PEDIATRIC LOGISTIC ORGAN DYSFUNCTION-2 (PELOD-2) SCORE AS A MODEL FOR PREDICTING MORTALITY IN PEDIATRIC BURN INJURY

SCORE "PEDIATRIC LOGISTIC ORGAN DYSFUNCTION 2 (PELOD 2)" ET PRÉDICTION DE MORTALITÉ CHEZ L'ENFANT BRÛLÉ

Dewi R.,[1]✉ Christie C.D.,[1] Wardhana A.,[2] Fadhilah R.,[1] Pardede S.O.[1]

[1]Department of Child Health, Cipto Mangunkusumo Hospital, Jakarta, Indonesia
[2]Division of Plastic, Reconstructive and Aesthetic Surgery, Cipto Mangunkusumo Hospital, Jakarta, Indonesia

SUMMARY. Multiple organ dysfunction syndrome (MODS) is an important cause of mortality in burn injury. Pediatric Organ Logistic Dysfunction (PELOD)-2 score as a descriptive scoring system for organ dysfunction has been highly predictive of mortality in children with suspected infection, but its usefulness for burn patients is unknown. All pediatric burn patients hospitalized in Cipto Mangunkusumo Hospital (CMH) in Jakarta, Indonesia, from January 2012 to January 2017 were studied. Gender, age, nutritional status, burn characteristics, total body surface area burned (%TBSA), depth of burn, inhalation injury, time interval to resuscitation and surgery, day one ABSI and PELOD-2 score, and mortality as outcome were recorded. Bivariate and multivariate analysis logistic regressions were done to generate a mortality prediction model. Mortality rate among subjects was 20.3%. Bivariate analysis showed that extensive %TBSA, depth of burn, presence of inhalation injury, PELOD-2 score and ABSI score in pediatric burn patients were significantly associated with mortality ($p<0.001$). In multivariate analysis, only PELOD-2 score was independently associated with mortality. PELOD-2 score mortality prediction rate was far lower than actual mortality. Mortality rate by the new model was close to the actual mortality rate. Our new combined model could be used to calculate probability of death based on day 1 PELOD-2 score in pediatric burn patients.

Keywords: PELOD-2 score, burn, children, mortality

RÉSUMÉ. *La mort après brûlure est fréquemment due à une défaillance multiviscérale. Le score PELOD 2 s'est révélé efficace dans la prédiction de mortalité de l'enfant septique mais n'a pas été évalué chez l'enfant brûlé. Tous les enfants brûlés hospitalisés dans l'hôpital Cipto Mangunkusumo de Djakarta (Indonésie) entre janvier 2012 et janvier 2017 ont été évalués. L'âge, le sexe, l'état nutritionnel, la surface brûlée, sa profondeur, l'existence d'une inhalation de fumées, les délais jusqu'à la réanimation et la chirurgie, ABSI et PELOD 2 à J1 et mortalité (20,3%) ont été colligés. Des analyse bivariée puis multivariée ont été réalisées afin de construire un modèle prédictif de mortalité. PELOD 2 comme ABSI étaient de bons prédicteurs de mortalité, les prédictions de PELOD 2 s'avérant très optimistes. Toutefois, seul PELOD 2 apparaissait comme un prédicteur indépendant de mortalité. Un modèle combinant les mortalités prédites par ABSI et PELOD 2 s'est avéré mieux corrélé à la mortalité observée. Il pourrait être utilisé chez les enfants brûlés.*

Mots-clés : *score PELOD 2, brûlure, enfants, mortalité*

✉ Corresponding author: Rismala Dewi, MD, Department of Child Health, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo Hospital, Jakarta, 71 Diponegoro St., Jakarta, Indonesia 10430. Tel.: +62 811810112; email: dewi22juli@gmail.com
Manuscript: submitted 16/05/2019, accepted 17/06/2019

Introduction

Burn injury may lead to temporary or permanent disability and to death. In 2014 the World Health Association (WHO) estimated that 265.000 deaths per year worldwide are caused by burn injuries.[1] Children are a susceptible population to burn injury due to their slow reaction to heat and limited mobility, as well as their undeveloped immune system. In Cipto Mangunkusumo Hospital (CMH) in Jakarta, Indonesia, it was found that 30% of burn patients in 2000-2010 were children, with a mortality rate of 28% in 2012.

