PELOD-2: An Update of the PEdiatric Logistic Organ Dysfunction Score

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Objective: Multiple organ dysfunction syndrome is the main cause of death in adult ICUs and in PICUs. The PEdiatric Logistic Organ Dysfunction score developed in 1999 was primarily designed to describe the severity of organ dysfunction. This study was undertaken to update and improve the PEdiatric Logistic Organ Dysfunction score, using a larger and more recent dataset.

Design: Prospective multicenter cohort study.

Setting: Nine multidisciplinary, tertiary-care PICUs of university-affiliated hospitals in France and Belgium.

Patients: All consecutive children admitted to these PICUs (June 2006–October 2007).

Intervention: None.

Measurements and Main Results: We collected data on variables considered for the PEdiatric Logistic Organ Dysfunction-2 score during PICU stay up to eight time points: days 1, 2, 5, 8, 12, 16, and 18, plus PICU discharge. For each variable considered for the PEdiatric Logistic Organ Dysfunction-2 score, the most abnormal value observed during time points was collected. The outcome was vital status at PICU discharge. Identification of the best variable cutoffs was performed using bivariate analyses. The PEdiatric Logistic Organ Dysfunction-2 score was developed by multivariable logistic regressions and bootstrap process. We used areas under the receiver-operating characteristic curve to evaluate discrimination and Hosmer-Lemeshow goodness-of-fit tests to evaluate calibration. We enrolled 3,671 consecutive patients (median age, 15.5 mo; interquartile range, 2.2–70.7). Mortality rate was 6.0% (222 deaths). The PEdiatric Logistic Organ Dysfunction-2 score includes ten variables corresponding to five organ dysfunctions. Discrimination (areas under the receiver-operating characteristic curve = 0.934) and calibration (chi-square test for goodness-of-fit = 9.31, $p = 0.317$) of the PEdiatric Logistic Organ Dysfunction-2 score were good.

Conclusion: We developed and validated the PEdiatric Logistic Organ Dysfunction-2 score, which allows assessment of the severity of cases of multiple organ dysfunction syndrome in the PICU with a continuous scale. The PEdiatric Logistic Organ Dysfunction-2 score now includes mean arterial pressure and lactatemia in the cardiovascular dysfunction and does not include hepatic dysfunction. The score will be in the public domain, which means that it can be freely used in clinical trials. (*Crit Care Med* 2013; 41:1761–1773)

Key Words: intensive care units; multiple organ failure; outcome assessment; pediatric; scoring methods; severity of illness index

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All authors contributed to the study design drafted by Dr. Leteurtre. Drs. Leteurtre, Grandbastien, and Leclerc contributed to the clinical implementation of the study and supervision of the patients. Dr. Duhamel and Mr. Salleron designed and did the statistical analysis and verified its accuracy. Dr. Leclerc obtained funding and supervised the study. Dr. Leteurtre, Dr. Duhamel, Ms. Salleron, Dr. Grandbastien, and Dr. Leclerc had full access to all data. All authors helped draft this report or critically revised the draft. All authors reviewed and approved the final version of the report and had final responsibility for the decision to submit for publication.

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Describing the severity of illness of critically ill patients while they are in an ICU is very important: Reliable quality assurance and quality assessment cannot be done without such data. Furthermore, an accurate marker of severity of illness can be used as an outcome measure in clinical studies. Multiple organ dysfunction syndrome (MODS), defined as the presence of two or more organ dysfunctions, is a good candidate marker of severity of illness because MODS is the main cause of death in adult ICU (1) and in PICU patients (2, 3).

Several definitions of organ dysfunctions and several sets of diagnostic criteria of MODS have been published (4–6). In the PICU, the relationship between the number of organ dysfunction, which is somewhat quantitative, and mortality is better than it is between the presence or absence of MODS, which is dichotomous, and mortality (2, 6). Furthermore, it is important to develop scores that consider the higher and the lower risk of death associated with the different organ dysfunctions (2). Adult MODS scores were developed using mortality as a dependent variable (7, 8). It is with these considerations in mind, the Pediatric-Multiple Organ Dysfunction Score (P-MODS) (9), the PEdiatric Logistic Organ Dysfunction (PELOD) score (2, 10, 11), and a modified Sequential Organ Failure Assessment (SOFA) score for children were created (12). The PELOD was developed in 1999, more than a decade ago (10). It is by far the most frequently used score aiming to describe the severity of cases of P-MODS. Because of changes over time in case mix and clinical practice, the performance of prognostic and descriptive models deteriorate, and there is a need to re-calibrate them (13). Furthermore, the PELOD was not free of some limitations; for example, a Brazilian study reported that the PELOD kept a very good discriminative capacity in Brazilian PICUs, but its calibration was poor (14). Also, even though PELOD is quantitative, it is discontinuous, which may cause problems when doing some statistical analyses (15). This study was undertaken to update and to improve the PELOD score, using a larger and more recent dataset.

METHODS

The 33 university-affiliated PICUs that were members of the Groupe Francophone de Réanimation et Urgences Pédiatriques (GFRUP) were invited to participate: nine PICUs provided, on a voluntary basis, the information requested (eight in France and one in Belgium). All consecutive children admitted to these PICUs between June 21, 2006, and October 31, 2007, were included. Children with a history of prematurity and hospitalized after birth were enrolled. Patients over 18 years and newborns who were premature (< 37-wk gestation) and admitted at birth were excluded. Although the period of data collection varied between units, for each unit, all patients admitted consecutively during the study period were included.

