J. Anesth (1994) 8:72–77

Journal of
Anesthesia

Changes of oxygen transport variables and serum lactate during open-chest cardiac massage in dogs

MICHIHIKO FUKUI, TETSUO HATANAKA, MASAMI YOSHIOKA, TSUTOMU YAN, NOBUAKI SHIME, and YOSHIFUMI TANAKA

Department of Anesthesiology, Kyoto Prefectural University of Medicine, 465 Kawaramachi-Hirokoji, Kamikyo-ku, Kyoto, 602 Japan

Abstract: The aim of this study was to investigate the influence of critically low cardiac output (CO) upon oxygen transport. We especially focused on the changes of mixed venous oxygen saturation ($S\bar{v}O_2$) in the presence of oxygen consumption ($\dot{V}O_2$) debts. Additionally, we examined the correlation between the cumulative oxygen deficit (Def$\dot{V}O_2$) and serum lactate. Def$\dot{V}O_2$ was calculated as the integrated area under the tissue $\dot{V}O_2$) deficit (baseline $\dot{V}O_2$—actual $\dot{V}O_2$) and time curve. To produce severe low CO, we performed open-chest cardiopulmonary resuscitation (CPR) in 11 anesthetized dogs for 1 h. We made the measurements before (baseline values) and during the CPR at 10-min intervals. Supply-dependent $\dot{V}O_2$ was observed when CO decreased below 40 ml·min^{-1}· kg^{-1}. The mean value of $S\bar{v}O_2$ in the range of supply-dependent $\dot{V}O_2$ was 13 ± 2% and did not change significantly during 1 h of CPR. The changes of lactate from baseline values were linearly correlated with Def$\dot{V}O_2$ (r = 0.62, $P < 0.01$), but absolute values of serum lactate were not.

Key words: Oxygen debt, Oxygen consumption, Tissue oxygen extraction, Cardiogenic shock, Mixed venous oxygen saturation, Cardiopulmonary resuscitation

Introduction

As the cardiac output (CO) decreases below a critical level, impairing the ability of tissues to extract oxygen, tissue oxygen consumption ($\dot{V}O_2$) is decreased and becomes supply-dependent [1,2]. Then the values of mixed venous oxygen saturation ($S\bar{v}O_2$) are determined by the ability of tissue oxygen extraction: $S\bar{v}O_2$ shows maximum compensatory decreases in intact tissue oxygen extraction, and becomes abnormally high when the ability of tissue to extract oxygen deteriorates. Recent studies demonstrated that the ability of tissue oxygen extraction is lowered in cases of adult respiratory distress syndrome (ARDS) and septic shock [3–5]. Such shock patients fail to maintain adequate $\dot{V}O_2$ with normal or high $S\bar{v}O_2$, and this affects the critical threshold [3]. Inadequate tissue oxygen extraction has not been studied in acute cardiogenic shock [6,7] because there are no experimental methods which can maintain critically lowered CO [8]. To study this problem, we performed open-chest cardiopulmonary resuscitation (CPR) to produce critical CO in dogs, and investigated the changes of $S\bar{v}O_2$ in the presence of $\dot{V}O_2$ debts.

Additionally, we examined the possibility of estimating the cumulative oxygen deficit (Def$\dot{V}O_2$) from serum lactate levels during low CO. Def$\dot{V}O_2$ is generally believed to be associated with the subsequent development of organ failure in patients with shock [2], and is calculated as the integrated area of the $\dot{V}O_2$ deficit (needed $\dot{V}O_2$—actual $\dot{V}O_2$) and time curve [8]. However, since this estimation is too complicated to determine in all shock patients, it is necessary to investigate simpler parameters which reflect the changes in Def$\dot{V}O_2$. The increase of Def$\dot{V}O_2$ is thought to facilitate anaerobic metabolism and may cause proportional lactate production in tissues. The changes of serum lactate have been well studied during shock [3,5,10,11], but its correlation with Def$\dot{V}O_2$ has not.

