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Mortality Prediction in a Neurosurgical Intensive Care Unit

Predikce úmrtnosti na neurochirurgické jednotce intenzivní péče

Abstract

Aim: The ability to estimate factors influencing intensive care outcome, especially mortality, is highly important to patient care worldwide. Several clinical variables have been identified for the general intensive care unit (ICU) setting with high mortality predictive ability. However, the application of such predictors in the neurosurgical ICU setting is not yet established. The study was aimed to assess the predictive ability of the variables associated with mortality in a tertiary neurosurgical ICU. *Material and methods:* All neurosurgical patients admitted to ICU during a 5-month period in 2011 were recruited to the study (n = 258). A logistic regression model was used for data analysis and odds ratios were calculated for each predictor. *Results:* The observed hospital mortality rate was 3.49%. The four resulting predictors of mortality were: increased body temperature of 0.1 °C OR = 1.21, 95% CI 1.02–1.44; 1 mg/dl increase in blood glucose level OR = 0.93, 95% CI 0.87–0.99; one point increase on the Glasgow Coma Scale (GCS) eye subscale OR = 0.26, 95% CI 0.07–0.89; and 1 day increase in the length of stay prior to ICU admission OR = 1.14 (1.05–1.24). These predictors were put into a regression model and the area under the receiver operating characteristic curve (AUC) was 0.968, 95% CI 0.923–1.000. *Conclusion:* The body temperature, blood glucose level, GCS eye response and the length of hospital stay prior to ICU admission may be hospital mortality predictors in a neurosurgical ICU. Accordingly, a new predictive model should be developed.

Souhrn

Cíl: Celosvětově je pro péči o pacienty velmi důležité, abychom byli schopni identifikovat faktory, které ovlivňují výsledky intenzivní péče, obzvláště mortalitu. Byla identifikována řada klinických proměnných, které velmi dobře predikují mortalitu na všeobecných jednotkách intenzivní péče (JIP). Použití takových prediktorů na neurochirurgických JIP nebylo zatím zkoumáno. Cílem naší studie bylo zhodnotit prediktivní schopnost proměnných spojených s mortalitou v terciární neurochirurgické JIP. *Meteriál a metody:* Do studie byli zapojeni všichni neurochirurgičtí pacienti přijatí na JIP během pětiměsíčního období roku 2011 (n = 258). Data byla analyzována pomocí logistické regrese a pro každý prediktor bylo vypočítáno odds ratio. *Výsledky:* Zjištěna byla hospitalizační mortalita 3,49 %. Identifikovány byly čtyři prediktory mortality: tělesná teplota zvýšená o 0,1 °C OR = 1,21, 95% CI 1,02–1,44; zvýšení hladiny glukózy v krvi o 1 mg/dl OR = 0,93, 95% CI 0,87–0,99; zvýšení o jeden bod na zrakové podstupnici Glasgow Coma Scale (GCS) OR = 0,26, 95% CI 0,07–0,89; a prodloužení hospitalizace předcházející přijetí na JIP o 1 den OR = 1,14 (1,05–1,24). Tyto prediktory byly vloženy do regresního modelu, přičemž plocha pod křivkou (AUC) činila 0,968, 95% CI 0,923–1,000. *Závěr:* Jako prediktory nemocniční mortality na neurochirurgické JIP mohou sloužit tělesná teplota, hladina glukózy v krvi, zraková odpověď na GCS a délka hospitalizace před přijetím na JIP. Je proto třeba vyvinout nový prediktivní model.

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Autoři deklarují, že v souvislosti s předmětem studie nemají žádné komerční zájmy.
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Key words

temperature – length of stay – Glasgow Coma Scale score – emergency admission – performance

Klíčová slova

teplota – délka hospitalizace – skóre Glasgow Coma Scale – urgentní příjem – výkon

Introduction

There are three main considerations where practice or other differences among intensive care units' (ICU) performance might matter: effectiveness; patient outcomes [1], efficiency; resource utilization for a given outcome, length of stay [2], and qualitative factors; complication rate, morbidity and rate of infection [3]. Nevertheless, the limitation of these factor assessments is still existed because of the unique patient variability especially in neurosurgical patient, e.g., physiologic response to surgery [4], anatomical lesion, endocrine axes path integration [5], patient phenotype [6], ventilator and pain management [7,8], etc.