Ethical Considerations

The PELOD score does not require that more measurements be done than in standard practice. The study and its database were declared safe and were approved by the French authorities (Commission Nationale de l'Informatique et des Libertés) on February 7, 2007. The study design was approved by the ethics committee of the Société de Réanimation de Langue Française on April 27, 2007.

Item Selection

The variables used to create and validate the PELOD-2 were abstracted from the PELOD (Glasgow Coma Score, pupillary reactions, heart rate, systolic blood pressure, creatinine, Pao_2/Fio_2, $Paco_2$, mechanical ventilation, WBCs, platelets, aspartate transaminase, prothrombin time, and international normalized ratio) and the P-MODS (lactate, Pao_2/Fio_2, bilirubin, fibrinogen, and blood urea nitrogen) scores (2, 8). Furthermore, the mean arterial pressure, which is an item of the SOFA score for adults, was added because it is considered a good marker of organ perfusion (9).

Data Management

Patients were monitored until they died or were discharged from the PICU, whichever happened first. Our team of investigators showed in 2010 that one does not need to collect data on the items of the PELOD everyday: Thus, we collected data during PICU stay according to the set of 8 days (days 1, 2, 5, 8, 12, 16, and 18, plus the discharge day) that were identified as the optimal time points to estimate the daily PELOD (dPELOD) scores (16). Days were counted by 24-hour interval, from the time of admission to 24 hours after admission and so on. Variables were measured only if the attending physician thought it appropriate (i.e., if justified by clinical status of patient). If a variable was not measured, we assumed that it was identical to the previous measurement (i.e., the physician thought the value of the variable had not changed) or normal (i.e., the physician thought the value of the variable was normal). Physiologic data from the preterminal period (the last 4 hr of life) were discarded (17). As for previously published severity and MODS scores, the most abnormal value of each variable observed during each of these time points was considered to build the PELOD-2 score.

Clinical data were prospectively recorded on a standardized case-report form. Previously trained physicians (one per center) entered data into a web-based database respecting confidentiality requirements (Epiconcept, Paris, France). A research assistant screened the database weekly for quality control and, if needed, sent a report to investigators. One quality control visit was done in each center during the study. Patients' data were collected anonymously, but investigators held a nominal list for quality control.

Statistical Analysis

Identification of Covariates and Their Cutoff. The association between the outcome (death/survival at PICU discharge) and each variable was first investigated using bivariate logistic regression. As the log-linearity assumption for continuous variables was not verified, they were transformed in categorical variables. This transformation process took into account two groups of variables according to literature data: those for which the normal values depend on the patient's age (namely heart rate, systolic and mean arterial pressure, and creatinine) and the others. The cutoffs were identified by using a decision tree

procedure with the Chaid method (14). The final cutoff values were validated on the basis of their clinical relevance, the results of the bivariate logistic regression, and the existence of a monotone relation between the death rates and the levels of the categorized variables (**supplemental data**, Supplemental Digital Content 1, http://links.lww.com/CCM/A639).

Identification of the Predictive Model. A multivariable logistic regression was performed with all variables (full model). The simplification of this full model was done using another multivariable logistic regression with backward selection at the level $p = 0.05$. The stability of the selected model was investigated using the bootstrap resampling method (16) (supplemental data, Supplemental Digital Content 1, http://links.lww.com/CCM/A639).

Creation of the PELOD-2 Score. For some categorized variables, some levels were pooled according to the odds ratio estimates. All cutoff values were rounded to the nearest integer to have a user-friendly score. The model was rebuilt considering these simplifications (supplemental data, Supplemental Digital Content 1, http://links.lww.com/CCM/A639). The PELOD-2 was obtained from the coefficients of this final multivariable logistic regression. The coefficients were multiplied by two and rounded to the nearest integer to have a user-friendly score.

Validation. The comparison of the PELOD-2 between the two groups (death/survival) was performed by a Student *t* test. The discriminant power of the PELOD-2 score was estimated using the area under the receiver-operating curve (AUC) with 95% CI, and calibration was assessed using the Hosmer-Lemeshow chi-square test. We addressed the optimism bias using a bootstrap resampling method. The stability of the score was estimated by cross validation (17) (supplemental data, Supplemental Digital Content 1, http://links.lww.com/CCM/A639). We used a logistic regression to investigate the relation between each organ dysfunction and mortality. We used a stepwise multiple regression to evaluate the relative weight of each organ dysfunction on the PELOD-2 scoring system. For these two analyses, the independent variables were ordinal variables of each organ dysfunction.

Comparison Between the PELOD and PELOD-2 Scores. The PELOD score was computed and calibrated using a logistic regression to compare distribution and AUC of both scores.

The results are expressed by medians and interquartile ranges (IQR) or means and SD for continuous variables and by frequencies and percentages for categorical variables. Statistical analyses were performed using SAS software version 9.2 (SAS Institute, Cary, NC). A *p* value of less than 0.05 was considered statistically significant.

