Contribution of Arterial Redox Potential Measurement to the Care of Critically Ill Patients

Shogo TANIGUCHI, Kenji KODAMA, Hiroyuki MATSUYAMA,
Kazuo IRITA and Junichi YOSHITAKE

175 arterial and 122 urinary samples from 20 patients admitted in ICU for organ system failure (OSF) were analysed. Besides arterial blood gases and lactate, electrolyte concentrations, pH, rH_2 and specific resistance (R) in blood and urine were measured. Redox potential (E) and base excess were calculated from these data. Patients were defined as having MOSF if their organ systems met failure criteria during their ICU stay. Data were classified with corresponding number of OSF developed in the patients when samples were obtained. Acid-base balance or base excess alone could not be used to predict the severity of illness as assessed by increasing number of organ system failures. Significant elevations in blood lactate concentrations were observed only in patients with four, five or six OSF. A lack of correlation between blood lactate and severity of OSF indicates that blood lactate is not valid as a guide to ultimate outcome of the patients. Arterial redox potentials progressively decreased with increasing number of OSF, therefore, it can be stated that the serial measurements of arterial redox potential are useful in assessing the patient's status or predicting their ultimate outcome.

(Key words: redox potential, multiple organ system failure, acid-base balance, lactate)

(Taniguchi S, Kodama K, Matsuyama H et al.: Contribution of arterial redox potential measurement to the care of critically ill patients. J Aesth 1: 125–131, 1987)

In recent years the advent of ICU has demanded more attention to the monitoring and the management of acid-base and electrolyte status[1,2,3]. The diagnosis and particularly the assessment of severity of many respiratory conditions rely on blood gases analysis[4], that is determination of Po_2 and Pco_2 values. The same is true for the management of patients on ventilators. Since the kidney is fundamentally involved in the regulation of electrolytes in the body fluids and the excretion and reabsorption of acid and base, it is obvious that the electrolyte and water balance is inevitably and intimately associated with acid-base balance[5]. Many other metabolic disorders involve disturbances of acid-base balance, for example, the lactic acidosis associated with shock[6,7,8]. Previously we reported the analytical method for the measurements of bioelectronic factors in the body fluids such as pH, rH_2, specific resistance (R), redox potential (E), milliamperes and microwatts with the BE-Vincent apparatus[9]. As shown in the physico-chemical principles underlying the measurement of pH, the pH, rH_2 and E are inseparably linked[10,11], hence it is impossible to look upon them apart from others as often happens for pH measurement. Some of ICU patients tend to deteriorate

---

Department of Anesthesiology, Faculty of Medicine, Kyushu University, Fukuoka, Japan

Address reprint requests to Dr. Taniguchi: Department of Anesthesiology, Faculty of Medicine, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka, 812 Japan

Table 1. The salient clinical features of the series

Patient	Age	Sex	Diagnosis	Operation	Sample		Length of ICU stay (day)	Course
					B	U		
1	65	F	IHD	CABG	22	19	49	S
2	75	M	Ruptured abdominal aortic aneurysm	Resection & Reconstruction	9	0	12	N
3	57	M	Hepatolithiasis & Hepatoencephalopathy	Drainage	8	6	10	N
4	72	M	Gastric cancer, IHD	Exploratory laparotomy	2	2	3	S
5	67	M	Meningitis & Respiratory failure	None	5	5	10	S
6	58	F	Post CPR	None	3	3	4	N
7	57	M	Esophageal cancer	Resection & Reconstruction	12	12	12	S
8	34	F	Vertebral tumor	Tumor resection	9	8	18	S
9	41	M	AR, Tr, MR	MVR, AVR, TAP	6	6	6	S
10	39	F	IE, MR	MVR	20	16	54	N
11	69	M	IHD	CABG	6	4	11	S
12	83	M	Aspiration pneumonia ARDS	None	2	2	5	S
13	64	M	Nephrotic syndrome ARDS	None	4	3	22	S
14	47	M	P/O MVR, AVR, TVR Valvular failure	MVR	8	0	12	N
15	34	M	Crohn's disease	None	6	6	8	N
16	63	F	Post CPR	None	4	4	5	N
17	51	M	IHD, LOS	CABG	13	0	19	N
18	50	M	Pontine hemorrhage	None	2	2	3	N
19	6	F	Traffic accident	Hemostasis	5	0	6	N
20	72	M	MS, TR	MVR	29	24	37	N

