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Comparing Pediatric Index of Mortality 3, Pediatric Logistic Organ Dysfunction 2 (PELOD-2), and Modified PELOD-2 scores for Mortality Prognosis in Vietnamese Children with Multiple Organ Dysfunction Syndrome

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Abstract:

Objective: To evaluate the performance of three scores, the Pediatric Index of Mortality 3 (PIM-3), the Pediatric Logistic Organ Dysfunction 2 (PELOD-2), and the modified PELOD-2 scores, in predicting mortality in multiple organ dysfunction syndrome (MODS) children in Vietnam.

Material and Methods: This cross-sectional study of MODS children admitted to the pediatric intensive care unit (PICU) of a central children's hospital in the Mekong Delta, Vietnam, was undertaken from April 2019 to June 2021. All three scores were evaluated using receiver operating characteristic (ROC) curves for discrimination and the Hosmer-Lemeshow goodness-of-fit test for calibration.

Results: Of eighty-four subjects, the median age was 24.5 months and the overall mortality rate was 63.1%. ROC curve analysis showed that the area under the curve of PIM-3, PELOD-2, and modified PELOD-2 for predicting the death of MODS children were 0.77, 0.89, and 0.89, respectively. With individual cut-offs, the PIM-3, PELOD-2, and modified PELOD-2 scores had sensitivities for predicting mortality of 81.1%, 79.2%, and 81.1%, respectively, and specificities

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of 61.3%, 87.1%, and 80.6%, respectively. All three scores performed well in the Hosmer-Lemeshow goodness-of-fit test, indicating high calibration between predicted and observed mortalities (PIM-3: χ^2=4.36, p-value=0.823; PELOD-2: χ^2=4.837, p-value=0.775; modified PELOD-2: χ^2=6.082, p-value=0.638).

Conclusion: The PELOD-2 and modified PELOD-2 scores showed a better mortality prognosis than the PIM-3 score. Compared to the PELOD-2, the modified PELOD-2 with fewer parameters can still predict mortality well in Vietnamese children with MODS when using a cut-off score ≥9.

Keywords: children, modified PELOD-2, MODS, mortality, PELOD-2, PIM-3

Introduction

Multiple organ dysfunction syndrome (MODS), a common and fatal event, is commonly seen in pediatric intensive care units (PICU). The reported incidence of MODS in children admitted to PICUs ranges from 11.0% to 56.0%, and the reported mortality rate from MODS ranges from 11.0% to 57.0%.[1]

Because of hemodynamic instability, critically ill patients are at elevated mortality risk. The PICU provides qualified and experienced healthcare staff for severely ill children to reduce mortality in severely ill children. Scoring systems for use in the PICU enable the assessment of illness severity and the estimation of mortality by giving quantitative assertions about the severity, prognosis, and progress of a disease. A severity-of-illness scoring system is beneficial for objectively estimating the outcomes and prognoses of PICU patients, including MODS children.[2]

Several organ dysfunction scoring systems are currently available to predict the risk of mortality based on the number of dysfunctional organs on admission. The Pediatric Index of Mortality 3 (PIM-3) score is used to predict the mortality of PICU patients, and the PIM-3 is a valuable tool for the early prediction of child mortality.[3] The Pediatric Logistic Organ Dysfunction (PELOD) score, created in 1999 to describe the severity of MODS, is the major score currently utilized in the PICU. Leteurtre et al. (2013) developed the PELOD-2 score for children. The PELOD-2 score, an updated version of the PELOD score, was recently validated to demonstrate sensitive discrimination and good calibration in critically ill pediatric patients.[4]

However, the lactate measurement necessary for PELOD-2 cannot be conducted in most resource-constrained settings. And there are limited data assessing the performance of PELOD-2 and PIM-3 in MODS patients. Therefore, we aimed to evaluate the performance of the PIM-3 score, PELOD-2 score, and a modified PELOD-2 score (eliminating lactate), in predicting the death of MODS patients admitted to the PICU in a southern Vietnamese city.

Material and Methods

Study design and subjects

This was a cross-sectional study of patients admitted to the PICU of a central children's hospital in the Mekong Delta region, Vietnam from April 2019 to June 2021.

