THE SEVERITY OF DISEASE MEASUREMENTS AMONG THAI MEDICAL INTENSIVE CARE UNIT PATIENTS

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Abstract. Since the diversity of diseases and complexities of treatments keeps on increasing, a precision of evaluation system that shows a strong and stable relationship to outcomes is needed. The APACHE II severity of disease classification system is an example that proved to be valid for large numbers of patients in different countries. Data from 334 Thai medical ICU patients were collected prospectively in order to validate the APACHE II system, and compare the findings with previous reports. Despite some differences in disease categories, the results showed close relation between APACHE II scores and the hospital mortality rate. The predictive power for death was strong with a specificity of 95% and correct prediction of 83% at the risk level of 0.5. The actual to predicted death ratio, an indicator of hospital performance, in this studied group was 1.17 and was close to the findings of most centers in USA. By providing a measure of severity of disease, APACHE II classification system can provide Thai researchers with a useful tool for clinical researches and improving the treatment of critically ill patients.

INTRODUCTION

As the complexity of medical practice has increased, intensive care service has become a crucial portion of critical care medicine. The intensive care unit, where most of the life threatening vital organ failure conditions are monitored and treated, therefore rapidly gained its favor since the 1960s (Relman, 1980). To expect the lowest mortality and best outcome, invasive monitoring and high-technology treatment could not be avoided. These approaches exposed patients to new iatrogenic risks and to increased costs of medical care (Puri *et al,* 1980; Relman, 1980; Schroead *et al,* 1979). Furthermore, the ability to support multiple organ-system failure may lead to prolonged suffering and postponement of inevitable deaths, particulary in some chronically ill and elderly patients. This unplanned and unlimited growth of medical expenditure became a major concern in industrial and developing countries which tried to keep up with modern technology (Knaus *et al,* 1982). Questions then arose as to how to weigh up the risks and the benefits of ICU treatment and how to limit treatment of the chronically ill. A good precision of evaluation is undoubtly needed to reach such goals. However, this precision has been limited by the diversity of diseases and differing arrangements among hospitals providing such care (Relman, 1980; Knaus *et al,* 1986). A severity of disease classification system which is able to show a strong, stable relationship between severity of illness and subsequent probability of death from various diseases will, therefore, be appropriate for this precision. A good severity assessment system not only helps physicians in rationing of ICU services, but also in comparing the overall severity and efficacy of treatment among different ICU settings in the same or different countries (Knaus *et al,* 1982; 1986; Strauss *et al,* 1986). Furthermore, it plays an important role in clinical research by giving an objective weighing system to help matching groups of patients with equal severity, prior to treatment allocation (Knaus *et al,* 1984). Acute physiology and chronic health evaluation (APACHE) developed in 1981 was an example of physiologically based objective classification systems (Knaus *et al,* 1981). It was tested and showed a strong relationship between severity of illness and probability of death over a wide variety of ICU treated conditions (Knaus *et al,* 1981, 1982, 1982, 1984). The system was refined and simplified later into the APACHE II which used information from fewer, readily available measurements but maintained the accuracy of the original system (Knaus *et al,* 1985). It was designed to stratify patients prognostically by risk so that different treatment programs could be more accurately compared. Since the original report, APACHE II has been used in rationing and evaluation of outcome of intensive care (Knaus *et al,* 1986; Strauss *et al,* 1986), stratification of prognosis in specific groups of diseases (Johnson *et al,* 1986; Knaus *et al,* 1989; Macher *et al,* 1989), adjunct to treatment decision making (Chang and Jacob, 1986), and management of intensive care units (Wagner *et al,* 1987). Most of these studies were done in the western world where people had better economic status and more technological advancement when compared to developing Southeast Asian countries. We therefore carried out this study in the medical intensive care unit of Ramathibodi Hospital, Thailand, in order to validate the APACHE II severity of disease classification system. Results from the study which included the overall patients' profile, disease severity, outcome of treatment, and hospital performance were also compared with previous worldwide reports.

