SUPPLEMENTARY DATA.

Statistical analysis

- Identification of covariates and their cutoffs

The association between the outcome (death/survival at ICU discharge) and each variable was first investigated using bivariate logistic regression. For continuous variables, two groups were considered: those variables for which the normal values do not change with patient's age and those for which normal values change with patient's age (heart rate, systolic and mean arterial pressure and creatinine).

Age independent continuous variables

The log-linearity assumption of the logistic model was checked by categorizing each variable in 10 groups (corresponding to deciles) and by looking at the plot of the logit of observed percentages of death in each class. As this assumption was not verified, all these continuous variables were transformed in categorical variables. The cutoffs were identified using a decision tree procedure in which the outcome was the dependent variable (death/survival). This was performed by the Chaid method using the maximization of the chi-square test (1)

Age dependent continuous variables

As there were no literature data allowing to compute z-scores according to different age groups for mean arterial pressure, the following procedure was used: first, we considered five strata of age (in months) for children, according to the Pediatric Advanced Life Support (PALS) (2), and we added one stratum for neonates: <1, 1–11, 12–23, 24–59, 60–143 and ≥144 months. Second, for each age dependent variable, a linear regression was performed with the 5 strata of age as independent variables with age less than 1 month as reference level. The residuals computed from the linear regression were analyzed by the CHAID method to identify a primary set of non age-dependent cutoffs (1). Third, the age dependent

variable cutoffs were calculated using the coefficients of the linear regression model and the primary set of non age-dependent cutoffs.

Validation of cutoffs

For each categorized variable, an additional modality corresponding to missing data (variable not measured) was created. This allowed associating to each categorized variable an ordinal variable coded from 0 (reference level corresponding to the missing data modality) to k (modality associated to the higher risk of death). The relationships between the outcome and each ordinal variable considered as categorical were evaluated by using bivariate logistic regressions. 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 relationship between the death rates and the levels of the ordinal variables. Because the observed differences between death rates in level 0 (modality corresponding to missing data) and level 1 (modality having the lower risk of death) were nearly equal, these modalities were pooled to build the predictive model.

- 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. In the simplification procedure, each categorical variable having *k* modalities was transformed in *k-1* binary variables.

The stability of the selected model was investigated using the bootstrap resampling method with 500 replicates (3) . Bootstrap resampling is a method to get replicates of the initial dataset used for the multivariable analysis. Multivariable logistic regressions with a backward selection at the level 0.2 were performed on each of these replicates. The variable was kept in the final model if it was selected in at least 70% of these 500 analyses. Otherwise, selection frequencies of all possible pairs of variables were considered to cope with the problem of the correlated variables. In case of the selection of a pair of variable in more than 90% of replicates, the variable with the higher inclusion frequency was selected.

Finally, when at least one modality was selected by the bootstrap procedure, the corresponding categorical variable was retained for the simplified predictive model.

- Creation of the PELOD-2 score

A multivariable logistic regression was performed using the variables selected by the previously described procedure. Two simplifications were performed: first, when the odds ratio of the first risk level had a significant level greater than 0.2, the corresponding level of the categorized variables was pooled with the reference; second, when two levels were associated with values of odds ratios nearly equal (differences less than 0.5), these levels were pooled. The choice of 0.2 for the significant level was a compromise between the need for avoiding the over-fitting adopting the parsimony principle (4) and the need for building a continuous score having a good discriminant power.

The cut-off values were rounded to the nearest integer in order to have a user friendly score. The model was rebuilt taking into account these simplification and influential observations were checked using the Pearson residuals.

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 in order to have a user friendly score.

- Validation

The discriminant power of the PELOD-2 was estimated using the area under the ROC curve (with 95% confidence interval) and the calibration was assessed using the Hosmer Lemeshow chi-square test. Because these parameters are estimated using the sample on which the score is developed, their values are generally biased (optimism bias (5)). Thus, a bootstrap resampling method with 500 replicates was employed to adjust for optimism bias. The stability of the score was estimated by cross validation. This procedure works as follows: for each patient *i*, a model *M-i* is derived from the sample obtained after elimination of the patient *i*. The cross validation score for *i* is computed from the coefficients of this model *M-i* with the characteristics of the patient *i*. The cross validation score can be considered as a new covariate. This covariate is then introduced in a logistic model and the predictive model

is considered as validated if the parameter associated with this new covariate is close to 1 (5).

