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Original Article

Modifying the PELOD-2 score to predict mortality in critically ill patients

Melda Melda, Rina Triasih, Nurnaningsih

Abstract

Background The PELOD-2 score, which has been widely used to predict multiple organ dysfunction, may be used to predict mortality. Nevertheless, blood gas analyses (BGA) and lactate measurements required for the PELOD-2 cannot be performed in most limited resource settings.

Objective To evaluate the performance of modified PELOD-2, without BGA and lactate, to predict mortality in critically ill children.

Methods This retrospective cohort study in critically ill children admitted to the pediatric intensive care unit (PICU), Dr. Sardjito Hospital, Yogyakarta, was undertaken from January to December 2018. The modifications to the PELOD-2 score were PELOD-2A (without BGA), PELOD-2B (without lactate), and PELOD-2C (without BGA and lactate). The modified PELOD-2 scores were evaluated using receiver operating characteristic (ROC) curve for discrimination, and Hosmer-Lemeshow goodness-of-fit test for calibration.

Results Of 130 subjects, 68 (52.3%) died. A PELOD-2 score cut-off of 6.5 and modified PELOD-2A, 2B, and 2C had sensitivities for predicting mortality of 73.5%, 67.7%, 70.6%, and 63.2%, respectively, and specificities of 75.8%, 77.4%, 77.4%, and 79%, respectively. The area under curve (AUC) of the PELOD-2 score was 78.3 (95%CI 70.5 to 86.2). The AUCs of the modified PELOD-2 scores ranged from 76.8 (95%CI 68.7 to 84.9) to 77.9 (95% CI 69.9 to 85.8). The positive predictive values of PELOD-2 and modified PELOD-2A, 2B, 2C were 76.9%, 76.7%, 77.4% and 76.8%, respectively. The Hosmer-Lemeshow goodness-of-fit test showed good calibration for PELOD-2 (x^2=8.74; P=0.27) and modified PELOD-2A (x^2=4.91; P=0.67).

Conclusion The PELOD-2A, modified without BGA, can still predict mortality well in critically ill PICU patients when using a cut-off score ≥ 6.5. **[Paediatr Indones. 2021;61:61-8 ; DOI: 10.14238/pi61.2.2021.61-8**].

Keywords: *PICU; mortality; critically-ill children; PELOD-2 score*

The mortality rate of children admitted to the pediatric intensive care unit (PICU) is high, especially in developing countries, varying from 6.5% in China[1] and 12.9% in Pakistan,[2] to 37.4% in Saudi Arabia.[3] The mortality rate in the PICU of Dr. Sardjito General Hospital, Yogyakarta in 2018 was 27.19% (unpublished data).

Several well-known tools to predict disease severity and mortality in PICU patients have been developed, namely, the pediatric risk of mortality (PRISM) and pediatric index of mortality (PIM). Also, the pediatric logistic organ dysfunction (PELOD) score is often used to assess multiple organ dysfunction.[4] The PELOD tool is a descriptive score including parameters for the cardiovascular, respiratory, hematology, central nervous, renal and hepatic systems.[5] In 2013, the tool was improved and validated, with better discrimination and calibration, and termed PELOD-2. This latest version added mean arterial pressure and lactatemia as components

From the Department of Child Health, Universitas Gadjah Mada Medical School/Dr. Sardjito Hospital, Yogyakarta, Indonesia.

Corresponding author: Melda, Department of Child Health, Universitas Gadjah Mada Medical School, Jalan Kesehatan no. 1 Sekip Yogyakarta 55284, Indonesia. Telp. +62-274-561616, +62-817803381; Fax. +62-274-583745; Email: meldachang@yahoo.com.

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of cardiovascular dysfunction and eliminated liver dysfunction from the scoring system.[6] A 2018 Cipto Mangunkusumo Hospital (CMH) Jakarta Report stated that a PELOD-2 cut-off score of 10 to predict multiple organ dysfunction severity in sepsis patients had 85.5% AUC (95%CI 74.5 to 96.5) and positive predictive value (PPV) of 82%.[7]

Critically ill PICU patients commonly experience multiple organ dysfunction. Such a severe condition may ultimately lead to death in PICUs.[8] Critically ill children with multiple organ dysfunction syndrome (MODS) had 11.3 times higher mortality rates compared to patients without MODS, with a predicted mortality rate of 35-50%.[9] Therefore, PELOD-2 score may be able to be used to predict mortality. Nevertheless, blood gas analysis (BGA) and lactate examination, which are two of the score parameters, cannot be performed in PICUs with limited resources. As such, we aimed to assess the performance of the PELOD-2 score and modifications, eliminating lactate and BGA, in predicting mortality in critically ill PICU patients.

