Yonsei Medical Journal
Vol. 45, No. 1, pp. 29-37, 2004

Predictive Comparisons of Procalcitonin (PCT) Level, Arterial Ketone Body Ratio (AKBR), APACHE III Score and Multiple Organ Dysfunction Score (MODS) in Systemic Inflammatory Response Syndrome (SIRS)

Young-Joo Lee[1], Chan-Hee Park[2], Jang-Woon Yun[1], and Young-Suk Lee[1]

[1]Department of Anesthesiology, [2]Nuclear Medicine, Ajou University School of Medicine, Suwon, Korea.

Procalcitonin (PCT) is a newly introduced marker of systemic inflammation and bacterial infection. A marked increase in circulating PCT level in critically ill patients has been related with the severity of illness and poor survival. The goal of this study was to compare the prognostic power of PCT and three other parameters, the arterial ketone body ratio (AKBR), the acute physiology, age, chronic health evaluation (APACHE) III score and the multiple organ dysfunction score (MODS), in the differentiation between survivors and nonsurvivors of systemic inflammatory response syndrome (SIRS). The study was performed in 95 patients over 16 years of age who met the criteria of SIRS. PCT and AKBR were assayed in arterial blood samples. The APACHE III score and MODS were recorded after the first 24 hours of surgical ICU (SICU) admission and then daily for two weeks or until either discharge or death. The patients were divided into two groups, survivors (n=71) and nonsurvivors (n=24), in accordance with the ICU outcome. They were also divided into three groups according to the trend of PCT level: declining, increasing or no change. Significant differences between survivors and nonsurvivors were found in APACHE III score and MODS throughout the study period, but in PCT value only up to the 7th day and in AKBR only up to the 3rd day. PCT values of the three groups were not significantly different on the first day between survivors and nonsurvivors. Receiver operating characteristic (ROC) curves for prediction of mortality by PCT, AKBR, APACHE III score and MODS were 0.690, 0.320, 0.915 and 0.913, respectively, on the admission day. In conclusion, PCT could have some use as a mortality predictor in SIRS patients but was less reliable than APACHE III score or MODS.

Key Words: Arterial ketone body ratio, acute physiology, age, chronic health evaluation III score, mortality prediction, multiple organ dysfunction score, procalcitonin, receiver operating characteristic curve, systemic inflammatory response syndrome

INTRODUCTION

Procalcitonin (PCT), a calcitonin precursor, is a newly introduced marker of systemic infection and is undetectable in healthy individuals. PCT is induced with systemic reactions of organisms such as bacteria, fungi and parasites, rather than being induced by viral or localized infection.[1,2] PCT reflects the extent of systemic inflammation due to infection, but in cases of severe infection and the course of inflammatory factors together with the potential onset of progressive organ failure generally determine patient prognosis.[3,4] PCT can also be induced with prolonged shock of non septic origin, e.g. hypovolemic or cardiogenic shock,[5] trauma,[6,7] postoperative period after extended surgical procedure[8] and pancreatitis,[9] which belongs to systemic inflammatory response syndrome (SIRS). PCT induction without any bacterial focus is feasible considering that high concentrations of proinflammatory cytokines and other mediators can be detected in the plasma of patients with these diseases. PCT also acts as a mediator during acute inflammation rather than just as a marker of infection.[10] Furthermore, the

Received October 7, 2003
Accepted October 31, 2003

This work was supported by 1997 grant from "Department of Medical Science, The Graduate School, Ajou University".

Reprint address: requests to Dr. Young-Joo Lee, Department of Anesthesiology, Ajou University School of Medicine, San 5 Wonchun-dong, Paldal-gu, Suwon 442-746, Korea. Tel: 82-31-219-6025, Fax: 82-31-219-5579, E-mail: leeyj@ajou.ac.kr

marked increase in circulating PCT levels in critically ill patients has been related with the severity of illness and poor survival. PCT values quickly fall once the acute inflammation has waned, whereas, plasma levels fail to return to normal in the case of persistent systemic inflammation secondary to infection.