Methods

This experiment was performed in accordance with the Guideline for Animal Experiments, Kyoto Prefectural University of Medicine. The study protocol was approved by the Ethics Committee of the Department of Anesthesiology of the University.

Eleven mongrel dogs weighing 8.0 to 15.0 kg (mean 10.8 kg) were used. Anesthesia was induced with 150 mg ketamine given intramuscularly and inhalation of 2% to 5% enflurane through a mask. With intramuscular administration of 100 mg succinylcholine to facili-

Address correspondence to: M. Fukui
Received for publication on August 5, 1992; accepted on April 8, 1993

tate tracheal intubation, anesthesia was maintained with pure oxygen and 1% enflurane. Continuous positive pressure ventilation was done with a Harvard-type animal respirator (B-2, Igarashi Ika Kogyo, Tokyo, Japan). The positive end-expiratory pressure level was maintained at 5 cmH_2O. Respiratory rate was maintained at 12–15 cycles·min^{-1} and tidal volume was adjusted to maintain end-tidal PCO_2 at 35–45 mmHg before the initiation of CPR. The respiratory mode was not changed during CPR.

Bilateral thoracotomy crossing a sternum at the 4th intercostal space, insertion of a 5-Fr thermodilution catheter through a surgically exposed external jugular vein into the pulmonary artery, and cannulation of a common carotid artery were done. Correct position of the pulmonary catheter was confirmed by direct palpation of the pulmonary artery and pressure monitoring. Body temperatures were maintained at the baseline levels with circulating water blankets and infrared heaters. About 1 h after these surgical procedures, 4 mg pancuronium to prevent convulsions during CPR and 3000 IU heparin were administered intravenously. Ventricular fibrillation was induced with an AC fibrillator, and direct cardiac massage was performed by one person to maintain the CO as constant as possible in each dog.

CO was measured by the thermodilution method in duplicate using 2 ml of 0.9% saline at 0°C (9520A, Edwards Laboratories, Santa Anna, Calif.). Arterial oxygen saturation (Sao_2), $S\bar{v}O_2$, and hemoglobin (Hb) were measured with a Hemoximeter (OSM3, Radiometer, Copenhagen, Denmark). Arterial lactate was measured with an enzyme electrode analyzer YSI27 (Yellow Springs Instrument, Yellow Springs, Ohio). One ml each of arterial and mixed venous blood samples were simultaneously drawn for the measurements, and CO measurements were done immediately after obtaining the blood samples. These measurements were taken 7 times in each dog: before CPR (baseline measurement) and at 10-min intervals for 1 h during CPR.

Measured values of CO were divided by body weight. $\dot{V}O_2$ were calculated using the following equation:

$$\dot{V}O_2 = 0.134 \times Hb \times (SaO_2 - S\bar{v}O_2) \times CO \quad (1)$$

To determine $\dot{V}O_2$ deficit (needed $\dot{V}O_2$ − actual $\dot{V}O_2$), the baseline value of $\dot{V}O_2$ was used as the needed $\dot{V}O_2$ in each animal. The percent changes of $\dot{V}O_2$ from the baseline were calculated, and decreases below 80% were defined as the presence of $\dot{V}O_2$ debts in consideration of a maximum error of more than 10% in the measurements of $\dot{V}O_2$ [4,12]. Def$\dot{V}O_2$ was calculated from the integrated area under the $\dot{V}O_2$ deficits and time curve.

Mean values and their standard deviations (SD) were calculated, and the following parameters were evaluated: (1) changes of all the values of CO, $S\bar{v}O_2$, and $\dot{V}O_2$ during 1 h of CPR, (2) estimation of a critical level for CO necessary to maintain baseline $\dot{V}O_2$ levels using the regression line between CO and $\dot{V}O_2$ below 80%, (3) changes of $S\bar{v}O_2$ in the range of $\dot{V}O_2$ debts based on the relationship between $S\bar{v}O_2$ and $\dot{V}O_2$, (4) relationship between $S\bar{v}O_2$ and CO, (5) estimation of critical CO levels based on increases of Def$\dot{V}O_2$ and serum lactate using the changing patterns of each dogs, and (6) correlation between Def$\dot{V}O_2$ and serum lactate levels.

