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The Usefulness of Perfusion Index for Predicting Mortality in Pediatric Intensive Care Unit

Perfüzyon İndeksinin Çocuk Yoğun Bakım Ünitesinde Mortaliteyi Öngörmede Kullanılabilirliği

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Abstract

Introduction: The aim of this study is to the usefulness of the perfusion index to predict mortality in the pediatric intensive care unit.

Methods: The study included patients aged >28 days and <18 years old, who were admitted to Mersin University Faculty of Medicine, Department of Pediatric Intensive Care Unit between 2018 and 2019. Characteristic variables of patients, pediatric risk of mortality III and pediatric logistic organ dysfunction scores, the reason for hospitalization, surgical history, underlying disease, mechanical ventilation, transfusion, perfusion index value at the zeroth hour (at the admission) and at the sixth hour, lactate levels, and prognosis were recorded.

Results: A total of 372 patients who met the study criteria were included in the study. Median perfusion index values at the zeroth and sixth hours were significantly lower in patients who were exitus than the survivors (p<0.001). Considering mortality and organ failure scores, the median values of pediatric risk of mortality III and pediatric logistic organ dysfunction scores were higher in those who were exitus and when compared with the perfusion index values at the zeroth hour, a negative significance was found between them. In receiver operating characteristic analysis, the specificity and sensitivity values for mortality were 90.1% and 75.9% at a perfusion index cut-off of ≤0.63, respectively.

Conclusion: Perfusion index is a reliable method to predict mortality for patients admitted to pediatric intensive care unit.

Keywords: Perfusion index, pediatric intensive care unit, mortality

Öz

Giriş: Bu çalışmanın amacı perfüzyon indeksinin çocuk yoğun bakım ünitesinde mortaliteyi öngörmede kullanılabilirliğinin araştırılmasıdır.

Yöntemler: 2018-2019 yıllarında, >28 gün- <18 yaş aralığında Mersin Üniversitesi Tıp Fakültesi, Çocuk Yoğun Bakım Ünitesi'ne yatan hastalar çalışmaya alındı. Hastaların karekteristik değişkenleri, pediyatrik ölüm riski III, pediyatrik lojistik organ disfonksiyon skorları, yatış nedeni, cerrahi öyküsü, altta yatan hastalık, mekanik ventilatör izlemi, transfüzyon, perfüzyon indeksi 0. saat (yatış anında) ve 6. saat değerleri, laktat ölçümleri ve devir/taburcu bilgileri kaydedildi.

Bulgular: Çalışma kriterlerine uygun 372 hasta çalışmaya dahil edildi. Perfüzyon indeksi 0. ve 6. saat medyan değerleri eksitus olan hastalarda anlamlı derecede düşüktü (p<0,001). Mortalite ve organ yetmezliği skorları bakımından pediyatrik ölüm riski III ve pediyatrik lojistik organ disfonksiyonu medyan değerleri eksitus olanlarda daha yüksek saptanırken perfüzyon indeksi 0. saat ile karşılaştırıldığında aralarında negatif bir anlamlılık saptandı. Alıcı işletim karakteristiği analizinde perfüzyon indeksi ≤0,63 cut-off değerinde mortalite için spesifitesi %90,1 iken sensitivitesi %75,9 saptandı.

Sonuç: Perfüzyon indeksinin non-invazif bir yöntem olarak çocuk yoğun bakım ünitesinde mortalitenin öngörülmesinde kullanılabileceğini düşünmekteyiz.

Anahtar Kelimeler: Perfüzyon indeksi, çocuk yoğun bakım ünitesi, mortalite

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Introduction

The perfusion index (PI) is a parameter calculated as the ratio of pulsatile arterial blood flow [alternating current (AC)] to non-pulsatile [direct current (DC)] in the peripheral tissues measured by the pulse oximeter (AC/DC x 100). The mean PI value of 1.4 is considered normal. The PI provides that peripheral perfusion can be monitored non-invasively and continuously using pulse oximetry.[1,2]

