Original Article

Is an Increase in Lactate Concentration Associated with Cardiac Dysfunction after the Fontan Procedure?

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Purpose: To investigate how blood lactate concentration changes in the early postoperative course after the Fontan procedure, and whether such a change is associated with postoperative hemodynamics.
Materials and Methods: Eight pediatric patients who underwent the Fontan procedure for congenital heart disease were included. Enrollment criteria were body weight >10 kg and staged Fontan procedure following the bidirectional Glenn procedure. Blood lactate concentration and central venous oxygen saturation (SvO_2) were measured at five points: before skin incision, upon intensive care unit (ICU) admission, 15 minutes before, 15 minutes after, and 2 hours after extubation. Cardiac index (CI) was continuously monitored using the pulse contour technique.
Results: Lactate concentration increased in the ICU, peaking from 15 minutes before (2.7±1.3 mmol/L) to 15 minutes after (3.0±1.3 mmol/L) extubation. Values returned to normal parameters (1.0±0.1 mmol/L) within 48 hours. The CI values were also higher immediately after extubation (4.0±0.6 L/min/m^2) than at ICU admission (3.3±0.6 L/min/m^2) and before extubation (3.6±0.6 L/min/m^2) (p=0.012). No significant change in central SvO_2 or blood pressure (BP) was evident during the study period.
Conclusion: In the early postoperative period after the Fontan procedure, blood lactate concentration increased temporarily around the time of extubation but the increase was not associated with hemodynamic deterioration. (Ann Thorac Cardiovasc Surg 2005; 11: 301–6)

Key words: Fontan procedure, lactate, pulse contour, cardiac output

Introduction

Blood lactate concentration has proven to be one of several reliable parameters for evaluating hemodynamic state in post-cardiac-surgery patients. In general, low output syndrome leads to poor peripheral circulation and high lactate concentration. After cardiac surgery for congenital heart disease, high lactate concentration is associated with high morbidity and mortality.[1)] Even so, the relationship between blood lactate concentration and cardiac output has not been thoroughly investigated in congenital heart disease patients, especially after the Fontan procedure.

The Fontan procedure, involving total cavopulmonary connection, is a definitive operation for patients with univentricular physiology, where a single ventricle propels blood through two resistant components: that is, systemic and pulmonary vascular resistance in series.[2)] Although drastic circulatory changes, such as a decreased cardiac output, occurs after the Fontan procedure,[3)] postoperative changes in lactate concentration have not been reported in detail. Even if lactate does increase, because of the typically small body size and abnormal cardiac morphology of Fontan patients, it is difficult to measure

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Table 1. Patient's characteristics

No.	Age (y)	Weight (kg)	Diagnosis
1	16	29	Ebstein's anomaly, atrial septal defect, ventricular septal defect, pulmonary stenosis
2	5	17	Mitral atresia, double outlet right ventricle
3	3	14	Atrioventricular discordance, double outlet right ventricle, pulmonary atresia
4	10	30	Mitral atresia, double outlet right ventricle
5	4	14	Tricuspid atresia
6	6	16	Pulmonary atresia with intact ventricular septum
7	1	13	Double outlet right ventricle
8	9	19	Double outlet right ventricle, pulmonary atresia

Table 2. Intraoperative parameters

No.	Anesthesia time (min)	Operation time (min)	CPB time (min)	ACC time (min)	Blood loss (ml)	Transfusion (ml)	Hb (g/dl)
1	810	680	242	87	680	1,910	14.2
2	600	450	133	45	220	160	12.5
3	600	440	0	0	200	0	9.3
4	570	455	0	0	400	0	13.8
5	645	520	0	0	190	0	12.9
6	560	460	0	0	165	0	10.9
7	575	460	0	0	100	0	12.1
8	385	295	0	0	350	0	8.2

CPB, cardiopulmonary bypass; ACC, aortic cross clamp; Hb, hemoglobin level when entering the intensive care unit

cardiac output and clarify how increased lactate is related to low cardiac output in the early postoperative period.