Methods

The study was conducted at Dr. Sardjito General Hospital, Yogyakarta, Indonesia, involving patients aged 1 month to 18 years. The inclusion criteria were critically ill PICU patients hospitalized from January to December 2018 who had complete PELOD-2 score data within the first 24 hours of admission. Those with incomplete medical record data (demographic, clinical, laboratory, and outcomes) were excluded. Subjects' data were obtained retrospectively from medical records.

The PELOD-2 score parameters are presented in **Table 1**. We made three modifications to PELOD-2: PELOD-2A (without BGA), PELOD-2B (without lactate) and PELOD-2C (without BGA and lactate).

A minimum required sample size of 130 patients was estimated to detect the primary outcome of mortality, with statistical significance of 95% (alpha error=0.05). Data were analyzed using *SPSS version 20.0*. The performance of the scoring systems was evaluated by assessing discrimination and calibration. The AUC of each scoring system ROC curve was calculated to evaluate discriminative ability. The interpretation of the AUC was as follows: >0.9 indicated excellent discrimination, 0.8-0.9 indicated good discrimination, 0.7-0.8 indicated satisfactory discrimination, 0.6-0.7 indicated poor discrimination, and 0.5-0.6 indicated that the scoring system did not predict better than mere chance. The calibrations of the scoring systems were assessed using Hosmer-Lemeshow goodness of fit test. Good calibration performance was defined as no difference between observed and expected values, with P values > 0.05.

This study was approved by the Ethics Committee of the Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada and the Research and Education Committee of Dr. Sardjito General Hospital.

Results

Of 434 PICU patients aged > 1month to 18 years in year 2018, 198 were eligible for inclusion, and 130 were selected for analysis using simple random sampling. The study flow chart is presented in **Figure 1**. Sixty-eight patients (52.3%) died during hospitalization. The characteristics of subjects are shown in **Table 2**. Around 60% of the patients were less than 5 years of age, and overall median age was 37 (IQR 6.5 - 131) months. The proportion of males to females was similar.

The median non-survivors' PELOD-2 score was significantly higher than that of the survivors' group (**Table 3**). The optimal cut-off values of the original PELOD-2 and modified versions of PELOD-2 to predict mortality were the same, at 6.5 (**Figure 2**). **Table 4** shows the sensitivity, specificity, PPV, and negative predictive value (NPV) of a cut-off score of 6.5 for the original and modified versions of PELOD-2. The AUCs of the four PELOD-2 versions ranged from 77% to 78%, which indicated that all of them were satisfactory predictors of mortality (**Table 5**).

Calibration of the PELOD-2 and PELOD-2A was good (P>0.05). However, the calibration of PELOD-2 score to PELOD-2B and PELOD-2C showed low calibration performances (P<0.05). Discrimination test results of the original and modified versions of PELOD-2 are shown in **Table 5**. Using the obtained cut-off value, diagnostic study was done to assess sensitivity, specificity, positive predictive value

Table 1. The PELOD-2 scoring system

Organ dysfunction and variable	Scoring system						
	0	1	2	3	4	5	6
Neurological	≥11	5-10			3-4		
Glasgow Coma Scale							
Pupillary reaction	Both reactive					Both fixed	
Cardiovascular							
Lactatemia, mmol/L	< 5.0	5-10.9			≥11		
Mean arterial pressure, mmHg							
0 - <1 month	≥ 46		31-45	17-30			≤ 16
1-11 months	≥ 55		39-54	25-38			≤ 24
12-23 months	≥ 60		44-59	31-43			≤ 30
24-59 months	≥ 62		46-61	32-44			≤ 31
60-143 months	≥ 65		49-64	36-48			≤ 35
≥144 months	≥ 67		52-68	38-51			≤ 37
Renal							
Creatinine (mmol/L)							
0 - < 1 month	≤ 69		≥ 70				
1-11 months	≤ 22		≥ 23				
12-23 months	≤ 34		≥ 35				
24-59 months	≤ 50		≥ 51				
60-143 months	≤ 58		≥ 59				
≥144 months	≤ 92		≥ 93				
Respiratory							
PaO_2, mmHg/FiO_2	≥ 61		≤ 60				
$PaCO_2$, mmHg	≤ 58	59 - 94		≥ 95			
Mechanical ventilation	No			Yes			
Hematological							
White blood cell count, x 109/L	> 2		≤ 2				
Platelets, x 109/L	≥ 142	77-141	≤ 76				
PELOD-2 score =							