One major cause of death in burn patients is multiple organ dysfunction syndrome (MODS). The American Burn Association found that 50% of deaths from burn injury were caused by organ failure.[2,3] However, only a few studies have investigated MODS as a burn complication, especially in pediatric populations.

Scoring systems to predict outcome in burn patients have been developed for years to make it easier to make a treatment plan. Abbreviated Burn Score Index (ABSI) is one of the indexes most widely used by both burn surgeons and pediatric intensivists to predict burn outcome. ABSI consists of 5 variables that can be easily calculated at the time of admission to predict mortality immediately. However it does not count organ failure as one of the major causes of mortality from burn.[4,5]

Pediatric Logistic Organ Dysfunction (PELOD) score is a frequently used scoring system to describe multiple organ dysfunction in pediatric patients. First developed in 1999, PELOD score was modified to PELOD-2 score, which allows the assessment of the severity of multiple organ dysfunction syndrome with good validity.[6] It consists of 10 variables which represent 5 organ dysfunctions (*Table I*). A higher PELOD-2 score correlates with a higher number of organ failures and mortality rate.

A study by Leclerc et al. demonstrated its good validity for predicting mortality in children in the Pediatric Intensive Care Unit (PICU) with suspected infection.[7] Given its potential for mortality prediction, the biggest issue with PELOD-2 for burn patients is that PELOD-2 does not include total body surface area (%TBSA) of burned skin as the greatest factor affecting outcome in burn patients.

We designed a study to compare the performance of two scores (PELOD-2 and ABSI) in predicting mortality. We also tried to implement a combined scoring system that used PELOD-2 and other prognostic factors that are considered important in predicting burn patient mortality. This study was approved by the Research Ethics Committee, Faculty of Medicine, Universitas Indonesia (645/UN2.F1/ETIK/2017).

Methods

This was a retrospective review study to compare the mortality prediction value of the PELOD-2 Score and ABSI in pediatric burn patients. The study was conducted at the Cipto Mangunkusumo Hospital (CMH) in Jakarta from January 2012 to January 2017. Data were obtained from the medical records of pediatric burn patients hospitalized in the emergency department and burn unit of CMH. The inclusion criteria were children (aged 0-18 years) and pediatric burn patients who met the hospitalization criteria in the CMH burn unit from January 2012 to January 2017. The exclusion criteria were patients who had incomplete medical records, non-hospitalized or outpatient burn cases, and patients who only underwent wound care/skin graft or advanced infection management in the burn unit. The total sampling method was used in this study. Subjects were assessed for demographics (gender and age), nutritional status, burn characteristics (total of body surface area burned [%TBSA], depth of burn and presence of inhalation injury), treatment (time interval to resuscitation and surgery), ABSI, PELOD-2 score and mortality as outcome. %TBSA was calculated using the Lund-Browder chart method, classified into 3 groups (<20%, 20-40%, and >40%) based on the study by Sheridan et al. expecting that TBSA <20% is compensated while TBSA>40% is associated with a high risk of mortality.[8] ABSI and PELOD-2 scores were recorded once within the first 24hrs from hospital admission and calculated using the scoring system as published.

Data were exported to Microsoft excel and analysed by SPSS 20.0. Descriptive statistics were calculated to find frequency, mean and median of the

Table I - Pediatric Logistic Organ Dysfunction Score - (PELOD-2)[6]