MATERIALS AND METHODS

Intensive Care Unit structure

The medical intensive care unit of the Department of Medicine, Ramathibodi Hospital, Mahidol University, was a mixed medical intensive care and coronary care unit. It had 8 beds in the first six months of study and was extended to 10 beds in the rest of the period. The unit was fully equipped with both invasive and non-invasive cardiac and respiratory monitoring systems, volume ventilators, and hemodialysers. Two teams of medical house staff, two persons per team, undertook 24 hour in-unit physician coverage. Admission, disharge, and most treatment decisions were guided by fulltime attending physicians and the chief of ICU. Cases admitted to the unit were primarily medical patients, surgical admissions were seldom and limited to patients from medical wards who underwent emergency surgery. Formal training programs and continuing education for house staff physicians were provided and arranged by the chief of ICU. At the same time, intensive care nurses acquired knowledge and skill from the attending staff, the chief of ICU and clinical nurse specialists. Patient to nurse ratio in the unit was approximately 1.5:1.

Patient data collection

Data were collected prospectively from every case admitted to the ICU during June 1989 to June 1990. These were recorded in the standard forms by one of the authors (SK) and the house staff in charge. The same author was then responsible for data editing, extensive error checking, and analysis. Excluded from the study were patients age under 15, and patients who died shortly after admission before complete laboratory tests and evaluation could be done.

Initial information collected from each patient included age, sex, major indication for ICU admission, other concomittent diagnoses, and operative status. After 24 hours of ICU stay, each clinical record was reviewed for physiologic data following the APACHE II system (Knaus *et al,* 1985). These included the 12 routine physiologic measurements, along with patient's age and chronic health status. They were scaled to the assigned weight points and summed up to be the first day APACHE II score. Detailed definitions for the components of APACHE II are provided in Fig 1. Data collection, which included the ICU and hospital outcome, was intended not to interfere with the primary physician's investigation plans and decision concerning treatment.

Analysis

Descriptive analysis was done concerning general patients' profiles, major diagnoses and outcome of treatments as expressed by hospital mortality rate (Table 1, 2; Fig 2). Patients' APACHE II scores were tabulated, within five points, aganist number of patients and hospital mortality rate (Fig 3, 4). Certain aspects of the results from the survivors were compared with the non survivors and the levels of significance were tested by unpaired T-Tests (Table 3).

The probability of hospital death for each patient was estimated using a multiple logistic regression analysis that included the patient's diagnostic category weight, the first day APACHE II score, and the emergency postoperative status (Knaus *et al,* 1985). Diseases or diagnostic categories were classified and weighted according to the APACHE II serverity of disease classification system (Knaus *et al,* 1985) (Table 4). This pretreatment risk stratification of the patients were tabulated and the actual and predicted death rates were compared (Fig 4). Classification matrices at different decision criteria or predicted risk levels were derived to

The apache II severity of disease classification system

Physiologic variable	High abnormal range					Low abnormal range			
	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature - rectal (°C)	O ≥ 41°	O 39°-40.9°		O 38.5°-38.9°	O 36°-38.4°	O 34°-35.9°	O 32°-33.9°	O 30°-31.9°	O ≤ 29.9°
Mean arterial pressure-mmHg	O ≥ 160	O 130-159	O 110-129		O 70-109		O 50-69		O ≤ 49
Heart rate (ventricular response)	O ≥ 180	O 140-179	O 110-139		O 70-109		O 55-69	O 40-54	O ≤ 39
Respiratory rate- (non-ventilated or ventilated)	O ≥ 50	O 35-49		O 25-34	O 12-24	O 10-11	O 6-9		O ≤ 5
Oxygenation: A-aDO$_2$ or PaO$_2$ (mm Hg) a. FIO$_2$ ≥ 0.5 record A-aDO$_2$	O ≥ 500	O 350-499	O 200-349		O < 200				O
b. FIO$_2$ < 0.5 record only PaO$_2$					O PO$_2$ > 70	O PO$_2$ 61-70		O PO$_2$ 55-60	O PO$_2$ < 55
Arterial pH	O ≥ 77	O 7.6-7.69		O 7.5-7.59	O 7.33-7.49		O 7.25-7.32	O 7.15-7.24	O < 7.15
Serum sodium (mMol/l)	O ≥ 180	O 160-179	O 155-159	O 150-154	O 130-149		O 120-129	O 111-119	O < 110
Serum potassium (mMol/l)	O ≥ 7	O 6-6.9		O 5.5-5.9	O 3.5-5.4	O 3-3.4	O 2.5-2.9		O < 2.5
Serum creatinine (mg/100 ml) (Double point score for acute renal failure)	O ≥3.5	O 2-3.4	O 1.5-1.9		O 0.6-1.4		O < 0.6		
Hematocrit (%)	O ≥ 60		O 50-59.9	O 46-49.9	O 30-45.9		O 20-29.9		O < 20
White blood count (total/mm3) (in 1,000s)	O ≥ 40		O 20-39.9	O 15-19.9	O 3-14.9		O 1-2.9		O < 1
Glasgow coma score (GCS): Score = 15 minus actual GCS									
[A] Total Acute physiology score (APS): Sum of the 12 individual variable points									
Serum HCO$_3$ (venous-mMol/l) (Not preferred, use if no ABGs)	O ≥ 52	O 41-51.9		O 32-40.9	O 22-31.9		O 18-21.9	O 15-17.9	O < 15