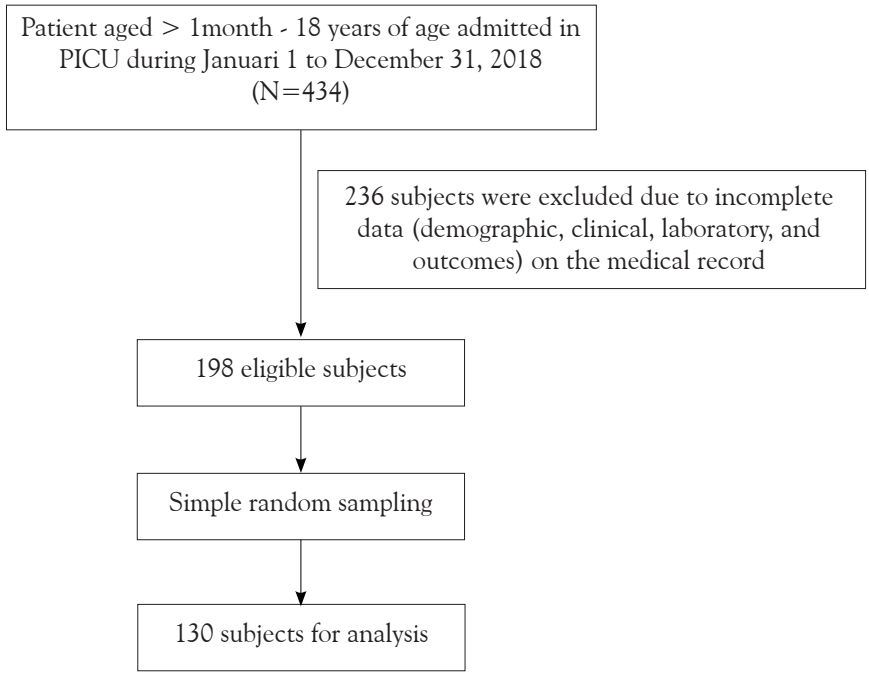

Figure 1. Study flow

Table 2. Subjects' characteristics

Characteristics	Survivors (n = 62)	Non-survivors (n = 68)	Total (N=130)	P value
Sex, n (%)				0.357
Male	26 (41.9)	34 (50)	60 (46.2)	
Female	36 (58.1)	34 (50)	70 (53.8)	
Age, n (%)				0.954
1-11 mo	19 (30.6)	23 (33.8)	42 (32.3)	
≥ 12-23 mo	8 (12.9)	8 (11.8)	16 (12.3)	
≥ 24-59 mo	11 (17.7)	9 (13.2)	20 (15.4)	
≥ 60-143 mo	12 (19.4)	13 (19.1)	25 (19.2)	
≥ 144 mo	12 (19.4)	15 (22.1)	27 (20.8)	
Nutritional status, n(%)				0.319
Severely wasted	13 (21.0)	14 (20.6)	27 (20.8)	
Wasted	20 (32.2)	18 (26.5)	38 (29.2)	
Normal	28 (45.2)	30 (44.1)	58 (44.6)	
Overweight	1 (1.6)	6 (8.8)	7 (5.4)	
Ventilator use, n(%)				0.001
Yes	37 (59.7)	62 (91.2)	99 (76.2)	
No	25 (40.3)	6 (8.8)	31 (23.8)	
Underlying disease, n(%)				
Respiratory	5 (8.0)	21 (30.9)	26 (20)	
Neurology	18 (29.0)	12 (17.6)	30 (23.1)	
Gastrointestinal	14 (22.6)	7 (10.3)	21 (16.2)	
Tropical infection	0	2 (2.9)	2 (1.5)	
Hemato-oncology	4 (6.5)	8 (11.8)	12 (9.2)	
Cardiovascular	2 (3.2)	4 (5.9)	6 (4.6)	
Immunology	0	1 (1.5)	1 (0.8)	
Surgery	14 (22.6)	8 (11.8)	22 (16.9)	
Other	5 (8.1)	5 (7.3)	10 (7.7)	
Median length of stay (range), days	6 (0-73)	3 (1-31		0.001

Table 3. Median total scores of the original and modified versions of PELOD-2 for survivors and non-survivors

Score	Survivors (n=62)		Non-survivors (n=68)	
	Median	IQR	Median	IQR
PELOD-2	5	3-6.25	9	6-13
PELOD-2A	4	3-6	9	6-12
PELOD-2B	4.5	3-6	8	6-12
PELOD-2C	4	3-6	8	5.25-11.75

Note: IQR= interquartile range

(PPV), negative predictive value (NPV) and accuracy of PELOD-2 score and each of its modifications. **Table 6** describes diagnostic test performance and odds ratio to mortality outcome.