This 30-bed PICU is in a tertiary-care children's hospital, where critically ill pediatric patients are admitted. The study inclusion criteria were meeting the MODS diagnostic criteria of Proulx (1996)[5] at the time of arrival to the PICU, and age from 1 month to 15 years. The exclusion criteria were length of PICU stay <24 hours, death within the first 24 hours of admission, or incomplete clinical data.

Data collection

The clinical and laboratory data were collected on the first day of admission. The dependent variable was the outcome of children with MODS (survival and non-survival). Non-survivors were patients who died in the hospital and severely ill patients who died at home within 24 hours after being discharged. Data were collected for the day-1 PELOD-2, its modified score, and 1-hour PIM-3 score calculations. The PIM-3 includes 10 variables: systolic blood pressure (mmHg), pupillary reaction to light, PaO_2 to FiO_2 ratio, base excess (mmol/L), mechanical ventilation, elective admission to the Emergency Department (ED), recovery after surgical procedure, and diagnosis.[3]

For the PELOD-2 score, five organ systems (cardiovascular, neurologic, respiratory, hematologic, and renal) were evaluated and 10 variables were collected (mean blood pressure, lactatemia, Glasgow Coma Scale, pupillary reaction, PaO_2/FiO_2 ratio, $PaCO_2$, mechanical ventilation, leukocyte count, platelet count, serum creatinine). The highest number of points in the PELOD-2 for an organ system is 10, and the maximum PELOD-2 score is 33.[4]

In this study, the modification to the PELOD-2 score was designated as modified PELOD-2, a modified PELOD-2 without the lactate variable. The scoring of the modified PELOD-2 is the same as the original PELOD-2 scoring.

Statistical analysis

All statistical analyses were performed using R version 4.1.2. Frequencies and percentages were used to express categorical variables. The quantitative variables were median, inter-quartile range (IQR), mean, and standard deviation (S.D.). The Chi-square test or Fisher's exact test was utilized to investigate the significance of a relationship between two categorical variables. The independent-sample t-test or Wilcoxon test was used to identify significant differences in the mean and median quantitative variables between the two groups of patients.

The area under the receiver operating characteristic curve (AUC-ROC) and its 95% confidence interval (CI) were calculated to assess the model's discrimination between survivors and non-survivors. We used the De-Long test to compare the two AUCs with each other. The best cut-off was determined to be the one with the highest Youden index. Odds ratio and Fisher's Exact Test were used to evaluate the diagnostic performance of scores against mortality outcome.

The Hosmer–Lemeshow goodness-of-fit analysis was used to verify calibrations and the degree of agreement between predicted and observed mortalities as determined by the PIM-3, PELOD-2, and modified PELOD-2 scoring systems. If p-value≥0.05, the model's predicted value was substantially compatible with the actual value, suggesting that the prognostic model was well calibrated and could be used in that population.

Ethics statement

The ethical and scientific aspects of the research were evaluated and approved by the Ethics Committee of Can Tho University of Medicine and Pharmacy on February 19, 2019 (Ethics approval No. 162).

Results

Patient characteristics

A total of 306 critically ill patients were admitted to the study PICU during the study period. Among them, 84 patients fulfilled the inclusion criteria for this study. In these patients, the death rate was 63.1% (53/84). The median age of children was 24.5 months (IQR: 8-94), with 31.0% (26/84) being infants. There was no difference in survival between males and females (Table 1).

The respiratory system was the most affected organ in terms of organ dysfunction in 91.7% of the children, followed by the cardiovascular system (86.9%). The neurological and respiratory systems failure rates were significantly higher in the non-survivors.

