Risk Factors for Predicting Mortality in a Paediatric Intensive Care Unit

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Abstract

Rapid advances in critical care technology and rising cost of medical care have spurred the development of outcome analysis including mortality risk prediction. The main objective of this study was to assess the risk factors contributing to mortality in our paediatric intensive care unit (PICU). This is a cohort study, consisting of consecutive admissions to the PICU from 1 January to 31 December 1997. The factors studied included multi-organ dysfunction syndrome (MODS), Pediatric Risk of Mortality III (PRISM III) scores in the first 24 hours (PRISM III-24), mechanical ventilation, renal replacement therapy, age, and diagnosis-related groups. Univariate and multivariate statistical methods were used. Univariate analysis showed that need for mechanical ventilation, renal replacement therapy, presence of MODS involving 3 or more organs and PRISM III-24 scores were significantly associated with outcome (P <0.0005). Relative risk of mortality in the presence of MODS and PRISM III-24 scores ≥8 were 11.3 (95% CI: 3.3 to 38.3) and 15.8 (95% CI: 2.0 to 127.8), respectively. Using Cox Proportional Hazards model, the relative risk of mortality for any new admission could be calculated by the equation $RR = e^{0.1032*P}$***, where P = PRISM III-24 scores.***

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Key words: Mortality, Multi-organ dysfunction, Outcome analysis, PRISM III

Introduction

Following the rapid advances in medical therapy and critical care technology over the past 30 years, coupled with the spiralling cost of medical care, outcome analysis including mortality risk prediction has become a challenge for the modern day intensivists.[1] During the early 90s, the focus has shifted from the more traditional quality assurance methods and mortality risk prediction, to another aspect of outcome analysis, that is to identify faulty processes or risk factors that produce poor outcomes. Attempts to address and subsequently eliminate, if not attenuate such factors would lead to an improvement of care. Scarce resources can also be channelled into areas where the greatest amount of benefits could be seen.[2] Most tertiary paediatric intensive care units (PICUs) account for 10% of the total paediatric beds of the hospital, incurring a significant proportion of the costs and budget.

In the context of intensive care management, a rational and objective way to define and quantify severity of illness is through the development of probability models predicting mortality risk.[1,3] Such models will allow an increased understanding of the effectiveness of different medical interventions, development of standards that may guide health care providers in optimizing the use of available medical resources. Moreover, the use of this information may aid in the decision making process by physicians and parents.

The Paediatric Risk of Mortality (PRISM) scoring system is a physiology-based predictor for PICU patients.[4] This was the most widely used system which has been validated in units in Africa, South America, Europe and Asia. Recently, a new scoring system, PRISM III, an updated second generation scoring system, included over 11,000 consecutive admissions in 32 PICUs which have 5-fold more patients than the previous studies, has been validated for use in the United States.[3] PRISM III has resulted in several improvements over the original PRISM. In addition, PRISM III has an important role in clinical study protocols as it acts as a severity index for patient comparison. This then allows the investigators to ascertain whether a new therapy or an investigation affects the patient outcome.[5-7]

The main objective of this study was to assess the risk factors contributing to the increased mortality in our PICU, in particular, the usefulness of the PRISM III scoring system as an outcome indicator.

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Materials and Methods

Characteristics of PICU

The PICU in the National University Hospital (NUH) is an 8-bedded ICU within a 95-bedded Children's Medical Centre, which admits paediatric patients ≤18 years of age, from both medical and surgical subspecialties. Patients undergoing cardiac surgery are admitted to a separate cardiothoracic intensive care unit for immediate postoperative care, and are only transferred to the PICU when they are stable. Because of the location of the hospital, the PICU serves mainly the population in the western region of Singapore. The PICU also caters for critically ill patients in the paediatric liver, bone marrow and renal transplantation programmes. There are at least 3 doctors on duty each day who will answer to calls at the PICU as well as the Accident and Emergency department, thus minimizing the little delay that exists before ICU admissions (lead-time bias). The volume of patients seen in our PICU averages about 29 patients per month or 159 patient-days per month.