RESULTS

The nine participating PICUs were devoted to medical, trauma, and postoperative care (including cardiac surgery) and were representative of the 33 university-affiliated PICUs of the GFRUP in terms of recruitment (medical/surgical, neonatal/pediatric) (supplemental data, Supplemental Digital Content 1, http://links.lww.com/CCM/A639 for details on the nine participating and the 24 nonparticipating sites). Patients

TABLE 1. Baseline and Clinical Characteristics, Reason for Admission and Primary Disease at Entry, and Outcomes of Children Admitted to Nine PICUs (June 2006–October 2007)

Characteristics and Outcomes	Value
Baseline characteristics	
Gender (male), *n* (%)	2,097 (57.1)
Age (mo), median (IQR)	15.5 (2.2; 70.7)
0 to < 1, *n* (%)	627 (17.1)
1–11, *n* (%)	1,068 (29.1)
12–23, *n* (%)	399 (10.9)
24–59, *n* (%)	559 (15.2)
60–143, *n* (%)	562 (15.3)
≥ 144, *n* (%)	456 (12.4)
Recovery post procedure,[a] *n* (%)	955 (26.0)
Pediatric Index of Mortality 2 score (predicted death rate in %) median (IQR)	1.42 (0.78; 4.34)
Primary reason for PICU admission, *n* (%)	
Respiratory	1,664 (46.6)
Neurologic	662 (18.5)
Cardiovascular	673 (18.8)
Hepatic	40 (1.1)
Genitourinary	96 (2.7)
Gastrointestinal	205 (5.7)
Endocrine	57 (1.6)
Musculoskeletal	45 (1.3)
Hematologic	45 (1.3)
Miscellaneous/undetermined	99 (2.7)
Mixed	85 (2.4)
Cause of primary diseases at entry, *n* (%)	
Infection	863 (23.5)
Trauma	325 (8.9)
Congenital disease	1,123 (31.0)
Drug poisoning	72 (2.0)
Cancer	120 (3.3)
Diabetes	41 (1.1)
Allergic/immunologic diseases	55 (1.5)
Miscellaneous/undetermined	1,072 (29.2)
Elective PICU admission,[a] *n* (%)	970 (26.4)
Outcomes	
Mechanical ventilation, *n* (%)	1,926 (52.5)
Length of ICU stay (d), median (IQR)	2 (1; 5)
Mortality, *n* (%)	222 (6.0)

[a]According to Pediatric Index of Mortality 2 instructions.
Total number of patients included in the study are 3,671.
IQR = interquartile range.

were enrolled for a median period of 15 months (IQR, 7–16). The median number of admissions per PICU during the study period was 442 (IQR, 132–581).

Among 3,675 consecutively screened children, two older than 18 years and two with incomplete data were excluded. Thus, 3,671 patients were retained for analysis, including 222 who died in the PICU (mortality rate, 6.0%). Baseline characteristics and outcomes of the enrolled population are detailed in **Table 1**. The proportion of medical and surgical cases was 66.5% to 33.5%. The median age was 15.5 months (IQR, 2.2–70.7).

The bivariate analyses demonstrated that all the candidate variables were predictive of death except bilirubin ($p = 0.53$); these 17 significant variables are listed with their cutoffs in **Tables 2** and **3**. Mean arterial pressure and systolic blood pressure provided similar information; we selected mean arterial pressure to describe cardiovascular dysfunction. The results of the multivariable logistic regression performed on these 16 variables are reported in the supplemental data (Supplemental Digital Content 1, http://links.lww.com/CCM/A639) (full model). After backward selection with bootstrap validation, 10 variables were retained (**Table 4**). From the results of this multivariable analysis, the following levels were pooled with the reference level: lactatemia (mmol/L) between 3.97 and 5.37, Pa_{O_2} (mm Hg)/F_{IO_2} ratio between 60.5 and 136.3, noninvasive ventilation, and WBC count ($\times 10^9$/L) between 2.15 and 4.09 (significant level > 0.2). For creatinine, the two levels of risk had nearly equal odds ratio values (2.42 and 2.90, respectively); they were pooled in a unique class (≥ cutoff 1). All cutoff values were rounded to be more user friendly, when appropriate. The final logistic regression, which considered these simplifications, is detailed in **Table 5**. Finally, the PELOD-2 includes 10 variables involving five organ dysfunctions. For each variable, the severity level is ranging from 0 (normal) to a maximum of 6 (**Table 6**).

The AUC of the PELOD-2 was 0·942 (95% CI, 0.925–0.960). The calibration assessed by the Hosmer-Lemeshow chi-square test was equal to 6.74 ($p = 0.565$) (supplemental data, Supplemental Digital Content 1, http://links.lww.com/CCM/A639). After correction for the optimism bias, the AUC and the calibration of the PELOD-2 were 0.934 and 9.31 ($p = 0.317$), respectively. The cross validation covariate was associated with a β value of 0.89 close to 1.

Median PELOD-2 score was 4 (IQR, 2–7); mean PELOD-2 score was 4.8 (SD, 4.3). PELOD-2 was significantly ($p < 0.0001$) higher in nonsurvivors than in survivors (mean, 14.9 [SD, 6.1] vs mean, 4.2 [SD, 3.2], respectively).

All organ dysfunctions retained in the PELOD-2 score were closely related to the risk of mortality. The maximum points for each organ ranged between 2 and 10. Neurologic and respiratory dysfunctions were the most important markers, explaining, respectively, 48% and 29% of the variance with respect to the risk of mortality (**Table 7**). **Figure 1** shows the distribution of patients for each organ dysfunction.

Five hundred fifty-six (15%) patients had no organ dysfunction, 1,016 (28%) patients had one, 994 (27%) patients had two, and 1,105 (30%) patients had three or more. **Table 8** shows mean PELOD-2 scores and outcome stratified by number of organ dysfunctions.