To investigate changes in lactate concentration in the early postoperative period after the Fontan procedure, and whether the increase in lactate is associated with impaired cardiac output, we serially measured lactate concentration and cardiac output using arterial pulse contour analysis.[4] We hypothesized that, because of impaired cardiac output, soon after Fontan surgery lactate concentration would temporarily increase.

Materials and Methods

The study was approved by the institutional ethics committee of the National Cardiovascular Center (Osaka, Japan), and written informed consent was obtained from the parents of each patient. Eight patients undergoing the Fontan procedure between 2001 June and 2002 February were included in this study (Table 1). Enrollment criteria were: 1) body weight >10 kg; 2) staged Fontan procedure following the bidirectional Glenn procedure; 3) meeting the indication of the Fontan operation; pulmonary vascular resistance[5] <4 Unit · m^2; and pulmonary artery index >250 mm^2/m^2.

The surgical procedure is outlined in Table 2. Using an 18- or 20-mm internal diameter (ID) Gore-Tex® tube graft, each patient received the construction of an extracardiac channel from the inferior vena cava (IVC) to the pulmonary arteries. Six patients (#3 to #8) did not require cardiopulmonary bypass (CPB) (off-pump Fontan),[6] and five (#3 to #7) of these six patients underwent the Fontan procedure under the placement of temporary bypass between the atrium and the IVC. On the other hand, the CPB was used to repair concomitant intracardiac anomalies in two patients (#1 and #2), and these patients required blood transfusion (1,910 ml and 160 ml). After the opearation, no atrioventricular valve regurgitation or pulmonary artery stenosis were recognized. On the intensive care unit (ICU) admission, dopamine was administered in 7 patients (3.8±1.4 μg/kg/min) and nitroglycerin in all patients (0.42±0.16 μg/kg/min).

Arterial blood pressure (BP), heart rate (HR), pulmonary artery pressure, central venous pressure (CVP), and pulse oximeter signal (PM-1000; Nellcor Inc., Hayward, CA) were continuously monitored in all patients. The catheter for left atrial pressure (LAP) measurement was inserted by surgeons after weaning from the CPB. We used a calibrated gas analyzer (ABL 700; Radiometer, Copenhagen, Denmark) to measure arterial blood gas, blood lactate, and base excess along with central venous oxygen saturation (SvO_2) in the right-sided superior vena cava at five points in time: before skin incision, at the admission to the ICU, and 15 minutes before, 15 minutes after, and 2 hours after extubation. Lactate concentration was also measured at 24 and 48 hours after ICU admission in addition to those five points.

Cardiac index (CI) was continuously monitored by arterial pressure contour analysis (PiCCO; Pulsion Medical Systems, Munich, Germany). After anesthetic induction, we inserted a central venous catheter (5.5 Fr, Arrow; Arrow International Corp., Germany) into the internal jugular vein and femoral vein, and a PiCCO catheter (4 Fr, PV2014L13, Pulsion Medical Systems) into the femoral artery. Before skin incision and at ICU admission, according to the manufacturer's instructions, we calibrated the PiCCO system by injecting 5 ml cold saline (0°C). Maximal rising rate of ventricular pressure (dP/dt max) was also continuously measured by PiCCO.

The IVC pressure was measured by the catheter into the femoral vein during temporary bypass when off-pump Fontan procedure was carried out.

Oxygen consumption index ($\dot{V}O_2I$), and extraction ratio (ER) were calculated using the following formulae:

$$\dot{V}O_2I = 1.34 \times Hb \times CI \times (SaO_2 - SvO_2)$$

$$ER = 100 \times (1 - SvO_2/SaO_2)$$

CI, cardiac index; Hb, hemoglobin; and SaO_2, arterial oxygen saturation.

Core temperature was continuously measured at the urinary bladder and skin surface temperature at the forehead. The PiCCO catheter was removed 3 hours after extubation.