Organ dysfunctions and variables	Points by severity level						
	0	**1**	**2**	**3**	**4**	**5**	**6**
Neurologic							
• Glasgow coma score	≥11	5-10			3-4		
• Pupillary reaction	Both reactive					Both fixed	
Cardiovascular							
• Lactatemia (mmol/L)	<5.0	5.0-10.9			≥11.0		
• Mean arterial pressure (mmHg) (months)							
0-<1	≥ 46		31-45	17-30			≤ 16
1-11	≥ 55		39-54	25-28			≤ 24
12-23	≥ 60		44-59	31-43			≤ 30
24-59	≥ 62		46-61	32-44			≤ 31
60-143	≥ 65		49-64	36-48			≤ 35
≥144	≥ 67		52-66	38-51			≤ 37
Renal							
• Creatinine (µmol/L) (months)							
0-<1	≥ 69		≥ 70				
1-11	≥ 22		≥ 23				
12-23	≥ 34		≥ 35				
24-59	≥ 50		≥ 51				
60-143	≥ 58		≥ 59				
≥144	≥ 92		≥ 93				
Respiratory							
• PaO_2 (mmHg)/FiO_2	≥ 61		≤ 60				
• $PacO_2$ (mmHg)	≥ 58	59-94		≥ 95			
• Invasive ventilation	No			Yes			
Hematologic							
• WBC Count ($x10^9$/L)	>2		≤ 2				
• Platelet ($x10^9$/L)	≥142	77-141	≤ 76				

Relationship between number of organ dysfunctions, PELOD-2 score, and mortality rate		
Number of organ dysfunctions	PELOD-2 Score Mean (SD)	Mortality rate (%)
0	0 (0.0)	0.4
1	2.3 (0.8)	0.3
2	4.9 (1.3)	1.2
3	7.5 (2.0)	7.1
4	11.5 (4.4)	30.5
5	16.8 (5.2)	59.0

SD = Standard deviation

demographic and clinical characteristics. Normality testing was conducted on numerical data using the Kolmogorov-Smirnov test. Numeric data was customarily presented as mean if normally distributed, and median if not. Subjects who died were compared to those who survived using the Chi-Square or Fisher test and t-test or Mann-Whitney as appropriate, with $p<0.05$ considered as statistically significant. Logistic regression was calculated for variables with $p<0.25$. The final model was re-tested with logistic regression to assess its performance in predicting mortality as well as calibration and discrimination profile using Hosmer and Lemeshow Test and Receiver Operator Curve.

Results

There were 190 pediatric patients with a burn diagnosis admitted to the Cipto Mangunkusumo Hospital (CMH) from January 1, 2012 to December 31, 2017. A total of 148 subjects were eligible for this study. ABSI score, as a standard severity index used in CMH, was calculated for each of them. PELOD-2 score was calculated for only 133 subjects due to incomplete laboratory examination.

There were 118 survivors and 30 non-survivors in this study. Demographic characteristics of survivors and non-survivors are shown on *Table II*. Mortality rate was found to be 20.3%. Mortality was higher among subjects who had more extensive TBSA, higher depth of burn, inhalation injury, higher PELOD-2 score and higher ABSI score with $p<0.05$ for each.

Mean PELOD-2 value for non-survivors in this study was 12.03±4.09. This value was higher than the PELOD-2 cut off point of 11, which represents 30.5% mortality rate and 4 organ dysfunctions, but less than the cut off point of 16, which is associated with 59% mortality rate and 5 organ dysfunctions (*Table I*).

Mean value for ABSI in non-survivors was 9.07±2.05, which falls into the serious category in ABSI scoring and is associated with 50-70% mortality rate.

Logistic regression analysis using the backward method was conducted on variables that had $p<0.25$ on bivariate analysis (%TBSA, depth of burn, inhalation injury, PELOD-2 Score, ABSI Score, and time interval to resuscitation). Using the backward method, variables that had a weak association with mortality were removed respectively from the analysis (depth of burn, %TBSA, inhalation injury, time interval to resuscitation, and ABSI). Only PELOD-2 score was found to be independently correlated to mortality (OR 4,38; 95% CI 1,37-13,96) (*Table III*).

A new combined mortality prediction model was developed for this population using the logistic regression model. With the new model, probability of death was calculated with the equation $p=1/1/(1+e^y)$, y representing mortality risk. The comparison of scoring formulae for PELOD-2, ABSI and the new model is shown in *Table IV*.

