

## Base deficit in the immediate postoperative period of open-heart surgery and patient outcome

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### Abstract

**Background:** Base deficit is a non-respiratory indicator of acid base status that evaluates the severity of shock at the cellular level. Base deficit results from cellular metabolism of pyruvate under anaerobic conditions. In this situation, base deficit is a sensitive marker of the magnitude of anaerobic metabolism and tissue oxygen deficit [1]. Several studies have shown a strong positive correlation between base deficit and the risk of morbidity and mortality in clinical situations such as circulatory shock, extracorporeal support and in children after operation for complex congenital heart disease.

**Methods:** 136 consecutive cases with coronary artery disease and valvular heart disease were scheduled in the study. 20 variables were determined during the preoperative, intraoperative and postoperative periods. Statistical univariate analysis was performed differentiating patients whose initial base deficit after weaning from cardiopulmonary bypass was  $-8$  meq and these whose base deficit was equal or more than  $-8$  meq.

**Results:** 39 patients had base deficit levels less than  $-8$  (Group A) and 91 had a level of  $\geq -8$  meq/L (Group B). Patients with a base deficit level of  $-8$  meq/L or more were older and most of them were women. The prevalence of left ventricular ejection fraction less than 30% and coronary artery disease was not significantly higher in patients with base deficit of  $\geq -8$  meq/L. No difference was found according to the presence of hypertension or diabetes in patients with base deficit levels of  $-8$  or higher than in those with base deficit levels less than  $-8$  ( $P > 0.05$ ). In the univariate analysis of preoperative variables, there were no differences with respect to factors such as age, sex, diabetes, preoperative hemoglobin level, hypertension, emergency operation and redo operation. Congestive heart failure was different between the two groups ( $P < 0.05$ ). Three variables had a statistically significant difference in the univariate analysis and two of them were highlighted by the linear logistic model.

**Conclusion:** The value of base deficit which was measured during the immediate postoperative open-heart surgery period is correlated with the volume of fresh frozen plasma and blood transfusion after open heart surgery and using of intra-aortic balloon pump after surgery.

**Keywords:** cardiac surgery, outcome, base deficit

### Introduction

The base deficit is a non-respiratory indicator of acid-base status that evaluates the severity of

shock at the cellular level. A drop in the total number of base or buffers such as bicarbonate, hemoglobin and plasma protein reflect imbalance between tissue oxygen supply and demand. Base deficit results from cellular metab-

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olism of pyruvate under anaerobic conditions [1]. Therefore, base deficit is related to the total oxygen debt and the magnitude of tissue hypoperfusion [2,3]. Several studies have suggested that base deficit has prognostic value in patients with circulatory shock [4, 5, 6]. A base deficit from 0 to -2 is considered normal, but mildly inadequate cellular and tissue perfusion is reflected in a base deficit between -3 and -5, a moderate abnormal base deficit is between -6 and -9 and a severe base deficit abnormality is -10 or lesser. Advanced age or alcohol use could falsely increase the base deficit level [1]. The purpose of this study is to test the hypothesis that an elevated base deficit level in open heart surgery patients could be an indicator of impaired systemic oxygen utilization and portends poor outcome.

### Methods

This study was a retrospective analysis of a prospectively-collected database. The study population included all patients (136 consecutive) admitted to cardiac intensive care after open heart surgery between August 2002 and June 2004. The patients in this study (n=136) had mean age of  $54 \pm 10.67$  years. There were 88 men and 47 women. Patients with alcohol abuse and more than 75 years of age were excluded from the study. Base deficit was obtained from the first arterial blood sample after weaning from cardiopulmonary bypass. Patients were divided into those who maintained a persistently high base deficit of ( $\geq -8$  meq/L) (Group B) and those who achieved base deficit ( $< -8$  meq/L) (Group A). Variables were compared with T-test (continuous variable),  $\chi^2$ , as a univariate analysis and a linear regression model, was performed on the variables and showed to have a statistically significant difference in univariate analysis with determination of the odds ratio. ROC curve was obtained for determination of sensitivity and specificity of this test. Factors considered for univariate analysis included: age, sex, body surface area, diabetes,