[B] Age points:
Assign points to age as follows:

Age(yrs)	Points
≤ 44	0
45-54	2
55-64	3
65-74	5
≥ 75	6

[C] Chronic health points
If the patient has a history of severe organ system insufficiency or is immuno-compromised assign points as follows:

a. for nonoperative or emergency postoperative patients - 5 points
b. for elective postoperative patients - 2 points

Definitions
Organ insufficiency or immuno-compromised state must have been evident prior to this hospital admission and conform to the following criteria:

Liver: Biopsy proven cirrhosis and documented portal hypertension; episodes of past upper GI bleeding attributed to portal hypertension; or prior episodes of hepatic failure/encephalopathy/coma.

Cardiovascular: New York Heart Association Class IV.

Respiratory: Chronic restrictive, obstructive, or vascular disease resulting in severe exercise restriction, *i.e.*, unable to climb stairs or perform household duties; or documented chronic hypoxia, hypercapnia, secondary polycythermia, severe pulmonary hypertension (>40mmHg), or respirator cependency.
Renal: Receiving chronic dialysis.

Immuno-compromised: The patient has received therapy that suppresses resistance to infection, e.g., immuno-suppression, chemotherapy, radiation, long term or recent high dose steroids, or has a disease that is sulliciently advanced to suppress resistance to infection. e.g., leukemra, lymphoma, AIDS.

APACHE II score
Sum of [A] + [B] + [C]

[A] APS points ____________
[B] Age points ____________
[C] Chronic health points ____________
Total APACHE II ____________

Fig 1–The APACHE II severity of disease classification system.

demonstrate the predictive power of APACHE II system when applied to this study group of Thai patients (Table 5).

Table 1

Patient profiles.

Variable	Mean ± SD
Age (year)	56.01 ± 18.23 (15 - 98)*
Diagnoses (number)	2.54 ± 1.18 (1 - 6)*
ICU stay (day)	6.56 ± 7.11 (1 - 41)*
Hospital stay (day)	18.78 ± 33.61 (1 - 376)*

( )* minimum to maximum values
Total cases = 334; female : male = 171 : 163
Hospital death = 117 (35.02%)

RESULTS

There were 334 cases enrolled in this study with more female than male patients (Table 1). The overall hospital mortality rate was 35.02%. Most patients had multiple organ system failure and the average number of dignoses per patient was 2.54 ± 1.8. The age distribution shown in Fig 2 indicated that more than fifty percent of cases populated in the age range 51-80, and patients at the extreme age groups, below 21 and above 80 year-old, accounted for only 10 percent of cases.

Table 2 lists the major indications for ICU admissions and their corresponding mortality rates. In addition to the worldwide common medical indications (cardiac, respiratory, and infectious), there were some tropical disease conditions such as complicated malaria, severe tetanus, leptospirosis,

Table 2

Major indications for ICU admission.