The results of these experiments were statistically analyzed using the analysis of variance (ANOVA). P values < 0.05 were considered significant.

Results

The mean values of baseline measurements were as follows: CO was 130 ± 21 ml·min^{-1}·kg^{-1}, $S\bar{v}O_2$ was 76.5 ± 6.9%, Hb was 15.8 ± 1.4 g·dl^{-1}, arterial lactate level was 3.2 ± 1.6 mmol·l^{-1}, and $\dot{V}O_2$ was 6.5 ± 1.0 ml·min^{-1}·kg^{-1}. SaO_2 ranged from 98% to 100% during the experiments. In all dogs, the decreases of pulmonary arterial temperature were within 1°C.

Figure 1 shows the sequential changes in CO, $S\bar{v}O_2$, and $\dot{V}O_2$ in 11 dogs. Each CO significantly decreased to a different level at the beginning of CPR ($P < 0.01$), but did not change significantly during CPR. The values of $S\bar{v}O_2$ and $\dot{V}O_2$ also decreased at the beginning of CPR ($P < 0.01$), but showed no significant changes during CPR.

There was a significant linear correlation between the values of CO and the percent changes of $\dot{V}O_2$ in the range of less than 80% of the baseline ($Y = 2.16X + 5.14$, $r = 0.78$, $P < 0.01$) (Fig. 2). Using the extrapolation of the regression line to 100% of $\dot{V}O_2$, the critical level of CO was estimated at 40 ml·min^{-1}·kg^{-1}.

Figure 3 shows the relationship between $S\bar{v}O_2$ and $\dot{V}O_2$ during CPR. In the presence of $\dot{V}O_2$ debts ($\dot{V}O_2 <$ 80%), the mean value of $S\bar{v}O_2$ was estimated at 13 = 2%.

Figure 4 shows the relationship between CO and $S\bar{v}O_2$ during CPR. The lines in the figure are the mathematical drawings of all points representing a constant $\dot{V}O_2$ of 7 ml·min^{-1}·kg^{-1}, Hb of 18 g·dl^{-1} (solid line) and 11 g·dl^{-1} (dotted line) in Eq. 1. Almost all Hb values in this study were within this range. The points at which these lines intersect the X axis ($S\bar{v}O_2 = 0$) are the mathematical borders of CO needed to maintain $\dot{V}O_2$ with a compensatory decrease in $S\bar{v}O_2$. The actual values of $S\bar{v}O_2$ decreased along these lines in response to the decrease of CO. Further decreases of CO below the low limit did not cause significant increases in $S\bar{v}O_2$.