IHD=ischemic heart disease, CABG=Aorto-coronary bypass graft, CPR=cardiopulmonary resuscitation, IE=infectious endocarditis, ARDS=Adult respiratory distress syndrome, LOS=Low output syndrome, B; blood, U; urine

despite of all our efforts to maintain and/or correct their acid-base balance. This may be due to our one-sideness in evaluation of their body fluid and our ignorance of bioelectronic status[12]. This is the first study that shows the significance of the arterial and urinary bioelectronic factors in care of critically ill patients.

Materials and Methods

This study included 20 ICU patients (14 males and 6 females, age: 6 to 75 yr). The salient clinical features of this group are summarized in table 1. Observation time varied from 3 to 54 days (mean: 15.3 days). There were a total of 306 observation days for the series. There were 11 non-survivors in this study. Physiologic and therapeutic data pertaining to the circulatory, respiratory, hepatic, renal, gastrointestinal and neurologic function of each patient were daily obtained. The criteria for failure of above mentioned organ systems were based on clinical findings, laboratory data and supportive therapies (table 2). Patients were defined as having multiple organ system failure (MOSF) if two or more organ systems met failure criteria during their ICU stay, regardless of whether the organ failure occured simultaneously or

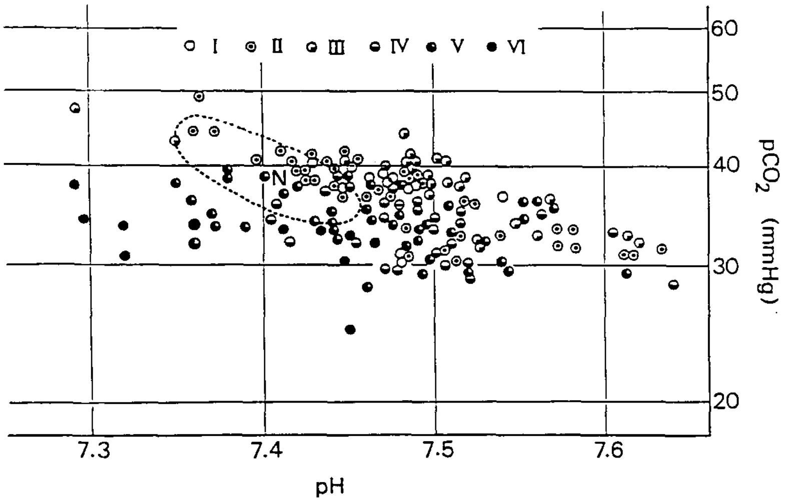

Fig. 1. Arterial acid-base status obtained from 175 measurements of 20 ICU patients. They are plotted on the pH-log (Pco$_2$) diagram. Roman number represents the number of OSF, and N represents normal area.

Table 2. Criteria for organ system failure (OSF*)

Cardiovascular system
1. Myocardial infarction
2. Cardiac arrest
3. Continuous iv infusions or inotropic agents to maintain blood pressure and/or cardiac output
Respiratory system
1. Mechanical support needed
Hepatic system
1. Total bilirubin > 3 mg/dl
2. GOT, GPT > 100 U
Renal system
1. BUN > 50 mg/dl
2. Creatinine > 3 mg/dl
Gastrointestinal system
1. GI bleeding
Neurologic system
1. Only respond to noxious stimuli

*OSF defined by meeting one or more criteria for a given system

not. The arterial and urinary samples were obtained at an appropriate time interval, and 175 arterial and 122 urinary samples were analyzed in this series. Data were classified with corresponding number of OSF developed in the patients when samples were obtained (table 3). The pH, rH$_2$ and specific resistance (R) of blood and urine were measured with BE-Vincent apparatus, and redox potential (E) was calculated. Laboratory analyses of blood and urine were done as follows; arterial blood gases and acid-base balance with ABL-2, serum and urinary electrolyte concentrations with electrolyte analyzer NOVA 10 and 2, blood lactate concentrations with OMRON lactate analyzer, blood glucose with Dextrometer and hematocrit by centrifugation method.