Arterial ketone body ratio (AKBR) represents the redox potential of hepatic cell mitochondria. At first, AKBR was applied as an indicator of hepatic reserve following hepatic surgery, now it is a key indicator in the assessment of any changes of vital functions throughout the entire body. However, there is strong evidence to show that it is correlated closely with hepatic functions in cases of not only primary hepatic disease but also hemorrhage shock, hypoxia and multiple organ dysfunction, and can be a predictor of outcome.[11-13] The APACHE scoring system is probably the most widely used critical care scale. The APACHE III score has been recently introduced to objectively estimate patient risk on a daily base for mortality and other important outcomes.[14]

The multiple organ dysfunction score (MODS) is a scoring system to quantify the severity of multiple organ dysfunction syndrome as an outcome in critical illness.[15]

Our study compared the prognostic power of PCT with these other parameters, AKBR, APACHE III score and MODS, between survivors and nonsurvivors, and observed the correlations between these parameters and SIRS. We also evaluated whether or not the trend of plasma PCT levels could predict the clinical outcome of SIRS.

MATERIALS AND METHODS

The study was carried out on 95 patients over 16 years old with the criteria of SIRS who had been admitted to the surgical ICU (SICU). We designed a retrospective study in the 24-bed SICU of University Hospital from September 1998 to February 2001. The patients comprised 72 males and 23 females, with an age range from 17 to 81 years (mean 47 years). The mean length of stay in the ICU was 17 days (range, 2-110 days) with a mortality rate of 25.3%. Age, body weight, sex and length of stay in the ICU showed no difference between nonsurvivors and survivors (Table 1). Sixty-eight of the 95 were transferred from the operating room and 27 from a ward or the emergency room. The most common diagnosis of the subjects was multiple trauma (n=40), followed by thoraco-abdominal operation (n=32) (Table 2). Informed consent was obtained before enrollment from conscious patients, or from the nearest kin for unconscious patients. The study protocol was approved by the institutional review board (IRB) of the University Hospital.

The plasma PCT concentrations and AKBR were assayed with arterial blood samples and the APACHE III score and MODS were measured after the first 24 hours admission to the ICU, and then daily for two weeks until either discharge or death. Data were collected prospectively and analyzed retrospectively. The subjects were divided into two groups, survivors (n=71) and nonsurvivors (n=24), in accordance with the clinical outcome. Included in the nonsurvivors were those who died in the ICU and those who

Table 1. Demographic Characteristics

	Total	Survivors	Nonsurvivors
Number of patients	95	71 (74.7%)	24 (25.3%)
Age (years)	46.5 ± 16.8	47.0 ± 17.5	45.1 ± 15.0
Sex (M/F)	72/23	55/16	17/7
Body weight (kg)	64.8 ± 10.6	64.3 ± 11.1	64.2 ± 10.1
Operation (yes/no)	74/21	56/15	18/6
Length of ICU stay (days)	16.9 ± 17.1	15.5 ± 17.6	20.5 ± 21.9

Values of age, body weight and length of ICU stay are mean ± SD.

Table 2. Diagnosis of the Study Population

	Total	Survivors	Nonsurvivors
Multiple trauma	40	31	9
Hepatobiliary disease	14	10	4
Dissecting aneurysm	7	4	3
Esophageal cancer	6	4	2
UGI bleeding	5	4	1
Pancreatitis	5	3	2
Inhalation burn	4	3	1
ICH	4	3	1
Postpartum DIC	3	3	0
Others	7	6	1

ICH, intra cranial hemorrhage; DIC, diffuse intravascular coagulation.
UGI, upper gastrointestinal.

were hopelessly discharged and died within 48 hours after the discharge.

The patients were divided into three groups according to the trend of the plasma PCT values: group 1, with declining PCT values; group 2, with increasing or persistently elevated values; and group 3, with unchanging or low values. A PCT cut-off value of 2.0 ng/ml, with best sensitivity and specificity, was used to assign patients to the three groups.

The definition of SIRS is characterized by the presence of at least two of the following four criteria: a) fever or hypothermia (temperature > 100.4°F [>38°C] or 96.8°F [<36°C]), b) tachycardia (>90 beats/min), c) tachypnea (>20 breath/min or $PaCO_2$ < 4.3 kPa [<32 mm Hg] or the need for mechanical ventilatory support) and d) an altered white blood cell count of >12,000 or <4000 cells/L, and the presence of 10% band forms, respectively.[16]

We used immunoluminometric assay for measurement of plasma PCT level using commercially available LUMItest PCT (BRAHAMS Diagnostica, Berlin, Germany). This immunoluminometric assay is based on the reaction of two antigen-specific monoclonal antibodies that bind PCT (as antigen) at the calcitonin and katacalcin segments.