Figure 5 shows the changes of CO, lactate, and

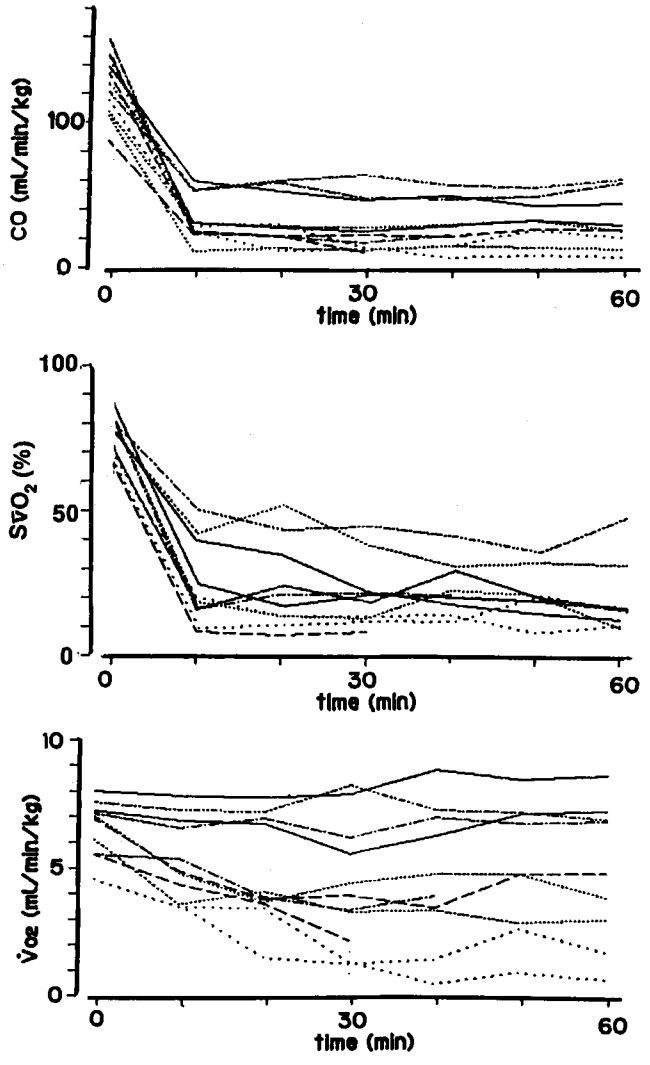

Fig. 1. Changes of coronary output (CO)·BW^{-1}. $S\bar{v}O_2$, and $\dot{V}O_2$ before and during cardiopulmonary resuscitation (CPR) in 11 dogs

Def$\dot{V}O_2$ in 11 dogs. The results were arranged according to the mean CO values during CPR. The values of Def$\dot{V}O_2$ plateaued or did not change in cases where CO exceeded 30 ml·min^{-1}·kg^{-1} during CPR (from #1 to #4), but increased continuously in other cases. The critical CO level at which Def$\dot{V}O_2$ continuously increased was found at 29.2 ml·min^{-1}·kg^{-1}. Because serum lactate increased continuously in all animals, a critical CO level was not clearly identified based on these changes. Larger increases of lactate were observed in dogs with larger Def$\dot{V}O_2$; however, the increments varied in pattern: some were proportional to Def$\dot{V}O_2$ and others plateaued.

Figure 6 shows the positive correlation between all Def$\dot{V}O_2$ values and changes in lactate from the baseline ($r = 0.62$, $P < 0.01$). However, absolute values of serum lactate were not correlated with Def$\dot{V}O_2$ values.

Discussion

In this study, neither $S\bar{v}O_2$ nor $\dot{V}O_2$ showed significant changes during CPR. The estimated critical CO levels of 30 and 40 ml·min^{-1}·kg^{-1} were about one-third of the resting state, which was reported to be a normal threshold [1,5,6]. The $S\bar{v}O_2$ of 13%, the estimated mean value in the range of supply-dependent $\dot{V}O_2$, was similar to the previously reported lowest levels: occasional values of less than 20% were reported by clinical studies of cardiogenic shock [6,7] and heavy exercise [13]. These results imply that the ability of tissue oxygen extraction is intact for 1 h of progressively reduced CO.

The ability of tissue to extract oxygen is generally believed to be determined by effective capillary flow and mitochondrial density in tissues [13,14]. If the number of mitochondria dose not change, inadequately