In order to attenuate this pitfall; Acute Physiology and Chronic Health Evaluation (APACHE) score, Simplified Acute Physiology Score (SAPS) have been initiated. These scales can clinically simplify and categorize critically ill patient with its high mortality predictive ability as shown in the area under the receiver operating characteristic curve (AUC) of 0.76–0.90 [9,10] for general ICU and 0.81–0.89 [11–13] together with sensitivity/specificity over 74% [14] for neurosurgical ICU. However, the differences of scale prediction have not been established, especially in neurosurgical patients lately.

Some articles accentuated the predictive mortality performance of the Glasgow Coma Scale score and its subscales, such as motor score, they found it less time-consuming but simpler and more effective with the AUC of 0.86–0.88 [15,16] and sensitivity/specificity of over 65% [14]. Unfortunately, the use of this less complex system has been questioned because testing was conducted on a sample that included 8% of post-operative neurosurgical patients only [15].

Therefore, this retrospective cohort study was performed to identify parameters associated with hospital mortality and their predictive performance in patients of a large single tertiary neurosurgical ICU.

Tab. 1. Demographics and patient characteristics.

Characteristics		Number (%)
Sex	male	110 (42.6)
	female	148 (57.4)
ASA physical status classification	I	26 (10.08)
	II	143 (55.43)
	III	71 (27.52)
	IV	13 (5.04)
	V	5 (1.94)
Type of admission	elective	244 (94.6)
	emergency	14 (5.4)
Diagnosis	cerebral tumor	202 (78.3)
	cerebral vascular lesion	16 (6.2)
	spinal tumor	4 (1.6)
	spinal spondylosis	11 (4.3)
	other	25 (9.7)
Admission criteria	impaired level of consciousness	34 (9.1)
	impaired airway protection	22 (5.9)
	progressive respiratory impairment or the need for mechanical ventilation	30 (8.0)
	seizures	13 (3.5)
	clinical or evidence of raised intracerebral pressure	40 (10.7)
	threatening medical complications	19 (5.1)
	monitoring purpose	217 (57.9)

ASA – American Society of Anesthesiologists.

Materials and methods

This study had been registered by the Thai Clinical Trials Registry with the identification number TCTR 20151012001. Approval for the study (No. 10/2555) was received from the Prasat Neurological Institutional Ethics Committee (Chairman: Suchart Hanchaipiboonkul) on Feb 8, 2012, and written informed consent was obtained from all patients or legal relatives in case of unconsciousness. All post-operative neurosurgical patients who met ICU admission criteria [17] by having impaired level of consciousness, impaired airway protection postoperatively, progressive respiratory impairment or the need for mechanical ventilation, seizures, clinical or other evidence of raised intracerebral pressure, threatening intraoperative medical complications, or the need for monitoring in a neurosurgical intensive care unit at Prasat Neurological Institute, Bangkok, during February 1–July 31, 2011 were included consecutively. Demographics and parameters including body temperature, mean arterial pressure, heart rate, respiratory rate, arterial oxygen tension (PaO_2), arterial carbon dioxide tension ($PaCO_2$), arterial pH, serum sodium, serum potassium, BUN, creatinine, hematocrit, white blood cell count, Glasgow Coma Scale score (scored 1 on the verbal subscale if the patient was intubated), 24-hour urine output recorded until the time of assessment, blood glucose, albumin, bilirubin and duration of hospital stay before ICU admission were collected at baseline within 30 min after admission by certified neurosurgical registrar nurses. The clinical parameters were measured by a patient monitoring system (Drager, Infinity Delta XL, Germany, 2011) and laboratory testing was done with a standardized automatic machine (Beckman Coulter hematology analyzer, XLH 780, USA 2011; Beckman Coulter chemistry analyzer, Unicel DXC 800, USA, 2010). Hospital death was derived from medical records with the Glasgow Outcome Scale at the day of discharge.

For demographic data, descriptive statistics were analyzed and reported as mean, standard deviation (SD), median, minimum-maximum, 95% confidence interval (95% CI), number and percent. Logistic regression model was calculated using Stata software version 13.1 (Texas, USA, 2013) to determine the association between the measured pa-

Tab. 2. Bivariated analysis of study variables categorized in tertiles on hospital mortality.