AKBR was obtained under sufficient blood glucose level (120 - 200 mg/dl) to exclude the possible effect of fasting on AKBR and patients with overt diabetes mellitus were excluded for the probable effects of excessive ketogenesis. AKBR above 1.0 was regarded as normal, between 0.7 and 1.0 as subnormal, between 0.4 and 0.7 as warning, between 0.25 and 0.4 as critical, and below 0.25 as terminal. Acetoacetate and β-hydroxybutyrate concentrations in the arterial blood were measured enzymatically using methods reported by Mellaby et al.[17] The enzyme, 3-hydroxybutyrate dehydrogenase and Keto 340 system II (Sanwa Chemical Co. Ltd., Nagoya, Japan) were used to determine acetoacetate and β-hydroxybutyrate.

The APACHE scoring system, introduced by Knaus et al.,[14] is probably the most widely used critical care scale. The APACHE III prognostic system consists of two options: an APACHE III score and an APACHE III predictive equation. The APACHE III system is based on 17 physiologic variables, an interactive coma scale, age, and comorbid conditions. The APACHE score is calculated by summing the coded variables for each category. A 5-point increase in APACHE III score (range 0-299) is associated with an increased risk of in-ICU death.

MODS, introduced by Marshall et al.,[15] consists of six organ systems: (1) the respiratory system ((PaO_2/FIO_2 ratio), (2) the renal system (serum

creatinine concentration), (3) the hepatic system (serum bilirubin concentration), (4) the cardiovascular system (pressure-adjusted heart rate, PAR= heart rate × right atrial pressure/mean BP), (5) the hematologic system (platelet count), and (6) the central nerve system (Glasgow Coma Scale). Each organ system is assigned 4 points (range, 1-24).

Statistics

The data were analyzed using SPSS. PC, version 10.0 statistical program. All data were expressed as mean SD. Two-group comparison (survivors vs. nonsurvivors) of normally distributed data were made by Student t-test, and comparison of not normally distributed data were analyzed by the Mann-Whitney U test. Nominal data were analyzed by the Chi-square. The trend of PCT level was analyzed with the Kruskal-Wallis one way analysis of variance. The correlations of the four parameters, PCT, AKBR, APACHE III score and MODS, were expressed as Spearman correlation coefficients. Receiver operating characteristic (ROC) curves of the four parameters for prediction ofmortality were plotted, and the respective areas under the curve were calculated. All tests were two-tailed, and a probability (P) of less than 0.05 was considered statistically significant.

RESULTS

There were significant differences between survivors and nonsurvivors in the PCT level, AKBR, APACHE III score and MODS on the admission day, however not in AKBR during the subsequent fourteen days (Table 2).

Fig. 1 depicts the changes of PCT, AKBR, APACHE III score and MODS between survivors and nonsurvivors during the study period, from the first to fourteenth day of ICU stay. Mean plasma PCT concentrations of nonsurvivors revealed more variable changes in comparison with those of survivors and a significant difference was noted from the first day to the 7^{th}. AKBR of the nonsurvivors was significantly lower than that of the survivors only in the first three days. APACHE III score and MODS showed a significant difference between the survivors and nonsurvivors during the study period. According to Spearman correlation (Table 3), on the admission day there

Table 3. Procalcitonin level, APACHE III Score, MODS and AKBR between Survivors and Nonsurvivors on Admission and Fourteen Days

		Survivors n=71	Nonsurvivors n=24
	D1		
	D1-14	n=348	n=154
Procalcitonin (ng/ml)	D1	7.59 ± 22.23	27.61 ± 66.39*
	D1-14	6.19 ± 19.37	16.87 ± 38.23†
AKBR	D1	0.76 ± 0.405	0.51 ± 0.283*
	D1-14	0.947 ± 0.454	0.911 ± 0.479
APACHE III	D1	52.3 ± 20.2	93.0 ± 29.8‡
	D1-14	45.3 ± 18.5	76.2 ± 27.4‡
MODS	D1	5.7 ± 3.6	10.5 ± 3.5‡
	D1-14	5.4 ± 3.3	10.2 ± 4.0‡