Indication	Cases	Death (%)
Cardiovascular		
Acute myocardial infarction	54	10 (18.51)
Unstable angina	39	2 (5.12)
Arrhythmia	25	2 (8.0)
Pulmonary edema	18	10 (55.55)
Conduction disorder	10	1 (10)
Pulmonary		
COPD	11	4 (36.36)
Bronchial asthma	8	0 (0)
Fulminating pneumonia	17	9 (52.94)
ARDS	9	8 (88.88)
Infectious		
Septic shock	27	19 (70.37)
Severe sepsis	20	9 (45)
Complicated malaria	8	1 (12.5)
Severe tetanus	3	2 (66)
Post cardio-pulmonary resuscitation	25	20 (80)
DKA/Hyperosmolar	5	0 (0)
Paraquat poisoning	4	3 (75)
Intracranial hemorrhage	8	6 (75)
Emergency postoperative	11	2 (18.18)
Miscellaneous	32	9 (28.12)
Total	334	117

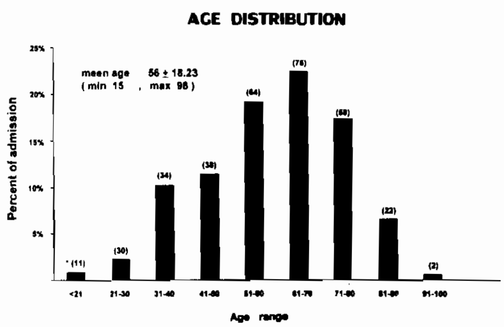

Fig 2–Number of patients presented by percents of admission at various patients's age range.
*( ) - actual number of cases

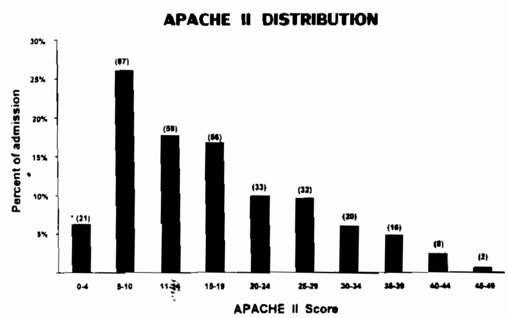

Fig 3–Number of patients presented by percents of admission at various APACHE II score ranges.
*( ) - actual number of cases

and paraquat poisoning. Surgical indications accounted for only 3.3% of total admissions. The highest mortality rates fell in the groups of patients admitted following cardiopulmonary resuscitation, ARDS, septic shock, paraquat poisoning, and intracerebral hemorrhage. Comparisons between survivors and non-survivors showed no statistical difference in most epidemiological variables (Table 3). However, striking differences were found in the stratified acute physiology, chronic health, and

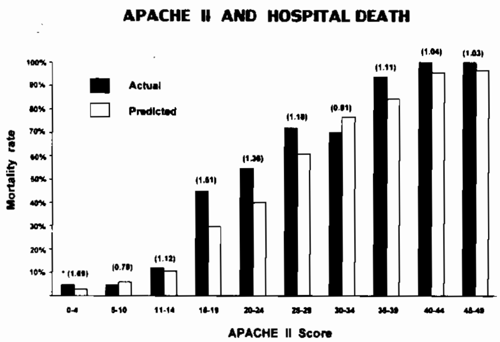

Fig 4–Illustration of the actual and predicted hospital mortality rate at various APACHE II score ranges. The predicted mortality rate in each group was calculated by the summation of individual's risks of death divided by the number of patients of the group.

APACHE II scores.

The distribution of APACHE II scores shown in Fig 3 demonstated that over 60% of cases had APACHE II scores in the range between 5 to 19. The highest and the mean ± SD APACHE II scores of the group were 46 and 16.57 ± 10.41 respectively. Plots of APACHE II score versus actual and predicted hospital mortality rate are shown in Fig 4. The APACHE II score range that gave a 50% mortality rate in this group was 20-24, and more than 75% of patients died if the scores exceeded 35. The highest survivor's APACHE II score in this group was 36. Calculation of the predicted hospital death revealed the group predicted mortality rate of 29.79%. This, together with the actual hospital death rate, resulted in an actual to predicted hospital death ratio of 1.17. Actually, the ratios were close to 1 in most APACHE II score ranges, except for the ranges 15-19 and 20-24, which had ratios of 1.54 and 1.37, respectively. The predictive power of the APACHE II system for this group of patients is shown in the classification matrices derived at different risk levels of death (Table 4). For a given risk level, every patient with a risk of death equal to or greater than the risk level was predicted to die. At the risk level of 50%, the specificity, positive predictive value, and correct prediction for death of the APACHE II system were 95%, 88%, and 83%, respectively. Both specificity and positive predictive value for death increased with the increasing levels of risk, and approached 100% at the risk level of 80%. However, the increase in specificity was achieved at the expense of sensitivity.