Discussion

The mortality rate in our study was 52.3%, similar to previous reports of 56.4% in Dr. Sardjito General Hospital in 2012 and 40.58-45.7% in Mohammad Hoesin Hospital, Palembang, South Sumatera, in 2016.[9-11] However, this rate was higher than most recent data in Dr. Sardjito General hospital in 2018 (unpublished data), and those in other countries such as Egypt (39.6%)[12] and Pakistan (28.7%),[13] and far higher than in developed nations of France and Belgium (6.0%).[14]

Mortality in critically ill PICU patients has been associated with MODS, which can be predicted by PELOD-2. Our subjects' median PELOD-2 score was 6.5 (IQR 3.75-10), with non-survivors' score significantly higher than survivors' score (9 *vs.* 5, respectively; P=0.001). A cut-off point of 6.5 showed a moderate performance in predicting mortality, with 73.5% sensitivity, 75.8% specificity, and 78.3% AUC. A national referral hospital in Jakarta reported that a lower cut-off score of > 4.5 had better sensitivity (84.3%) and specificity (84.5%) for predicting

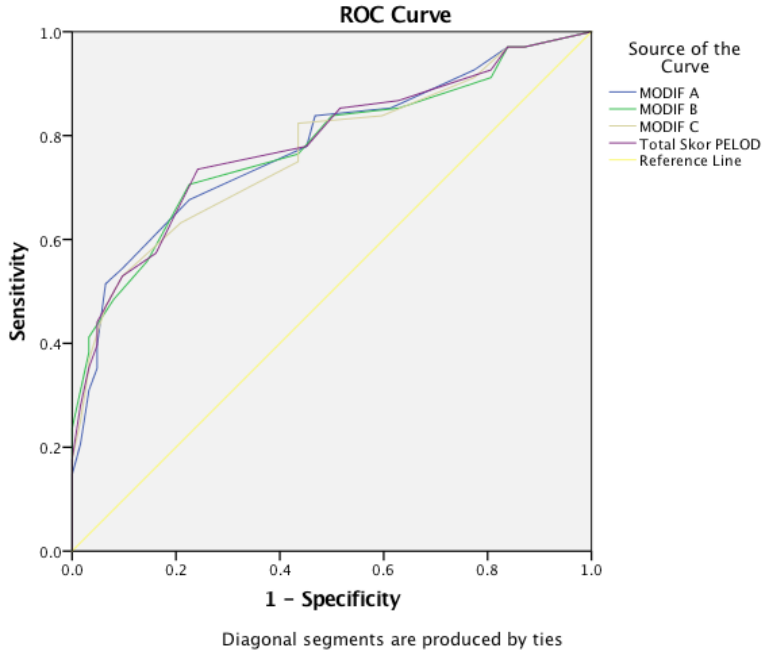

Figure 2. ROC curve of the original and modified versions of PELOD-2 to predict mortality

Table 4. The performance of the original and modified versions of PELOD-2 (total score ≥ 6.5) to predict mortality

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	PLR (%)	NLR (%)
PELOD-2	73.5	75.8	76.9	72.3	3.04	0.35
Modified 2A	67.6	77.4	76.7	68.6	3.00	0.42
Modified 2B	70.6	77.4	77.4	70.6	3.13	0.38
Modified 2C	63.2	79.0	76.8	66.2	3.02	0.57

Note: PPV=positive predictive value, NPV=negative predictive value, PLR=positive likelihood ratio, NLR=negative likelihood ratio

Table 5. Discrimination and calibration of the original and modified versions of PELOD-2

	PELOD-2	Modified PELOD-2A (without BGA)	Modified PELOD-2B (without lactate)	Modified PELOD-2C (without BGA and lactate)
Discrimination AUC value (95%CI)	0.78 (0.71 to 0.86)	0.78 (0.70 to 0.86)	0.78 (0.67 to 0.86)	0.77 (0.69 to 0.85)
Callibration				
x2 Hosmer-Lemeshow	8.74	4.91	16.87	16.71
P value	0.27	0.67	0.03	0.03
Observed death, %	76.9	76.7	77.4	76.8
Expected death, %	73.5	67.6	70.6	63.2
Standardized mortality rate (SMR)	1.05	1.13	1.10	1.22

Table 6. Diagnostic performance of PELOD-2 score and its modification to mortality outcome

