Original Article

Performance of the Paediatric Index of Mortality 3 and Paediatric Logistic Organ Dysfunction 2 Scores in Critically Ill Children

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Abstract

Introduction: The Paediatric Index of Mortality 3 (PIM 3) and Paediatric Logistic Organ Dysfunction 2 (PELOD 2) scores were recently revised. We aimed to assess the performance of these scores in a contemporary cohort of critically ill children. Materials and Methods: This is a single-centre prospective study conducted in a multidisciplinary paediatric intensive care unit (PICU). Consecutive PICU admissions over 1 year were included and admission PIM 3 and PELOD 2 scores were calculated. The performance of each of the scores was evaluated by calculating the area under the curve (AUC) of the receiver operating characteristic (ROC) and the Hosmer-Lemeshow goodness-of-fit test for the outcome of PICU mortality. Results: A total of 570 patient admissions were eligible for this study. The median age of patients was 3.1 (interquartile range [IQR]: 0.4, 8.9 years). Overall median PIM 3 and PELOD 2 scores were 1.2 (IQR: 0.4, 3.2) % and 4 (IQR: 2, 7), respectively. The overall mortality rate was 35/570 (6.1%). The PIM 3 and PELOD 2 scores had good discrimination for mortality (AUCs 0.88 [95% confidence interval (CI) 0.85, 0.91] and 0.86 [95% CI 0.83, 0.89], respectively). Goodness-of-fit was satisfactory for both scores. Higher PIM 3 and PELOD 2 scores were also associated with decreasing ventilator and PICU-free days. Conclusion: PIM 3 and PELOD 2 scores are robust severity of illness scores that are generalisable to a contemporary cohort of critically ill children in Singapore.

Ann Acad Med Singapore 2018;47:285-90

Key words: Multiple organ dysfunction syndrome, Paediatric intensive care unit, Patient outcome assessment, Severity of illness index

Introduction

Initially designed to provide an indication of the risk of death in certain subsets of critically ill patients, the use of severity of illness scores in critically ill patients has evolved and these scores are now more often used to internally and externally benchmark quality of intensive care, and as markers of severity of illness for analysis in clinical studies.[1,2] Severity scores allow for more meaningful comparisons of mortality rates reported by different centres because they can be used to account for more severe presentation at centres with higher reported mortality. These scores are derived from large datasets of critically ill patients whereby clinical or demographic variables are investigated for their strength of association with the outcome of interest (e.g. mortality).[3]

The Paediatric Index of Mortality (PIM) score was designed to predict paediatric intensive care unit (PICU) mortality using variables which were present on admission to the PICU as a benchmark of the quality of care provided by the respective PICU.[4] Because of improvements in mortality rates in most PICUs, organ dysfunction is increasingly used as a surrogate outcome to mortality.[2,5] Hence, over the

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years, investigators started to examine organ dysfunction as an outcome in critically ill children.[6] The Paediatric Logistic Organ Dysfunction (PELOD) score was designed as a descriptive outcome score.[5] Both the PIM and PELOD scores had subsequently undergone extensive validation in other cohorts of patients across the globe.[6-10]

The performance of severity scores changes with time due to the changing case-mix of patients and improvements in the provision of critical care.[2,3,11] As such, intermittent revisions are required to ensure that they remain robust for clinical practice. These revisions require external validation to ensure generalisability. Hence, this study aimed to assess the performance of the recently updated PIM 3 and PELOD 2 scores in a contemporary cohort of critically ill children in Singapore. We postulated that both the PIM 3 and PELOD 2 scores had good discriminatory power in this cohort.