Data Collection

This was a cohort study from 1 January to 31 December 1997. Consecutive admissions to the PICU were included. Those patients who stayed less than 2 hours in the PICU were excluded from the study. Re-admissions to the PICU during the same hospitalization were analyzed as separate patients, as there was a possibility of a different outcome at each admission. The exact time of admissions and discharge were recorded to the nearest minute and length of stay calculated to the nearest hour. Diagnosis-related groups were divided into the indication for admission and the primary disease. Three special aspects of clinical care were recorded. Firstly, in those who were on mechanical ventilation, the site of intubation, mode of ventilation, duration and the occurrence of reintubation were recorded. Secondly, for those on renal replacement therapy, the mode, duration, indication and complications were recorded. Finally, the presence of multi-organ dysfunction syndrome as defined by Pollack (Appendix I),[8] involving 3 or more organs (henceforth indicating the presence of MODS in this study) was recorded along with details including the specific systems involved, the timing of onset and the duration of MODS. PRISM III was scored in the first 24 hours only, i.e. PRISM III-24. This involved age-related physiological parameters, including systolic blood pressure, heart rate, temperature, pupillary reflexes, mental status, acidosis (pH and total CO_2), pCO_2, pO_2, glucose, potassium, creatinine, blood urea, white blood cell count, platelet count, and prothrombin or partial thromboplastin time (Appendix II).[3] Outcome analysis was defined either as "death" or "discharged", and where applicable, the causes of death were recorded. Data were collected by one observer supervising 3 other observers to minimize variability.

Statistical Analysis

Statistical analysis was performed using both univariate as well as multivariate analysis. Risk factors that were deemed to significantly contribute to mortality after univariate analysis were further analysed using the multivariate model, namely the Cox Proportional Hazards model. The factors studied included MODS, PRISM III-24, mechanical ventilation, renal replacement therapy, age, and diagnosis-related groups. The Cox Proportional Hazards model was also used to ascertain the relative risks for mortality due to these risk factors.

Results

Over the one-year study period, there were 283 admissions to the PICU, with 13 deaths, which translated to a mortality rate of 4.5%. This was comparable to other reported PICU studies, which ranged from 2.2% to greater than 15%.[3,4,9] In our PICU, pulmonary causes formed the major indication for ICU admission (21.7%), closely followed by general paediatric surgical (14.1%), neurological (13.8%) and cardiovascular (13.0%) problems (Table I). Six patients (2.1%) had some form of renal replacement therapy, 16 patients (5.7%) fulfilled the criteria of MODS involving 3 or more organs, while 89 patients (31.5%) had mechanical ventilation.

Univariate analysis showed that the need for mechanical ventilation, renal replacement therapy, presence of MODS and PRISM III-24 were significantly associated with outcome (P<0.0005) (Table II). With regards to age-related mortality, although there was a tendency for neonates to have a higher mortality, this did not reach statistical significance. For the univariate analysis, the diagnosis-related groups were divided into 2 broad

TABLE I: DIAGNOSIS-RELATED GROUPS AS INDICATION FOR ADMISSION

Diagnosis-related groups	Percentage admission
Medical	
Respiratory System	21.7
Central Nervous System	13.8
Cardiovascular System	13.0
Gastrointestinal System	5.1
Endocrine - Metabolic	3.3
Sepsis	2.5
Renal System	2.5
Haematology - Oncology	1.8
Others	3.3
Surgical	
General Paediatric Surgery	14.1
Cardiothoracic Surgery	8.7
Orthopaedic Surgery	3.3
Ear, Nose & Throat Surgery	1.1
Dental Surgery	0.4

TABLE II: UNIVARIATE ANALYSIS OF RISK FACTORS VERSUS MORTALITY

Risk factor		Mortality (%)	Significance (Fisher's Exact Test)
Mechanical ventilation	No	0.01	*P* <0.0005
	Yes	13.4	
Renal replacement	No	0.03	*P* <0.0005
	Yes	66.7	
MODS	No	0.01	*P* <0.0005
	Yes	56.3	
PRISM III-24 ≥8	No	0.005	*P* <0.0005
	Yes	0.23	
Age ≤1month	No	0.04	ns
	Yes	0.08	
Diagnosis-related group	Surgical	0.01	ns
	Medical	0.06	

MODS: multi-organ dysfunction syndrome; PRISM III-24: Pediatric Risk of Mortality III scores in the first 24 hours; ns: not significant

categories, namely, medical and surgical causes. Although the surgical admissions had only a third of the mortality risk as compared to medical admissions (relative risk = 0.35), this did not reach statistical significance. However, the presence of MODS increased the risk of mortality by 11.3 times (Fig. 1).