Table 1 General characteristics of the study sample

Characteristic	Total (n=84)	Survivors (n=31)	Non-survivors (n=53)	p-value
Age (months)				
Median (IQR)	24.5 (8-94)	27 (14-118)	18 (7-54)	0.123
Male sex, n (%)	58 (69.0)	25 (80.6)	33 (62.3)	0.13
Required vasoactive agents, n (%)	68 (81.0)	20 (64.5)	48 (90.6)	0.008
Required mechanical ventilation, n (%)	70 (83.3)	20 (64.5)	50 (94.3)	0.001
Main diagnosis, n (%)				0.011
Sepsis	44 (52.3)	13 (41.9)	31 (58.5)	
Cardiovascular diseases	21 (25.0)	13 (41.9)	8 (15.1)	
Respiratory diseases	5 (6.0)	3 (9.7)	2 (3.8)	
Other	14 (16.7)	2 (6.5)	12 (22.6)	
Number of organ failures, n (%)				<0.001
2	33 (39.3)	24 (77.4)	9 (17.0)	
3	27 (32.1)	6 (19.4)	21 (39.6)	
4	19 (22.6)	1 (3.2)	18 (34.0)	
5	4 (4.8)	0 (0.0)	4 (7.6)	
6	1 (1.2)	0 (0.0)	1 (1.9)	
Organ dysfunction, n (%)				
Neurological	30 (35.7)	0 (0.0)	30 (56.6)	<0.001
Respiratory	77 (91.7)	25 (80.6)	52 (98.1)	0.009
Cardiovascular	73 (86.9)	25 (80.6)	48 (90.6)	0.314
Hematological	50 (59.5)	17 (54.8)	33 (62.3)	0.661
Gastrointestinal	11 (13.1)	2 (6.5)	9 (17)	0.201
Hepatic	5 (3.2)	1 (3.2)	4 (7.6)	0.647
Nephrological	3 (3.6)	0 (0.0)	3 (5.7)	0.293

n=number of cases, S.D.=standard deviation, IQR=interquartile range

Table 2 PIM-3, PELOD-2, and modified PELOD-2 scores in the study MODS children

Score	Total (n=84)	Survivors (n=31)	Non-survivors (n=53)	p-value
PIM-3				
Mean PDR (S.D.), %	32.8 (32.8)	14.0 (16.3)	43.8 (35.1)	<0.001
Median PDR (IQR), %	18.7 (5.7-50.2)	6.1 (2.9-18.3)	33.3 (10.9-82.7)	<0.001
PELOD-2				
Mean (S.D.)	12.1 (6.06)	7.19 (3.16)	15.0 (5.47)	<0.001
Median (IQR)	12 (7-16)	7 (5-8)	15 (11-19)	<0.001
Mean PDR (S.D.), %	37.9 (36.5)	8.4 (13.1)	55.2 (34.7)	<0.001
Median PDR (IQR), %	27.5 (3.5-71.3)	3.5 (1.4-5.5)	60.8 (19.1-91.0)	<0.001
modified PELOD-2				
Mean (S.D.)	10.8 (5.16)	6.68 (2.8)	13.3 (4.65)	<0.001
Median (IQR)	10 (7-15)	7 (4.5-8)	14 (10-16)	<0.001
Mean PDR (S.D.), %	29.8 (32.1)	5.91 (7.6)	43.8 (32.7)	<0.001
Median PDR (IQR), %	12.9 (3.5-60.8)	3.5 (1.2-5.5)	49.3 (12.9-71.3)	<0.001

PIM-3=Pediatric Index of Mortality 3, PELOD-2=Pediatric Logistic Organ Dysfunction 2, MODS=multiple organ dysfunction syndrome PDR=predicted death rate, S.D.=standard deviation, IQR=interquartile range

Compared to the survivor group, the non-survivor group had significantly higher PIM-3, PELOD-2, and modified PELOD-2 scores (all p-value<0.001) (Table 2).

Discrimination of scores for the predictive ability for mortality

In our study, ROC curve analysis showed that the AUCs of the PIM-3, PELOD-2, modified PELOD-2 scores for predicting the mortality of children with MODS were 0.77 (95% CI: 0.67-0.87), 0.89 (95% CI: 0.82-0.96), and 0.89 (95% CI: 0.82-0.95), respectively (all p-value<0.001; Table 3, Figure 1).

There were significant differences in the AUCs between the PELOD-2 and PIM-3 scores (Z-score=2.891, p-value=0.003) and the modified PELOD-2 and PIM-3 scores (Z-score=2.812, p-value=0.004). However, the difference between the AUCs of the PELOD-2 score and the modified PELOD-2 score (Z=0.15, p-value=0.877) was not significant.