Variables		Mortality		Total	OR	95%CI	P value
		Yes n (%)	No n (%)				
PELOD-2	≥6.5	50 (76.9)	15 (23.1)	65	8.70	3.94 to 19.23	0.001
	<6.5	18 (27.7)	47 (72.3)	65			
Modified 2A	≥6.5	46 (76.7)	14 (23.3)	60	7.17	3.28 to 15.68	0.001
	<6.5	22 (31.4)	48 (68.6)	70			
Modified 2B	≥6.5	48 (77.4)	14 (22.6)	62	8.23	3.73 to 18.16	0.001
	<6.5	20 (29.4)	48 (70.6)	68			
Modified 2C	≥6.5	43 (76.8)	13 (23.2)	56	6.48	2.96 to 14.22	0.001
	<6.5	25 (33.8)	49 (66.2)	74			

Cut-off point ≥ 6.5 both the original and modified PELOD-2B had an eight-times increase in mortality than patients with score < 6.5

mortality in PICU patients.[15] The difference may have been caused by differing severity or underlying disease of the patients. In Jakarta, 65% of the patients were surgical cases, whereas those in our study had predominantly neurology and respiratory problems.[15]

We conducted this study to evaluate three modifications of PELOD-2, based on the fact that facilities/PICUs in developing countries may lack the capability to perform BGA and serum lactate measurements, which are parameters of PELOD-2. All 3 modified versions of PELOD-2 [without BGA (2A), without lactate (2B), and without BGA and lactate (2C)] had similar ability to predict mortality as the original PELOD-2, with AUC around 0.78. However, only PELOD-2 and PELOD-2A score had good calibration. This finding indicates that serum lactate level is important in predicting mortality. A study reported a significant relationship between serum lactate level on admission with mortality in critically ill children (OR 1.38; 95%CI 1.30 to 1.46).[16] Another study reported good predictive value of one-time lactate evaluation in predicting mortality in PICU patients, in which the first 24-hour serum lactate level had better sensitivity and specificity compared to the first 6-hour serum lactate level.[17] A serial lactate evaluation was also beneficial to predict mortality, as shown by a Yogyakarta study that reported higher serial serum lactate level in non-survivors than in survivors (RR 4.92; 95%CI 1.77 to 13.65).[18]

Despite concerns about the poor calibration result, in limited resource settings, modifying PELOD-2 without BGA and serum lactate may still be useful for clinicians to predict mortality in PICU patients, where facilities for BGA and serum lactate are unavailable. This suggestion is based on the similarity of predictive values between PELOD-2C (without BGA and lactate) and the original PELOD-2. Nevertheless, when using this modified PELOD-2C to make a clinical decision, the clinician should be aware of the limitations and consider the potential harm and benefits.

Young children are more likely to be admitted to the PICU. Thirty-two % of our subjects were aged 1 to 11 months, similar to previous studies in Jakarta, which reported 27.9%[15] and in France and Belgium, which reported 29.1%.[6] Young children are also at greater risk of mortality due to infection or sepsis. In our study, 13/32 children aged less than one year died, with sepsis as the main underlying diagnosis. The immature immune system of young children may be an influencing factor.

Non-survivors length of stay was shorter than that of survivors (3 *vs.* 6 days, respectively). In contrast, a study in France and Belgium documented that LOS of survivors was shorter (4 days) than in our study.[14] Ventilator use in our setting was quite high, at 76.2% of all subjects and 91.2% of non-survivors. Other studies reported far less ventilator use, with 52% in Egypt,[6] 52.5% in Portugal,[14] and 52% in France.[13] Many factors may cause these differences, one of which is the underlying condition of the patient. In our study, the three most common conditions were cerebrospinal diseases (21.3%), respiratory problems (20%), and surgical (16.9%) issues. In a Portugal study, cardiovascular problems were reported to be the

most common underlying disease (23.9%), followed by respiratory (16.9%), and neurologic diseases (14.9%). [19]

The retrospective design of this study is one of the limitations, as well as subjective evaluations such as of heart rate, Glasgow coma score, and pupil reaction by different practitioners. In addition, there were potential subjects who could not be included because of incomplete medical data. A prospective study should be conducted to evaluate the use of the modified PELOD-2 in limited resource settings, or to develop a simple and feasible scoring system to predict mortality in children admitted to the PICU.

In conclusion, a modified version of PELOD-2, without BGA and/or without lactate, can be used to predict mortality in critically ill pediatric patients with precautions. A cut-off point > 6.5 on both the original and modified PELOD-2 has an eight-times increase in mortality than patients with score < 6.5.

Conflict of Interest

None declared.

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