*$p<0.05$ vs. survivors.
†$p<0.01$ vs. survivors.
‡$p<0.001$ vs. survivors.
Values are mean ± SD.
AKBR, arterial ketone body ration; APACHE, acute physiology, age, chronic health evaluation; MODS, multiple organ dysfunction score.
D1, first day of ICU stay; D1-14, from the first day to 14th day of ICU stay.

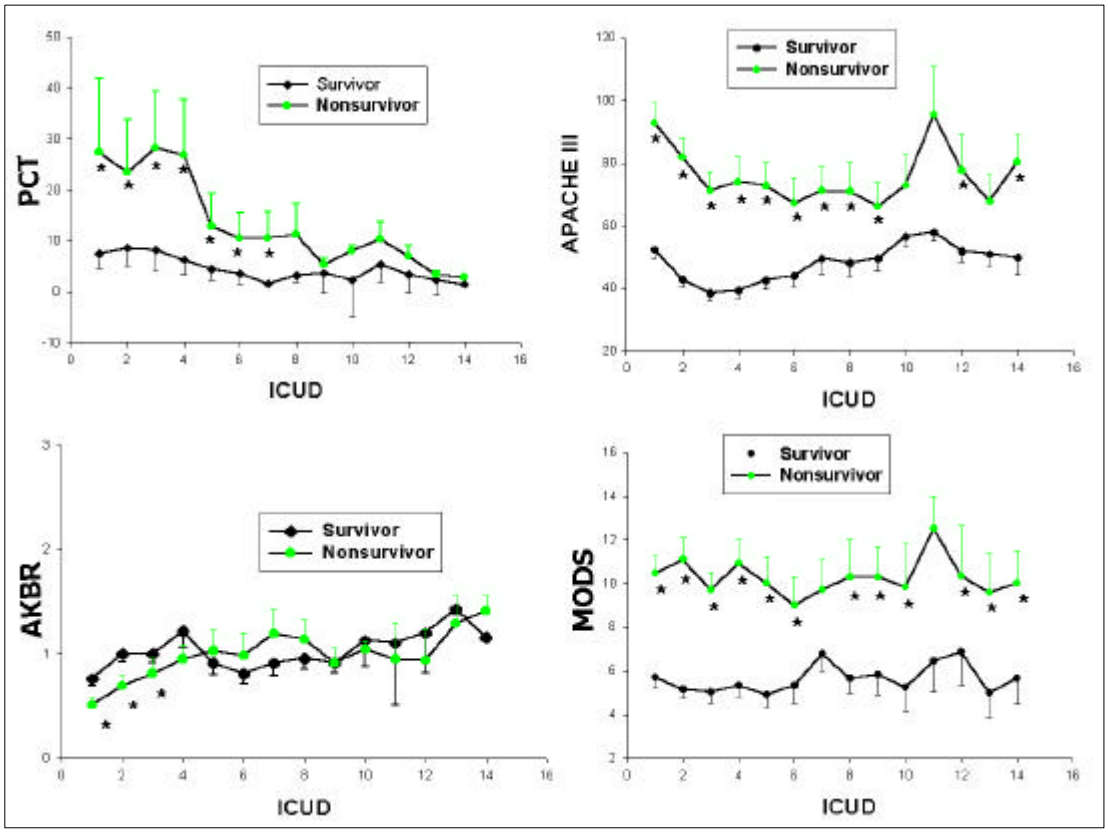

Fig. 1. Changes of the four parameters during 14 days of ICU stay between survivors and nonsurvivors. Values represent the mean ± SE. *: $p<0.001$ †: $p<0.01$ ‡: $p<0.05$ compared with survivors. Left upper, changes of plasma procalcitonin level. Left lower, changes of arterial ketone body ratio (AKBR), Right upper, changes of APACHE III score. Right lower, changes of multiple organ dysfunction score (MODS).