Materials and Methods

We conducted a single-centre prospective cohort study of all patients admitted to a multidisciplinary 16-bedded PICU of a university-affiliated, tertiary referral hospital. In addition to medical and general surgical patients, our PICU cares for children who require neurosurgery, open heart and vascular surgery, as well extracorporeal membrane oxygenation support. Consecutive children <18 years admitted to the PICU from 1 April 2015 to 31 March 2016 were included. This study was approved by the SingHealth Centralised Institutional Review Board (reference number: 2015/2231) and waiver of consent was granted as all data collected were performed as part of routine clinical care. This cohort study was conducted and reported in close accordance with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[12]

PIM 3 and PELOD 2 Scores

PIM 3 scores were calculated from data extracted within the first hour of PICU admission.[2] The PELOD 2 score on admission was calculated from data extracted within the first 24 hours of PICU admission.[11] For the PELOD 2 scores, the most abnormal value within the day was recorded. This was done according to published equations and directions.

Data Extraction

All clinical data were collected prospectively on a standardised case report form. In addition to the parameters required for calculation of the PIM 3 and PELOD 2 scores, we also extracted data on patient demographics (e.g. age, gender, presence of comorbidities), category of admission (cardiac surgical, cardiac non-surgical, trauma, respiratory, neurological non-surgical, surgical non-cardiac and other medical diagnosis), type of admission (elective or non-elective), intubation/extubation dates, and admission/discharge dates.[2,11] Patients were monitored daily until discharge from PICU or death. Bedside data was extracted by study team members who underwent standardised training and were blinded. The completed database was counter-checked for inconsistencies or potential errors by an independent party not involved in clinical care of these patients (CPH). Inconsistent data were verified based on the patient's case notes.

Outcomes

The primary outcome was PICU mortality. The secondary outcomes were 28-days ventilator-free days (VFD) and 28-days intensive care unit-free days (IFD). VFD was defined as days alive and free from invasive mechanical ventilation for up to 28 days. IFD was defined as days alive and discharged from the PICU for up to 28 days. Patients who died were considered to have a VFD and IFD of 0. This is to eliminate mortality as a competing interest in evaluating ventilator and PICU duration. Patients were followed-up until PICU discharge or for a minimum of 28 days.

Statistical Analysis

Categorical variables were presented as frequency (proportion). Continuous variables were presented as median interquartile range (IQR). Differences between the distributions of categorical variables were compared using the chi-squared or Fisher's exact test, as deemed appropriate. We compared differences between continuous variables with the Wilcoxon rank sum or Kruskal Wallis test, where appropriate. We evaluated the predictive performance of each of the 2 scores (PIM 3, PELOD 2) to correctly predict death prior to PICU discharge. The performance of each of the scores was first evaluated using receiver operating characteristic (ROC) analysis with calculation of the area under the ROC curve (AUC) and 95% binomial confidence interval (CI). Next, we computed the number of expected deaths in each decile of increasing predicted probability of death for both the PIM 3 and PELOD 2 scores. Decile cutoffs were chosen based on distribution of each of the scores in our cohort. The sum of predicted probabilities within each decile was used to calculate the number of expected deaths. Calibration was assessed by the Hosmer-Lemeshow goodness-of-fit test for deciles of probabilities. We report observed and expected mortalities in each decile of predicted probability. We performed all statistical analyses using STATA 14.0 (StataCorp, College Station, TX) and considered a P value <0.05 statistically significant.

Results

Over the 1-year study period, there were 572 PICU admissions. All were assessed for eligibility and followed-up until PICU discharge. Two patients were eventually excluded due to missing outcome data because they were

transferred to another facility during critical illness. Hence, 570 patients were included in our final analysis (Table 1). The overall median age was 3.1 (0.4, 8.9) years including 3 patients who were >18 years of age. The majority of admissions (342/570 [60%]) were emergency admissions. The most common category of admission was surgical non-cardiac 137/570 (24%). The overall median PIM 3 and PELOD 2 scores on admission were 1.2 (0.4, 3.2) % and 4 (2, 7), respectively. The overall mortality rate was 35/570 (6.1%). The median time of death was 4 (1, 12) days after PICU admission. The observed mortality of each category of admission were 5/107 (4.7%) in cardiac surgical, 6/42 (14.2%) in cardiac non-surgical, 3/27 (11.1%) in trauma, 8/89 (9.0%) in respiratory, 4/72 (5.6%) in neurological, 2/137 (1.5%) in surgical non-cardiac and 7/96 (7.3%) in other medical diagnosis. The median IQR duration of mechanical ventilation and PICU stay was 1 (0, 3) and 2 (2, 4) days, respectively. The median IQR VFD and IFD was 27.0 (25.0, 28.0) and 26.0 (24.0, 26.0), respectively.