The PI value can also provide information about peripheral vasomotor tonus. Low PI represents high peripheral vasomotor tonus whereas high PI represents low peripheral vasomotor tonus. In other words, perfusion decreases as the PI value decreases. Therefore, it is thought that PI can be used to determine the severity of the disease in critical patients in the intensive care unit (ICU). In a limited number of studies on this subject, low PI value has been shown to be compatible with peripheral perfusion disorder.[2]

However, normal values and limits in pediatric patients are not clear. While there are studies on this subject in newborns, there is no study involving children.[3] Therefore, there is a need for new studies to investigate the use of PI in predicting prognosis in pediatric intensive care units (PICU). This study aimed to reveal the effectiveness and usability of PI in predicting mortality in PICU and to investigate the correlation of PI with pediatric risk of mortality III (PRISM III) and pediatric logistic organ dysfunction (PELOD) scores, which were scoring systems used to predict mortality and morbidity.

Materials and Methods

The study included patients within the age range of >28 days to <18 years, who were admitted to Pediatric ICU between September 2018 and September 2019. The following parameters of the patients whose file information could be accessed were recorded: Characteristic and demographic variables, PRISM III and PELOD scores, reason for hospitalization, presence of surgery, underlying disease, mechanical ventilation, transfusion status, PI values at the zeroth hour (at the time of hospitalization) and sixth hour, lactate levels and prognosis (survive or exitus). The admission diagnosises with low number of patients (<5) were evaluated in a group called the other. The PI value was recorded when it was in its brightest and steady-state using the Masimo Root™ device with the help of pulse oximeter. Patients whose PI value was measured incorrectly due to technical problems or not measured and those with missing information in their files were excluded from the study. The study was approved by Mersin University Clinical Research and Ethics Committee (2019/169). Informed consent was obtained from the patients.

Statistical Analysis

The Shapiro-Wilk test was used to determine whether continuous variables distributed normally. Student's t-test and One-Way ANOVA tests were used for the comparison of parameters following a normal distribution whereas the Mann-Whitney U test was used for the comparison of parameters that did not follow a normal distribution. Descriptive data were expressed as mean and standard deviation for normally distributed parameters whereas the parameters that did not follow a normal distribution were expressed as minimum, maximum, median, and 25-75% percentages. Spearman's rank correlation coefficient was used for the correlation coefficient of continuous measurements. Receiver operating characteristic (ROC) analysis was used to determine the cut-off point for the PI value at the zeroth hour. A p-value of <0.05 was considered statistically significant.

Results

A total of 372 patients, including 188 (50.5%) females and 184 (49.5%) males, who met the study criteria, among 380 patients who were hospitalized in the PICU were included in the study. The mean age of the patients was 77.7±72.0 months. The mean age was 70.7±69.1 months in female patients and 84.7±74.5 months in male patients. Characteristic features of patients and mean PI values at zeroth hour are shown in Table 1.

The mean PI value was found to be higher in male patients compared to females (p=0.04). The PI value was found to increase with advancing age. There was no statistically significant correlation between PI and fever, saturation, white blood cell, and platelet count. There was an inverse statistical significance between the PI value and respiratory rate and heart rate whereas a positive statistical significance was found with high blood pressure. The comparison of the PI values at the zeroth and sixth hours showed that the sixth-hour measurements were significantly higher (p<0.001). Table 2 shows the comparison of all parameters and statistical significance.

The differences between PI values in terms of hospitalization were found to be significant (p<0.001). When these differences were examined, the zeroth-hour PI values of the patients hospitalized due to sepsis, septic shock, and disseminated intravascular coagulation (DIC) were found to be lower compared to those of patients hospitalized due to trauma and post-operative reasons (p=0.015). The zeroth hour PI values of the patients hospitalized due to sepsis, septic shock, and DIC were lower than those of patients hospitalized due to other reasons (p=0.001). A statistically significant difference was observed between patients hospitalized due