The distribution of the PELOD-2 is different from that of the PELOD: The PELOD-2 is a continuous score that can take all integer values from 0 to 33 (**Fig. 2**). The value of the AUC of

TABLE 2. Identification of Cutoff Values for Age-Dependent Variables

	Age (mo)					
Variable and Cutoff	**< 1**	**1–11**	**12–23**	**24–59**	**60–143**	**≥ 144**
Creatinine (μmol/L)						
Cutoff 1	70	22	34	50	58	93
Cutoff 2	94	47	59	75	83	117
Heart rate (beats/min)						
Cutoff	207	215	203	191	176	167
Mean arterial pressure (mm Hg)						
Cutoff 1	16	25	30	32	35	37
Cutoff 2	30	39	44	46	49	51
Cutoff 3	46	55	60	62	65	67
Systolic arterial pressure (mm Hg)						
Cutoff 1	22	38	47	49	54	58
Cutoff 2	34	49	58	60	65	69
Cutoff 3	43	58	67	69	74	78
Cutoff 4	52	68	76	79	84	87
Cutoff 5	63	79	87	90	95	98

TABLE 3. Candidate Variables for the Pediatric Logistic Organ Dysfunction-2 Score

Variable	Survivors ($n = 3,449$) (%)	Nonsurvivors ($n = 222$) (%)	p
Non–age-dependent variables			
Glasgow Coma Score			
3–4	53 (1.54)	103 (46.61)	
5–10	337 (9.77)	28 (12.67)	< 0.001
≥ 11	3,059 (88.69)	91 (40.99)	
Pupillary reaction			
Both fixed	37 (1.07)	108 (48.65)	
Both reactive	108 (98.93)	114 (51.35)	< 0.001
Lactatemia (mmol/L)			
< 3.97	3,121 (90.49)	106 (47.75)	
3.97–5.36	158 (4.58)	20 (9.01)	
5.37–11.06	136 (3.94)	43 (19.37)	< 0.0001
≥ 11.07	34 (0.99)	53 (23.87)	
Uremia (mg/dL)			
< 27	2,205 (63.93)	71 (31.98)	
27–36	595 (17.25)	29 (13.06)	< 0.0001
≥ 37	649 (18.82)	122 (54.95)	
Pao_2 (mm Hg)/Fio_2 ratio			
< 60.5	81 (2.35)	47 (21.27)	
60.5–136.2	250 (7.25)	23 (10.41)	< 0.001
≥ 136.3	3,118 (90.40)	152 (68.47)	
$Paco_2$ (mm Hg)			
< 58.5	3,099 (89.85)	155 (69.82)	
58.5–94	315 (9.13)	49 (22.07)	< 0.0001
≥ 94.5	35 (1.01)	18 (8.11)	
Ventilation			
No	1,470 (42.62)	10 (4.50)	
Noninvasive	261 (7.57)	4 (1.80)	< 0.001
Invasive	1,718 (49.81)	208 (93.69)	
WBC count ($\times 10^9$/L)			
< 2.15	85 (2.46)	34 (15.32)	
2.15–4.0	170 (4.93)	21 (9.46)	< 0.0001
≥ 4.1	3,194 (92.61)	167 (75.23)	
Platelets ($\times 10^9$/L)			
< 76.5	237 (6.87)	72 (32.43)	
76.5–141	287 (8.32)	36 (16.22)	< 0.0001
≥ 141.5	2,925 (84.81)	114 (51.35)	

(*Continued*)

TABLE 3. (*Continued*). Candidate Variables for the Pediatric Logistic Organ Dysfunction-2 Score

Variable	Survivors ($n = 3,449$) (%)	Nonsurvivors ($n = 222$) (%)	p
Fibrinogen (mg/dL)			
< 81	92 (2.67)	31 (13.96)	
81–146	156 (4.52)	32 (14.41)	< 0.0001
≥ **147**	3,201 (92.81)	159 (71.62)	
Aspartate transaminase (IU/L)			
< 111.5	3,102 (89.94)	122 (54.95)	
111.5 to < 339.5	235 (6.81)	48 (21.62)	< 0.0001
≥ 340	112 (3.25)	52 (23.42)	
Prothrombin time (s)			
< 34.5	110 (3.19)	61 (27.60)	
34.5–55	335 (9.71)	56 (25.34)	
55.5–69	418 (12.12)	29 (13.12)	< 0.001
≥ **69.5**	2,586 (74.98)	76 (34.23)	
International normalized ratio			
< 3	3,429 (99.42)	217 (97.75)	
≥ 3	20 (0.58)	5 (2.25)	0.0149
Age-dependent variables[a]			
Mean arterial pressure (mm Hg)			
< Cutoff 1	21 (0.61)	39 (17.57)	
Cutoff 1–cutoff 2	276 (8.0)	69 (31.08)	< 0.0001
Cutoff 2–cutoff 3[	1,654 (47.96)	95 (42.79)	
≥ **Cutoff 3**	1,498 (43.43)	19 (8.56)	
Systolic arterial pressure (mm Hg)			
< Cutoff 1	15 (0.43)	42 (18.92)	
Cutoff 1–cutoff 2	58 (1.68)	33 (14.86)	
Cutoff 2–cutoff 3	193 (5.60)	38 (17.12)	< 0.0001
Cutoff 3–cutoff 4	519 (15.05)	47 (21.17)	
Cutoff 4–cutoff 5	1,057 (30.65)	45 (20.27)	
≥ **Cutoff 5**	1,607 (46.59)	17 (7.66)	
Heart rate (beats/min)			
< Cutoff 1	3,286 (95.27)	180 (81.08)	< 0.0001
≥ Cutoff 1	163 (4.73)	42 (18.92)	
Creatinine (μmol/L)			
< Cutoff 1	2,255 (65.38)	49 (22.07)	
Cutoff 1–cutoff 2	785 (22.76)	73 (32.88)	< 0.0001
≥ Cutoff 2	409 (11.86)	100 (45.05)	

[a]Cutoff of age-dependent variables is described in Table 2.
Reference levels are in bold font.