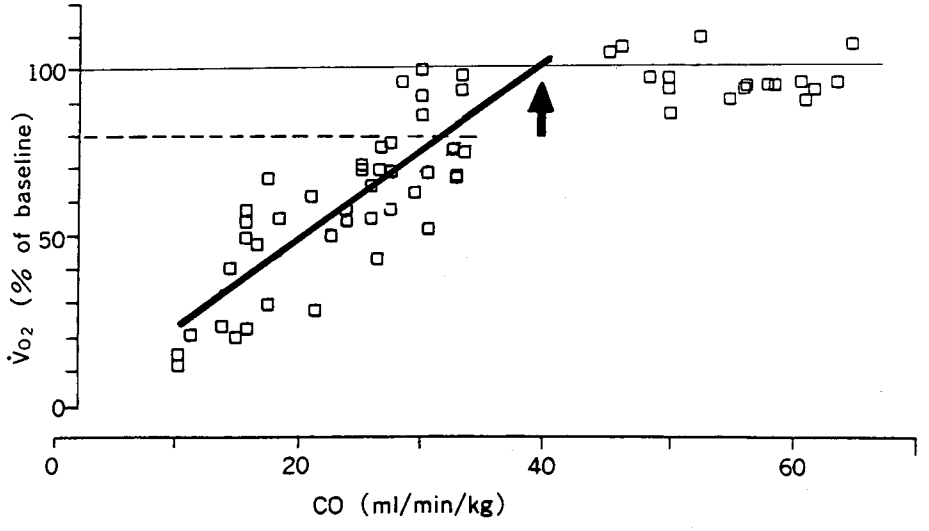

Fig. 2. Relationship between CO·BW^{-1} and the percent changes of $\dot{V}O_2$ from the baseline measurements. When CO decreased below the estimated critical point shown by the *arrow*, the values of $\dot{V}O_2$ showed a supply-dependent decrease

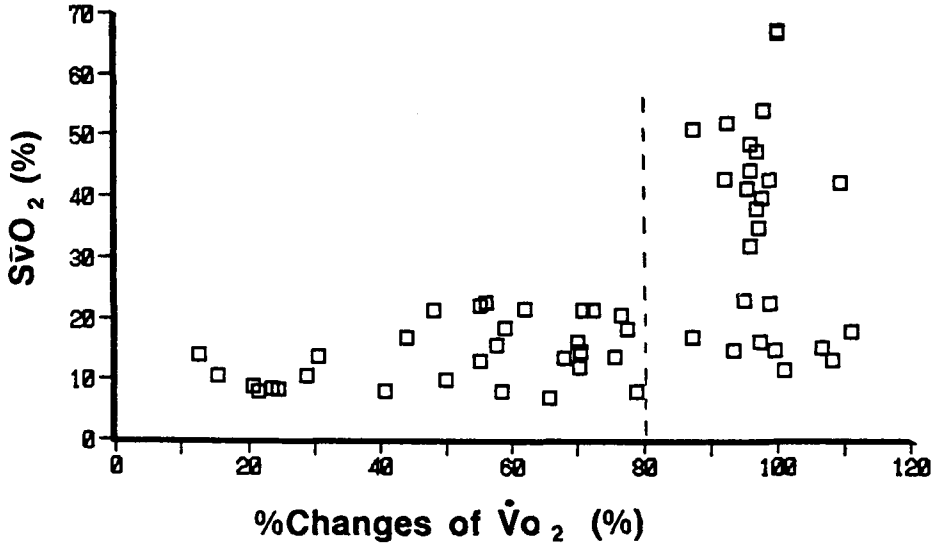

Fig. 3. Relationship between $S\bar{v}O_2$ and the percent change of $\dot{V}O_2$ during CPR