Mechanical ventilation

For ventilation in the ICU, we used V.I.P. Bird ventilators (Bird Corp., Palm Springs, CA) for patients with body weight <15 kg and Servo 300 ventilators (Siemens Life Support Systems, Iselin, NJ) for those with body weight ≧15 kg. Initial ventilatory settings were: assist-control mode; pressure-control ventilation (PCV), 17 cm H_2O; inspiratory time, 0.8-1.0 s; and positive end-expiratory pressure, 3 cm H_2O. We adjusted the pressure-control level and respiratory rate to obtain a tidal volume of 10 ml/kg and normocapnia. Inspired oxygen fraction was initially reduced to ≦0.6. Once spontaneous breathing efforts emerged, the pressure-control level was reduced to 7-10 cm H_2O. When circulatory and respiratory conditions stabilized, endotracheal tubes were removed.[7] These procedures enabled weaning from mechanical ventilation as quickly as possible.

Statistical analysis

Data are presented as mean±SD. Variables were analyzed using non-parametric Friedman tests. When significant differences were found, we performed a post hoc analysis using Wilcoxon signed rank tests. Spearman correlation coefficients were used to evaluate whether lactate concentration correlated with the pre- and intra-operative parameters. All statistical analysis was performed with a software package *Statview for Macintosh* (Abacus Concepts, Berkeley, CA). Statistical significance was set at $p<0.05$.

Results

Tracheal tubes were removed 3.1±1.1 hours after ICU admission, which corresponded to 6.2±1.9 hours after the commencement of Fontan circulation. No complications arose due to the PiCCO technique. The stay in the ICU was 7±3 days (range, 4 to 14 days) and discharge from hospital came at 52±34 days (range, 24 to 129 days) after the operation.

Figure 1 shows changes in blood lactate concentration. Lactate concentration significantly increased from 0.9±0.3 mmol/L (before skin incision) to 1.6±0.5 mmol/L (at the ICU admission) and then 2.7±1.3 mmol/L (15 minutes before extubation) and 3.0±1.3 mmol/L (15 minutes after extubation). It then declined to 2.4±1.1 mmol/L (2 hours after extubation) (p=0.012). Six patients had maximal concentration of lactate between 15 minutes before and after extubation. For the other two patients, throughout the measurement period, the lactate level gradually decreased for one and increased for the other. The lactate level decreased to 1.5±0.2 mmol/L at 24 hours and 1.0±0.1 mmol/L at 48 hours after ICU admission.

Figure 2 shows changes in CI values. For all patients, from 15 minutes before to 15 minutes after extubation, CI values increased (3.6±0.6 L/min/m^2 to 4.0±0.6 L/min/m^2) (p=0.012). PiCCO data for CI change (patient #7) is shown in Fig. 3. CI values declined remarkably after the start of Fontan circulation and then gradually increased during the operation.

In the ICU, the CI values increased when the patient returned to consciousness and decreased again after extubation, at which time dP/dt max significantly increased. Core temperature significantly increased from 36.5±0.6°C at the ICU admission to 37.8±0.7°C after extubation (p=0.012). SvO_2 did not significantly change throughout the monitoring period (Table 3).

There was no correlation between lactate concentra-

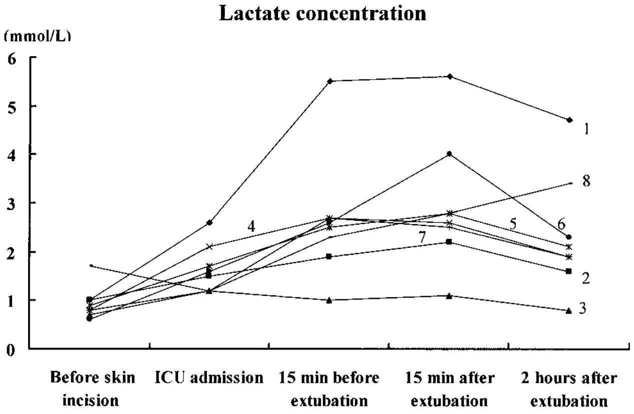

Fig. 1. Changes in blood lactate concentration at the perioperative period of the Fontan procedure. The numbers in this figure correspond to the patient numbers in Table 1.