Table S1: Description of the nine participating sites

	Number of admissions	Age, months, median (IQR)	Gender (male), n (%)	Death, n (%)
Besançon	130	11.9 (0.3-65.6)	78 (60.00)	7(5.38)
Brest	42	18.7 (0.5-109.4)	22 (52.38)	3 (7.14)
Bruxelles	442	16.8 (6.1-57.8)	238 (53.85)	11(2.49)
Grenoble	132	12.2 (2.9-70.6)	71 (53.79)	5 (3.79)
Lille	645	22.8 (6.4-69.5)	387 (60.00)	36 (5.58)
Lyon	581	32.7 (5.0-103.5)	329 (56.63)	23 (3.96)
Paris (R Debré)	838	14.6 (2.4-75.2)	481 (57.40)	55 (6.56)
Toulouse	348	4.3 (0.1-49.9)	205 (58.91)	40 (11.49)
Trousseau	513	2.8 (0.1-53.1)	286 (55.75)	42 (8.19)

Table S2: Description of PICUs of the Groupe Francophone de Réanimation et Urgences Pediatriques (GFRUP)

Centre	Medical		Surgical		Neonatal		Pediatric	
	Yes	No	Yes	No	Yes	No	Yes	No
1	1		1		1		1	
2	1		1			1	1	
3	1		1		1		1	
4	1			1	1		1	
5	1			1	1		1	
6	1		1			1	1	
7	1		1			1	1	
8	1		1			1	1	
9	1		1			1	1	
Other GFRUP PICUs	24	0	18	6	14	10	24	0
Total	33	0	25	8	18	15	33	0

Table S3: Multivariable logistic regression (full model)

Variable and cutoff	Odds ratio	95% confidence interval	Pr > Chi square
Glasgow coma score ≥11	1		
Glasgow coma score [5-10]	1.93	(1.14-3.27)	0.0155
Glasgow coma score [3-4]	6.59	(3.43-12.69)	<.0001
Pupillary reaction, both reactive	1		
Pupillary reaction, both fixed	12	(6.45-22.36)	<.0001
Lactatemia (mmol/L) <3.97,	1		
Lactatemia (mmol/L) [3.97-5.37[	1.25	(0.62-2.51)	0.537
Lactatemia (mmol/L) [5.37-11.07[	1.77	(0.96-3.24)	0.0679
Lactatemia (mmol/L)>11.07	5.78	(2.69-12.44)	<.0001
Mean arterial pressure (mm Hg) ≥ cutoff 3 [a]	1		
Mean arterial pressure, [cutoff 2 - cutoff 3[[a]	2.18	(1.21-3.96)	0.0104
Mean arterial pressure, [cutoff 1-cutoff 2[[a]	3.48	(1.74-6.95)	0.0004
Mean arterial pressure, <cutoff 1 [a]	17.89	(6.33-50.57)	<.0001
Heart rate (beats/min) <cutoff 1	1		

