Original Article

Full outline of unresponsiveness score as a predictor of outcomes in critically ill pediatric patients

Novita Purnamasari Assa, Dyah Kanya Wati, Ida Bagus Subanada, Soetjiningsih, Made Kardana, Made Sukmawati

Abstract

Background Mortality predictions are very important for improving service quality in the pediatric intensive care unit (PICU). The full outline of unresponsiveness (FOUR) is a new coma scale and is considered capable of predicting mortality and outcome.

Objective To assess the ability of FOUR scores to predict outcomes of critically ill patients in the PICU.

Methods This prospective cohort study included children aged 1 months - 18 years who were admitted to the PICU. Subjects were assessed by FOUR, grouped into score < 9 or score >9, and followed until outcomes were obtained. Bivariate analysis to assess the risk of death was made by cross-tabulation and the strength of the association in the form of risk ratio by Chi-square test. Multivariate analysis was done by logistic regression test.

Results Of 94 subjects, 47 had FOUR scores ≤9 and 47 subjects had FOUR >9. Bivariate analysis revealed that PICU patients with FOUR score ≤9 had a higher risk of death than those with FOUR score >9 (RR 12.5; 95%CI 3.1 to 49.8; P<0.0001). Multivariate analysis revealed that FOUR score, length of stay ≤7 days, and non-surgical disease significantly increased the risk of mortality in PICU patients (by 42.8 times, 8.9 times, and 5.9 times, respectively).

Conclusion The FOUR scores have good ability to predict the outcomes of critically ill pediatric patients. A FOUR score ≤9 at the beginning of treatment is significantly associated with the outcome of mortality during treatment in the PICU. **[Paediatr Indones. 2020;60:77-82; doi: http://dx.doi.org/10.14238/pi60.2.2020.77-82].**

Keywords: *full outline of unresponsiveness score; critically ill; prognosis outcome; pediatric intensive care unit*

Critical illness is a condition that requires support of vital organs to prevent failure that can cause death. This support can either be mechanical or pharmacological assistance. The pediatric intensive care unit (PICU) is a facility or a separate unit, which is designed for the treatment of children with medical, surgical, trauma, or other life-threatening conditions, who require intensive care, as observation is comprehensive and specialized.[1]

Mortality in PICU patients remains very high. Several factors contribute to the outcome of critically ill patients in the PICU, such as age, sex, nutritional status, mechanical ventilation support, length of stay, type of disease, intellectual disability, cerebral palsy, and major congenital abnormalities.[2] Predicting the outcomes is very important to improving service quality in the PICU. The usual PICU mortality scoring systems include pediatric logistic organ dysfunction

From the Department of Child Health, Universitas Udayana Medical School/ Sanglah Hospital, Denpasar, Bali.

Corresponding author: Dyah Kanya Wati, Department of Child Health, Udayana University Medical School, Sanglah Hospital, Pulau Nias Street, Denpasar - 80114, Indonesia. Ph +62-361-244038, Fax +62-361-244038, Email: dyahpediatric@yahoo.com.

(PELOD), pediatric risk of mortality (PRISM), and pediatric index of mortality (PIM). Of the many scoring systems used, each has advantages and disadvantages. PELOD II, PRISM III, and PIM3 scores have many variables in order to cover many organ systems, so they require extensive examinations.[3-6]

The full outline of unresponsiveness (FOUR) score is a new coma scale developed with consideration of the limitations of the Glasgow coma scale (GCS) useful for intensive care. In addition to evaluating consciousness, some studies noted that FOUR was able to predict the outcomes of critically ill patients in the PICU.[7-9] The FOUR cut-off score for predictors of mortality is 9.[7,10]

Studies on the role of FOUR score as a mortality predictor in critically ill children in the PICU have been limited. We aimed to assess the ability of FOUR scores to predict outcomes of critically ill patients in the PICU.

Methods

This prospective cohort study included children aged 1 month - 18 years who were admitted to the PICU, Sanglah Hospital, Bali, Indonesia from February to April 2018. Patients with intellectual disability, cerebral palsy, and major congenital abnormalities were excluded. Subjects were divided into two groups, those with FOUR score ≤9 and those with FOUR score >9, and followed until an outcome was obtained. FOUR scores were checked by residents on duty, with an inter-rater reliability of 0.890. Components of the FOUR score are shown in **Table 1**.[7] Subjects were included by consecutive sampling and sample size was calculated based on unpaired categorical comparative analytics, with alpha 0.05 and power 0.8. The minimum required sample size for each group was 47 subjects.