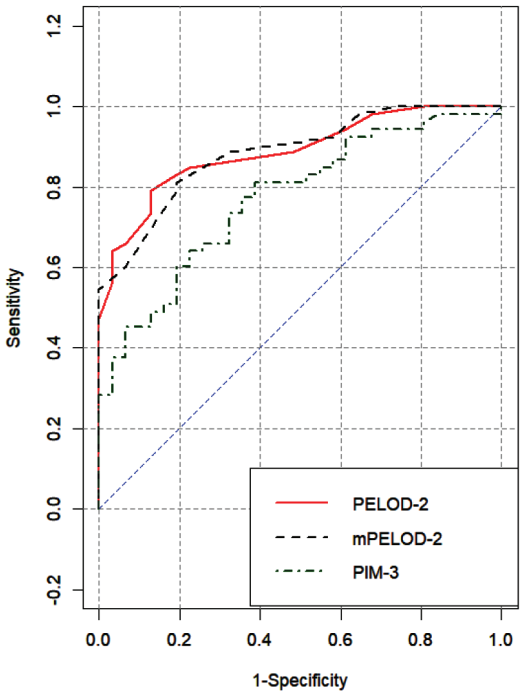

Figure 1 AUC ROC analysis of PIM-3, PELOD-2, and modified PELOD-2 scores

Table 3 Discrimination and diagnostic performances of the PIM-3, PELOD-2, and modified PELOD-2 scores to predict mortality

Parameter	PIM-3	PELOD-2	Modified PELOD-2
Cut-off	8.8	11	9
ACC (%)	73.8	82.1	81.0
Se (%)	81.1	79.2	81.1
Sp (%)	61.3	87.1	80.6
PPV (%)	78.2	91.3	87.8
NPV (%)	65.5	71.1	71.4
PLR	2.1	6.1	4.2
NLR	0.3	0.2	0.2

ACC=Accuracy, Se=sensitivity, Sp=specificity, PPV=positive predictive value, NPV=negative predictive value, PLR=positive likelihood ratio, NLR=negative likelihood ratio, OR=odds ratio

Diagnostic performance of the three scoring systems

The optimal cut-off values of the PIM-3 score, the original PELOD-2 score, and the modified PELOD-2 score to predict mortality were 8.8, 11, and 9, respectively. Using the obtained cut-off values, a diagnostic study was done to assess the diagnostic parameters of PELOD-2, modified PELOD-2, and PIM-3 scores (shown in Table 3). Table 3 also summarizes the diagnostic test performances for mortality prognoses with the individual cut-offs (all p-value<0.001).

Calibration performance of the three scoring systems

The Hosmer-Lemeshow test was used to calibrate the models across the deciles of mortality risk, as shown in Table 4. There were no statistically significant

differences in observed and predicted fatalities (PIM-3: p-value=0.823; PELOD-2: p-value=0.775; modified PELOD-2: p-value=0.638).

Discussion

It is critical to have access to reliable scores predicting mortality. The regular application of a scoring system allows the prediction of outcomes and the enhancement of optimal care in situations where resources are limited.

Demographic and clinical characteristics

Our study found a mortality rate of roughly 63.1%, similar to some other studies in Vietnam[6,7] but higher than studies from other countries.[8,9] This can be explained by our study including only subjects with multi-organ failures, whereas in Malhotra's study[8], all patients admitted to the intensive care unit were included. Furthermore, the PICU facilities in our center were not as well equipped as those of intensive care units in developed countries.

The mean and median ages of patients in our study were 51.36 months and 24.5 months, respectively. With a median age of 23 months, our findings are comparable to those of Proulx et al. (1996) (0.06-204 months of age).[5] This age was higher than in other studies in our country on MODS children, such as Tran et al. (2013) at Hue Central Hospital with an average age of 39.2 months[6] and Luong et al. (2006) at Vietnam National Children's Hospital of 30.42 months.[10] This difference might be due to the disease pattern of each region, and the undeveloped immune systems of young children may have a role.

We found that the most injured organs in multiple organ dysfunction were respiratory, cardiovascular, and hematological, at 91.7%, 86.9% and 59.5%, respectively. This finding is consistent with other studies conducted in Vietnam, i.e. according in the Tran et al. (2013) study, respiratory damage was 87.7%, cardiovascular damage was 75.4%, and hematological damage was 61.4%.[6]

Discrimination

For the PELOD-2 score, the area under the ROC curve of the PELOD-2 score was 0.89 (95% CI: 0.82-0.96), revealing the ability to predict very well the risk of mortality of children with MODS in a PICU in a developing country, which has seldom been documented. There have