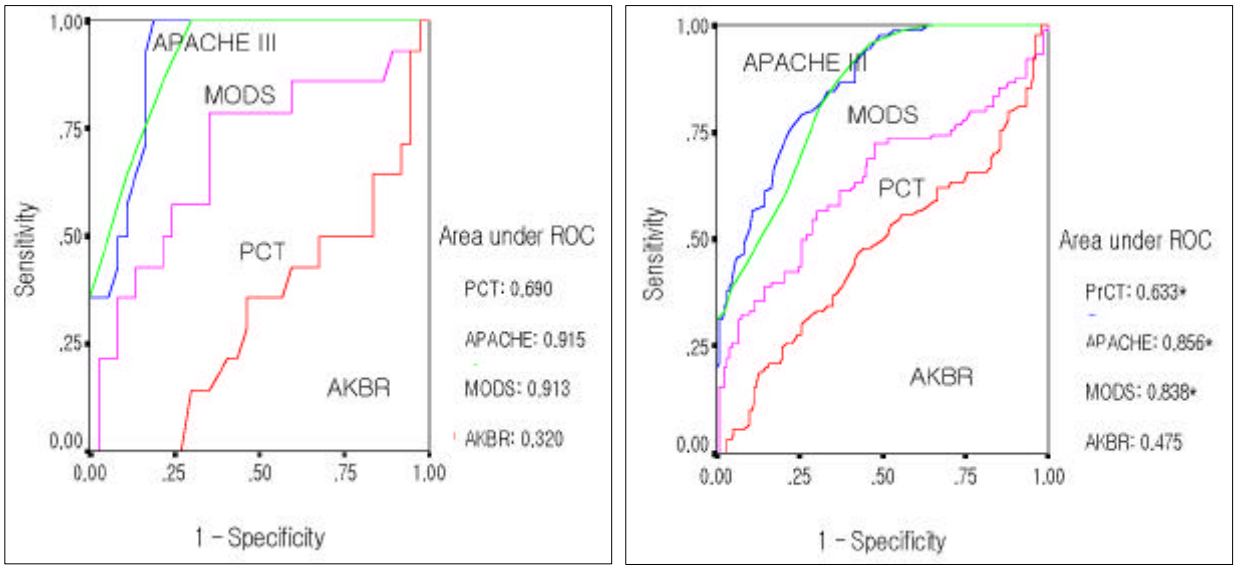

Fig. 2. Mortality receiver operating characteristic (ROC) curves, with area under the curve of procalcitonin (PCT) level, arterial ketone body ratio (AKBR), APACHE III score, and multiple organ dysfunction score (MODS). Left, ROC curves of 4 parameters on admission. Right, ROC curves of 4 parameters during fourteen days.

Table 4. Spearman Correlation of Four Parameters on Admission

	Procalcitonin	APACHE III	MODS	AKBR
Procalcitonin	1.000	0.374*	0.424*	0.015
APACHE III		1.000	0.697*	-0.297
MODS			1.000	-0.220
AKBR				1.000

*$p<0.001$
AKBR, arterial ketone body ratio; APACHE, acute physiology, age, chronic health evaluation; MODS, multiple organ dysfunction score.

Table 5. Admission and Fourteen days' Procalcitonin level, APACHE III Score, MODS and AKBR between Survivors and Nonsurvivors of Three grouped by Procalcitonin Pattern