The FOUR score is a description of a situation without a complete response in order to provide more detailed neurological abnormalities that might give a prognosis for critically ill patients. There are four components that are valued in FOUR, namely, eye, motor, brain stem, and respiration, each of which has a maximum value of 4.[7] Data are grouped according to the cut-off point from previous study, namely (1) FOUR score ≤9 and (2) FOUR score >9.[8] Outcome is the final condition of the patient, either died or survived.

Table 1. The Full Outline of Unresponsiveness (FOUR) score[7]

FOUR score
Eye response
4 = eyelids open or opened, tracking, or blinking to command
3 = eyelids open, but not tracking
2 = eyelids closed but open to loud voice
1 = eyelids closed but open to pain
0 = eyelids remain closed to pain
Motor response
4 = thumbs up, fist, or peace sign
3 = localizing to pain
2 = flexion response to pain
1 = extension response to pain
0 = no response to pain or generalized myoclonus status
Brainstem reflex
4 = pupillary and corneal reflexes present
3 = one pupil wide and fixed
2 = pupillary or corneal reflexes absent
1 = pupillary and corneal reflexes absent
0 = absent pupillary, corneal, and cough reflex
Respiration
4 = regular breathing patterns, not intubated
3 = Cheyne-Stokes breathing pattern, not intubated
2 = irregular breathing patterns, not intubated
1 = breathing at speeds above ventilator, intubated
0 = apnea or breathing with ventilator speed.

Subject characteristics are presented descriptively. Bivariate analysis to assess the risk of death was made by cross-tabulation and risk ratio using Chi-square test. Multivariate analysis by logistic regression test was done to assess the pure effect of FOUR score in predicting mortality, with a P<0.05 level of significance. The data were analyzed with *SPSS 20.0* software. This study was approved by the Research Ethics Committee of Udayana Medical Faculty/Sanglah Hospital, Denpasar.

Results

During the study period, 95 children met the age criterion, but 1 patient was excluded because of cerebral palsy. Hence, the total sample size was 94 subjects. Characteristic data collected were age, gender, nutritional status, use of mechanical ventilation, length of stay, and type of disease. Characteristics of subjects according to FOUR score group are shown in **Table 2**. Most subjects were aged ≤5 years. The majority of subjects in both groups were male and had malnutrition. Mechanical ventilation was used

by 44 subjects (93.6%) in the FOUR <9 group, and 5 (10.6%) in the FOUR >9 group. The length of stay for most subjects was ≤7 days and the most common illness types were surgery and respiratory.

The association between FOUR score and mortality in critically ill patients in the PICU was analyzed using Chi-square test. **Table 3** shows that FOUR ≤9 had a significantly higher risk of mortality than FOUR score >9 (RR 12.5; 95%CI 3.1 to 49.8; P<0.0001). Multivariate logistic regression analysis was used to adjust the confounding variables such as length of stay ≤7 days and non-surgical disease.

Table 4 shows the multivariate analysis where FOUR score, length of stay ≤7 days, and non-surgical disease significantly increased the risk of mortality in PICU patients (by 42.8 times, 8.9 times, and 5.9 times, respectively).

Discussion

The mortality of pediatric patients in the PICU is remains high. The pediatric intensive care unit of Sanglah General Hospital managed 604 critically ill patients during the period of February to April 2018. The net death rate (NDR) at the Sanglah Hospital PICU in 2016 was 19.66, while the gross death rate (GDR) was 24.08%. Several factors contribute to the outcome of critically ill PICU patients, such as age, sex, nutritional status, mechanical ventilation support, length of stay, intellectual disability, cerebral palsy, and major congenital abnormalities.[2]