TABLE 4. Multivariable Logistic Regression After Backward Selection With Bootstrap Validation

Variable and Cutoff	Coefficient	Odds Ratio (95% CI)	*p*
Glasgow Coma Score			
≥ 11		1	
5–10	0.635	1.89 (1.12–3.18)	0.017
3–4	1.904	6.71 (3.58–12.59)	< 0.0001
Pupillary reaction			
Both reactive		1	
Both fixed	2.481	11.95 (6.48–22.03)	< 0.0001
Lactatemia (mmol/L)			
< 3.97		1	
3.97–5.37	0.326	1.39 (0.70–2.74)	0.347
5.37–11.07	0.642	1.90 (1.05–3.43)	0.033
> 11.07	1.814	6.13 (2.93–12.83)	< 0.0001
Mean arterial pressure (mm Hg)			
≥ Cutoff 3[a]		1	
Cutoff 2–cutoff 3[a]	0.841	2.32 (1.28–4.18)	0.005
Cutoff 1–cutoff 2[a]	1.372	3.94 (2.00–7.79)	< 0.0001
< Cutoff 1[a]	2.961	19.31 (6.88–54.21)	< 0.0001
Creatinine (μmol/L)			
< Cutoff 1[a]		1	
Cutoff 1–cutoff 2[a]	0.883	2.42 (1.49–3.94)	< 0.0001
≥ Cutoff 2[a]	1.065	2.90 (1.69–4.99)	< 0.0001
Pao_2 (mm Hg)/Fio_2 ratio			
> 136.3		1	
60.5–136.3	−0.197	0.82 (0.44–1.53)	0.535
< 60.5	0.889	2.43 (1.27–4.67)	0.008
$Paco_2$ (mm Hg)			
< 58.5		1	
58.5–94.4	0.529	1.70 (1.00–2.88)	0.050
≥ 94.5	1.604	4.97 (1.94–12.76)	0.001
Ventilation			
No ventilation		1	
Noninvasive ventilation, yes	0.166	1.18 (0.28–5.05)	0.823
Invasive ventilation, yes	1.446	4.25 (2.02–8.93)	< 0.0001
WBC count (× 10^9/L)			
≥ 4.10		1	
2.15–4.09	−0.276	0.76 (0.36–1.60)	0.468
< 2.15	0.693	2.00 (0.95–4.19)	0.067
Platelets (× 10^9/L)			
≥ 141.5		1	
76.5–141.4	0.399	1.49 (0.84–2.64)	0.172
< 76.5	0.782	2.19 (1.27–3.77)	0.005

[a]Cutoffs of age-dependent variables are defined in Table 2.

TABLE 5. Final Logistic Regression Defining the Pediatric Logistic Organ Dysfunction-2 Score

Type of Variables and Cutoffs	Coefficient	Odds Ratio (95% CI)	*p*	Pediatric Logistic Organ Dysfunction-2 Points
Glasgow Coma Score				
≥ 11		1		
5–10	0.650	1.92 (1.14–3.22)	0.014	1
3–4	1.942	6.97 (3.74–12.99)	< 0.0001	4
Pupillary reaction				
Both reactive		1		
Both fixed	2.510	12.30 (6.68–22.65)	< 0.0001	5
Lactatemia (mmol/L)				
< 5.0		1		
5.0–10.9	0.508	1.66 (0.98–2.83)	0.062	1
≥ 11.0	1.804	6.07 (3.08–11.96)	< 0.0001	4
Mean arterial pressure (mm Hg)				
≥ Cutoff 3[a]		1		
Cutoff 2–cutoff 3[a]	0.806	2.24 (1.25–4.02)	0.007	2
Cutoff 1–cutoff 2[a]	1.332	3.79 (1.93–7.43)	< 0.0001	3
< Cutoff 1[a]	2.891	18.01 (6.52–49.77)	< 0.0001	6
Creatinine (μmol/L)				
< Cutoff 1[a]		1		
≥ Cutoff 1[a]	0.959	2.61 (1.68–4.06)	< 0.0001	2
Pao_2 (mm Hg)/FIo_2 ratio				
≥ 61		1		
≤ 60	0.964	2.62 (1.39–4.94)	0.003	2
$Paco_2$ (mm Hg)				
≤ 58		1		
59–94	0.484	1.62 (0.97–2.73)	0.068	1
≥ 95	1.514	4.55 (1.79–11.52)	0.001	3
Ventilation				
No or noninvasive		1		
Invasive	1.384	3.99 (2.07–7.70)	< 0.0001	3
WBC count (× 10^9/L)				
> 2		1		
≤ 2	0.761	2.14 (1.04–4.40)	0.039	2
Platelets (× 10^9/L)				
≥ 142		1		
77–141	0·373	1.45 (0.82–2.57)	0.200	1
≤ 76	0·782	2.19 (1.30–3.67)	0.003	2

[a]Cutoffs of age-dependent variables are defined in Table 2.