Table 4 Hosmer-Lemeshow test for deciles of risk

PIM-3				PELOD-2				Modified PELOD-2			
Value	n	O	E	Value	n	O	E	Value	n	O	E
0.25-0.32	9	3	2.48	0.05-0.15	11	1	1.25	0.05-0.17	12	1	1.35
0.32-0.40	8	2	2.83	0.15-0.29	11	5	2.92	0.17-0.31	5	3	1.22
0.40-0.44	8	5	3.42	0.29-0.39	10	2	3.85	0.31-0.35	10	2	3.45
0.44-0.54	9	4	4.53	0.39-0.51	2	1	0.97	0.35-0.46	8	4	3.69
0.54-0.64	8	5	4.77	0.51-0.77	13	9	8.99	0.46-0.69	8	6	5.43
0.64-0.73	8	6	5.56	0.77-0.88	6	5	5.19	0.69-0.84	7	5	5.49
0.73-0.79	9	5	6.73	0.88-0.92	6	5	5.51	0.84-0.94	11	9	9.85
0.79-0.86	8	7	6.56	0.92-0.95	8	8	7.55	0.94-0.96	8	8	7.69
0.86-0.95	8	7	7.32	0.95-0.99	8	8	7.83	0.96-0.99	8	8	7.85
0.95-0.99	9	9	8.80	0.99-1	9	9	8.962	0.99-1	7	7	6.98
$\chi^2(8)=4.36$, p-value=0.823				$\chi^2(8)=4.837$, p-value=0.775				$\chi^2(8)=6.082$, p-value=0.638			

PIM-3=Pediatric Index of Mortality 3, PELOD-2=Pediatric Logistic Organ Dysfunction 2, n=number of cases, O=Observed death value, E=Expected death value

been many studies on the PELOD-2 score in the world. El-Nawawy's study comparing the PELOD and PELOD-2 scores of 200 patients aged between 1 month and 13 years who were admitted to a PICU in Egypt showed that the PELOD-2 score was significantly higher in the non-survivors group than in the survivors. The predictive ability of mortality was excellent, with an area under the ROC curve of 0.91 (95% CI: 0.86-0.94).[11] Similarly, Zhong et al.'s (2020) research on 516 children with sepsis admitted to a PICU in China found comparable results with an area under the ROC curve of 0.916. (95% CI: 0.888-0.938).[12] These studies demonstrated that, despite differences in the studies' inclusion criteria for patients in the PICUs, the PELOD-2 score was a useful tool for predicting mortality in that population.

We found that the PIM-3 score could also predict the risk of death at a good level with the area under the ROC curve of 0.77 (95% CI: 0.67-0.87). In a study by Straney, the area under the ROC curve of the PIM-3 score was 0.89, higher than in our study.[3] This was probably due to differences in the study samples. Probably because our study sample was patients with multiple organ dysfunctions, while the Straney study included all patients admitted to the intensive care unit, the mortality rate in our study was 63.1%, much higher than the 3.7% in the Straney study. Similar to our study, a study of 202 children admitted to a PICU evaluating the value of the PIM-3 score in India in 2018 also reported similar results to our study, with the area under the ROC curve of 0.75 (95% CI: 0.67-0.81), lower than the Sankar et al. study.[13]

The AUC of the PELOD-2 score in our study was higher than that of the PIM-3 score (0.89 versus 0.77, with p-value=0.003). When the modified PELOD-2 score was compared to the PIM-3 score, similar findings were reached (0.89 versus 0.77, p-value=0.004). As a result, the original and modified PELOD-2 scores predicted the probability of mortality better than the PIM-3 score. This can be partially explained by the PIM-3 score, which evaluated patients within the first hour of ICU admission, whereas the original and modified PELOD-2 scores did so within the first 24 hours, reflecting the fact that some patients did not have obvious severe symptoms in the first hours of admission, while these manifestations became clearer later, leading to the differences in the scores. We found no significant difference in the AUCs of the PELOD-2 and modified PELOD-2 scores when we compared them (Z=0.15, p-value=0.877). This is comparable to the research of Melda et al. (2021).[14]