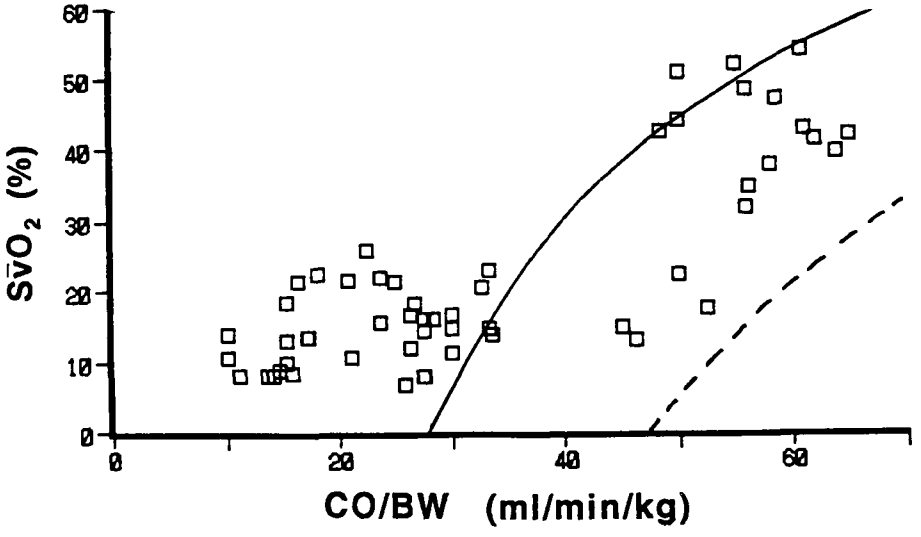

Fig. 4. Relationship between all the values of $CO \cdot BW^{-1}$ and $S\bar{v}O_2$ during CPR. The *lines* represent a constant $\dot{V}O_2$ of 7 $ml \cdot min^{-1} \cdot kg^{-1}$, Hb of 18 $g \cdot dl^{-1}$ (*solid line*) and 11 $g \cdot dl^{-1}$ (*dotted line*)

regulated capillary flow, maldistribution of blood flow, is thought to lower the extraction oxygen [2,3,5]. This impaired oxygen extraction was observed in cases of ARDS and septic shock [1,3,5], but not in patients with acute myocardial infarction (MI) [6,7], and impaired extraction was also not detected in cases of MI in our study of CPR. Maldistributed blood flow is considered to be a basic physiologic deficit in all shock status [2], but we infer that the symptoms are etiologically characteristic of ARDS and septic shock.

Recent shock studies reported that hyperlactacidemia generally occurs in settings in which tissues are well perfused [11], and that the increases of serum lactate facilitated by anaerobic metabolism do not correlate well with any oxygen transport variables [3,5]. Our study of open-chest CPR also did not identify a critical CO threshold of lactate increase or positive correlation between absolute values of serum lactate and $Def\dot{V}O_2$. The changes of serum lactate from baseline values correlated with $Def\dot{V}O_2$, but the correlation was not enough to estimate $Def\dot{V}O_2$. We infer that the poor relationship between blood lactate and oxygen transport variables during shock may be caused by the inhibited lactate production in tissue and/or impaired lactate washout from tissue to the vascular system. There are no adequate studies on these problems, but it is known that ionized lactate hardly diffuses across membranes and is hardly transported from capillary to central circulation by decreased tissue blood flow [10,13]. To assess overall lactate metabolism, we must measure lactate not only in serum but in tissue levels.

We infer that the experimental model of open-chest CPR satisfied the methodological problems to continue critically low CO status. However, to assess such possi-