TABLE 6. Scoring the Pediatric Logistic Organ Dysfunction-2 Score

Organ Dysfunctions and Variables[a]	Points by Severity Levels						
	0	1	2	3	4	5	6
Neurologic[b]							
Glasgow Coma Score	≥ 11	5–10			3–4		
Pupillary reaction	Both reactive					Both fixed	
Cardiovascular[c]							
Lactatemia (mmol/L)	< 5.0	5.0–10.9			≥ 11.0		
Mean arterial pressure (mm Hg)							
0 to < 1 mo	≥ 46		31–45	17–30			≤ 16
1–11 mo	≥ 55		39–54	25–38			≤ 24
12–23 mo	≥ 60		44–59	31–43			≤ 30
24–59 mo	≥ 62		46–61	32–44			≤ 31
60–143 mo	≥ 65		49–64	36–48			≤ 35
≥ 144 mo	≥ 67		52–66	38–51			≤ 37
Renal							
Creatinine (μmoL/L)							
0 to < 1 mo	≤ 69		≥ 70				
1–11 mo	≤ 22		≥ 23				
12–23 mo	≤ 34		≥ 35				
24–59 mo	≤ 50		≥ 51				
60–143 mo	≤ 58		≥ 59				
≥ 144 mo	≤ 92		≥ 93				
Respiratory[d]							
Pao_2 (mm Hg)/FIo_2	≥ 61		≤ 60				
$Paco_2$ (mm Hg)	≤ 58	59–94		≥ 95			
Invasive ventilation	No			Yes			
Hematologic							
WBC count (× 10^9/L)	> 2		≤ 2				
Platelets (× 10^9/L)	≥ 142	77–141	≤ 76				

[a]All variables must be collected, but measurements can be done only if justified by the patient's clinical status. If a variable is not measured, it should be considered normal. If a variable is measured more than once in 24 hr, the worst value is used in calculating the score. FIo_2: fraction of inspired oxygen.

[b]Neurologic dysfunction: Glasgow Coma Score: use the lowest value. If the patient is sedated, record the estimated Glasgow Coma Score before sedation. Assess only patients with known or suspected acute central nervous system disease. Pupillary reactions: nonreactive pupils must be > 3 mm. Do not assess after iatrogenic pupillary dilatation.

[c]Cardiovascular dysfunction: Heart rate and mean arterial pressure: do not assess during crying or iatrogenic agitation.

[d]Respiratory dysfunction: Pao_2: use arterial measurement only. Pao_2/FIo_2 ratio is considered normal in children with cyanotic heart disease. $Paco_2$ can be measured from arterial, capillary, or venous samples. Invasive ventilation: the use of mask ventilation is not considered invasive ventilation.

Logit (mortality) = −6.61 + 0.47 × PELOD-2 score.

Probability of death = 1/(1 + exp [−logit(mortality)]).

PELOD-2 was near to the value obtained for the PELOD on the training set (0.98 [95% CI, 0.960–0.999], published in 1999) (10). After recalibration on the present data, the AUC of the PELOD-2 was significantly higher than the AUC of the PELOD 0.857 (95% CI, 0.834–0.879), $p < 0.0001$.

DISCUSSION

We developed and validated the PELOD-2, a continuous scale that allows assessment of the severity of cases of MODS in the PICU. This updated version of the PELOD includes 10 variables involving five organ dysfunctions. Compared with the

TABLE 7. Relative Contribution of Each Organ Dysfunction to Mortality (Logistic Regression) and to the Pediatric Logistic Organ Dysfunction-2 score (Multiple Regression)

Dysfunction	Maximum Value in Each Dysfunction	Logistic Regression	Multiple Regression
		p	Partial R^2
Neurologic	9	< 0.0001	0.48
Respiratory	8	< 0.0001	0.29
Cardiovascular	10	< 0.0001	0.12
Renal	2	< 0.0001	0.08
Hematologic	4	< 0.0001	0.03

