Acta Med Okayama 1996; 50(6): 285-292

Continuous Measurement of Tissue Oxygen and Carbon Dioxide Gas Tensions in Dog Liver in Ischemia/Reperfusion

Atsushi Urakami*, Ryuji Hirai, Tetsuya Ota, Hiroyuki Soga, Sugato Nawa and Nobuyoshi Shimizu

Second Department of Surgery, Okayama University Medical School, Okayama 700, Japan

An experiment was conducted to determine whether the oxygen and carbon dioxide gas tensions in liver tissue (PtO_2 and $PtCO_2$, respectively) reflect the state of microcirculation and/or metabolism in the ischemic liver. Subjects were divided into three groups: group 1, 30 min ischemia; group 2, 60 min ischemia; group 3, four times of intermittent 15 min ischemia after every 10 min of reperfusion. PtO_2, $PtCO_2$ and tissue blood flow (TBF) were measured by mass spectrometry, comparatively studied with the serum GOT level as an indicator of liver tissue damage. Furthermore, the time point at which the $PtCO_2$ increase for 1 min initially became less than 1/2 of the maximum value was located on the transit curve of $PtCO_2$, referred to as the critically anaerobic (CA) point, with which new indices of critically anaerobic score (CAS) and time (CAT) (see details in text) were developed. The profiles of PtO_2 and $PtCO_2$ during ischemia and reperfusion were clearly demonstrated, and the CA point was observed 12.7 ± 2.9 min after induction of ischemia. PtO_2 was positively correlated with TBF and negatively with the serum GOT level. Furthermore, not only CAS but also CAT were significantly correlated with PtO_2, TBF, and the serum GOT level. It was concluded that $PtCO_2$ reflects the state of anaerobic tissue metabolism during ischemia and PtO_2 reflects the magnitude of microcirculatory disturbance and tissue injury caused by ischemia/reperfusion. Therefore, continuous monitoring of not only PtO_2 but also $PtCO_2$ is beneficial for patients undergoing hepatic surgery with ischemia.

Key words: liver, ischemia, oxygen, carbon dioxide, mass spectrometry

Although transient hepatic ischemia is a useful procedure to facilitate hepatic surgery, it is also known to cause liver injury (1, 2). Therefore, measurement of the oxygen (O_2) gas tension in liver tissue (3, 4) (PtO_2) is useful to measure the balance between O_2 supply and demand and the metabolic state in ischemia. On the other hand, many investigators have been little concerned with the carbon dioxide (CO_2) gas tension in tissue ($PtCO_2$), and few studies have been done using $PtCO_2$ as an indicator of tissue metabolism (5-9). The purpose of this study was to examine whether or not PtO_2 and $PtCO_2$ accurately reflect the state of microcirculation and/or metabolism in ischemic liver tissue so that ischemia/reperfusion injury can be predicted and prevented.

Materials and Methods

Animal preparations. Eighteen adult mongrel dogs, weighing 8-13 kg, were examined. Anesthesia was induced by an intramuscular injection of 25 mg/kg of ketamine hydrochloride and 0.3 mg/kg of atropine sulfate, and was established by an intravenous injection of 30 mg/kg of sodium pentobarbital and 0.2 mg/kg of pancuronium bromide. Additional doses were given as needed. After an intra-venous line was established with instillation of Ringer's lactate solution (20 ml/kg/h), endotracheal intubation was done, and ventilation was mechanically controlled with 50 % oxygen, a tidal volume of 15 ml/kg, and a respiration rate of 15 times/min. After laparotomy, the blood influx from the hepatic artery and portal vein into the left three lobes was obliterated using a vascular clamp, a model of partial (70 %) liver ischemia being prepared (10), in which reperfusion was achieved by releasing the vascular clamp. A plastic catheter was in-

* To whom correspondence should be addressed.

serted into a left femoral artery, and was used to monitor the arterial blood pressure, which was expressed as a mean, and also to draw blood samples for measurement of serum GOT levels, that were determined before ischemia and after 2 h of reperfusion and were used as an index of liver tissue damage. The liver temperature was measured with a needle thermometer placed into the left medial lobe and was kept between 37.0 and 38.0 °C during the experiment by using an electric warmer and heat lamps. The subjects were divided into three groups; group 1 (n = 6), ischemia for 30 min; group 2 (n = 6), ischemia for 60 min; group 3 (n = 6), four times of intermittent 15 min ischemia after every 10 min of reperfusion. In all groups, reperfusion was continued for 2 h after ischemia.