As %TBSA is known to have a great impact on mortality, and is accounted for in the ABSI score but not in the PELOD-2 score, we attempted to include %TBSA in the scoring system. Patients were divided into 3 groups based on %TBSA as ABSI predicts mortality over a range, not a specific percentage. We found that compared to actual mortality, neither PELOD-2 score nor ABSI alone showed lower probability of death for almost all %TBSA groups, except that the ABSI mortality prediction rate was higher in the <20% TBSA group. Prediction with the new combined model was closest to actual mortality among all scoring systems in all %TBSA groups, but was higher in the TBSA>40% group compared to actual mortality (*Table V*).

Using the Hosmer and Lameshow Test, the new combined model was found to have a good calibration performance ($p=0.74$). *Fig. 1* shows the excellent discrimination profile of the new model ($p<0.05$, area 90-100%) using Receiver Operator Curve (ROC). Cut-off value of the new model to predict mortality was -2.043.

Discussion

This was the first study to assess PELOD-2 performance as a scoring system to predict mortality in pediatric burn patients. In our new model we also calculated several factors that were considered im-

Table II - Bivariate analysis of demographic characteristics and mortality

Variable	Survivor	Non-survivor	OR	95%CI	P
Subjects (%)	118 (79,7)	30 (20,3)	-	-	-
Age (years) Median (range)	3 (0-18)	4 (0-18)	-	-	0,366
Age group					0,891
0-4 years (%)	72 (61)	19 (63,3)	1		
5-10 years (%)	26 (22)	7 (23,3)	1,02	0,38-2,71	
11-18 years (%)	20 (17)	4 (13,3)	0,76	0,23-2,48	
Gender					0,304
Boys (%)	75 (63,6)	16 (53,3)	1		
Girls (%)	43 (36,4)	14 (46,7)	1,53	0,68-3,43	
Nutritional status					0,991
Severely wasted (%)	5 (4,2)	1 (3,3)	1		
Wasted (%)	21 (17,8)	6 (20)	1,43	0,14-14,69	
Normal (%)	78 (66,1)	20 (66,7)	1,28	0,14-11,60	
Overweight (%)	6 (5,1)	1 (3,3)	0,83	0,04-16,99	
Obese (%)	8 (6,8)	2 (6,7)	1,25	0,09-17,65	
Total Body Surface Area Burned (TBSA)					<0,001
<20% (%)	76 (64,4)	1 (3,3)	1		
20-40% (%)	37 (31,4)	8 (26,7)	16,43	1,98-136,31	
>40% (%)	5 (4,2)	21 (70)	319	35,34-2883,01	
Depth of burn					<0,001
II (%)	83 (70,3)	9 (30)	1		
II-III (%)	33 (28)	19 (63,3)	5,31	2,18-12,93	
III (%)	2 (1,7)	2 (6,7)	9,22	1,16-73,61	
Inhalation injury					<0,001
No (%)	106 (89,8)	12 (40)	1		
Yes (%)	12 (10,2)	18 (60)	13,25	5,16-34,03	
PELOD-2 Score, median (range) or mean±SD	1 (0-7)	12.03±4,09	-	-	<0,001
ABSI Score, median (range) or mean±SD	5 (0-12)	9,07±2,05	-	-	<0,001
Time interval to surgery					0,083
<24 hours (%)	13 (17,3)	9 (33,3)	1		
>24 hours (%)	62 (82,7)	18 (67,3)	0,42	0,15-1,13	
Time interval to resuscitation					0,307
<24 hours (%)	104 (88,1)	29 (96,7)	1		
>24 hours (%)	14 (11,9)	1 (3,3)	0,26	0,03-2,03	

OR = Odds Ratio; CI = Confidence Interval; SD = Standard Deviation

Table III - Multivariate analysis of variables significant for mortality

Variable	B	SE	EXP (B) (95%CI)	P
PELOD-2 Score	1,477	0,592	4,38(1,37-13,96)	0,013
Constant	-9,428	3,942	-	0,017

B = Regression Coefficient; SE = Standard Error, EXP (B) = Odds Ratio for predictors

Table IV - Probability of death scoring formulae for PELOD-2, ABSI and the new combined model