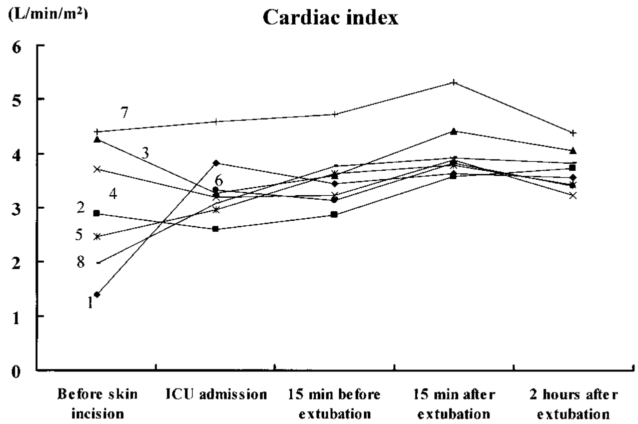

Fig. 2. Changes in cardiac index values at the perioperative period of the Fontan procedure. The numbers in this figure correspond to the patient numbers in Table 1.

tion and preoperative parameters such as pulmonary artery index and pulmonary artery resistance, or between lactate concentration and intraoperative parameters such as urine output, core and skin surface temperature, base excess, IVC pressure after IVC clamping during the use of temporary bypass.

Discussion

The main findings of this study are: 1) after the Fontan procedure, blood lactate concentration increases immediately after extubation of tracheal tubes and returns to normal within 48 hours; 2) when lactate concentration peaks, CI data is also high.

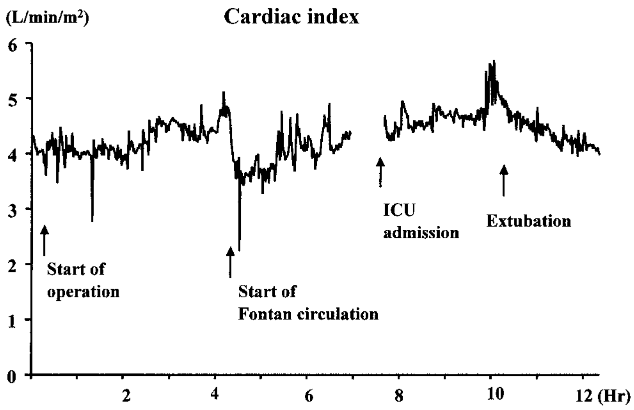

Fig. 3. Representative tracing of cardiac index data during and after the Fontan procedure. This patient (#7) underwent Fontan procedure without the support of cardiopulmonary bypass.

Clinical implication

In general, increasing lactate concentration indicates diminishing tissue perfusion and oxygen delivery:[8] in patients undergoing repair surgery for congenital cardiac anomaly, high lactate predicts postoperative morbidity and mortality.[9-12] Charpie et al.[9] have reported that when blood lactate increases at a rate greater than 0.75 mmol/L per hour after neonatal cardiac surgery, it indicates that extracorporeal membrane oxygenation or other mechanical support is more likely to be needed. These findings, however, may not be applicable to patients with Fontan circulation, because total cavopulmonary connection drastically changes hemodynamics. In this study, we found that both blood lactate and CI values increased at around the period of extubation. Our findings suggest that increased lactate does not necessarily result solely from impaired hemodynamics or hypoxia. Although our study offers scant evidence as to why blood lactate increases even while CI is improving, there are several plausible explanations.

First, poor peripheral tissue perfusion during the intraoperative or postoperative period has been reported to be a common cause of oxygen imbalance that promotes lactate production.[12,13] We found that the gradual increase in lactate in the ICU was associated with increases in $\dot{V}O_2I$ and ER. Even though these changes were not significant (Table 3), they could be signs of poor peripheral perfusion. The poor peripheral perfusion could be promoted by increased metabolic rate related to rewarming,[13] awakening, and increased work of breathing. The elevation in lactate especially at around the period of tracheal tube extubation may result from these complex situations. Furthermore, improvement in peripheral perfusion