The PRISM III-24 scoring system has a range of 0 to 74. Our data suggested that mortality tended to occur when the PRISM III-24 score was 4 or more (Fig. 2). We selected a cut-off point of 8 for further analysis, as the relative risk of mortality was highest at this point, and thus a better predictor of mortality. Analysis of the 2 groups PRISM III-24 <8 and PRISM III-24 ≥8, showed that there was a 15.8 times increased risk of mortality (95% CI: 2.0 to 127.8) in the latter group (Fig. 3).

A multivariate analysis was subsequently performed using Cox Proportional Hazards Model (forward stepwise entry with the following co-variates: PRISM III-24, renal replacement therapy and mechanical ventilation). MODS was excluded from the analysis because it was a more useful late predictor of mortality, since it was a terminal event in many patients. As the mortality rate for patients with MODS was inordinately high, including it as a factor would skew the analysis.

Using this model, only PRISM III-24 score was found to be an independent predictor of mortality. The relative risk of mortality between any 2 scores was given by the equation $RR = e^{0.1032(P1-P0)}$, where P0 and P1 were the respective PRISM III-24 scores. Hence, the relative risk of mortality for any new admission (where P0 = 0) could be further defined by the equation $RR = e^{0.1032*P}$, where P = PRISM III-24 score of the patient. The incremental mortality risks at the various PRISM III-24 scores for this

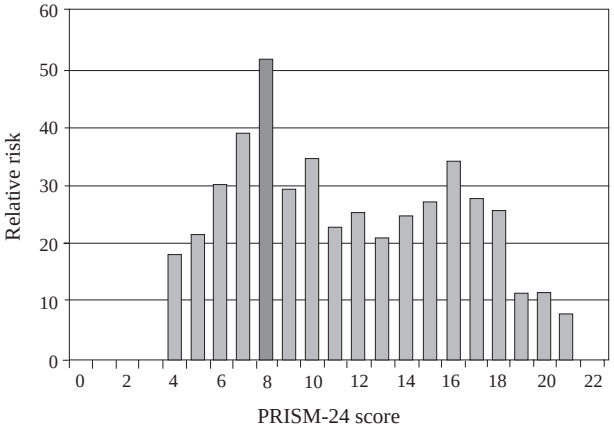

Fig. 2. Bar chart showing that mortality correlated positively with increasing PRSIM-24 scores. The relative risk for mortality was highest when the PRISM III-24 score was 8.

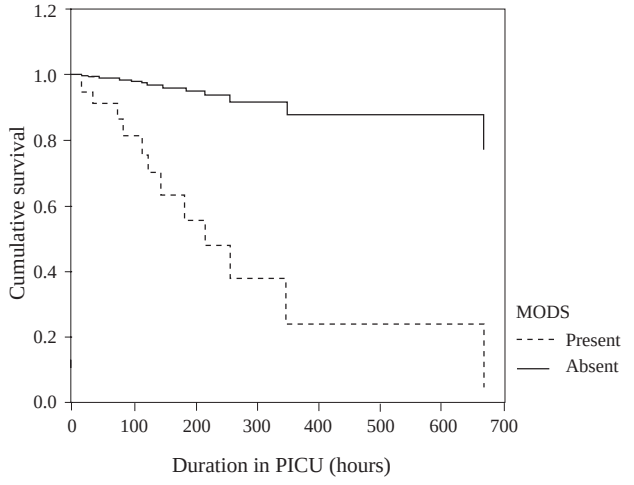

Fig. 1. Survival functions in relation to presence or absence of MODS using the Cox Proportional Hazards model. Relative risk of mortality in the presence of MODS was 11.3 (95% CI: 3.3 to 38.3).