Performance of PIM 3 Score

The PIM 3 score AUC of the ROC curve for the entire cohort for PIM 3 score was 0.88 (95% CI 0.85, 0.91). This indicates good discriminating ability and it accurately predicted mortality in 95.4% of patients (Fig. 1). Calibration described by the Hosmer-Lemeshow test through stratification for deciles of probabilities was not significant (P = 0.297) (Table 2). The total number of expected deaths was 23/570 is equal to the sum of individual predicted probabilities by PIM 3 score. The number of observed deaths was higher (35/570 [6.1%]). The resulting standardised mortality ratio (SMR) was 1.54 (95% CI 1.24, 2.03) but goodness-of-fit test suggested adequate model fit. The VFD and IFD also showed a decrease from the first to fourth PIM 3 quartiles (P <0.001) (Table 3).

Performance of PELOD 2 Score

The PELOD 2 score AUC for PELOD 2 score was 0.86 (95% CI 0.83, 0.89) and it accurately predicted mortality in

Table 1. Characteristics of Patients Admitted to the Paediatric Intensive Care Unit (n = 570)

Characteristics	Total (n = 570), n (%)	Survivors (n = 535), n (%)	Non-Survivors (n = 35), n (%)	*P* Value
Age				0.841
0 to <1 month	61 (10.7)	59 (11.0)	2 (5.7)	
1 to 11 months	125 (21.9)	116 (21.7)	9 (25.7)	
12 to 23 months	63 (11.1)	60 (11.2)	3 (8.6)	
24 to 59 months	86 (15.1)	79 (14.8)	7 (20.0)	
60 to 143 months	134 (23.5)	127 (23.7)	7 (20.0)	
≥144 months	101 (17.7)	94 (17.7)	7 (20.0)	
Male gender	348 (61.1)	324 (60.6)	24 (68.6)	0.377
Category of admission				0.019
Cardiac surgical	107 (18.8)	102 (19.1)	5 (14.3)	
Cardiac non-surgical	42 (7.4)	36 (6.7)	6 (17.1)	
Trauma	27 (4.7)	24 (4.5)	3 (8.6)	
Respiratory	89 (15.6)	81 (15.1)	8 (22.9)	
Neurological non-surgical	72 (12.6)	68 (12.7)	4 (11.4)	
Surgical non-cardiac	137 (24.0)	135 (25.2)	2 (5.7)	
Other medical diagnoses	96 (16.8)	89 (16.6)	7 (20.0)	
Comorbidities*	333 (58.4)	310 (57.9)	23 (65.7)	0.479
Elective admission	228 (40.0)	223 (41.7)	5 (14.3)	0.001
Mechanical ventilation	302 (53.0)	270 (50.5)	32 (91.4)	<0.001
Duration of mechanical ventilation (days), median (IQR)	1 (0, 3)	0 (0, 2)	4 (2, 11)	<0.001
Duration of PICU stay (days), median (IQR)	2 (2, 4)	2 (2, 4)	5 (2, 13)	0.003

IQR: Interquartile range; PICU: Paediatric intensive care unit

*Examples of comorbidities include significant congenital heart disease, chronic lung disease, chronic renal failure, chronic liver failure, malignancies and genetics syndromes.

Categorical variables are presented in counts (percentages). Continuous variables are presented in median (interquartile range).