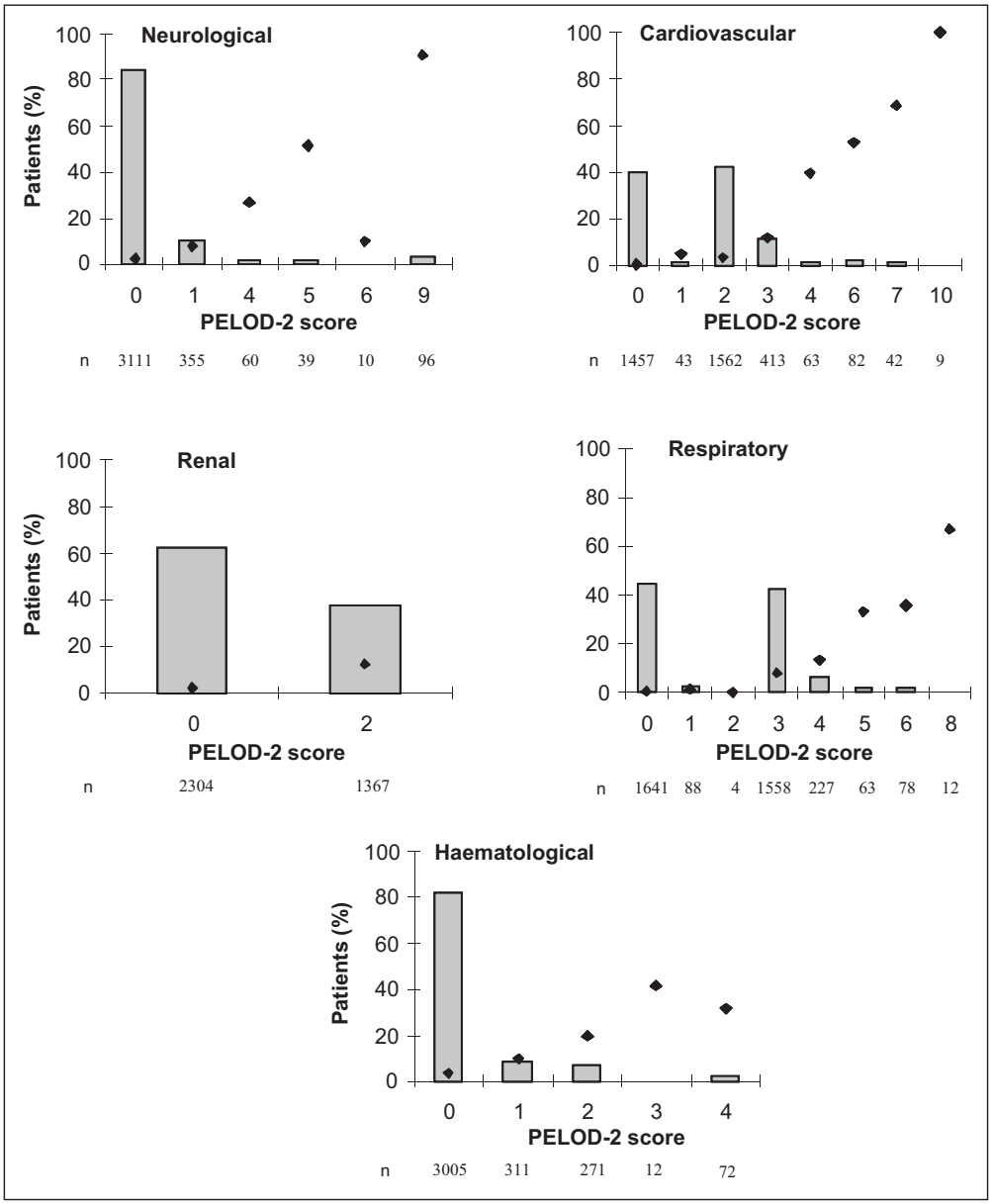

Figure 1. Patients' distribution and mortality rate for each organ dysfunction score. *Black diamond* = mortality rate, PELOD-2 = Pediatric Logistic Organ Dysfunction-2.

previous version, the PELOD-2 now includes mean arterial pressure and lactatemia in the cardiovascular dysfunction, which are present in the SOFA and the P-MODS scores. On the other hand, the PELOD-2 does not include hepatic dysfunction, which was part of the first version of the PELOD. Hepatic dysfunction was linked with mortality in PELOD but accounted for in only 0.1% of its variance (2), and it did not predict death in the P-MODS (9) score.

To be useful, a descriptive index, such as the PELOD-2, should be clinically credible, accurate, user friendly, and generalizable and provide useful additional information to clinicians and scientists (18). What remains to be determined is if the responsiveness of the PELOD-2 to preventive and/or therapeutic interventions is good, if so, this will support the idea that the PELOD-2 can be used as an outcome measure in randomized clinical trials. The responsiveness of a test is good if the test reacts significantly to active therapeutic approach, when the response of the test is in the right direction and when the response of the test is proportional to the stimulus, as demonstrated for the PELOD (19). Thus, it makes

TABLE 8. Relationship Between the Number of Organ Dysfunctions, the Pediatric Logistic Organ Dysfunction-2 Score, and Mortality

Number of Organ Dysfunctions	No. of Patients (%)	Pediatric Logistic Organ Dysfunction-2 score Mean (SD)	Deaths: No. of Patients (%)
0	556 (15.2)	0 (0.0)	2 (0.4)
1	1,016 (27.7)	2.3 (0.8)	3 (0.3)
2	994 (27.1)	4.9 (1.3)	12 (1.2)
3	687 (18.7)	7.5 (2.0)	49 (7.1)
4	318 (8.7)	11.5 (4.4)	97 (30.5)
5	100 (2.7)	16.8 (5.2)	59 (59.0)

sense to believe that the responsiveness of the PELOD-2 should be good, but it remains to be proven.

Descriptive scores, like the PELOD, and predictive scores, like the Pediatric Risk of Mortality score (17) and the Acute Physiology and Chronic Health Evaluation system (20), need to be updated regularly because patients' demographics, disease prevalence, monitoring, treatment, and mortality rates change over time. In the future, scoring systems are likely to become more complex and dependent on new information technology. They may require additional variables, adjustment for treatment limitations, and diagnostic precision (21). For example, a noninvasive variable, such as Spo_2/Fio_2 ratio instead of Pao_2/Fio_2 ratio (22), might be considered more appropriate and/or more informative.