Table 3. Number of sampling used for arterial and urinary analysis in the patients with organ system failure

	1OSF	2OSF	3OSF	4OSF	5OSF	6OSF	Total
Blood	13	49	28	26	28	11	175
Urine	13	33	27	19	24	6	122

Statistical analysis

Values were expressed as mean±SD. Statistical analyses were performed by either unpaired, student's t-test and regression analysis. Statistical significance was defined as $P < 0.05$.

Results

In figure 1 the arterial acid-base status obtained from 175 measurements in 20 ICU patients are plotted on a pH-log (Pco$_2$)

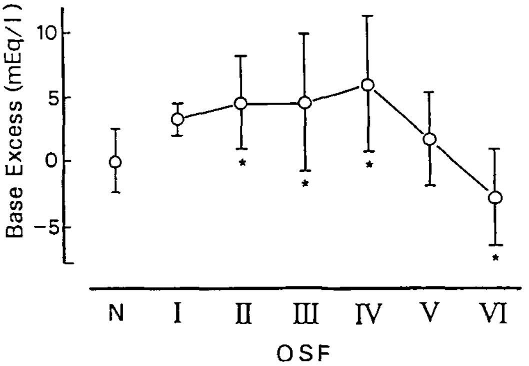

Fig. 2. Changes in base excess in the patients with MOSF

All values are represented mean±SD. $^*P<0.05$

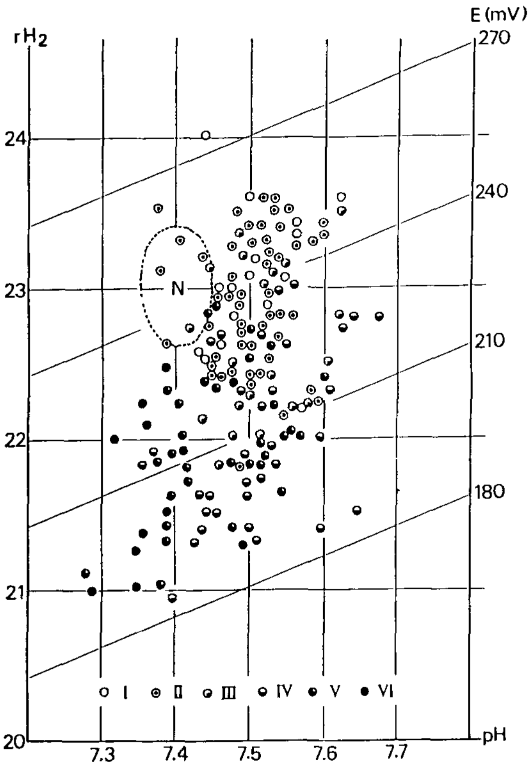

Fig. 3. A total of 175 arterial bioelectronic data of the patients with MOSF

They are plotted on the pH-rH_2 diagram. Roman number represents the number of OSF, and N represents normal area.

diagram. The patients were mechanically ventilated if necessary, hence their P_{CO_2} values were mostly remained between 30 and 40 mmHg. The pH values were near or above normal range, however, 1 of the values obtained from the patients with three OSF and 4 of the values from the patients with six OSF were as low as around 7.29. The base excess was proposed as the standard index of the metabolic component of acid-base imbalance. Figure 2 shows the changes of base excess in the patients with OSF. From these results it is considered that there was no consistent alterlations in acid-base balance corresponding to increasing number of OSF in our series of the patients.