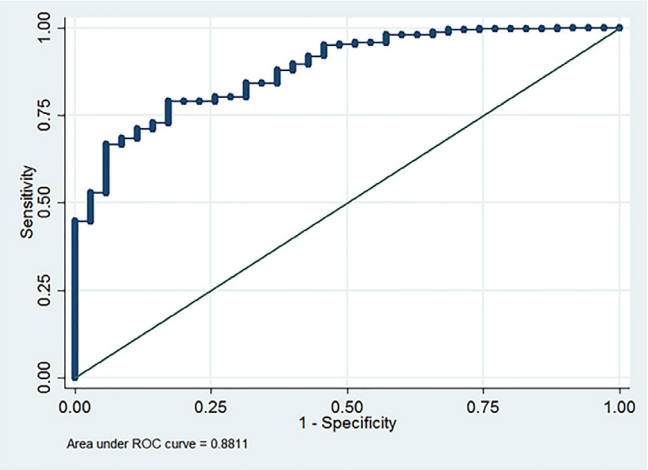

Fig. 1. Receiver operating curve for PIM 3 (Paediatric Index of Mortality 3) score for all patients.

94.9% of patients (Fig. 2). The expected number of deaths was 32/570 and this was equal to the sum of individual predicted probabilities by PELOD 2 score. The resulting SMR was 1.08 (95% CI 0.89, 1.36). In the calibration described by the Hosmer-Lemeshow test (only 7 distinct quantiles due to presence of ties), through stratification of probabilities was also not significant ($P = 0.243$), indicating acceptable goodness-of-fit (Table 2). The VFD and IFD also showed a decrease from the first to fourth PELOD 2 quartiles ($P < 0.001$) (Table 3).

Discussion

Our study evaluated the updated PIM 3 and PELOD 2 scores and demonstrated that they were robust in assessing the severity of illness in a contemporary cohort of PICU patients. Both the PIM 3 and PELOD 2 scores had good discrimination for mortality (AUCs of 0.88 [95% CI 0.85, 0.91] and AUC 0.86 [95% CI 0.83, 0.89]), respectively. Higher PIM 3 and PELOD 2 scores were robust not only

Table 2. Hosmer-Lemeshow Test for Deciles of Probabilities for PIM 3 and PELOD 2 Scores

PIM 3				PELOD 2*			
Mean Probability of Death	Number of Patients	Observed Deaths	Expected Deaths	Mean Probability of Death	Number of Patients	Observed Deaths	Expected Deaths
0.0016	58	0	0.0931	0.0013	63	1	0.0847
0.0026	57	0	0.1495	0.0032	119	1	0.3849
0.0042	57	0	0.2382				
0.0066	57	0	0.3774	0.0078	119	0	0.9335
0.0099	57	2	0.5627				
0.0129	58	0	0.7505	0.2015	105	4	2.1158
0.0167	56	4	0.9361				
0.0309	57	5	1.7588	0.0448	68	6	3.0455
0.0469	57	5	2.6715	0.0997	53	3	5.2865
0.2676	56	19	14.9867	0.4783	43	20	20.5655
$P = 0.297$				$P = 0.243$			

PELOD 2 score: Paediatric Logistic Organ Dysfunction 2 score; PIM 3 score: Paediatric Index of Mortality 3 score
*Only 7 distinct quantiles due to presence of ties.

Table 3. Ventilator-Free Days and Paediatric Intensive Care Unit-Free Days Associated with PIM 3 and PELOD Scores in Quartiles of Predicted Probabilities

	PIM 3			PELOD 2		
Quartiles	Number of Patients	VFD	IFD	Number of Patients	VFD	IFD
First quartile	143	28 (28, 28)	26 (26, 26)	184	28 (28, 28)	26 (25, 26)
Second quartile	143	26 (26, 27)	25 (24, 26)	119	28 (26, 28)	26 (25, 26)
Third quartile	143	28 (26, 28)	26 (24, 26)	139	26 (24, 27)	25 (21, 26)
Fourth quartile	143	22 (2, 26)	20 (0, 24)	130	23 (4, 26)	21 (2, 25)

IFD: Intensive care unit-free days; PELOD 2 score: Paediatric Logistic Organ Dysfunction 2 score; PIM 3 score: Paediatric Index of Mortality 3 score; VFD: Ventilator-free days
Continuous variables are presented in median (interquartile range).