Table 1. Characteristics of the patients

		Number (n)	Percent (%)	PI 0.h	p
Gender	Female	188	50.5	1.63±1.20	0.040
	Male	184	49.5	1.90±1.32	
Causes of hospitalization	1- Sepsis, septic shock, disseminated intravascular coagulation (DIC)	60	16.1	1.31±1.16	<0.001
	2- Respiratory and infectious diseases	64	17.2	1.57±1.10	
	3- Neurological diseases	56	15.1	1.54±0.78	
	4- Trauma and post-operative patients	142	38.2	1.93±1.32	
	5- Hematological diseases and bleeding	12	3.2	2.12±2.09	
	Other	38	10.2	2.45±1.38*,†,‡,#	
Surgical operation	No	304	81.7	1.77±1.28	0.829
	Yes	68	18.3	1.74±1.20	
Underlying disease	No	163	43.8	2.12±1.41	<0.001
	Yes	209	56.2	1.49±1.07	
Mechanical ventilation in the first 24 hours	No	313	84.1	1.85±1.29	0.001
	Yes	59	15.9	1.34±1.02	
Transfusion	No	340	91.4	1.82±1.28	0.007
	Yes	32	8.6	1.19±0.96	
Result	Survived	343	92.2	1.85±1.25	<0.001
	Exitus	29	7.8	0.83±1.06	

Characteristics of the patients staying in the pediatric intensive care unit, perfusion index values, and significance level of perfusion index comparisons (p<0.05) *: Refers to the differences with the first category; †: Refers to the differences with the second category; ‡: Refers to the differences with the third category, #: Refers to the differences with the fourth category, PI: Perfusion index, h: Hour

to respiratory and infectious diseases and those hospitalized due to other diseases (p=0.016). There was a statistically significant difference between patients hospitalized due to neurological diseases and those in the other group (p=0.007).

The PI value of the group with a comorbidity or an underlying disease was found to be lower (p<0.001). There was no significant difference between patients undergoing post-traumatic or elective surgery and requiring intensive care and those not undergoing surgery and staying in the ICU (p=0.829).

There was a positive linear relationship between hemoglobin value and PI during hospitalization. The PI value was found to be lower in patients who received erythrocyte transfusion during hospitalization compared to those who were not transfused (p=0.07). When the effect of transfusion on PI was evaluated, no significant difference was observed between PI measured at sixth and zeroth hours.

The zeroth hour PI values of the patients, who received mechanical ventilation due to respiratory failure, hemodynamic instability, severe septic shock, and multiple organ failure, were found to be lower than those who were not received mechanical ventilation (p=0.001). Similarly, the sixth hour PI values were found to be significantly higher in those who received mechanical ventilation (p<0.02).

A negative correlation was found between PI and lactate. The PI value was seen to decrease significantly as the lactate value increased (p<0.01) (Table 2).

Comparison of vital signs, lactate values, and mean hemoglobin levels of the patients, who recovered and died, and statistically significant differences are shown in Table 3. There was a significant decrease in systolic and diastolic blood pressure and a significant increase in lactate values in patients who were exitus compared to those who were transferred to the service or discharged.

There was a significant decrease in the median PI values at zeroth and sixth hours in patients who were exitus. When mortality and organ failure scores of the patients were evaluated, median PRISM III and PELOD scores were found to be higher in those who were exitus compared to those who survived (Table 4).

A negative significance was found between PI values and PRISM III and PELOD scores. In patients with high PRISM III and PELOD scores, the PI value was found to be low. In receiver operating characteristic (ROC) analysis, the specificity and sensitivity values for mortality were 90.1% and 75.9% at a PI cut-off of ≤0.63, respectively (Figure 1).