Diagnostic performance

The optimal PELOD-2 cut-off to differentiate mortality probability was found to be a score equal to or greater than 11 points in the current study, which is similar to the cut-off found by Wulandari et al. (2019), but higher than in the study by Ta et al. (2021) at Vietnam National Children's Hospital, which had a cut-off point of 8.5 points.[15,16] The PELOD-2 score demonstrated sensitivity, specificity, positive predictive value, and negative predictive value of 79.2%, 87.1%, 91.3%, and 71.1%, respectively, with a cut-off of 11 points. This study's findings are comparable to those of El-Nawawy et al. (2017), who found that with a cut-off of 9 points, the PELOD-2 score had sensitivity, specificity, positive predictive value, and negative predictive value of 76.9%, 92.0%, 76.0%, and 92.0%, respectively.[11] The sensitivity of the PELOD-2 score was only 35.7% in Wulandari's study, with a cut-off of 11 points, while the specificity was 93.8%.[16]

With an individual cut-off, the diagnostic performance was similar among all three scores. This was also reported by Melda et al. (2021)[14] and Suari et al. (2021)[17], who did not find any significant differences in the accuracy, sensitivity, specificity, positive predictive value, or negative predictive value in the PELOD-2 score with and without the lactate variable. This could be explained by the multivariable logistic regression analysis findings, which revealed that the blood lactate variable was not statistically significant

(p-value=0.557). The modified PELOD-2 score was inferior to neither the original version nor the PIM-3 score in predicting mortality.

Calibration

Regarding the calibrations in the prognosis of mortality in children with multiple organ dysfunctions, all three scores showed good results with the calibration tests, giving good predictions of mortality. A similarly good calibration for the PIM-3 score was reported by Lee et al. (2017) (χ^2=9.4, p-value=0.313).[18] In contrast to our results, however, PIM-3 had poor calibrations in other studies.[13,19] Poor calibrations have been associated with many issues, including variations in medical system performances, diverse case mixes, variations in death rates, illness patterns, and a scoring system equation's inability to model the real situation.[19] El-Nawawy et al. (2017) reported that when using the Hosmer-Lemeshow test for PELOD-2, the good result was obtained with a p-value of 0.27 (χ^2=9.9). This means that PELOD-2 had a better calibration result in the current study than PELOD did in the same type of patients.[11] A similar pattern was seen with a good calibration of the PELOD-2 score (p-value=0.42) by Deshmukh et al. (2020).[20]

Therefore, all three models were considered suitable for predicting mortality in MODS children due to good calibrations between predicted and observed mortalities. Our findings were consistent with other research conducted worldwide.[20,21]

Limitations

The study had some limitations. First, though it was a study conducted at a large central hospital during a time period of over 2 years, it was still single-center study with a quite small number of patients, and as a result, the findings may not be generalizable to the entire Vietnamese pediatric population. Thus, future research should include more Vietnamese PICUs to acquire more trustworthy and precise results. Second, all indicators in this study were obtained within 24 hours after admission, and no dynamic evaluation of the prognostic usefulness of the three scores was performed.

Implementations for clinical practice and further research

In Vietnam, quite a few children's intensive care centers do not include scores in their MODS treatment guidelines, while some use scores that do not present as continuous variables, limiting their usefulness. Such scores should be used as descriptors of MODS in critically ill patients and not to predict mortality. To the best of our knowledge, this study can be considered the first research to evaluate the specific three scores for their usefulness in assessing the probability of survival in children with MODS, and we found that all three scores, particularly the modified PELOD-2 score with fewer variables but still strong discrimination and calibration, can be useful for clinical practice. As the majority of the study population was septic children, these three scoring systems could also be useful in predicting the mortality of children with sepsis. More research is needed to evaluate the performance of these scores in septic children.

The modified PELOD-2 score is less complicated than the original PELOD-2 score, making evaluation more accessible and standardized training of PICU clinicians more straightforward. However, when using this modified PELOD-2 score to make a therapeutic decision, the practitioners should be aware of the listed limitations. More multicenter studies need to be carried out to obtain more reliable and accurate predictions of these scores for children in Vietnam and evaluate the validity of the modified PELOD-2 score for estimating the risk of death among Vietnamese MODS patients.

Conclusion

The study demonstrated that all three scores were suitable for mortality prognosis for MODS children. The PELOD-2 and modified PELOD-2 scores were more beneficial for predicting death in MODS patients in the PICU than the PIM-3 score. Moreover, in developing countries, with limited resource conditions such as some Vietnamese PICU centers, the modified PELOD-2 score has an advantage over the PELOD-2 score in having fewer variables, making assessment more economically acceptable and convenient for mortality outcome prognosis assessment due to its good discrimination and calibration.

Conflict of interest

There are no potential conflicts of interest to declare.

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