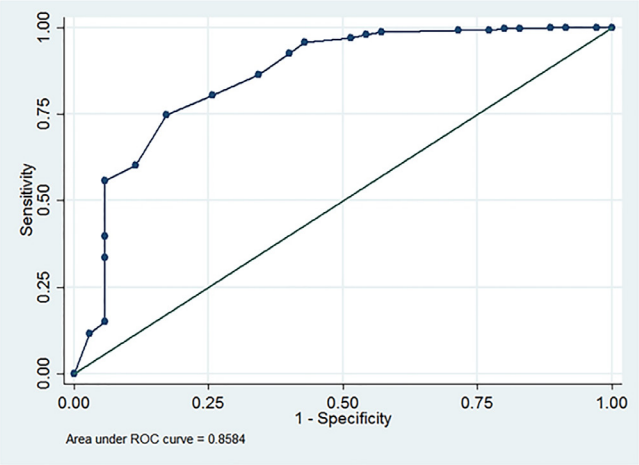

Fig. 2. Receiver operating curve for PELOD 2 (Paediatric Logistic Organ Dysfunction 2) score for all patients.

in predicting mortality but were also associated with decreasing VFD and IFDs.

Recently, both the PIM and PELOD scores were updated (PIM 3 and PELOD 2, respectively).[2,11] Compared to the PIM 2 model, the new PIM 3 model was developed based on a larger dataset across 4 countries to increase its generalisability.[2] In this recently updated version, necrotising enterocolitis was added to the list as a very high-risk diagnosis, whereas human immunodeficiency virus was removed from the list of high-risk conditions and admission following elective liver transplant was not included in the definition of liver failure (a high-risk code). This is the first prospective study to evaluate the performance of the PIM 3 score. Two previous retrospective validation studies of PIM 3 were conducted in Italy and Korea.[13,14] The former study (n = 11,109) showed that PIM3 scores had good discrimination with AUC that were fairly similar to our current study (AUC 0.88 [95% CI 0.86, 0.89]). However, the latter study (n =1710) showed only acceptable discrimination (AUC 0.76 [95% CI 0.72, 0.80]). In the Korean study, the reason for poorer discrimination was attributed to the high proportion of cardiac, haemato-oncological, and respiratory groups which carried a mortality rate higher than that estimated by severity scores.[14] In our study, we were not able to analyse subgroups of different admission categories because of insufficient patients. The total number of expected deaths was 23 as predicted by the overall PIM 3 score of 4.0%. However, the number of observed deaths was higher (35/570 [6.1%]) resulting in a SMR of 1.52. Our centre is 1 of 2 tertiary referral centres in Singapore and sees the largest number of PICU admissions nationwide. All mortalities are discussed at a monthly quality forum to identify preventable factors. It is also possible that the higher SMR may be due to the small sample size and relatively small number of deaths. Differences in SMRs across studies are most likely due to differences in resources, skills and health access in different PICUs.