Table 2. Comparison of variables and statistical significance

		Age	PI 6.h	PRISM III	PELOD	Peak heart rate	Blood pressure (systolic)	Blood pressure (diastolic)	Saturation	Lactate	Hemoglobin	White sphere	Platelet count	Length of stay (day)
PI 0.h	r	0.290	0.820	-0.188	-0.179	-0.307	0.203	0.121	0.098	-0.190	0.194	-0.050	-0.058	-0.154
	p	<0.001	<0.001	<0.001	0.001	<0.001	<0.001	0.020	0.058	<0.001	<0.001	0.333	0.264	0.003
Age	r		0.294	-0.002	0.009	-0.526	0.356	0.187	0.078	-0.083	0.339	0.009	-0.288	-0.119
	p		<0.001	0.965	0.865	<0.001	<0.001	<0.001	0.133	0.110	<0.001	0.858	<0.001	0.022
PI 6h	r			-0.127	-0.120	-0.258	0.157	0.083	0.084	-0.184	0.139	-0.039	-0.085	-0.148
	p			0.015	0.021	<0.001	0.003	0.112	0.107	<0.001	0.007	0.461	0.104	0.005
PRISM III	r				0.801	0.018	-0.122	-0.169	-0.052	0.164	-0.133	0.019	-0.058	0.074
	p				<0.001	0.723	0.019	0.001	0.319	0.002	0.010	0.722	0.263	0.156
PELOD	r					0.038	-0.176	-0.203	-0.131	0.140	-0.113	0.010	-0.096	0.104
	p					0.468	0.001	<0.001	0.012	0.007	0.030	0.853	0.064	0.045
Peak heart rate	r						-0.101	0.009	-0.096	0.092	-0.304	0.027	0.198	0.114
	p						0.052	0.857	0.064	0.077	<0.001	0.599	<0.001	0.027
Systolic blood pressure	r							0.748	0.092	-0.020	0.151	0.020	-0.054	-0.070
	p							<0.001	0.077	0.707	0.004	0.696	0.298	0.178
Diastolic blood pressure	r								0.080	-0.025	0.138	0.048	0.024	-0.033
	p								0.123	0.631	0.008	0.356	0.644	0.522
O_2 saturation	r									-0.035	-0.049	-0.005	-0.008	-0.118
	p									0.508	0.347	0.930	0.879	0.023
Lactate	r										-0.144	0.091	-0.109	0.110
	p										0.006	0.082	0.036	0.035
Hemoglobin	r											-0.117	0.059	-0.039
	p											0.024	0.253	0.459
Leucocyte count	r												-0.064	-0.033
	p												0.216	0.525
Platelet count	r													0.025
	p													0.625

PI: Perfusion index, h: Hour, PRISM III: Risk of mortality score III, PELOD: Pediatric logistic organ dysfunction

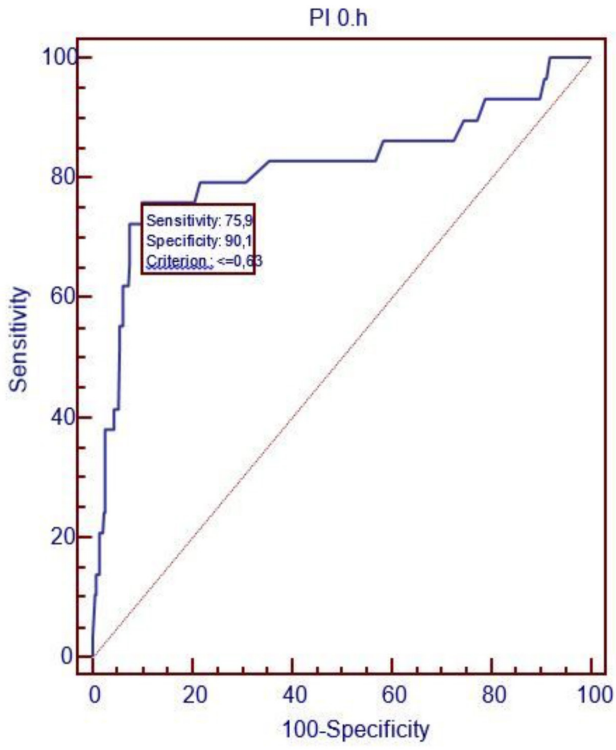

Figure 1. ROC analysis results

Discussion

The PI is a non-invasive measurement method made by using a pulse oximeter. There is no clear data on the normal and pathological values of PI in children, and current studies on this subject include patients in the newborn age group.[3,4] Granelli and Ostman-Smith[4] showed that a PI value of <0.7 may be indicative of disease in newborns and that the measurement should be repeated if the PI value is >4.5. In a study by Lima et al.[2] involving adult ICU patients, a PI value of <1.4 has been reported to be associated with poor peripheral perfusion. As it can be understood from these studies, the PI value varies according to the age and vasomotor tonus of the patient. The present study has provided information about the level of PI value in pediatric age groups in PICU patients. The median value of PI was 0.4 in patients who were exitus, while it was 1.4 in the group survived. We think that low PI value in the patients who were exitus was due to the presence of peripheral perfusion disorder, higher incidence of circulatory failure, and increased vasomotor tonus. So that the PI value can be used in clinical practice as an objective method for early diagnosis, particularly in cases of circulatory disorders that are not clinically noticeable. Compared with the study by Lima et al.[2], the PI values of the patients in the present study were lower. Considering the result that the PI value increases with advancing age, it can be said that the mean value is lower in children than that of adults. The result we found in this study that the PI value increases with advancing age also supports this hypothesis. Therefore,