Figure 3 shows a total of 175 arterial bioelectronic data of the patients with OSF plotted on a pH-rH_2 diagram. The characteristic factors for the normal healthy adults are located around the intersection of pH 7.4 and rH_2 23. The points that correspond to the patients with one and two OSF lay in slightly alkaline and normal oxidation-reduction state. These points moved to more reduced state with only slightest changes in acid-base balance with increasing number of OSF.

Figure 4 shows the acid-base (A) and pH-rH_2 (B) pathways of the patient with ruptured abdominal aortic aneurysm (patient number 2 in table 1). The arrows represent the directional change during and after surgery. This patient developed metabolic acidôsis during surgery, and his arterial pH had been 7.2. After admission in ICU, pH had risen to 7.6, and remained between 7.40 and 7.68 for several days. He developed six OSF and expired. The pH value of arterial blood was 7.3 immediately before death. The severity of illness as assessed by increasing number of OSF was not necessarily associated with the magnitude of acid-base embarrassment. On the other hand, pH-rH_2 pathway showed consistent shifts from alkline and normal oxidation-reduction state to slightly acidotic and more reduced state.

The changes in arterial and urinary redox potentials and specific resistances (R) are shown in figure 5. The arterial redox potentials decreased progressively with increasing number of OSF, whereas those of urine elevated consistently. But there was no correlation between arterial E and urinary E

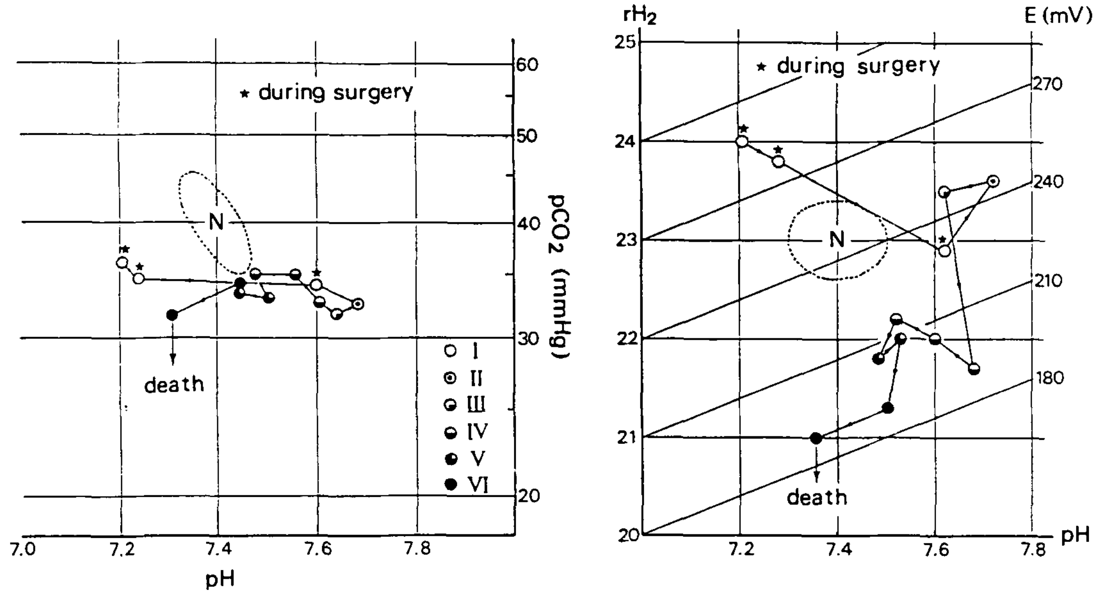

Fig. 4. The acid-base pathway (A) and pH-rH_2 pathway (B) of the patient with ruptured abdominal aortic aneurysm. Roman number represents the number of OSF, and N represents normal area.

Table 4. Relationship between two variables in the study samples

Variable 1	Variable 2	Samples	r	p values
arterial E	urinary E	122	−0.24	$P>0.05$
lactate	Base Excess	175	−0.27	$P>0.05$
lactate	arterial E	175	−0.14	$P>0.05$

($P > 0.05$, table 4).