DISCUSSION

The medical intensive care unit of Ramathibodi Hospital, Mahidol University has been established for over fifteen years. Few studies were done in the

Table 3

A comparison of survivors and non-survivors.

	Survivors (n = 217) mean ± SD	Non-survivors (n = 117) mean ± SD
Age	55.56 ± 17.41	56.85 ± 19.71
Number of diagnosis	2.28 ± 1.06	3.00 ± 1.26
*APS	8.06 ± 6.24	20.74 ± 9.82 (p = 0.000)+
**Chronic health	0.80 ± 1.89	1.96 ± 2.69 (p = 0.000)+
***APACHE II	11.72 ± 7.14	25.56 ± 9.53 (p = 0.000)+
Risk of death	14.57 ± 5.06	57.20 ± 6.01 (p = 0.000)+
ICU stay (day)	6.17 ± 5.96	7.27 ± 8.84
Hospital stay (day)	19.57 ± 33.47	17.32 ± 33.96

* Acute physiology score
** Chronic health points
*** APACHE II score (see Fig 1)
+ Statistically significant

Table 4

Calculation for risk of death and diagnostic category weight.

Calculation of risk of hospital death (R) was done following the formula:
ln (R/1-R) = - 3.517 + (APACHE II score × 0.146) + 0.603 (only if post emergency surgery + (diagnostic category weight)

Diagnostic categories and weighting system

Diagnostic category		Weighting
A. Nonoperative patients		
Respiratory failure from :	Asthma/allergy	- 2.108
	COPD	- 0.367
	Non cardiogenic pulmonary edema	- 0.251
	Post respiratory arrest	- 0.168
	Aspiration/poisoning/toxic	- 0.142
	Pulmonary embolus	- 0.128
	Infection	0
	Neoplasm	0.891
Cardiovascular failure from :	Hypertension	- 1.798
	Rhythm disturbance	- 1.368
	Congestive heart failure	- 0.424
	Hemorrhagic shock/hypovolemic	0.493
	Coronary artery disease	- 0.191
	Sepsis	0.113
	Post cardiac arrest	0.393
	Cardiogenic shock	- 0.259
	Dissecting aneurysm	0.731
Neurologic :	Siezure disorder	- 0.584
	ICH/SDH/SAH	0.723
Others :	Drug overdose	- 3.353
	Diabetic ketoacidosis	- 1.507
	GI bleeding	0.334
If not one of the specific groups above, then which major vital organ system was the principle reason for admission?		
	Metabolic/renal	- 0.885
	Respiratory	- 0.890
	Neurologic	- 0.759
	Cardiovascular	0.470
	Gastrointestinal	0.501
B. Postoperative patients		
	Hemorrhagic shock	- 0.682
	GI bleeding	- 0.617
	GI perforation/obstruction	0.060
	Sepsis	0.113

Table 5

Classification matrices at different risk levels of death for 334 ICU patients.

Level of risk*	Predicted			Value of prediction for death (%)				
	Alive	Dead	Total	Sensitivity	Specificity	Predictive value +ve	Predictive value -ve	Correct prediction
40%				75.21%	90.75%	81.48%	87.16%	85.32%
Actual alive	197	20	217					
Actual dead	29	88	117					
Total	226	108	334					
50%				60%	95%	88%	81%	83%
Actual alive	207	10	217					
Actual dead	47	70	117					
Total	254	80	334					
60%				47.0%	96.31%	87.3%	77.12%	79.04%
Actual alive	209	8	217					
Actual dead	62	55	117					
Total	271	63	334					
70%				37%	97%	88%	74%	76%
Actual alive	211	6	217					
Actual dead	74	43	117					
Total	285	49	334					
80%				27.35%	99.07%	94.11%	71.66%	73.95%
Actual alive	215	2	217					
Actual dead	85	32	117					
Total	300	34	334					
90%				13.67%	100%	100%	68.23%	69.76%
Actual alive	217	0	217					
Actual dead	101	16	117					
Total	318	16	334					