Scoring formula
• In hospital mortality risk via PELOD-2 y = -2.038 + (0.104 x PELOD-2 Score) • In hospital mortality risk via ABSI y = B0+ (B1x ABSI Score) • In hospital mortality risk via the new combined model y = 1.008 x (-9.428 + (1.477 x PELOD-2 Score) • Probability of death $p = 1/(1+e^{y})$

Table V - Predicted vs. actual mortality of scoring systems

Variable	%TBSA <20%	%TBSA 20-40%	%TBSA >40%
Probability of death via the new combined model (%)	1,7	16,6	80,3
Probability of death via PELOD-2 (%)	0,13	0,53	2,97
Probability of death via ABSI (%)	6,1	16,8	49,5
Actual mortality (%)	3,3	26,7	70

portant in previous studies. However, this study had several limitations. Firstly, there was a difference in population profile used in the PELOD-2 formulation and in this study. This study used subjects with burns admitted to the emergency department/burn unit, while the study in the PELOD-2 formulation used subjects with various primary diseases at entry.[6] Secondly, PELOD-2 score was only calculated once, within the first 24 hours of admission (d1qPELOD-2), which might not represent an optimal measurement of PELOD-2 score and changes over time. D1qPELOD-2 score was previously known as highly predictive of mortality among children admitted to the PICU with suspected infection, but nobody had investigated its usefulness in pediatric burn injury.[7]

Mortality rate in this study was 20.3%. This was higher than in the study by Rosanova et al.[9] conducted in Brazil (15%) and slightly lower than the

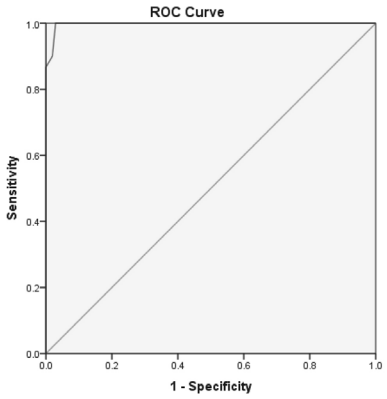

Fig 1 - Receiver operator curve of the new combined model

study by Agbernoku et al.[10] carried out in Ghana (21.3%). This is supported by a study by WHO, which found that Southeast Asian countries had the highest pediatric burn patient mortality rate.[1]

It is generally accepted that TBSA has a big impact on mortality. This study found that mortality rate was 16.43 times higher (95% CI 1,98-136,31) for 20-40% TBSA and 319 times higher (95% CI 35,34-2883,01) for TBSA>40%. Extensive burn could lead to reduced skin protection capacity, increased risk of infection, metabolic stress, and death.[11] Burn injury of >40% TBSA is often accompanied by hypovolemic or distributive shock due to great intravascular fluid loss. This could increase afterload and reduce heart contractility. Without adequate resuscitation, renal failure will occur due to reduced blood supply to the kidney.[12,13]

Non-survivors had a higher depth of burn than survivors in this study (p<0.001). Higher depth of burn can cause damage to skin structure and induce scar tissue formation, which disturbs the skin's function, delays the regeneration process, causes infection, and has a higher risk of mortality.[14]

In this study the presence of inhalation injury was associated with a 13.25-times (95% CI 5.16-34.03) higher risk of mortality. Inhalation injury was found to be an important factor causing mortality among burn patients in previous studies.[10,15-18] Inhalation injury can cause airway obstruction, laryngeal edema, mucosal and lung damage, acute respiratory distress syndrome, and even death.[19]

Bivariate analysis showed that non-survivors had higher PELOD-2 and ABSI scores (p<0.001) than survivors. On logistic regression, it was found that only PELOD-2, not ABSI, had a strong correlation to mortality. Meanwhile, in our study PELOD-2 mortality prediction score was far lower than the actual mortality rate. This might be because the mortality prediction rate was grouped based on %TBSA, while the PELOD-2 score itself does not include %TBSA. We found that many subjects in our study who had an extensive burn had a low PELOD-2 score.

We have proposed a new mortality prediction model with good calibration and discrimination value based on our logistic regression analysis in this population. The mortality prediction rate of this new combined model is closer to actual mortality than PELOD-2 and ABSI alone.