The PELOD 2 score was examined in several studies after its introduction in 2013. A single-centre prospective study conducted in Portugal (n = 556) showed AUC 0.94 (95% CI 0.90, 0.98). However, there was poor calibration with the goodness-of-fit test (P = 0.022).[15] A posthoc analysis of a multicentre point-prevalence study examined the performance of PELOD 2 score in a subpopulation of children who received plasma transfusions (n = 443).[16] In this subpopulation, PELOD 2 score demonstrated acceptable discrimination (AUC 0.76 [95 % CI 0.71, 0.81]) and calibration (P = 0.76).[16] The odds ratio for death was 1.30 (95 % CI 1.22, 1.39) for each increase in PELOD 2 point.[16] The largest multicentre prospective study involving 9 PICUs in France and Belgium (n = 3669) confirmed that PELOD 2 scores offered the best discrimination on the first day of admission (AUC 0.89 [95% CI 0.86, 0.91]) with good calibration (P = 0.47).[17] The latter 2 studies evaluated the change in serial PELOD 2 scores from day 1 and demonstrated a significant association with death, for each of the observation days. Our study, with a modest sample size of Asian patients, concurs with the previous few studies showing good discrimination and calibration and thus demonstrates the generalisability of the PELOD 2 score. Overall, the PELOD 2 score performed better than the PIM 3 score in this cohort as the 95% CI of SMR crossed 1. As opposed to previous studies which evaluated the PELOD 2 score over a series of time points, we evaluated PELOD 2 score only on day 1 of PICU admission for several reasons. The day 1 PELOD 2 score has superior performance compared to other time points.[17] Because PIM 3 scores are scored within the first hour of admission, we focused on Day 1 PELOD 2 score, so as to allow us to compare these 2 scores within the early period of PICU admission.

In addition to being the first prospective study to evaluate the performance of the PIM 3 score, our study also evaluated the association between higher PIM3 and PELOD 2 scores with VFD and IFD. Investigating alternative clinically important outcomes is necessary because of the improvement in mortality rates in most PICUs. Assuming that factors leading to increase in VFD and IFD also improves mortality, the use of these alternative end points allows for smaller sample sizes.[18] Though not originally designed to predict VFD or IFD, our study demonstrated that patients with a higher quartile of PIM 3 and PELOD 2 scores had progressively decreased VFD and IFD (Table 3). This data further corroborates the 2 scores as robust predictive tools.

Limitations of this study include the small sample size (n = 570) resulting in an underpowered Hosmer-Lemeshow

test. Even though our centre is the larger of 2 national PICUs, this is nevertheless a single-centre study, and hence results are not generalisable throughout Singapore. Other limitations related to the challenges involved in determining some of the variables in the severity scores. For example, some patients did not have arterial cannulas and partial pressure of arterial oxygen could not be measured; some patients were also sedated and Glasgow Coma Scale score could not accurately be ascertained. Normal variables were keyed into the algorithm if data was missing as per the original model.[2,11] To attempt to overcome the practical challenges faced in calculating these scores, we anticipate that in the next revision of these scores, alternative variables that require less invasive monitoring such as the oxygen saturation: fraction of inspired oxygen (SpO_2/FiO_2) ratio may be included instead of the partial pressure of arterial oxygen: fraction of inspired oxygen (PaO_2/FiO_2) ratio. Lastly, we did not perform any tests to determine the inter-rater agreement of the scores. This may have introduced bias, although evaluators underwent standardised training and were blinded.

Conclusion

In a contemporary cohort of critically ill children in Singapore, PIM 3 and PELOD 2 scores performed better in those in the highest quartile of severity of illness. In addition to predicting mortality, we demonstrated that these scores are also associated with VFDs and IFDs.

Acknowledgement

The authors would like to acknowledge Dr Lahn Straney from the School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia and Dr Stephane Leteurtre from the Jeanne de Flandre University Hospital, Lille, France for providing guidance on the use of the PIM 3 and PELOD 2 scores, respectively. This study was funded by the Paediatrics Academic Clinical Program Young Researcher Pilot Grant – the Principal Investigator for this grant is Dr JH Lee. Dr CP Hornik receives salary support for research from the National Center for Advancing Translational Sciences of the National Institutes of Health (UL1TR001117) and the United States' government for his work in paediatric and neonatal clinical pharmacology (Government Contract HHSN267200700051C, PI: Benjamin under the Best Pharmaceuticals for Children Act).

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