Table 3. Comparison of survive and exitus

	Survive (n=343)	Exitus (n=29)	p
Age (months)	77.6±72.1	77.9±72.8	0.985
Fever (°C)	36.46±0.98	35.91±1.61	0.080
Respiratory rate (/min)	32.14±14.67	35.21±11.36	0.273
Peak heart rate (/min)	125.62±32.30	134.07±33.24	0.178
Systolic blood pressure (mmHg)	110.22±19.17	98.76±23.93	0.003
Diastolic blood pressure (mmHg)	70.87±18.07	59.59±18.95	0.001
Saturation (%)	97.78±5.12	94.41±9.08	0.058
Lactate (mmol/L)	4.04±3.06	5.66±3.53	0.007
Hemoglobin (g/dL)	11.11±2.39	10.35±2.23	0.102

Comparison of vital signs, lactate, and hemoglobin values of patients, who were survive, with those who died

Table 4. Comparison of survive and exitus 2

	Survive (n=343)		Exitus (n=29)		p
	Min-max	Median (25-75% percentages)	Min-max	Median (25-75% percentages)	
PI 0.h	0.11-6.90	1.40 (0.96-2.50)	0.10-4.0	0.40 (0.265-0.765)	<0.001
PI 6.h	0.12-7.60	1.80 (1.10-2.98)	0.14-4.30	0.665 (0.3475-1.05)	<0.001
PRISM III	0-36	4 (0-7)	0-60	14 (5-24.5)	<0.001
PELOD	0-32	8 (0-8)	0-40	12 (1-28)	<0.001
Leucocyte count (x10³/µL)	0.06-659.9	14.08 (10.01-193)	0.03-123.2	12.87 (5.29-27.5)	0.806
Platelet count (x10³/µL)	1-1179	326 (239-420)	2-702	169 (42.5-357)	<0.001
Length of stay in ICU (days)	1-78	4 (3-8)	1-85	5 (1-24)	0.699

Comparison of the PI values, PRISM III and PELOD scores, white sphere, platelet count, and length of stay in ICU of patients, who were transferred to the service or discharged, and those who died. PI: Perfusion index, PRISM III: Risk of mortality score III, PELOD: Pediatric logistic organ dysfunction, ICU: Intensive care unit

normal values of PI should be determined according to age groups.

The PI values of patients hospitalized due to sepsis, septic shock, and DIC were found to be lower compared to those who were hospitalized due to other reasons. We attributed the low PI value to the fact that the vasomotor tonus increased and peripheral perfusion was low due to tissue oxygenation disorder in patients with sepsis. When the tissue perfusion was evaluated with lactate, one of the parameters globally examined in the case of septic shock, the PI value was low if the lactate levels were elevated. The positive correlation between hyperlactatemia and PI, which is one of the generally accepted indicators of circulatory disorder, is significant in terms of showing the clinical value of PI. The present study is of great importance since it is the first study to evaluate lactate and PI values together in terms of mortality in pediatric patients due to increased lactate levels and low PI values in patients who were exitus. In patients with pediatric shock, Hafez et al.[5] found a strong correlation between PI, lactate, and lactate clearance, and found that these variables provided comparable sensitivity and specificity for predicting outcomes. On the other hand, in a study involving newborns in which lactate and PI values were evaluated together, high lactate level (4 mg/dL) and low PI value (<0.5) were found to increase the incidence of premature of retinopathy and broncho pulmoner dysplasia in early term infants.[6] In a study by Bakker et al.[7] involving adults, lactate level has been reported to be one of the most important markers of hypoxia and hypoperfusion, and lactic acidosis may be a marker for mortality in critically ill patients.