		Group 1		Group 2		Group 3	
		Survivors 45	Nonsurvivors 7 (13.4%)	Survivors 11	Nonsurvivors 15 (57.7%)[a]	Survivors 15	Nonsurvivors 2 (11.8%)
D1	PCT (ng/ml)	2.92 ± 4.70	7.23 ± 7.83	21.10 ± 51.41	46.28 ± 84.26	1.02 ± 0.82	1.36 ± 0.93
	AKBR	0.775 ± 0.380	0.275 ± 0.163	0.733 ± 0.563	0.544 ± 0.270	0.752 ± 0.355	0.55 ± 9.481
	APACHE III	55.0 ± 23.5	85.8 ± 24.5†	56.6 ± 16.9	100.7 ± 34.3‡	45.9 ± 15.1	78.8 ± 15.9‡
	MODS	6.1 ± 3.0	7.4 ± 1.5	7.4 ± 3.8	12.3 ± 2.9†	4.1 ± 3.3	8.8 ± 3.6
D1-14	PCT (ng/ml)	4.23 ± 6.87	16.87 ± 36.04*	19.62 ± 44.5	22.41 ± 44.27	0.92 ± 0.72	2.08 ± 1.44†
	AKBR	1.019 ± 0.468	0.992 ± 0.439	0.817 ± 0.540	0.916 ± 0.427	0.830 ± 0.313	0.716 ± 0.571
	APACHE III	49.3 ± 18.0	65.4 ± 24.3‡	50.2 ± 20.7	80.1 ± 29.0‡	41.6 ± 11.8	76.5 ± 32.2‡
	MODS	5.5 ± 3.3	7.4 ± 1.8‡	7.0 ± 3.1	11.7 ± 4.0‡	0.9 ± 3.3	2.1 ± 3.8‡

Group 1, declining PCT pattern; Group 2, increasing or persistently elevated PCT; Group 3, unchanging or low level PCT; AKBR, arterial ketone body ratio; APACHE, acute physiology, age, chronic health evaluation; MODS, multiple organ dysfunction score.
Cut-off value of PCT among groups: 2 ng/ml.
*$p<0.05$ vs. survivors, †$p<0.01$ vs. survivors, ‡$p<0.001$ vs. survivors, [a]$p<0.01$ vs. group 1, 3.

was a significant correlation between PCT and APACHE III score (r=0.374), and between PCT and MODS (r=0.424), but a stronger correlation between APACHE III score and MODS (r=0.697). AKBR failed to reveal any correlation with any other parameter (Table 3).

Mortality ROC curves showed similar data with area under the curve of the admission and during fourteen days of ICU stay (Fig. 2). The area under the ROC curve of PCT (0.690) was less than that of APACHE III score (0.915) and MODS (0.913) for predicting the mortality on the admission day.

Table 4 shows the mortality between survivors and nonsurvivors of the three groups by the pattern of plasma PCT levels. Overall mortality of this study was 25.3%; in group 1, 7 out of 52 died (13.4%), in group 2, 15 out of 26 died (57.7%), and in group 3, 2 out of 17 died (11.8%). PCT levels and AKBR of the three groups on the first day revealed no significant difference between survivors and nonsurvivors. However, APACHE III score and MODS of not only the first day but also the fourteen days of the three groups demonstrated significant differences between the survivors and the nonsurvivors.

DISCUSSION

SIRS is a state of consistent progression of sys-

temic inflammatory responses caused by various inflammatory or non-inflammatory diseases, and remains one of the major causes of morbidity or mortality in patients admitted to the ICU.

We investigated the mortality prediction of PCT, AKBR, APACHE III score and MODS on admission and during 2 weeks of SICU stay in SIRS patients. We found significant differences between survivors and nonsurvivors for these four values. The mean plasma PCT level of nonsurvivors revealed variable changes compared with survivors, and although they both showed a declining trend, nonsurvivors had a significantly higher level from the first to the 7th day than survivors. All of our patients were in the state of SIRS on admission to the ICU, and were started on antibiotic and fluid therapy immediately. This may partially explain why nonsurvivors showed a declining trend. By the 7th day, 18 (75%) patients had died and the rest were chronic cases. Our nonsurvivors showed higher PCT levels than reported in other studies.[4-8,18-23] Giamarellos-Bourboulis[24] reported that PCT level was as high in SIRS as in sepsis. Some investigators have demonstrated that PCT value might increase during the first few days after surgery, depending on the nature and extent of the surgical procedure. After extensive and complex, abdominal, cardiac and thoracic surgeries, markedly elevated PCT values were frequently attained during the post operative period.[8,19-22] Higher PCT levels were associated with a severe injury, frequent onset of shock, and multiple organ dysfunction.[6,7] APACHE III score of the nonsurvivors in our study was high, 93 on admission to ICU, and it remained high throughout the study period. MODS 11 meant 3 to 4 organ dysfunctions when they were admitted.