Variables	N	Mortality (%)	Means	Median (range)	Crude odds ratio (95% CI)	p
age (years)			447.90 ± 15.11	47.5 (15–87)	0.71 (0.31 –1.66)	0.424
≤ 40	86	0.05				
41–55	89	0.03				
> 55	83	0.02				
heart rate (/min)			82.42 ± 16.54	80 (50–144)	1.87 (0.79–4.42)	0.138
≤ 74	97	0.01				
75–88	81	0.05				
> 88	80	0.05				
MAP (mm Hg)			108.29 ± 20.88	104 (58–166)	1.08 (0.47–2.47)	0.859
≤ 97	89	0.03				
98–116	92	0.03				
> 116	77	0.04				
temperature (X10°C)			36.43 ± 0.75	36.5 (34.0–39.0)	3.05 (1.12–8.26)	0.014*
≤ 36.1	99	–				
36.2–36.8	83	0.05				
> 36.8	76	0.07				
RR (/min)			18.22 ± 3.93	18 (10–28)	0.59 (0.22 –1.54)	0.256
≤ 16	101	0.04				
17–20	99	0.05				
> 20	58	–				
hematocrit (%)			34.99 ± 4.62	35.15 (22–49)	0.98 (0.43–2.23)	0.965
≤ 33.1	83	0.05				
33.2–36.9	89	0.01				
> 36.9	86	0.05				
WBC count (X103/μL)			13.99 ± 5.62	13.3 (4.4–38.4)	0.39 (0.14–1.06)	0.041*
≤ 11.45	90	0.07				
11.46–15.45	85	0.02				
> 15.45	83	0.01				
urine output per day (CC)			2,665.78 ± 1,082.23	2,460 (755–8,350)	0.99 (0.44–2.24)	0.989
≤ 2 150	86	0.03				
2 151–2 950	85	0.04				
> 2 950	87	0.03				
blood glucose (mg/dl)			165.82 ± 50.67	157.5 (87–442)	0.36 (0.13–0.97)	0.025*
≤ 138	83	0.06				
138.1–177.5	84	0.05				
> 177.5	91	–				
BUN (mg/dl)			10.51 ± 5.20	9.5 (3–39)	0.94 (0.42–2.11)	0.890
≤ 8	99	0.04				
8.1–11	79	0.03				
> 11	80	0.04				
creatinine (mg/dl)			0.80 ± 0.31	0.7 (0.4–3.2)	0.51 (0.18–1.42)	0.177
≤ 0.6	86	0.05				
0.61–0.9	121	0.04				
> 0.9	51	–				
sodium (mEq/l)			138.06 ± 3.79	138.3 (124.6–155.7)	0.59 (0.24–1.41)	0.219
≤ 137	86	0.05				
137.1–139.4	89	0.04				
> 139.4	83	0.01				

Tab. 2 – continuing. Bivariated analysis of study variables categorized in tertiles on hospital mortality.

Variables	N	Mortality (%)	Means	Median (range)	Crude odds ratio (95% CI)	p
albumin (g/dl)			3.05 ± 0.52	3.1 (1.4–5.4)	0.89 (0.39–2.00)	0.771
≤ 2.9	110	0.05				
2.91–3.3	75	0.01				
> 3.3	73	0.04				
bilirubin (mg/dl)			0.80 ± 0.38	0.75 (0.1–3.4)	0.69 (0.28–1.70)	0.408
≤ 0.6	97	0.04				
0.61–0.9	96	0.04				
> 0.9	65	0.02				
PaO_2 (mm Hg)			202.06 ± 87.02	200.5 (58–416)	0.84 (0.37–1.89)	0.670
≤ 154	87	0.05				
154.1–253.5	83	0.02				
> 253.5	88	0.03				
$PaCO_2$ (mm Hg)			37.98 ± 6.92	38 (17–59)	0.89 (0.39–2.05)	0.782
≤ 35	88	0.03				
35.01–41	92	0.04				
> 41	78	0.03				
pH (X100)			7.38 ± 0.07	7.38 (7.11–7.60)	2.34 (0.92–5.90)	0.056
≤ 7.35	92	–				
7.36–7.41	88	0.06				
>7.41	78	0.05				
GCS			10.36 ± 3.57	12 (3–15)	0.45 (0.10–2.05)	0.261
3–12	160	0.04				
13–14	89	0.02				
15	9	–				
GCSe			2.67 ± 0.93	3 (1–4)	0.15 (0.04–0.60)	0.006*
1–2	62	0.10				
3–4	196	0.02				
GCSv			2.69 ± 1.35	3 (1–5)	0.77 (0.19–3.15)	0.713
1–3	157	0.04				
4–5	101	0.03				
GCSm			5.00 ± 1.76	6 (1–6)	0.34 (0.08–1.41)	0.165
1–3	39	0.08				
4–6	219	0.03				
potassium (mEg/l)			3.79 ± 0.41	3.8 (2.57–5.11)	0.36 (0.13–0.99)	0.027*
≤ 3.63	84	0.07				
3.64–3.97	85	0.02				
> 3.97	89	0.01				
length of stay before ICU admission (days)			6.04 ± 9.51	3 (0–97)	19.19 (4.43–83.17)	< 0.001*
< 3	132	0.01				
3–24	119	0.03				
> 24	7	0.57				