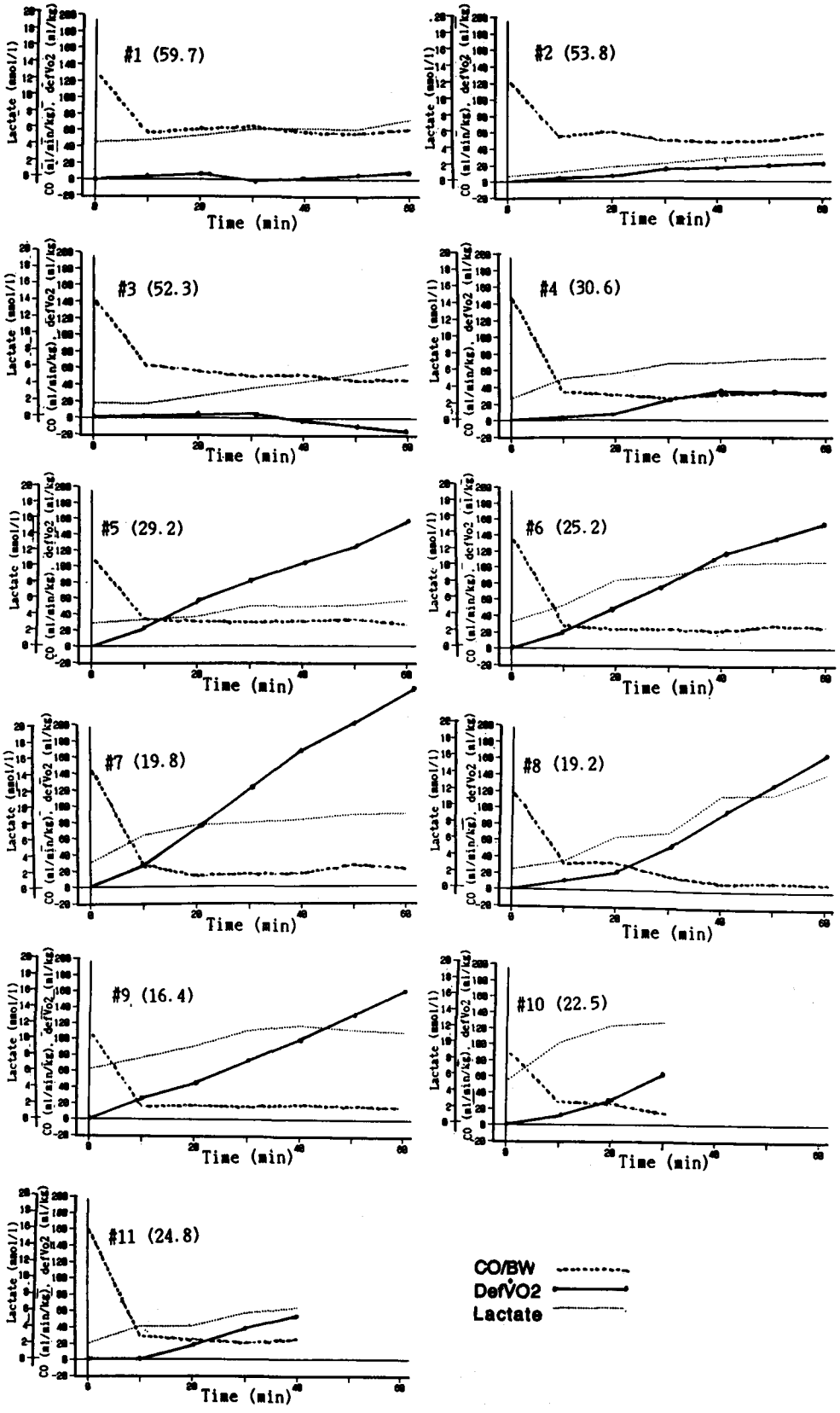

Fig. 5. Changes of CO·BW^{-1}, lactate, and Def$\dot{V}O_2$ before and during CPR in 11 dogs. The graph of each dog was sorted in order of the mean CO·BW^{-1} value during CPR except interrupted cases (#10, #11). The mean CO·BW^{-1} values are shown in *parentheses* next to the material numbers