In a baboon model of trauma, PCT level was elevated 2 hours after the start of reperfusion.[7] Assicot et al.[2] reported that IL-2 administration to renal cancer patients was followed by elevation of PCT, TNF-α, and IL-6, suggesting that cytokines were capable of releasing PCT independent to endotoxin release. The high PCT levels of our SIRS patients could be explained partially from the observation of these reports.

Increasing or persistently high PCT values indicated ongoing inflammatory disease activity and suggested a poor prognosis, whereas declining values indicated a diminishing inflammatory reaction, and thus, a favorable prognosis.[19] We arranged our patients into three group according to the trend of plasma PCT values: declining, increasing or persistently elevated, and unchanging or low level. Although the overall mortality of our study was 25.3%, mortality in the declining and unchanging or low PCT groups was almost equally low (13.4% vs. 11.8%). In the increasing or persistently elevated group, however, the mortality was 57.7%. Therefore the trend of increasing or decreasing PCT values could be a more accurate index for prognostic evaluation.

Area under the mortality ROC curve directly reflects the mortality prediction. In our study, admission day area under the ROC curves of the four parameters remained almost constant for fourteen days. Although elevated admission PCT was associated with a poor outcome, overall our ROC analysis demonstrated that a single PCT measurement was an inadequate predictor for mortality and that a trend study with multiple measurements was necessary for mortality prediction.

According to the analysis by Spearman correlation, probability depicted a significant correlation between PCT and both APACHE III score and MODS, but with correlation coefficients of only around 0.4, indicating that these were weak correlations. As noted in our previous reports[24,25] the correlation coefficient between APACHE III score and MODS was about 0.7, indicating a good correlation.

Yamamoto et al.[13] reported that when AKBR below 0.40 persists for more than 5 days, there was a high incidence of multiple organ failure and a 100% mortality. Also patients who showed AKBR between 0.4 and 0.25 had a higher incidence of postoperative complications than had those who showed ratios above 0.40. In our study, mean AKBR of nonsurvivors on admission was 0.51, and increased to 0.80 on the 3rd day. Only five of the 28 of nonsurvivors had AKBR below 0.4 during their ICU stay. In addition, AKBR of nonsurvivors was significantly lower than that of survivors on the first three days. AKBR, moreover, could not be correlated with any other parameters. Area under the ROC curve of AKBR was 0.320, which implied that AKBR could not be

used as an indicator of mortality in SIRS.

In our study, APACHE III score and MODS both showed a quite strong difference between survivors and nonsurvivors, not only on admission day but also during fourteen days of ICU stay. In the three groups by PCT trend, PCT level and AKBR showed no difference between survivors and nonsurvivors on the admission day, whereas APACHE III score and MODS showed significant differences in every study period. These findings confirmed that APACHE III score and MODS could be used for mortality prediction.

In conclusion, plasma PCT values could be used as a useful predictor of mortality but appeared to be less accurate than APACHE III score or MODS. Sequential measurements of PCT for 1 week are needed for clinical application with SIRS and also further study with a large number of SIRS patients is necessary to confirm the validity of these prognostic factors.