N – number, MAP – mean arterial pressure, RR – respiratory rate, GCS – Glasgow coma score, GCSe – eye subscale in Glasgow coma scale score, GCSv – verbal subscale in Glasgow coma scale score, GCSm – motor scale in Glasgow coma scale score, ICU – intensive care unit.
*Statistical significance at $p < 0.05$.

rameters and mortality. The values were presented as odds ratio and 95% CI. The area under the receiver operating characteristic curve (AUC) was analyzed to demonstrate the performance of the parameters and hospital mortality.

Results

258 patients fulfilling the admission criteria were enrolled. The mean age was 47.90 ± 15.11 years while the APACHE II score was 16.54 ± 5.85. The mean duration of surgery was 192.23 ± 87.57 min and the procedures were done as followed: craniotomy with lesion removal in 187 (72.48%) cases, craniotomy with vascular clipping in 15 (5.81%) cases, spinal surgery in 15 (5.81%) cases and other procedure in 41 (15.89%) cases. Overall mortality was 9 (3.49%) and there were no deaths during ICU admission. The mean ± SD and median (min.–max.) duration of patient stay in ICU was 2.36 ± 2.19 days and 2 (1–25) days. The median (min.–max.) length of hospitalization before ICU admission was 3 (0–97) days. Patient demographics and characteristics are shown in Tab. 1.

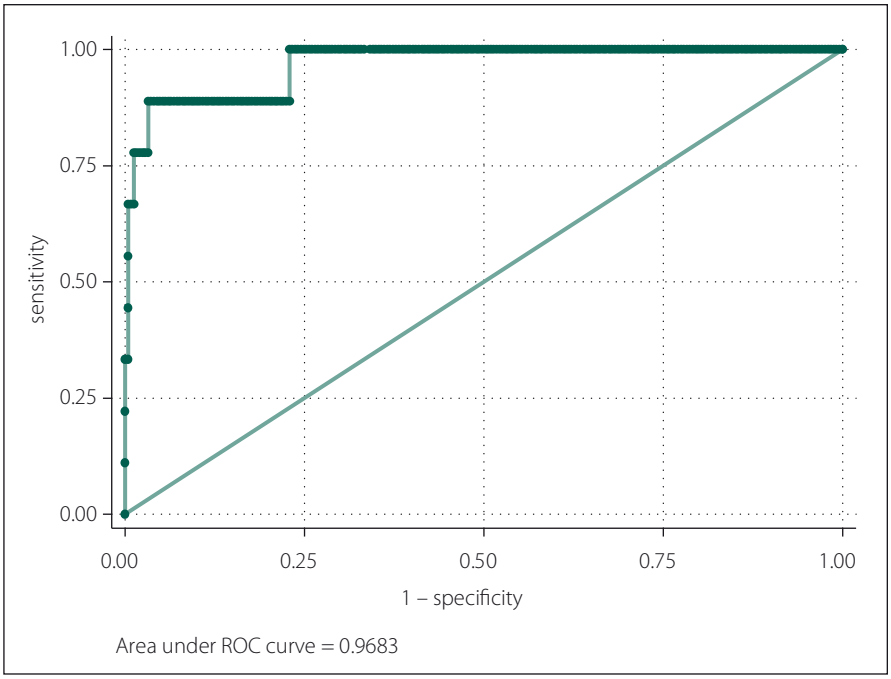
Among the 258 patients, the incidences of comorbidities, i.e. renal failure, acquired immune deficiency syndrome (AIDS), hepatic failure, lymphoma, metastatic cancer, leukemia, compromised immune system and cirrhosis were unidentified. The bivariate and multivariate analysis of parameters that possibly affected hospital mortality are presented in Tab. 2 and Tab. 3, resp. Crude odds ratio (95% CI) for type of admission (elective vs. emergency cases) was 2.27 (0.26–19.53; p = 0.497) and it was 0.87 (0.46–1.65; p = 0.660) for the comparison between diagnoses (cerebral tumor vs. other).

The AUC (95% CI) for the impact of body temperature, blood glucose, eye subscale of the Glasgow Coma Scale and duration of hospitalization prior to ICU admission on hospital mortality was 0.968 (0.923–1.000) as shown in Graph 1.