* Patients with risk of death equal to or greater than a given risk level were predicted to die.

past concerning epidemiological aspects, costs, and out comes (Buri *et al*, 1987; 1987). These studies illustrated the high cost of ICU treatment along with some inappropriate and improper investigations and treatments, particulary when comparisons between ward and ICU patients were done. However, these evaluations were mostly subjective, lacked precision and disease severities were not prognostically stratified. These made comparisons, in various aspects, between different institutions more difficult and it was not possible to evaluate the cost effectiveness of ICU treatments. This prospective study was done to validate the APACHE II severity of disease classification system when applied to this group of tropical disease patients. It was hoped that the clinical profiles and hospital performance could be evaluated and compared with the previous worldwide studies (Knaus *et al*, 1982, 1986; Chang and Jacobs, 1986).

The Thai patients' age and sex distribution were closely resemble to the USA patients (Knaus *et al*, 1982). Most patients (77%) were over 40 years of age with equal proportion of males to females. However, the Thai patients were significantly older than ICU patients in France and Saudi Arabia (Knaus *et al*, 1982; Chang and Jacobs, 1986). Furthermore, the mean ICU stay of 7 days was close to those found in most places in USA, but shorter than the French experience (11.08 days). This may partly be explained by the difference in hospital systems, and by admission and discharge criteria. Our unpublished data showed that there were 12-20 patients in the Department of Medicine who needed ventilatory support each day. This disproportionate demand and supply of ICU beds forced patients to be discharged from the ICU earlier, in order to yield a more rapid turnover rate. Like the American and French experiences, cardiovascular conditions were the most common admission indications (51%) in our group. This was followed by various sepsis conditions (23%), which included the well known tropical diseases of Southeast Asian countries such as complicated malaria, tetanus, leptospirosis, melioidosis and disseminated strongyloidosis. Since most patients in the sepsis group had multiple organ system failure, the mortality rate remained very high (62.8%). Future development of a pricise evaluation system for these regional diseases will be a great challange.

When APACHE II scoring system was spplied, our group yieled a mean APACHE II score of 16.57 with some left screw distribution when compared to the original study (Knaus *et al*, 1985) (Fig 2). However, Americans and Thais shared the similarity of having most of the nonoperative patients (77% *vs* 79%) fallen in the APACHE II score range of 5-29. Fig 4 demonstrates the close relation between the APACHE II score and the hospital mortality rate. In this study, each one-point rise in APACHE II score increased the hospital mortality rate by approximately 2%. These findings were similar to the original study and strongly supported the validity of the APACHE II scoring system. However, special attention should be paid in certain groups of diseases which had low first day APACHE II scores, but extremely high mortality rates. Examples were paraquat poisoning and severe tetanus. Since the number of these patients were small in this study (2.09%), deterioration of the APACHE II scoring system validity could not be identified. Following days, in instead of the first day, APACHE II scores might show a better relation to the mortality rate, provided the population is big enough.

Following the APACHE II disease category weighting system, the calculated predicted mortality rate or risk of death of the group was 29.79%. Tests of the system's predictive power at 50% risk level of death showed that the specificity, positive predictive value, and correct prediction were 95%, 88% and 83%, respectively. These were very close to the findings of the original studies (Knaus *et al*, 1985) and Saudi Arabia (Chang and Jacobs, 1986). Therefore, the strong predictive power of the APACHE II classification system was again confirmed and the system was proved to be applicable to this Southeast Asian population. Since the precision of risk stratification was stable and strong, the actual death to predicted death ratio of a given hospital would indicate the hospital performance or treatment efficacy. The hospital that showed favorable performance would have the ratio close to or less than 1. The present study yielded the group's actual to predicted death ratio of 1.17, a figure which was very close to most hospitals' ratios in the USA (Knaus *et al*, 1986). This should not be surprising, since most of our hospital systems, practice, and training programs followed the American standard.

Data from this study represent important baseline information from a Thai medical ICU, which was stratified in ways that severity of dieases and treatment efficacy could be compared internationally. The APACHE II severity of disease classification system was proved to be valid for the Thai patient population. The system, therefore, will provide Thai researchers with an important tool for improving the treatment of critically ill patients, nonrandomized clinical trials and multi-institutional studies of therapeutic efficacy.

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