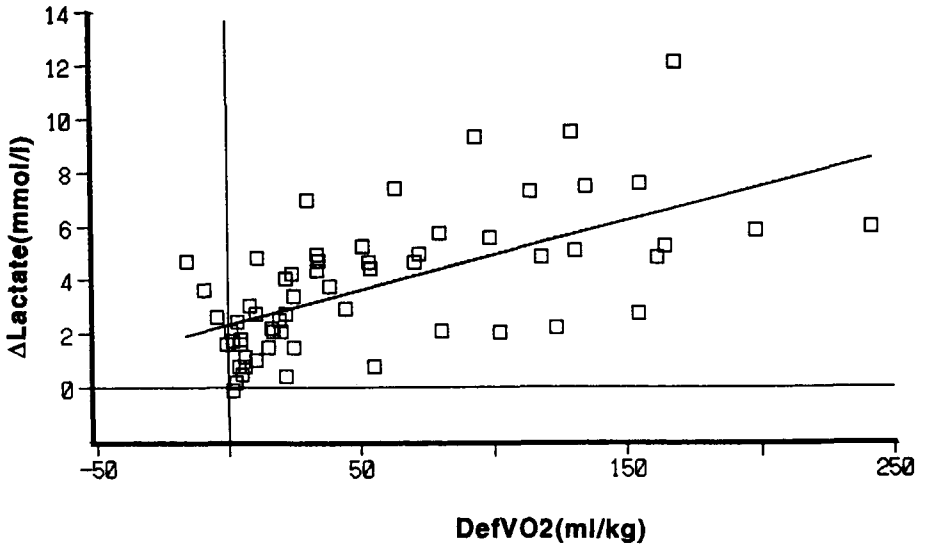

Fig. 6. Correlation between all the values of Def$\dot{V}O_2$ and the changes in lactate from baseline values (Δ lactate). The regression line: Y = 0.027X + 2.2

ble deterioration in tissue oxygen extraction, as demonstrated in ARDS and septic shock, we might have to continue CPR for longer than 1 h. Nonetheless, our study implies that vasodilation induced by an inhalation anesthetic [15] and anticoagulation by heparin are effective to prevent microcirculatory infarction and persistent uneven vasoconstriction that leads to maldistributed flow during CPR. For purposes of further clinical investigations of cardiogenic shock, a more accurate and immediate method of measuring $\dot{V}O_2$ would allow more detailed analysis of patients with unstable circulation.

Acknowledgments. This work was supported in part by a Grants-in-Aid for Encouragement of Young Scientists (Nos. 01771185, 04857171) from The Ministry of Education, Science and Culture, Japan.

References

1. Schumacker PT, Cain SM (1987) The concept of a critical oxygen delivery. Intensive Care Med 13:223–229
2. Shoemaker WC (1987) Circulatory mechanisms of shock and their mediators. Crit Care Med 15:787–794
3. Weg JG (1991) Oxygen transport in adult respiratory distress syndrome and other acute circulatory problems: Relationship of oxygen delivery and oxygen consumption. Crit Care Med 19:650–657
4. Handeln KB, Gronemeyer R, Held A, et al. (1991) Use of continuous noninvasive measurement of oxygen consumption in patients with adult respiratory distress syndrome following shock of various etiologies. Crit Care Med 19:642–649
5. Tuchschmidt J, Oblitas D, Fried JC (1991) Oxygen consumption in sepsis and septic shock. Crit Care Med 19:664–671
6. Edwards JD (1991) Oxygen transport in cardiogenic and septic shock. Crit Care Med 19:658–663
7. Creamer JE, Edwards JD, Nightingale P (1990) Hemodynamic and oxygen transport variables in cardiogenic shock secondary to acute myocardial infarction and response to treatment. Am J Cardiol 65:1297–1300
8. Schlichtig R, Pinsky MR (1988) Defining the hypoxic threshold. Crit Care Med 19:147–149
9. Shoemaker WC, Appel PL, Kram HB (1988) Tissue oxygen debt as a determinant of lethal and nonlethal postoperative organ failure. Crit Care Med 16:1117–1120
10. Leavy JA, Weil MH, Rachow EC (1988) Lactate washout following circulatory arrest. JAMA 260:662–665
11. Mizock BA, Falk JL (1992) Lactic acidosis in critical illness. Crit Care Med 20:80–93
12. Stetz CW, Miller RG, Kelly GE (1982) Reliability of thermodilution method in the determination of cardiac output in clinical practice. Am Rev Respir Dis 126:1001–1004
13. Jones NL (1988) Clinical exercise testing, 3rd edn. WB Saunders, Philadelphia, pp 28–34, 46–50
14. Wagner PD (1987) Handbook of physiology, the respiratory system volume IV. Bethesda, American Physiological Society, pp 257–281
15. Lowenstein E, Reiz S (1987) Effects of inhalation anesthetics on systemic hemodynamics and the coronary circulation. In: Kaplan JA (ed) Cardiac Anesthesia, 2nd edn. Grune and Stratton, Orlando, pp 3–31