Urinary R elevated markedly, whereas arterial R decreased significantly. Marked elevations in the specific resistance of urine obtained from the patients with OSF suggest that only small amounts of electrolytes were excreted through kidney. From these data it is suggested that the normal renal regulatory mechanisms maintaining proper redox potential and R in blood were progressively deteriorated in the patients with MOSF, subsequently derrangements of arterial redox potential and R were induced.

Figure 5 also shows the changes in arterial lactate values in the patients with OSF. Lactate values remained vertually unchanged in the patients with 1, 2 and 3 OSF. In the patients with 4, 5 and 6 OSF, their blood lactate concentrations were elevated significantly ($P < 0.05$). However, their lactate values were not necessarily high compared with those observed in the patients under major surgery. And there was no correlation between two variables: lactate and base excess, lactate and arterial E($P > 0.05$, table 4).

Discussion

In humans, the normal values of pH lie between 7.36 and 7.44[13]. The range of pH which is compatible with life for more than a short period of time is about 7.0–7.7[13]. In this study the range of pH in 20 patients was 7.29–7.65. This indicates the acid-base balance is not reliable in assessing the patient's status or predicting the ultimate outcome.

In our study the normal lactate value was 9.3±2.5 mg/dl. During impaired perfusion, tissue hypoxia stimulates anaerobic metabolism with consequent overproduction of lactate from pyruvate, although reduced splanchnic and renal blood flow may also impair lactate clearance by the liver and kidneys[7,8,14]. Lactate levels have, for many years, been considered to be representative of the degree of underperfusion and oxygen debt incurred during low flow states and hence to provide a valuable assessment of

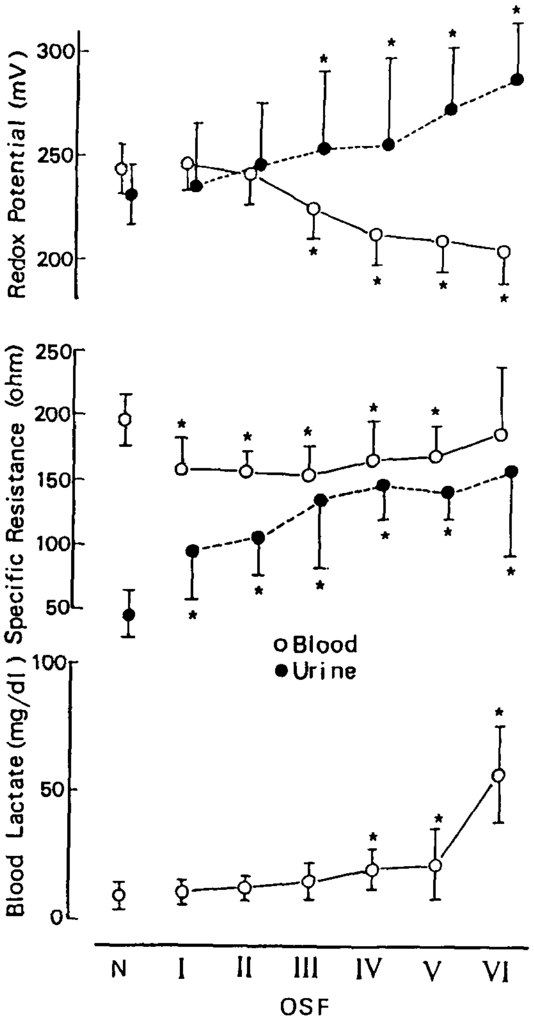

Fig. 5. Relationship between increasing number of OSF and the changes of redox potential, specific resistance and blood lactate concentration. Roman number represents the number of OSF, and N represents normal value. All values are represented mean±SD. *$P<0.05$

the severity of shock. Early studies suggested that a good correlation exists between lactate values encountered during shock and mortality, leading to the construction of probability curves for survival[6,8]. This view continues to be held by some investigators to the present days. Although initially excess lactate defined as a disproportionate elevation of lactate level in relation to that of pyruvate was believed to be more representative of the oxygen debt and hence to confer a greater prognostic index, later work showed that measurement of lactate without that of pyruvate was sufficiently valuable[7,14].