Table 3. Hemodynamic parameters

	units	Before skin incision	ICU admission	15 min before extubation	15 min after extubation	2 hrs after extubation
HR*	bpm	101±13	130±23†	133±17†	143±19†	131±14†
Mean BP	mmHg	69±12	77±9	78±10	78±14	79±9
CVP*	mmHg	10±2	15±3†	17±5†	15±4†	14±4†
LAP	mmHg	n.d.	6±2	8±4	6±4	5±4
dP/dt max*	mmHg/s	641±182	686±234	793±332	1,204±553‡	879±390
CI*	L/min/m^2	3.2±1.1	3.3±0.6	3.6±0.6	4.0±0.6‡	3.7±0.4
SvO_2	%	62±5	63±9	63±8	71±7	62±7
$\dot{V}O_2I$	ml/min/m^2	11.9±6.0	14.2±1.2	16.6±5.0	16.4±5.3	20.6±2.2
ER	%	27.6±9.7	33.8±8.7	33.7±7.2	26.3±5.5	33.1±8.1
Lactate*	mmol/L	0.9±0.3	1.6±0.5†	2.7±1.3†	3.0±1.3†	2.4±1.1†
PaO_2	torr	65±15	105±42	117±61	88±33	107±46
Core temp*	°C	36.9±0.6	36.5±0.6	37.7±0.6††	37.8±0.7††	37.8±0.8††

Data are presented as mean±SD.
HR, heart rate; BP, blood pressure; CVP, central venous pressure; LAP, left atrial pressure; dP/dt max, maximum rising rate of ventricular pressure, CI, cardiac index; SvO_2, mixed venous oxygen saturation; $\dot{V}O_2I$, oxygen consumption index; ER, extraction ratio; PaO_2, arterial oxygen pressure; temp, temperature.
*, $p<0.05$ using Friedman test; †, $p<0.05$ vs Before skin incision; ††, $p<0.05$ vs ICU admission; and ‡, $p<0.05$ vs 15 min before extubation.

brought about by increased CI might be insufficient to compensate for the increased metabolic rate.

Second, transfer of lactate from peripheral tissue into the blood stream is promoted when peripheral vasodilatation occurs.[7] In our study, in addition to the rise in CI values, core temperature increased after ICU admission (Table 3). These changes could possibly augment vasodilation and promote lactate transfer. These phenomena increased blood lactate levels even if lactate production is suppressed because of a stable condition.

Third, in general, CI data show instant values that are measured at each point. On the other hand, lactate concentration does not demonstrate instant values but reflect some changes in circulatory, respiratory, and metabolic condition for some periods of time. These may be reasons why lactate concentration does not necessarily correlate with the instantaneous CI value.

Because of the complicated cardiac structure and lack of appropriate catheter, measurement of cardiac output is difficult in patients undergoing congenital cardiac surgery.[14] During the Fontan procedure, the insertion of a Swan-Ganz catheter is impossible because systemic veins are directly anastomosed to the pulmonary artery. Although the Fick method, which uses expired gas analysis, is an alternative mode of measurement,[15] $\dot{V}O_2I$ calculation is prone to significant error in small children and SvO_2 monitoring is unreliable for patients who have residual intracardiac anomalies. PiCCO, on the other hand, is a novel device that enables continuous monitoring of cardiac output in children by means of transpulmonary thermodilution and arterial pulse contour analysis.[4,16,17] This technique requires neither blood sampling nor insertion of catheters into the heart. The cardiac output data from PiCCO is reported to correlate well with other techniques.[18]

Our current study contains several limitations. First, our sample was small (*n*=8) because, to avoid complications relating to cannulation,[18] we limited enrollment to patients with body weight greater than 10 kg. Second, the patient population and Fontan procedures performed in this study were not homogeneous, which makes an extrapolation of the findings directly to other patients difficult. Third, because all patients showed an uneventful clinical course and CI values remained at above 3.0 L/min/m^2 during this study, there might be no drastic lactate change correspondent with subtle hemodynamic change. We could have observed more drastic change of lactate concentration if we had enrolled the patients whose clinical course became much worse.

In conclusion, after the Fontan procedure, blood lactate concentration temporarily increased after extubation and decreased to within the normal range within 48 hours. The increase in lactate was not associated with decreased CI values, probably because the postoperative recovery in all patients was uneventful. Further investigation is needed to evaluate the usefulness of lactate measurement for patients who have undergone the Fontan procedure.

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