The use of mechanical ventilators in respiratory failure is life-saving but it is a fact that the mortality of patients receiving mechanical ventilation is higher than non-intubated patients. The PI values of the patients who received mechanical ventilation at the time of hospitalization have been found to be significantly low compared to those who did not receive mechanical ventilation. In a study by Su et al.[8] involving adult patients, in which the effects of mechanical ventilation and peripheral PI on prognosis were investigated, patients on the mechanical ventilator were also associated with a poor prognosis if the PI value was below 1.37 and the authors emphasized that patients with high mean airway pressure and low PI value had a poor prognosis. In a study by Er et al.[9] investigating whether PI can be used to estimate the mortality of adult patients on mechanical ventilation, it has been reported that PI cannot be a marker for long-term mortality (60 days), but it can be an independent marker for short-term mortality (7 days). There may be several reasons why the PI value of patients on mechanical ventilation may be lower than that of patients who are not mechanically ventilated. First of all, it may be expected that the PI value will be low in mechanically ventilated patients since they are usually a group of patients with a poor general condition which is mostly accompanied by circulatory failure. Furthermore, the physiological effects of mechanical ventilation increase the intrathoracic pressure, reducing venous return, right ventricular filling, and right heart rate. This results in decreased cardiac output and low perfusion. That's why the reason for the low PI values may also be due to these physiological effects of mechanical ventilation.

Among the scoring systems developed to provide and standardize the comparison of patients in PICU in terms of morbidity and mortality, PRISM III score is a marker of mortality whereas PELOD has been developed to assess organ failure. The values that are found to be high following the calculations indicate that the patient has a high likelihood of mortality or organ failure. In the present study, median PRISM III and PELOD values were found to be higher in patients who were exitus compared to patients transferred to the service or discharged. When evaluated together with PI, we found low PI values were correlating with high PRISM III and PELOD scores, and this result was statistically significant. The statistically significant correlation of PI value with PRISM III and PELOD scores supports the idea that PI can be a valuable parameter in predicting mortality in the PICU. The present study is of great importance in terms of being the first study in the literature showing the relationship between the PI value and PRISM III and PELOD scores in children.

We further used ROC analysis to assess the PI value and mortality. Our ROC analysis revealed different results in terms of cut-off point and the results obtained were more variable compared to the studies in the literature. In a study by De Felice et al.[10] involving newborns, the AUC, sensitivity, and specificity values for mortality were found to be 97%, 95.5% and 93.7% at a PI cut-off of 1.24 in ROC analysis, respectively The authors reported that PI can be associated with severe disease in neonates.[9] In a study by He et al.[11] involving adults, peripheral PI variability has been shown in patients with postoperative septic shock compared to the control group and sensitivity and specificity values have been found to be 65% and 92.3% at a PI cut-off of ≤0.2. There was a significant difference between the cut-off values in both studies. Although the cut-off value was high in the study involving neonates, the specificity and sensitivity were also found to be high whereas the data were analyzed using very low PI cut-off values in the study involving adults. In the present study, the AUC, specificity, and sensitivity were found to be 82%, 90.1%, and 75.9% at a cut-off value of ≤0.63, respectively. The ROC analysis has shown that PI may be an indicator of mortality. However, the fact that it is variable by age prevents obtaining exact information about the threshold value. The cut-off point for the present study was 0.63.

Study Limitations

This study has some limitations including being a single-center study and not having enough population size to generalize the results. There is a need for more comprehensive and multicenter studies.

Conclusion

The PI measurement is a non-invasive method that is measured peripherally using a pulse oximeter. However, it also has some disadvantages. The need for a special pulse oximeter, the necessity of keeping the pulse oximeter constant, and individual variations can be listed as some of its disadvantages. The results obtained from the present study have shown that the efficacy of PI in predicting mortality cannot be ignored. We believe that PI can be used to predict mortality in PICU since it is a non-invasive and easily applicable method.

Ethics

Ethics Committee Approval: The study was approved by Mersin University Clinical Research and Ethics Committee (2019/169).

Informed Consent: Informed consent was obtained from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.A., Design: A.E.A., Data Collection or Processing: M.A., Analysis or Interpretation: S.E., Literature Search: A.E.A., Writing: M.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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