In our unpublished study, the serial blood lactate measurements during and after surgery revealed that raised blood lactate was attributable to the greater intraoperative blood loss and extensive surgery regardless of occurrence of intraoperative shock and hypotention. After surgery elevated blood lactate returned to near normal levels within one day. In ICU their blood lactate values were remained near normal levels even if two or three OSF has developed as shown in this study.

From these facts it could be stated that elevation in blood lactate concentrations during surgery was originated from the metabolic responses of the patients to major surgery, and that the magnitude of lactate elevation was dependent upon the nature and severity of injury. The increase in arterial lactate concentrations observed in the patients with five or six OSF was probably resulted from the renal and hepatic failure which subsequently led to low lactate clearance. A lack of correlation between blood lactate values and severity of OSF indicates that blood lactate may not be valied as a guide to ultimate outcome of the patients.

As shown in figure 5, arterial redox potentials progressively decreased with increasing number of OSF. The ICU patients with less than 200 mV of arterial E value were likely to become fatal. It can be stated that the serial measurements of arterial redox potential are useful in assessing the patient's status or predicting their ultimate outcome. These data actually added much informations to facilitate our decision making in the clinical situation. Mechanisms which make arterial blood more reduced in the patients with MOSF are not known. Although the bioelectronic status in these patients may be modified by the various therapeutic interventions, we consider that the abolishion of hepatic and renal regulatory function in MOSF is most responsible.

In conclusion arterial and urinary bioelectronic factors can be used as a useful adjunct to the clinical evaluation of critically ill patients.

(Received May 29, 1987, accepted for publication May 29, 1987)

References

1. Churchill ED: Multiple, progressive, or sequential systems failure. Arch Surg 110: July, 779–781, 1975
2. Eiseman B, Beart R, Norton L: Multiple organ failure. Surg Gynecol Obstet 144:323–326, 1977
3. Draper EA, Kanaus WA, Wanger DP: Prognosis from combined organ system failure. Abstr Crit Care Med 11:23, 1983
4. Wilkinson JD, Pollack MM, Ruttimann UE, Glass NL, Yeh TS: Outcome of pediatric patients with multiple organ system failure. Crit Care Med 14:271–274, 1986
5. Law RO: Renal control of acid-base balance, Acid-base Balance. Manchester, Manchester University Press, 1982, pp. 27–49
6. Schuster HP: Prognostic value of blood lactate in critically ill patients. Resuscitation 11:141–146, 1984
7. Cohen RD, Simpson R: Lactate metabolism. Anesthesiology 43:661–673, 1975
8. Park R, Arieff AI: Lactic acidosis. New York, New York Medical Publishers, 1980, pp. 33–68
9. Taniguchi S, Matsuyama H, Irita K, Yoshitake J: The bioelectronic factors of human body fluids and intravenous replacement solutions. J Anesthesia 1:22–28, 1987
10. Elmut H: Die Definition der Factoren, Bioelectronik nach Vincent und Säuren-Basen-Haushalt in Theorie und Praxis. Heiderberg, Karl F. Haug Verlag GmbH, 1985, pp. 13–74
11. Ziegler E: The physicochemical principles of redox measurement, The Redox Potential of Blood in Vivo and in Vitro. Springfield, Thomas, 1965, pp. 34–73
12. Jellinek M. Castaneda M, Carvin PJ, Niehoff M: Oxidation-reduction maintenance in organ preservation. Arch Surg 120:439–442, 1985
13. Hainsworth R: Acid-base control in the whole body, Acid-base Balance. Manchester, Manchester University Press, 1982, pp. 75–95
14. Kreisberg RA: Pathogenesis and management of lactic acidosis. Ann Rev Med 35:181–193, 1984
15. Gryan L: The significance of blood lactate in intensive care. Intensive & Critical Care Digest 5:15–17, 1986