Heart rate (beats/min) ≥cutoff 1	1.59	(0.86-2.96)	0.1424
Creatinine (µmol/L)<cutoff 1 [a]	1		
Creatinine (µmol/L) [cutoff 1- cutoff 2[a]	2.48	(1.51-4.06)	0.0004
Creatinine (µmol/L) ≥cutoff 2[a]	2.82	(1.56-5.12)	0.0007
Uremia (mg/dL), <27	1		
Uremia (mg/dL), [27-36]	0.81	(0.46-1.45)	0.4758
Uremia (mg/dL), ≥ 37	0.88	(0.52-1.5)	0.6339
PaO_2 (mmHg)/FIO_2 ratio, >136.3	1		
PaO_2 (mmHg)/FIO_2 ratio, [60.5-136.3]	0.79	(0.42-1.49)	0.4559
PaO_2 (mmHg)/FIO_2 ratio, <60.5	2.32	(1.2-4.48)	0.013
$PaCO_2$ (mmHg), <58.5	1		
$PaCO_2$ (mmHg), [58.5-94·4]	1.69	(0.99-2.89)	0.0569
$PaCO_2$ (mmHg), ≥94.5	5.05	(1.95-13.1)	0.0009
Ventilation, no	1		
Ventilation, Non-invasive	1.28	(0.3-5.52)	0.4935
Ventilation, Invasive	4.17	(1.97-8.87)	0.0011
White blood cell count($\times 10^9$/L), ≥4.10	1		
White blood cell count ($\times 10^9$/L), [2.15-4.09]	0.75	(0.35-1.6)	0.4433
White blood cell count ($\times 10^9$/L), <2.15	2.03	(0.96-4.3)	0.0658
Platelets ($\times 10^9$/L), ≥141.5	1		
Platelets ($\times 10^9$/L), [76.5-141.4]	1.34	(0.73-2.45)	0.3495
Platelets ($\times 10^9$/L), <76·5	1.92	(1.07-3.46)	0.0304
Fibrinogen (mg/dL), ≥147	1		
Fibrinogen (mg/dL), [81-146]	1.3	(0.68-2.5)	0.4322
Fibrinogen (mg/dL), <81	1.13	(0.52-2.45)	0.7728
Aspartate transaminase (IU/L)<111.5	1		
Aspartate transaminase (IU/L) [111.5-<339.5]	1.15	(0.65-2.05)	0.6454
Aspartate transaminase (IU/L) ≥340	0.82	(0.4-1.71)	0.5969
Prothrombin time (seconds) ≥69.5	1		
Prothrombin time (seconds) [55.5-69]	1.24	(0.68-2.25)	0.4903
Prothrombin time (seconds) [34.5-55]	1.41	(0.8-2.49)	0.2429
Prothrombin time (seconds) <34·5	1.33	(0.61-2.92)	0.4832
International normalized ratio (INR) (seconds) <3	1		
International normalized ratio (INR) (seconds) ≥3	2.04	(0.37-11.33)	0.4166

[a]Cutoffs of age dependent variables are defined in table 2

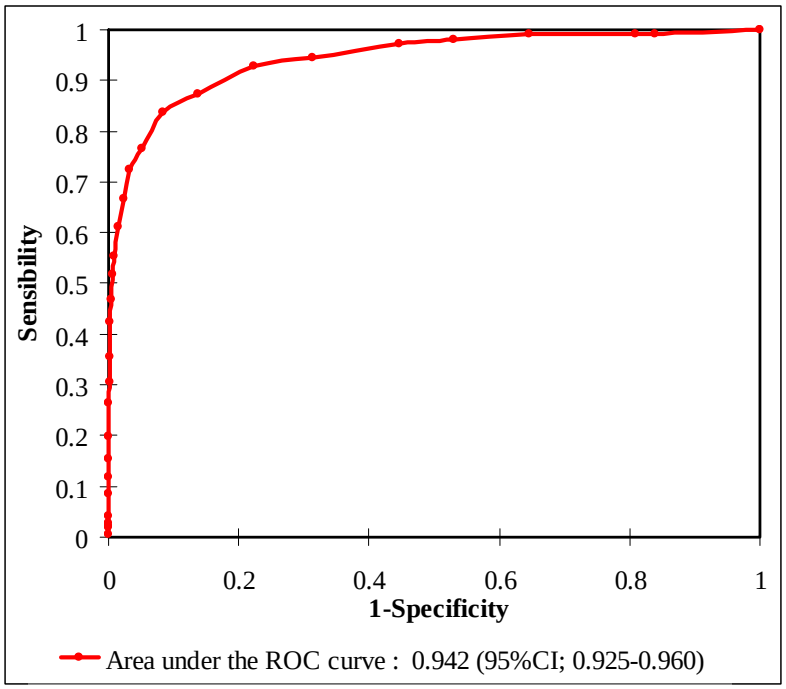

Figure S1: ROC curve of the PELOD-2 score

Table S4: Goodness-of-fit test for the PELOD-2 score.

Probability of death*	Total	Non survivors		Survivors	
		Observed	Expected	Observed	Expected
<0.0015	556	2	0.84	554	555.16
<0.0033	489	0	1.56	489	487.44
<0.0057	265	1	1.18	264	263.82
<0.0087	375	1	2.41	374	372.59
<0.0129	249	2	2.39	247	246.61
<0.0154	421	6	5.89	415	415.11
<0.0292	365	7	8.12	358	356.88
<0.0542	370	12	14.21	358	355.79
<0.2599	367	47	38.75	320	328.25
<1	214	144	146.65	70	67.35

***The observations are divided into 10 groups according to the SAS procedure.
Hosmer-Lemeshow Chi-square goodness of fit: p=0.565 with 8 degrees of freedom.

References

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