Table 2. Characteristics of subjects based on FOUR score groups

Variables	Total (N=94)	FOUR score group	
		Score ≤9 (n=47)	Score >9 (n=47)
Age, n (%)			
1-11 months	28 (29.8)	17 (36.2)	11 (23.4)
1-5 years	37 (39.4)	15 (31.9)	22 (46.8)
6-10 years	11 (11.7)	4 (8.5)	7 (14.9)
11-12 years	5 (5.3)	3 (6.4)	2 (4.3)
13-18 years	13 (13.8)	8 (17.0)	5 (10.6)
Sex, n (%)			
Male	55 (58.5)	29 (61.7)	26 (55.3)
Female	39 (41.5)	18 (38.3)	21 (44.7)
Nutritional status, n (%)			
Super-obese	2 (2.1)	1 (2.1)	1 (2.1)
Obese	4 (4.3)	1 (2.1)	3 (6.4)
Overweight	4 (4.3)	4 (8.5)	0
Well nourished	35 (37.2)	18 (38.3)	17 (36.2)
Moderate malnutrition	46 (48.9)	22 (46.8)	24 (51.1)
Severe malnutrition	3 (3.2)	1 (2.1)	2 (4.3)
Mechanical ventilation support, n (%)			
Yes	49 (52.1)	44 (93.6)	5 (10.6)
No	45 (47.9)	3 (6.4)	42 (89.4)
Length of stay, n (%)			
≤7 days	64 (68.1)	28 (59.6)	36 (76.6)
>7 days	30 (31.9)	19 (40.4)	11 (23.4)
Type of disease, n (%)			
Respiratory	28 (29.8)	15 (31.9)	13 (2.7)
Cardiovascular	14 (14.9)	6 (12.8)	8 (17.0)
Neurological	12 (12.8)	8 (17.0)	4 (8.5)
Hematologic & oncologic	2 (2.1)	1 (2.1)	1 (2.1)
Endocrine and metabolic	1 (1.1)	0	1 (1.1)
Gastrointestinal	2 (2.1)	1 (2.1)	1 (2.1)
Surgery	30 (31.9)	11 (23.4)	19 (40.4)
Kidney and urinary tract	3 (3.2)	3 (6.4)	0
Tropical infection	2 (2.1)	2 (4.3)	0

Table 3. Bivariate analysis of mortality outcome and FOUR score

Variables	Outcomes		RR	95% CI	P value
	Died	Survived			
FOUR score, n (%)					
≤9	25 (53.2)	22 (46.8)	12.5	3.1 to 49.8	<0.0001
>9	2 (4.3)	45 (95.7)			

Table 4. Multivariate analysis of FOUR score as a predictor of mortality in critically ill PICU patients

Variables	Exp (B)	95% CI	P value
FOUR score ≤9	42.8	8.0 to 227.5	<0.0001
Length of stay ≤7 days	8.9	2.1 to 37.2	0.003
Non-surgical disease	5.9	1.0 to 34.0	0.048

Age is an important predictive factor on PICU patient outcomes. The younger the age, the lower the maturity of the immune system. Less mature immune systems have lower ability to eradicate pathogens, increasing the risk of death in young children. In our study, 65 subjects (69%) were aged ≤5 years. This finding was similar to other PICU study. Children less than 5 years of age had a 0.6 times higher risk of death compared to groups over 5 years.[12]

The majority of our subjects were males (55 subjects; 58.5%), similar to a Dr. Cipto Mangunkusumo Hospital study in which 66.7% of subjects were male.[13] In addition, moderate malnutrition was most common in both groups, with 22 subjects (46.8%) in the FOUR ≤9 group and 24 subjects (51.1%) in the FOUR > 9 group. Similarly, a previous study reported that 54.5% of children treated in intensive care units had moderate malnutrition.[14] Malnutrition, either directly or indirectly, is associated with high mortality. The immune systems of malnourished children are weak, so these children are susceptible to infectious diseases, especially in developing countries.[15] One study reported mortality rates of critically ill patients accompanied by malnutrition to be 2.6 times higher than in those with good nutrition.[16]

Mechanical ventilation, while providing a positive, life-saving impact, can also have a negative impact in the form of intra-pulmonary and extra-pulmonary complications.[17,18] In our study, 49 subjects (52.1%) used mechanical ventilation. Most of these were in the FOUR ≤9 group.

Length of stay is also an important predictive factor of outcome of critically ill PICU patients. Length of stay also increases mortality (30%) compared to shorter length of treatment (20%).[19] In our study, the length of stay for most subjects was ≤7 days. In the FOUR ≤9 group, 59.6% had length of stay ≤7 days and 40.4% had length of stay > 7 days. This may have been due to age, comorbidity, hypermetabolism, organ failure, and/or nutritional deficiencies.[20]

The diagnosis at PICU admission is important for determining the prognosis. A previous study in a tertiary hospital in Jakarta found that the most common diagnosis in PICU patients was CNS infection (36.7%), followed by non-CNS malignancy (20%), non-CNS infection (16.7%), and CNS malignancy (13.3%).[10] In our study, patient diagnoses were grouped according to the type of disease with surgery in 31.9%, followed by respiratory in 29.8%, cardiovascular in 14.9%, and neurological in 12.8%. This observation may have been because our hospital receives referrals from the eastern part of Indonesia, so our PICU treats various surgical cases, namely, cases of pediatric surgery, neurosurgery, trauma surgery, and thoracic-cardiovascular surgery.