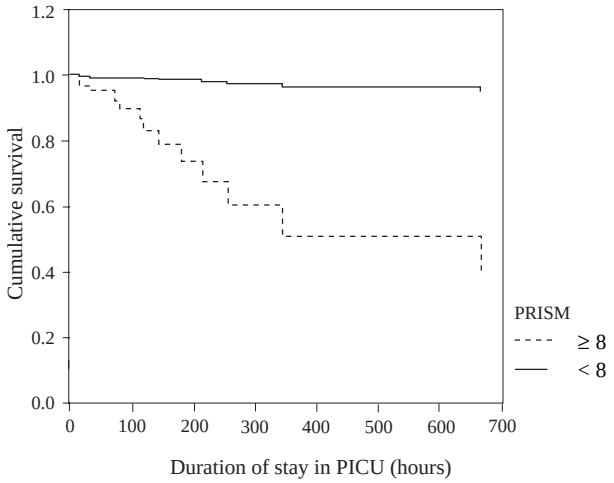

Fig. 3. Survival functions in relation to PRISM-III scores at cut-off score of 8 using the Cox Proportional Hazards model. Relative risk of mortality when PRISM III-24 ≥8 was 15.8 (95% CI: 2.0 to 127.8).

TABLE III: RELATIVE RISK OF MORTALITY AT VARIOUS PRISM III-24 SCORES

PRISM III-24 score	Relative mortality risk
0	1.0
5	1.6
10	2.8
15	4.7
20	8.1
25	13.0
50	185
74	2290

cohort of patients were calculated using this formula, and is outlined in Table III.

Discussion

Modern paediatric intensive care is characterized by increased sophistication, resulting in spiralling costs. Auditing the PICU is thus an integral component in health care planning and management. There is a need to accurately define prognosis, so that the physician can be guided in clinical decision-making, including the appropriateness of therapy.[10,11] Moreover, the impact of new technologies and medical intervention can be assessed in a more objective fashion.

Development of the PRISM III scoring system has greatly enhanced the paediatric intensivist's ability to measure outcomes in the PICU objectively. It permits the quantification of severity of illness through the development of probability models predicting mortality risks.[12] The PRISM III score utilizes appropriate age-adjusted physiologic variables unlike the original PRISM score where age was included as an explicit variable.[4] The logic of this approach was confirmed by our study, which showed that although mortality risk was higher in the neonate compared to the older age groups, this difference was not statistically significant.

This study has identified MODS and PRISM III-24 as effective tools in predicting mortality. Patients with MODS had an 11.3 times increased risk of mortality. MODS, however, suffers from the cumbersome way it collects its data, that is, throughout the whole PICU stay.[8] Thus, it has limited practical uses being a late indicator of mortality in most instances. On the other hand, PRISM III-24 is scored within the first 24 hours of admission. The defined parameters are easily measured, and this scoring system has proven to be more accurate than its predecessor, having been validated in 32 PICUs with a total of 11,165 admissions.[3]

The presence of mechanical ventilation and the need for renal replacement therapy were found to be significant risk factors in our cohort, only on univariate analysis. The small sample size and low number of events (death in this case) could account for the lack of significance on multivariate analysis. Diagnosis-related groups, similarly, suffered from this drawback, as the sample size of 283 was divided into too many categories. Classifying into "surgical" and "medical" admissions also was not related significantly to mortality. Many of the "surgical" admissions were elective cases, which carried low mortality risks, as trauma was the cause for admission into our PICU in only 2.5% of patients.

The PRISM III-24 scoring system was the single most important tool in predicting mortality in our PICU. Our data showed that there was a 15.8 times increase in mortality in children with a PRISM III-24 score of 8 or more (Fig. 3). This information would be useful to the attending physician, as it will allow him to address various ethical and clinical issues arising because of the critical state of the patient.