Conclusion

Extensive %TBSA, depth of burn, presence of inhalation injury, PELOD-2 score and ABSI score in pediatric burn patients were associated with mortality. We concluded that higher PELOD-2 score could be associated with a higher risk of mortality, but its predictive mortality value was lower than the actual mortality rate. Our new combined model could be used to calculate probability of death based on PELOD-2 score.

BIBLIOGRAPHY

1 Peden M et al. (eds.): Burns. In: "World Reports on Child Injury Prevention". World Health Organization, Geneva, 2008.
2 Miller SF, Bessey PQ, Schurr MJ et al.: National Burn Repository 2005: a ten-year review. J Burn Care Res, 27: 411-36, 2006.
3 Kallinen O, Maisniemi K, Böhling T, Tukiainen E, Koljonen V: Multiple organ failure as a cause of death in patients with severe burns. J Burn Care Res, 33(2): 206-11, 2012.
4 Berndston AE, Sen S, Greenhalgh DG, Palmieri TL: Estimating severity of burn in children: Pediatric Risk of Mortality (PRISM) score versus Abbreviated Burn Severity Index (ABSI). Burns, 39(6): 1048-53, 2013.
5 Halgas B, Bay C, Foster K: A comparison of injury scoring systems in predicting burn mortality. Ann Burn Fire Disasters, 31(2): 89-93, 2018.
6 Leteurtre S, Duhamel A, Salleron J, Grandbastien B et al.:

PELOD-2: an update of the pediatric logistic organ dysfunction score. Crit Care Med, 41: 1761-73, 2013.
7 Lacrec F, Duhamel A, Deken V, Grandbastien B, Leteurtre S: Can the Pediatric Logistic Organ Dysfunction (PELOD)-2 on day 1 be used in clinical criteria for sepsis in children? Pediatr Crit Care Med, 18(8): 758-63, 2017.
8 Rosanova MR, Stamboulian D, Lede R: Risk factor for mortality in burn children. Braz J Infect Ds, 18: 144-9, 2014.
9 Agbenorku P, Agbenorku M, Filfi-Yankson PK: Pediatric burn mortality risk factors in a developing country's tertiary burns intensive care unit. Int J Burn Trauma, 32: 151-8, 2013.
10 Krishnamoorthy V, Ramaiah R, Bhananker SM: Pediatric burn injury. Int J Crit Illn Inj Sci, 2: 128-34, 2012.
11 Nielson CB, Duethman NC, Howard JM, Moncure M, Wood JG: Burns: pathophysiology of systemic complications and current management. J Burn Care Res, 38: 469-81, 2017.
12 Ryan CM, Schoenfeld DA, Thorpe WP, Sheridan RL et al.: Objectives estimates of the probability of death from burn injuries. NEJM, 338: 362-6, 1998.
13 Moneadjat Y: Kedalaman luka dan luas luka bakar pediatrik. In: Mariam NS (ed.): "Luka Bakar Pediatrik", 23-37, 1st ed., Sagung Seto, Jakarta, 2016.
14 Rosanova MR, Stamboulian D, Lede R: Risk factor for mortality in burn children. Braz J Infect Ds, 18: 144-9, 2014.
15 Wolf SE, Rose JK, Desai MH, Mileski JP et al.: Mortality determinants in massive pediatric burns. An analysis of 103 children with > or = 80% TBSA burns (> or = 70% full-thickness). Ann Surg, 225: 554-65, 1997.
16 Karimi H, Motevalian SA, Momeni M, Safari Y, Ghadarjani M: Etiology, outcome and mortality risk factor in children burn. Surg Sci, 6: 42-9, 2015.
17 Dermijan G: Adjusting a prognostic score for burned children with logistic regression. J Burn Care Rehabil, 18: 313-6, 1997.
18 O'Keefe GE, Hunt J, Purdue GF: An evaluation of risk factors for mortality after burn trauma and the identification of gender dependent differences in outcomes. J Am Coll Surg, 192: 154-60, 2001.
19 Sheridan RL, Hinson MI, Liang MH: Long-term outcome of children surviving massive burns. JAMA, 283: 69-73, 2000.