The FOUR score consists of four components: assessment of brain stem reflexes, eye assessment, broad spectrum motor response, and the presence of abnormal breathing patterns as well as respiratory effort, with a rating scale of 0-4 for each component. The eye response describes the function of nerve nuclei III, IV, and VI in the mesencephalon, pons, and by two higher centers in the frontal and parieto-occipital lobes. Motor response describes the location of lesions in the brain. Examination of the brain stem reflex can help in a more complete and accurate coma depth assessment. Respiratory examination describes the normal interactions between the brain stem and cerebral cortex. The total FOUR score showed good prognostic value for predicting outcomes.[7,21]

Bivariate analysis revealed that FOUR score ≤9 had a significantly higher risk of mortality than FOUR score >9 in critically ill PICU patients (RR=12.5; 95%CI 3.1 to 49.8; P<0.0001). The association of

FOUR score with mortality based on existing references can be influenced by age, sex, nutritional status, mechanical ventilation support, length of stay, and type of disease. Multivariate analysis also showed surgical disease to have significantly lower mortality rates than non-surgical diseases. Data were grouped into surgical and non-surgical because a dichotomous nominal variable was needed to analyze for a relationship between the type of disease and outcome. Mortality was 6.7% in surgical cases and 39.1% in non-surgical cases. This difference was clinically significant. Because the difference was >15%, we subjected it to multivariate analysis because it might be a confounding factor. Non-surgical diseases included the respiratory, cardiovascular, neurological, hematologic and oncologic, endocrine, metabolic, and gastrointestinal systems, as well as kidney and urinary tract, and other disorders in accordance with the indications of PICU admission.

Multivariate analysis was performed to control for confounding variables (length of stay ≤7 days and non-surgical cases). The FOUR score ≤9 had a 42.8 times higher risk of poor prognosis in critically ill PICU patients (95%CI 8.0 to 227.5; P<0.0001). Other factors that played roles in this association between FOUR score and mortality were length of stay ≤7 days (P=0.003) and non-surgical cases (P=0.048). Factors that influence the length of stay are age, comorbidity, hypermetabolism, organ failure, and nutritional deficiencies.[20]

The limitation of this study was that the FOUR score cut-off was not self-determined, but from the previous literature.[8] In conclusion, FOUR score has good ability to predict outcomes of critically ill patients in the PICU. A FOUR score ≤9 at the beginning of treatment was significantly associated with mortality.

Conflict of interest

None declared.

Acknowledgments

Funding acknowledgment

References

1. UKK Emergensi dan Rawat Intensif Anak IDAI. Rawat intensif. In: Latief A, Pudjiadi AH, Kushartono H, Malisie RF, editors. Pelayanan Emergensi, Rawat Intermediet dan Rawat Intensif Anak. Jakarta: Badan Penerbit Ikatan Dokter Anak Indonesia; 2016. p. 1-36.

2. Pollack MM, Ruttimann UE, Wiley JS. Nutritional depletions in critically ill children: associations with physiologic instability and increased quantity of care. J Parenter Enteral Nutr. 1985;9:309-13. DOI: 10.1177/0148607185009003309.

3. Metta D, Soebardja D, Hudaya D. The use of pediatric logistic organ dysfunction (PELOD) scoring system to determine the prognosis of patients in pediatric intensive care units. Paediatr Indo. 2006;46:1-6. DOI: 10.14238/pi46.1.2006.1-6.

4. Pollack MM, Patel KM, Ruttimann UE. PRISM III: An updated pediatric risk of mortality score. Crit Care Med. 1996;24:743-52. DOI: 10.1097/00003246-199605000-00004.

5. Lacroix J, Cotting J, Severity of illness and organ dysfunction scoring in children. Pediatr Crit Care Med. 2005;6:126-34. DOI: 10.1097/01.PCC.0000161287.61028.D4.