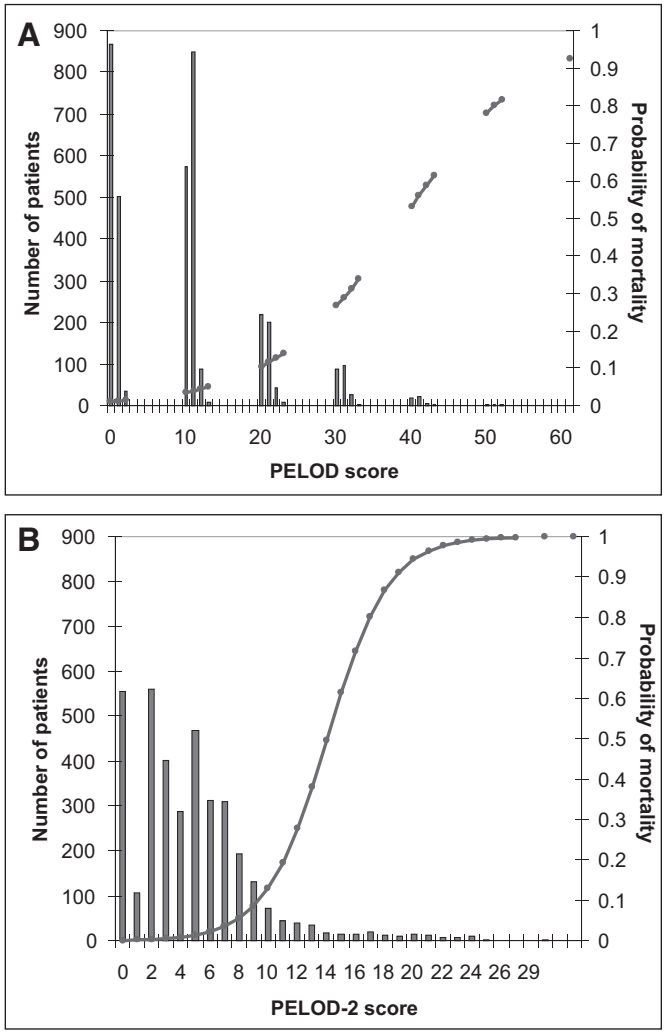

Figure 2. Descriptive characteristics of the Pediatric Logistic Organ Dysfunction (PELOD) (**A**) and PELOD-2 (**B**) scores in the study population. *Dotted lines* = probability of mortality calculated from the score according to the values of the score; *bars* = number of patients according to the values of the score.

MODS scores seem to satisfy most criteria proposed by Segers et al to assess the validity of a surrogate outcome, even though some authors underline that surrogate outcome endpoints have not yet been rigorously validated (23, 24). There is also evidence that MODS scores (PELOD, SOFA, MOD) can be a useful tool for clinical investigation: MODS scores are largely used as secondary endpoint and primary outcome measure when the mortality cannot be used as a primary outcome measure because its incidence rate is too low (25). This is particularly important in PICUs where mortality rate is much lower than in adult ICUs. In fact, the first version of the PELOD was used in many large multicenter studies (26–28). Also, MODS scores may be used to describe the effects of therapy, and most trials now include repeated measures of a MODS score as part of routine patient assessment (29).

The equation of probability of death that we used while doing the goodness-of-fit test (calibration) is given in **Table 6**. However, if the risk of death is to be predicted in a population different from that which PELOD-2 was developed and validated, this should be done using customization steps (first or second level of customization), as recommended in the literature (21). Also, we would emphasize that the aim of organ dysfuction scores, such as the P-MODS (9), PELOD (2), SOFA (8), MODS (7), and Logistic Organ Dysfunction (30) scores, is to describe the severity of illness of critically ill patients and not to predict mortality rate.

This study has some limitations. First, the data in this study were collected using the set of 8 days (days 1, 2, 5, 8, 12, 16, and 18, plus the PICU discharge) in PICU that were previously identified as the optimal time points for measurement of dPELOD (16). Thus, an abnormal value of a variable measured on a day outside this set could be missed; in theory, this could cause some underestimation

of the score. However, data of the day of discharge or death were recorded, and thus, worst values of variables of patients who died were taken into account up to 4 hours before death. Even though we considered the worst value of each variable over the PICU stay to build the PELOD-2, as performed with other organ dysfunction scores for adults (such as the MOD score of Marshall et al [7] and the SOFA score of Vincent et al [8]), this may have exaggerated the discrimination (AUC). Consequently, an external validation of the whole PICU stay and dPELOD-2 scores is needed. Second, the PELOD-2 was developed and validated with a dataset that originated from only two countries (France and Belgium). The population of our study was different from U.S. and U.K. populations (31, 32). Thus, the extensibility of our findings to other countries, particularly to PICUs that receive a higher percentage of cases from the operating room (32), has to be verified. Also, because of changes in case mix and clinical practice, the performances of prognostic models deteriorate over time. To counterbalance this deterioration, models often need to be customized (33). Third, interobserver variability was not studied for the PELOD-2 and should be evaluated in future studies on new populations. However, using an electronic clinical information system with an automated archiving method intelligently excluding unreliable variables values should decrease the risk of inaccurate data collection (34).

This study has several strengths. First, the data were collected from nine typical European multidisciplinary university-affiliated PICUs. Second, the score development used a large dataset of 3,671 consecutive patients. Third, it is continuous. Fourth, its adjusted discriminative value is 0.934, which is considered "excellent" in the scale advocated by Hanley et al (35) to estimate the descriptive value of a test.

In summary, we created and validated the PELOD-2, which has an excellent discriminative power. The PELOD-2 score now includes mean arterial pressure and lactatemia in the cardiovascular dysfunction and does not include hepatic dysfunction. We believe that the PELOD-2 allows assessment of the severity of cases of MODS in the PICU and can be useful as an outcome measure in clinical trials (36). The PELOD-2 will be available in the public domain, which means that it can be freely used in clinical trials, as it was the case with the PELOD (37).

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