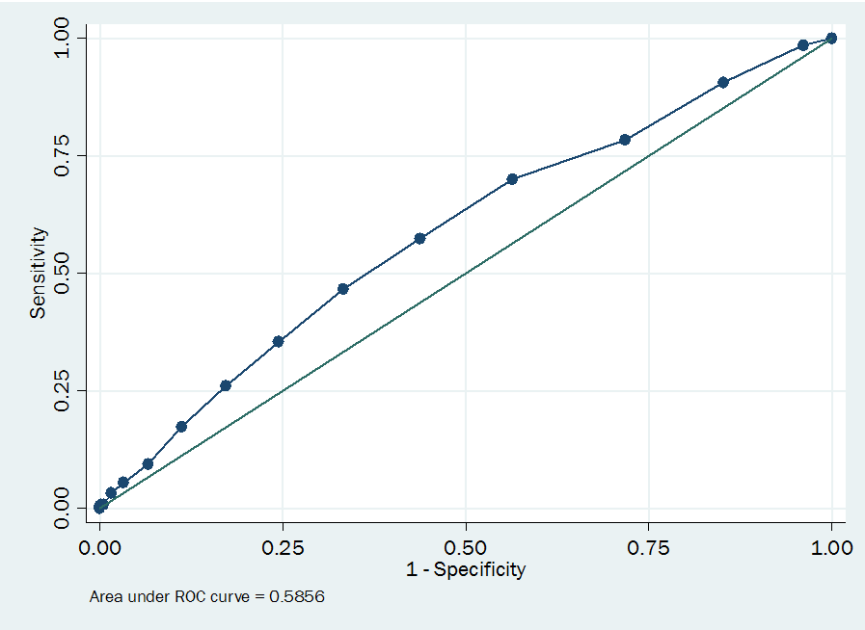

Figure 3: AUC-ROC for in-patient MET Call at any time during hospital admission 0.59 (95%CI: 0.55-0.62)

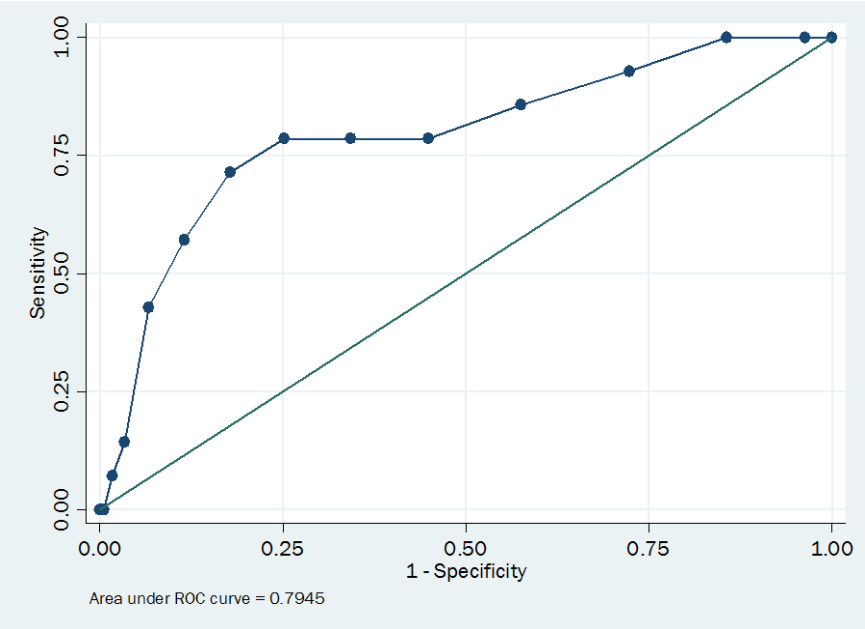

Figure 4: AUC-ROC for in-patient cardiac arrest at any time during hospital admission 0.79 (95%CI: 0.66-0.93)

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