APPENDIX I [MODS]

Criteria for Failure of Specific Organ Systems

Organ System	Criteria
Cardiovascular	MAP <40 mmHg (infants <12 months) MAP <50 mmHg (children ≥12 months) HR <50 bpm (infants <12 months) HR <40 bpm (children ≥12 months) Cardiac arrest Continuous vasoactive drug infusion for haemodynamic support
Respiratory	RR >90 /min (infants <12 months) RR >70 /min (children ≥12 months) PaO_2 <40 torr (in absence of cyanotic heart disease) $PaCO_2$ >65 torr PaO_2/FiO_2 <250 torr Mechanical ventilation (24 hours if postoperative) Tracheal intubation for airway obstruction or acute respiratory failure
Neurologic	Glasgow Coma Scale <5 Fixed, dilated pupils Persistent (>20 min) ICP >20 torr or requiring therapeutic intervention
Haematologic	Haemoglobin <5 g/dL WBC <3000 cells/mm^3 Platelets <20 000 /mm^3 Disseminated intravascular coagulopathy (PT >20 sec or aPT >60 sec in presence of positive FSP assay)
Renal	BUN >100 mg/dL (35.7 mmol/L) Serum creatinine >2 mg/dL (176 μmol/L) Dialysis
Gastrointestinal	Blood transfusions >20 ml/kg in 24 hours because of GI haemorrhage (endoscopic confirmation optional)
Hepatic	Total bilirubin >5 mg/dL and AST or LDH more than twice normal value (without evidence of haemolysis) Hepatic encephalopathy ≥grade II

AST: aspartate aminotransferase; BUN: blood urea nitrogen; FSP: fibrin split products; GI: gastrointestinal; HR: heart rate; LDH: lactic dehydrogenase; MAP: mean arterial pressure; PT: prothrombin time; aPTT: activated partial thromboplastin time; RR: respiratory rate; WBC: white blood cells

APPENDIX II [PRISM III - 24]

Variable	Age restrictions				Score appointed	Score given
Systolic blood pressure (mmHg)	Neonate	Infant	Child	Adolescent		
	40-55	45-65	55-75	65-85	3	
	<40	<45	<55	<65	7	
Temperature	All ages <33°C or >40°C				3	
Mental status	All ages: stupor or coma (GCS <8)				5	
Heart rate	Neonate	Infant	Child	Adolescent		
	215-225	215-225	185-205	145-155	3	
	>225	>225	>205	>155	4	
Pupillary reflexes	All ages = One pupil fixed, pupil >3mm				7	
	All ages = Both fixed, pupil >3mm				11	
Acidosis (pH) or total CO_2 (mmol/L)	All ages = pH 7.0-7.28 or total CO_2 5-16.9				2	
	All ages = pH <7.0 or total CO_2 <5				6	
pH	All ages = 7.48-7.55				2	
	All ages >7.55				3	
PCO_2 (mmHg)	All ages = 50.0-75.0				1	
	All ages >75.0				3	
Total CO_2 (mmol/L)	All ages >34.0				4	
Arterial PaO_2 (mmHg)	All ages = 42.0-49.9				3	
	All ages <42.0				6	
Glucose	All ages >11.0 mmol/L				2	
Potassium	All ages >6.9 mmol/L				3	
Creatinine (μmol/L)	Neonate	Infant	Child	Adolescent	2	
	>75	>80	>80	>115		
Urea (mmol/L)	Neonate	All other ages			3	
	>4.3	>5.4				
White blood cells	All ages < 3000 cells/mm^3				4	
Prothrombin time (PT) or partial thromboplastin time (PTT)	Neonate	All other ages			3	
	PT >22.0 sec or PTT >85.0 sec	PT >22.0 sec or PTT >57.0 sec				
Platelets (cells/mm^3)	All ages = 100,000 to 200,000				2	
	All ages = 50,000 to 99,999				4	
	<50,000				5	
Total PRISM III-24 score						

In summary, the paediatric intensivist will be faced with increasingly complex and difficult problems, with the development of new life-sustaining techniques that require a vast amount of resources. The physician will find that there is an increasing need to have an objective method of assessment to complement clinical decision-making.[7,13] The use of several such scoring systems may improve predictive power. Furthermore, such methods may need readjustment from time to time, as medical science advances and outcomes differ. Moreover, outcome analysis should not limit itself to survival versus demise, but should also include morbidity. Cost and workload analyses would also benefit from similar models.[1,7-9,14]

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