REFERENCES

1. Dandona P, Nix D, Wilson MF, Aljada A, Love J, Assicot M, et al. Procalcitonin increase after endotoxin injection in normal subjects. J Clin Endocrinol Metab 1994;79:1605-8.
2. Assicot M, Gendrel D Carsin H Raymond J Guilbaud J Bohuon C. High serum procalcitonin concentrations in patients with sepsis and infection. Lancet 1993;341:515-8.
3. Lind L, Bucht E, Ljunghall S. Pronounced elevation in circulating calcitonin in critical care patients is related to the severity of illness and survival. Intensive Care Med 1995;21:63-6.
4. Wanner GA, Keel M, Steckholzer U, Beier W, Stocker R Ertel W. Relationship between procalcitonin plasma levels and severity of injury, sepsis, organ failure, and mortality in injured patients. Crit Care Med 2000;26: 950-7.
5. Al-Nawas B, Krammer I, Shah PM. Procalcitonin in diagnosis of severe infections. Eur J Med Res 1996;1: 331-3.
6. Mimoz O, Benoist JF, Edouard AR, Assicot M, Bohuon C, Samii K. Procalcitonin and C-reactive protein during the early posttraumatic systemic inflammatory response syndrome. Intensive Care Med 1998;24:185-8,
7. Redl H, Schlag G, Toegel E, Assicot M, Bohuon C. Procalcitonin release patterns in a baboon model of trauma and sepsis: Relationship to cytokines and neopterin. Crit Care Med 2000;28:3659-63.
8. Meisner M, Tschaikowsky K, Hutzler A, Schick C, Schuttler J. Postoperative plasma concentration of procalcitonin after different types of surgery. Intensive Care Med 1998;24:680-4.
9. Rau B, Steinbach G Baumgart K, Mayer M, Grunet A, Beger HG. The role of procalcitonin and interleukin-8 in the prediction of infected necrosis in acute pancreatitis. Gut 1997;41:832-40.
10. Braithwaite S: Procalcitonin-marker or mediator? Crit Care Med 1998;26:977-8.
11. Ozawa K, Aoyama H, Yasuda k, Shimahara Y, Nakatani T, Tanaka J, et al. Metabolic abnormalities associated with postoperative organ failure. Arch Surg 1983;118:1245-51.
12. Ukikusa M, Ozawa K, Shimahara Y. Changes in blood ketone body ratio: Their significance after major hepatic resection. Arch Surg 1981;116:781-9.
13. Yamamoto Y, Ozawa K, Okamoto R, Kiuchi T, Maki A, Lin H. et al. Prognostic implications of postoperative suppression of arterial ketone body ratio: Time factor involved in suppression of hepatic mitochondrial oxidation-reduction state. Surgery 1990;107:289-94.
14. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. Prognosis in acute severity of disease classification system. Crit Care Med 1995;13:818-29.
15. Mashall JC, Cook DJ, Christou NV, Bernard GR, Sprung CL, Sibbald WJ. Multiple organ dysfunction score: A reliable descriptor of a complex clinical outcome. Crit Care Med 1995;23:1638-52.
16. Members of the American College of Chest Physicians/ Society of Critical Care Medicine Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference. Definition for sepsis and organ failure and guidelines for the innovative therapies in sepsis. Crit Care Med 1992;20:864-74.
17. Mellaby J, Williamson DH. Acetoacetate. Bergmeyer HU. editor. Methods of enzymatic analysis. Ist ed. New York: Academic Press; 1974. p.1446-51.
18. Davis TM, Assicot M, Bohuon C, St John A, Li GQ, Anh TK. Serum procalcitonin concentrations in acute malaria. Trans R Soc Trop Med Hyg 1994;88:670-3.
19. Meisner M, Hutzler A, Tschaikowsky K, Harig F, von der Emde J. Postoperative plasma concentration of procalcitonin and C-reactive protein in patients undergoing cardiac and thoracic surgery with and without cardiopulmonary bypass. Cardiovas Engineering 1998; 3:174-8.
20. Kuse ER, Langefeld I, Jaeger K, Kulpmann WR. Procalcitonin-a new diagnostic tool in complications following liver transplantation. Intensive Care Med 1998;24:680-4.
21. Hensel M, Volk T, Döcke WD, Kern F, Tschirna D, Egerer K, et al. Hyperprocalcitoninemia in patients with noninfectious SIRS and pulmonary dysfunction associated with cardiopulmonary bypass. Anesthesiology 1998;89:93-104.
22. Reith HB, Mittelkötter U, Debus ES, Kussner C, Thiede A. Procalcitonin in early detection of postoperative

complications. Dig Surg 1998;15:260-5.
23. Giamarellos-Bourboulis EJ, Mega A, Grecka P, Scarpa N, Koratzanis G, Thomopoulos G, et al. Procalcitonin: a marker to clearly differentiate systemic inflammatory response syndrome and sepsis in critically ill patient? Intensive Care Med 2002;28:1351-6.
24. Lee YJ, Chung KH, Wang HJ, Moon BK, Shim YH, Lee YS. Thyroid function, metabolism, and severity scorings in brain dead patients. Ajou Med J 1999;4:44-51.
25. Lee YJ, Chung SM, Hong JS, Moon BK, Wang HJ, Lee YS. Comparison of predictive indices of severity scorings, metabolism, and thyroid hormones in systemic inflammatory response syndrome. Kor J Anesthesiology 1999;37:799-806.