6. Shann F, Pearson G, Slater A, Wilkinson K. Pediatric index of mortality (PIM): a mortality prediction model for children in intensive care. Intensive Care Med. 1997;23:201-7. DOI: 10.1007/s001340050317.

7. Wijdicks EFM, Bamlet WR, Maramattom BV, Manno EM, McClelland RL. Validation of a new coma scale: the FOUR score. Ann Neurol. 2005;58:585-93. DOI: 10.1002/ana.20611.

8. Dewi R, Mangunatmadja I, Yuniar I. Perbandingan full outline of unresponsiveness score dengan glasgow coma scale dalam menentukan prognostik pasien sakit kritis. Sari Pediatri. 2011;13:215-20. DOI: 10.14238/sp13.3.2011.215-20.

9. Akavipat P. Endorsement of the FOUR score for consciousness assessment in neurosurgical patients. Neurol Med Chir. 2009;49:565-71. DOI: 10.2176/nmc.49.565.

10. Fischer M, Rüegg S, Czaplinski A, Strohmeier M, Lehmann A, Tschan F, *et al*. Inter-rater reliability of the full outline of unresponsiveness score and the glasgow coma scale in critically ill patients: a prospective observational study. Crit Care. 2010;14:R64. DOI: 10.1186/cc8963.

11. Dahlan MS. Besar sampel dalam penelitian kedokteran dan kesehatan. 4th ed. Jakarta: Epidemiologi Indonesia; 2016. p. 105-119.

12. Saraswati DD, Pudjiadi AH, Djer MM, Supriyatno B, Syarif DR, Kurniati N. Faktor risiko yang berperan pada mortalitas sepsis. Sari Pediatri. 2014;15:281-8. DOI: 10.14238/sp15.5.2014.281-8.

13. Yuniar, I, Latief A, Devaera Y, Fitriani S. Pemberian nutrisi pada pasien dengan penyakit kritis di ruang perawatan intensif anak RS Cipto Mangunkusumo. Sari Pediatri. 2014;16:254-9. DOI: 10.14238/sp16.4.2014.254-9.

14. Marlina L, Hudaya D, Garna H. Perbandingan Penggunaan Pediatric Index of Mortality 2 (PIM2) dan Skor Pediatric Logistic Organ Dysfunction (PELOD) untuk memprediksi kematian pasien sakit kritis pada anak. Sari Pediatri. 2008;10:262-7. DOI: 10.14238/sp10.4.2008.262-7.

15. Schaible UE, Kaufmann SHE. Malnutrition and infection: complex mechanisms and global impacts. PLoS Med. 2007;4:806-12. DOI: 10.1371/journal.pmed.0040115.

16. Correia MI, Waitzberg L. The impact of malnutrition on morbidity, mortality, length of hospital stay and costs evaluated through a multivariate model analysis. Clin Nutr. 2003;22:235-9. DOI: 10.1016/s0261-5614(02)00215-7.

17. Cheifetz IM. Invasive and noninvasive pediatric mechanical ventilation Respir Care. 2003;48:442-53; discussion 453-8. PMID: 12667269.

18. Principi T, Fraser DD, Morrison GC, Farsi SA, Carrelas JF, Maurice EA, et al. Complications of mechanical ventilation in the pediatric population. Pediatr Pulmonol. 2011;46:452-7. DOI: 10.1002/ppul.21389.

19. Adisasmito AW, Hadinegoro SR. Infeksi Bakteri Gram Negatif di ICU Anak: epidemiologi managemen antibiotik dan pencegahan. Sari Pediatri. 2004;6:32-9. DOI: 10.14238/sp6.1.2004.32-5.

20. Meilyana F, Djais J, Garna H. Status gizi berdasarkan subjective global assessment sebagai faktor yang memengaruhi lama perawatan pasien rawat inap anak. Sari Pediatri. 2010;12:162-7. DOI: 10.14238/sp12.3.2010.162-7.

21. Bordini AL, Luiz TF, Fernandes M, Arruda WO, Teive HAG. Coma scales: a historical review. Arq Neuropsiquiatr. 2010;68:930-7. DOI: 10.1590/S0004-282X2010000600019.

22. Iyer VN, Mandrekar JN, Danielson RD, Zubkov AY, Elmer JL, Wijdicks EFM. Validity of the FOUR score coma scale in the medical intensive care unit. Mayo Clin Proc. 2009;84:694-701. DOI: 10.1016/S0025-6196(11)60519-3.