preoperative hemoglobin level, congestive heart failure, hypertension, redo operation, emergency operation, CPB time, aortic cross clamp time, maximum and minimum CPB flow, neurological complication, myocardial infarction, mortality, hemodynamic stability, pulmonary complication, intra-aortic balloon pump use, gastrointestinal complication, renal failure, and infection. All patients were treated with the same CPB technique. After systemic heparinization, the aorta and vena cava were cannulated and CPB initiated using either roller or centrifugal pump, membrane oxygenators were used and the circuit was primed with 2 liters of a crystalloid solution (Ringer's lactate). Systemic temperature was decreased to  $28^\circ\text{C}$  during perfusion. Flow rate was maintained at  $2.2 \text{ l/min.m}^2$  at  $37^\circ\text{C}$  and  $2 \text{ l/min.m}^2$  at  $28^\circ\text{C}$ . Mean systemic arterial pressure was continuously monitored and maintained between 60 and 70 mmHg. Arterial blood samples were drawn after weaning from CPB and stored immediately on ice to prevent lactate production. Blood gas was measured on an ABG commercial analyzer (Nuva Company, USA). For the purpose of the study base deficit levels after CPB with a pump prime solution containing Ringer's lactate were expected to be normally between 0-2 meq/L, according to one previous study [1]. Hypertension and diabetes were diagnosed if the patient had a history of the condition. Congestive heart failure was defined as a present or previously documented episode of pulmonary edema in a patient with left ventricular dysfunction. Left ventricular function was evaluated by echocardiography. Myocardial infarction was documented by new Q wave or ST segment elevation on the electrocardiogram or CPK MB concentration higher than 100 IU/L within 48 hours after the operation. Low cardiac output syndrome was defined by inotropic drugs or intra-aortic balloon pump use for 24 hours or more; pulmonary dysfunction was defined as mechanical ventilation for 48 hours or more or acute respiratory failure necessitating

Variable	$\geq -8$ meq/L	$< -8$ meq/L	P value
Age (yr)	$55.3 \pm 12.4$	$63.1 \pm 10.58$	0.03
Men	61.1%	65.8%	NS
Women	38.9%	54.4%	0.04
Diabetes	29.4%	25.4%	NS
Preoperative hemoglobin level	$13.6 \pm 1.2$	$13.8 \pm 1.2$	NS
Congestive heart failure	2%	6.5%	0.04
Hypertension	35%	27%	NS
Redo operation	1.6%	7.1%	NS
Emergency operation	0	4.5%	NS

NS: Not significant

Table 1. Preoperative characteristics of 136 patients undergoing cardiac operation according to base deficit levels after CPB.

reintubation; renal failure was defined as creatinine of more than 1.5 mg/L; post operative mortality was defined as death occurring during hospitalization for operation.

### Results

Patients in the study (n=136) had a mean age of  $54 \pm 10.67$  years. There were 88 men and 47 women. Coronary artery bypass operation was performed in 80 cases of the study population and valvular operation in 56 cases. Among the patients included in the present study, 39 had base deficit levels less than -8 (A group) and 91 had a level of  $\geq -8$  meq/L (B group). Patients with a base deficit level of -8 meq/L or more were older and most of them were women. The prevalence of left ventricular ejection fraction less than 30% and coronary artery disease was not significantly higher in patients with base deficit of  $\geq -8$ . No differences were found according to the presence of hypertension or diabetes in patients with base deficit levels of -8 or higher than those with base deficit levels less than -8 (P value  $>0.05$ ). In univariate analysis of preoperative variables there were no differ-

ences in regard to factors such as diabetes, preoperative hemoglobin level, hypertension, emergency operation and redo operation. Congestive heart failure was different between the two groups (P value less than 0.05)(Table 1).

Factors such as cross clamp time, lowest hemoglobin during CPB, maximum CPB flow and minimum CPB flow were not significantly different between the two groups (P value  $<0.05$ ) (Table 2).

Postoperative factors such as hemodynamic stability, myocardial infarction, intra-aortic balloon pump use and inotropic drug use were significantly different between the two groups (P  $<0.05$ ) (Table 3). Factors such as infection, renal failure, gastrointestinal complications and pulmonary complications were almost the same in both groups (P  $>0.05$ )(Table 3).