Tab. 3. Multivariated analysis of study variables on hospital mortality.

Variables	Adjusted odds ratio (95%CI)	p
temperature (incremented every 0.1 °C)	1.21 (1.02–1.44)	0.030*
blood glucose (incremented every 1 mg/dl)	0.93 (0.87–0.99)	0.042*
GCSe (incremented every single score)	0.26 (0.07–0.89)	0.032*
length of stay before ICU admission (incremented every single day)	1.14 (1.05–1.24)	0.003*

GCSe – Eye subscale in Glasgow Coma Scale score, ICU – intensive care unit.
* Statistical significance at p < 0.05.



Graph. 1. The receiver operating characteristic curve of the model containing body temperature, blood glucose, eye subscale in Glasgow coma scale score and length of stay before ICU admission to the hospital mortality.

Discussion

Mortality prediction models for neurosurgical patients have not yet been established. Various scores have good discrimination in neurosurgical patients but have limited usage in this specific group of patients. The study variables included in our analysis were selected from the process of critical literature reviews that included both neurological and non-neurological searches. The radiologic finding was the abundance for data collection because of the time limited for primary evaluation. Together with the length of ventilator days and pathological report, radiological examination was initially considered for inclusion in the predictive model but the evidence showed to be insufficiently robust [18].

In this study, body temperature, duration of hospitalization prior to ICU admission, blood glucose and Glasgow Coma Scale eye subscale were demonstrated as the parameters affected to the mortality. The AUC statistics were not as strong as that for the complex scoring system but these can represent specifically well for the post-operative neurosurgical patients.

Mortality in the majority of neurosurgical patient is the consequence of primary neuronal damage but secondary insults from cascade events including brain edema, ischemia, excitotoxicity and dysregulation of homeostasis leading to cell death may occur [19]. Hyperthermia has for many years been known to have this harmful effect [20,21]. The odds ratio of 0.43 was reported for the association between lower body temperature and favorable outcome in severe stroke patient [22]. Additionally, many authors suggest that body temperature as well as any other vital signs, oxygenation and ventilation should be monitored and managed as part of immediate intensive care in traumatic brain injury patients, particularly hemorrhage stroke and cerebral infarction subgroups [23–25]. Interestingly, in

another study of neurosurgical patients, duration of hospital stay before ICU admission and duration of ICU stay in non-survivors were longer than that of survivors [26]. The severe grading derangement in physiology and pathology which possibly lead to acute clinical deterioration among the critically ill patients needed more time to optimize, correct and manage, were explained. However, the unavoidable morbidity associated with patients' condition might occur and result in mortality in the non-survivors group.

In our study, blood glucose level was a factor affecting mortality but had lower predictive power than in other subgroups of traumatic brain injury, or intracerebral hemorrhage with severe brain injury [27–29]. The impact of low mortality rate has previously been mentioned. Despite the statistically significant difference in blood glucose levels between survivors (168 ± 73.6 mg/%) and non-survivors (192 ± 101.6 mg/%) reported by Ramesh et al., multivariable analysis did not provide statistically significant findings [30]. However, the report of Natarajan et al which studied in neuromedical ICU especially in acute stroke patient, the initial blood glucose of over 115 mg/% was the main predictor of death and poor outcome at 90 days after discharge [31].

There were some studies showed the evidence of satisfaction of Glasgow Coma Scale score for the mortality prediction because of its simple and effective [11,15] but the authors discovered the inferiority in this study. The pitfall has been mentioned about its exclusion of the clinical brainstem indicators, furthermore, in some situation the score may possibly be obscured by intubation, aphasia or even language barrier [32] similar to our finding. The confrontation and the utilization with this issue should be concerned.

The limitations of our study to be realized were the low mortality rate in this specific group of patients even the study was performed in a largest neurosurgical institute of Thailand. By the way, the multicenter study may strengthen more appropriated model to this prediction. Secondly, most of the patients recruited were diagnosed cerebral tumor, only few were intracranial vascular lesion and none was traumatic brain injuries. Therefore the physiology, pathology, criteria of ICU admission and the withdrawal of treatment policy difference should be taken to account before generalized these results to any circumstances.

In conclusion, it should be emphasized that the accurate mortality prediction tools in critically ill neurosurgical patient is still needed. Body temperature, length of hospitalization before ICU admission, blood glucose and GCS eye subscale are the acceptable predictive variables for hospital mortality. The ongoing improvement of evidence based and economic concerned for the mortality predictor as well as the appropriated models should be continued to counterclaim the effectiveness and efficacy in patient care worldwide.

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