In linear regression with base deficit less than -8 as dependent variable, factors significantly associated with these variables included: preoperative hemoglobin, renal complication, ICU stay, and minimum hemoglobin during CPB.

According to ROC curve analysis the best threshold value of base deficit for predicting the

Variable	$\geq -8$ meq/L	$< -8$ meq/L	P value
CPB time	$83 \pm 21$	$90 \pm 17$	0.05
Clamp time	$46 \pm 8$	$43 \pm 13$	NS
Lowest Hgb (gr/l)	$11.3 \pm 1.3$	$11.8 \pm 1.7$	NS
Maximum CPB flow	$3996 \pm 1338$	$4267 \pm 985$	NS
Minimum CPB flow	$3263 \pm 845$	$3877 \pm 3514$	NS

NS: Not significant

Table 2. Intraoperative characteristics of 136 patients undergoing cardiac operation according to base deficit levels after CPB.

	$\geq -8$ meq/L	$< -8$ meq/L	P value
<b>Variable</b>			
Neurological complication	36.4%	43.6%	NS
Myocardial infarction	4%	15%	0.01
Mortality (hospital)	33.3%	66.7%	0.03
Hemodynamic stability	28.1%	71.9%	0.004
Pulmonary complication	27.3%	72.7%	NS
IABP	34.4%	55.6%	0.013
Gastrointestinal complication	39.2%	30.8%	NS
Inotropic drug use	57.1%	42.9%	0.001
Renal failure	0 %	43%	NS
Infection	46.7%	33.3%	NS
Death (in hospital)	3%	11%	0.04

NS: Not significant

Table 3. Postoperative characteristics of 136 patients undergoing cardiac operation according to base deficit levels after CPB.

occurrence of postoperative complications had a sensitivity and specificity of 65% and 75%, respectively (Fig. 1).

### Discussion

Outcome after cardiac operation is determined by preoperative characteristics of the patient in addition to intraoperative factors such as surgical technique, myocardial protection, and CPB. Several risk factor models have been developed to predict outcome after cardiac operation but very few consider intraoperative events [5-16]. Such intraoperative factors may identify the postoperative course. Monitoring of such factors during the surgical procedure may lead to early therapeutic intervention that might improve outcome. Cardiopulmonary bypass is widely used to maintain systemic perfusion and oxygenation during coronary artery bypass and other open heart surgery. Tissue hypo-perfusion with lactic acidosis during CPB

may occur despite normal gas concentration [10]. Therefore, high blood lactate level during CPB may reflect as base deficit and may be used as a marker of inadequate tissue oxygen delivery. The goal of this study was to evaluate the association between base deficit after CPB and postoperative morbidity and mortality in an adult cardiac surgical population. Under anaerobic condition, oxidative phosphorylation is not possible and ATP is produced from pyruvate and metabolized to lactate that is reflected as base deficit. In this situation, base deficit is a sensitive marker of the magnitude of anaerobic metabolism and tissue oxygen deficit [1]. Several studies have shown a strong positive correlation between base deficit and the risk of morbidity and mortality in clinical situations such as circulatory shock, extracorporeal support and in children after operation for complex congenital heart disease [1-4,17,18]. As early as 1964, Roder and Weil [2] documented that only

Variable	Unstandardized coefficients		Standardized coefficients	t.	P value
	B	Std. error	Beta		
Preoperative hemoglobin level	7.49	4.28	0.23	1.75	0.088
Renal complication	9.09	4.58	0.204	1.98	0.054
ICU stay	-1.92	0.85	-0.84	-2.24	0.031
Minimum hemoglobin during CPB	-1.39	0.49	-2.07	-2.83	0.007
Death	-1.2	0.39	-2.3	-1.25	.025

Table 4. Summary of linear regression of base deficit.

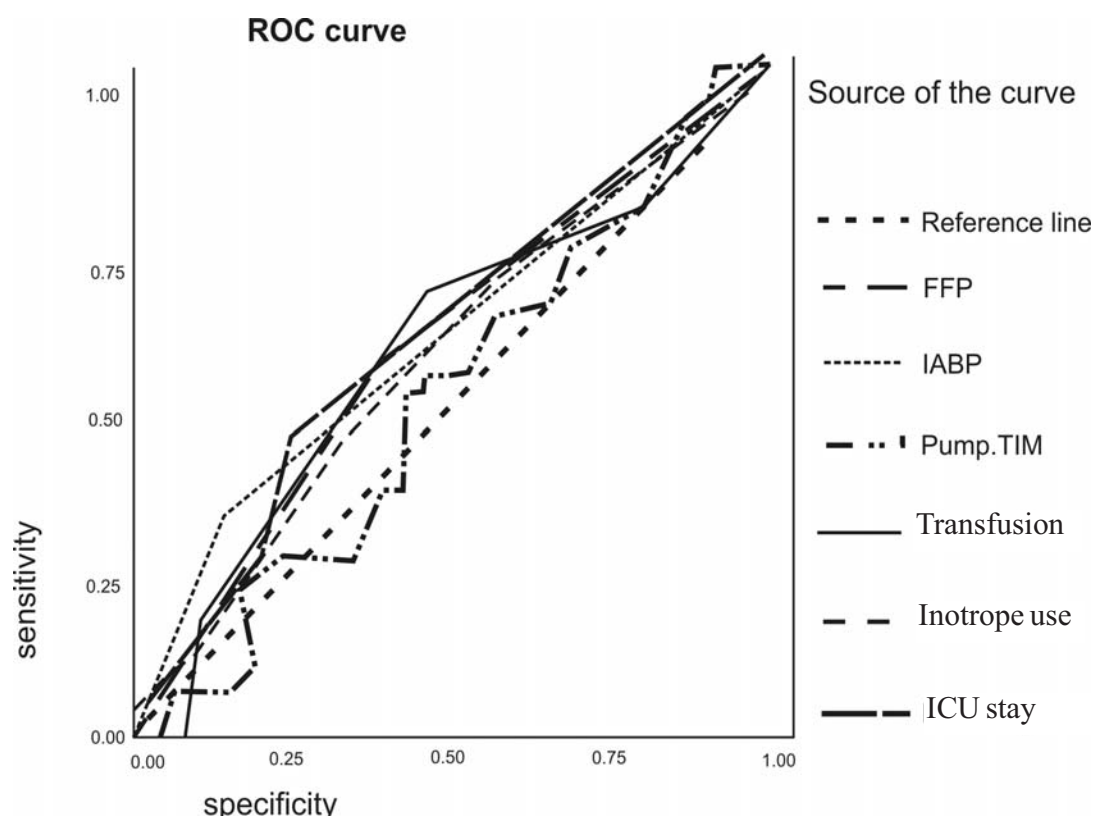


Fig. 1. ROC curve for prediction of postoperative variables and complications.

11% of patients with excess levels of base deficit survived circulatory shock. Later, these authors showed that as base deficit increased from  $-2$  to  $-8$  mmol/L the probability of survival from shock decreased from 9% to 1% [3]. These findings were confirmed more recently by other groups [1,4]. Moreover serial base deficit determination was also reported to be useful to assess response of patients in shock to therapy as a decrease in base deficit exceeding  $-6$  mmol/L [19]. In high risk general surgical patients a positive correlation between the estimated intraoperative oxygen deficit and postoperative base deficit was observed [20]. It was concluded that base deficit determination maybe used to assess the degree of accumulated oxygen deficit and in titrating therapy to support postoperative physiologic compensation.

Tissue perfusion and oxygenation during CPB is achieved by adjusting flow rate, temperature, gas flow, and hemoglobin to maintain oxygen delivery. Monitoring of the balance between oxygen supply and demand usually consists of serial arterial blood gas determination. In 1958, Clowes and colleagues [6] reported the occurrence of metabolic acidosis with base deficit determination during CPB. In some patients, early experimental evidence showed the critical value of high perfusion flow rate and hypothermia in preventing lactic acidosis and base deficit during CPB [6, 8].

Several contributing factors have been linked to regional tissue hypoperfusion and increased base deficit during CPB. Recently, at  $2.2$  l/min.m<sup>2</sup> at  $37^{\circ}\text{C}$ , hypoperfusion during CPB was related to the production of endoge-



nous vasoactive mediators and a decrease in arterial oxygen content during bypass was proposed as an important event in the generation of lactate and increased base deficit during an apparently adequate oxygen supply. Extreme hemodilution, hypothermia, low flow CPB, and excessive neurohormonal activation have also been linked to increased base deficit [10]. An abrupt increase in lactate concentration may result at the institution of CPB when priming solutions containing lactate are used. However, several studies comparing different priming solutions have shown that base deficits are lower than  $-1$  mmol/L, even when lactate is present in the priming fluid [9,14,15]. An impaired hepatic clearance of lactate during CPB related to a hypothermia-induced defect in pyruvate metabolism has also been suggested. In the immediate postoperative period, a hypermetabolic response characterized by increased oxygen consumption and carbon deficit production has been shown to occur at CPB [21-23]. Base deficit measurement usually indicates the need for volume resuscitation in the acutely injured patient. However severe base deficit in the ICU patient is due to perfusion impairment [25]. In one study [25], the base deficit has been specifically examined in the pediatric trauma population. Base deficit less than  $-4$  meq/L and the presence of a closed head injury were predictors of mortality. For this group, an admission base deficit of  $-8$  meq/L corresponded to a probability of mortality. Significant correlations were found between base deficit and emergency department systolic blood pressure, length of stay in the ICU, injury severity score and deficit value in the immediate postoperative period of coronary surgery with CPB [26]. Ten variables had a statistically significant difference in univariate analysis (Tables 1,2,3) and four of them highlighted by linear regression model, one of which was ICU stay postoperatively (Table 4).

Kincaid and colleagues [25] showed that, the admission value of the arterial base deficit strat-

ifies injury severity, predicts complications and is correlated with arterial lactate concentration. In theory, elevated base deficit and lactate concentration after shock and hypoperfusion such as CPB are related to oxygen transport imbalance at the cellular level. Subgroup analysis revealed that patients with a persistently high base deficit had higher rates of multiple organ failure compared with patients who achieved a low base deficit [25]. Patients with a persistently high base deficit had lower oxygen consumption and a lower oxygen utilization coefficient and higher lactate level compared with patients with a low base deficit. They conclude that in these patients, a high arterial base deficit is associated with altered oxygen utilization and an increased risk of multiple organ failure and mortality. Serial monitoring of base deficit may be useful in assessing the adequacy of oxygen transport and resuscitation process. The above response (high arterial base deficit) may be related to intraoperative oxygen deficit and may represent a high risk period for decompensation. In the present study, patients undergoing cardiac operation with base deficit of  $-8$  or less after CPB were older, more likely to be female, and were at higher risk according to the clinical study (Table 1). There were weak but significant correlations between CPB time and base deficit of more than  $-8$  meq/L, suggesting that higher base deficit levels are more likely to occur with long CPB duration but are dependent on other preoperative factors (Table 2). Postoperative mortality was significantly higher in patients with high base deficit after CPB. Moreover postoperative complications such as myocardial infarction, hemodynamic stability, IABP and inotropic drug use were significantly more frequent in these patients (Table 3). This group of patients also needed greater hospital care. Finally, a peaked base deficit of  $-8$  meq/L or less after CPB was identified as a strong independent predictor of mortality and morbidity by linear regression analysis and suggests that occult tissue hypoperfusion occurred during

CPB (Table 4). However, further studies are needed to evaluate the association between blood gas base deficit and occult oxygen deficit occurring during CPB. Identification of high base deficit during CPB should prompt further evaluation of all potential factors that may modify oxygen delivery and consumption. Several limitations are inherent to the present study. First, the population studied was heterogeneous including all the patients undergoing cardiac operation with CPB during 3 months. The proposed threshold value for base deficit levels differed from the value for base deficit chosen by other authors for different clinical situations. According to receiver under curve analysis (ROC), the best threshold value of base deficit for predicting postoperative complications had a sensitivity and specificity of 65% and 75%, respectively (Fig. 1). In conclusion, our data suggest that a base deficit level of -8 meq/L or less after CPB is associated with an increased risk of perioperative mortality and morbidity. Further studies are needed to determine if serial blood gas determinations during CPB and intervention based on base deficit value improve survival in cardiac surgical patients.

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