Measurement of PtO_2 and $PtCO_2$. Both PtO_2 and $PtCO_2$ were continuously measured using a mass spectrometer (11) (MEDSPECT-II, Chemetron, USA), and the data were obtained on each transit curve every 5 min from 15 min before ischemia until the end of reperfusion. A Teflon catheter (12) for each measurement of PtO_2 and $PtCO_2$ (PysioProbe, Research Medical Inc., USA) was inserted directly into the parenchyma of the left lateral lobe with care not to make a hematoma around the sensor. Calibration of the catheters was completed before and after every experiment.

Measurement of the liver tissue blood flow (TBF). The liver tissue blood flow (TBF) was measured by the argon clearance method (13-16) using also a mass spectrometer and determined before ischemia, after 5 min and 2 h of reperfusion, and is expressed in volume as ml/min/100 g of tissue weight.

Calculation of critically anaerobic score (CAS) and time (CAT). A careful analysis of the changes of the $PtCO_2$ during ischemia revealed that it showed initially an accelerated elevation, but the magnitude of the increase was gradually decelerated, and eventually it plateaued. So, the increase in $PtCO_2$ for every 1 min was obtained on the transit curve during both the acceleration and deceleration phases. Then, the time point when the increase initially became less than 1/2 of the maximum one was searched, and is referred to as the critically anaerobic (CA) point. From this CA point to the end of ischemia, the area below the $PtCO_2$ curve and the time interval were measured, and are referred to as the critically anaerobic score (CAS) and time (CAT; expressed in minutes), respectively (Fig. 1). When the CA point was not observed, both CAS and CAT were regarded as zero. In group 3, for the sake of convenience, the sum of areas and/or time intervals in four periods of ischemia thus obtained was taken as the CAS and CAT for this group, respectively. Correlations of the CAS and CAT with PtO_2, TBF and GOT were studied to determine the best indicator and/or predictor of ischemia/reperfusion injury.

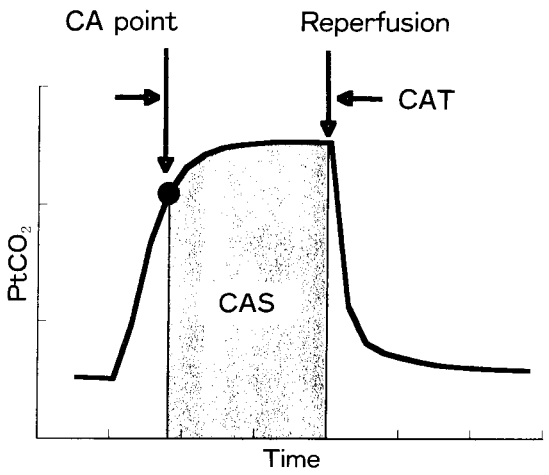

Fig. 1 Schematic presentation of the critically anaerobic (CA) point, CA score (CAS), and CA time (CAT).

Statistical analysis. Data were analyzed by ANOVA with post hoc testing by Fisher's protected least significant difference, and Statview 4.11 (Abacus Concepts, Inc., Shingle Springs, CA, USA.) was used for the statistical calculations. A simple linear regression analysis was also done to examine the correlation between two variables. All data are expressed as means ± SD, and $P < 0.05$ was defined as statistically significant.

All animals received humane care in accordance with the Principles of Laboratory Animal Care formulated by the National Society of Medical Research and the Guide for the Care and Use of Laboratory Animals prepared by the National Academy of Sciences and published by the National Institutes of Health (NIH Publication no. 80-23, revised in 1978).

Results

Serial changes of arterial blood pressure. The arterial blood pressure did not significantly change throughout the experiment in all three groups (Table 1).

Serial changes of PtO_2 and $PtCO_2$ during

Table 1 Serial changes of arterial blood pressure (mmHg)

Group	Before ischemia	Before 10 min of reperfusion	After 10 min of reperfusion	After 1 h of reperfusion	After 2 h of reperfusion
1	112.8 ± 21.8	118.0 ± 21.3	116.2 ± 22.5	112.2 ± 20.9	112.1 ± 20.3
2	116.3 ± 13.3	119.6 ± 16.7	113.4 ± 14.1	108.3 ± 22.6	103.5 ± 25.3
3	115.1 ± 14.4	117.4 ± 8.1	115.9 ± 5.9	113.3 ± 7.3	109.4 ± 4.1

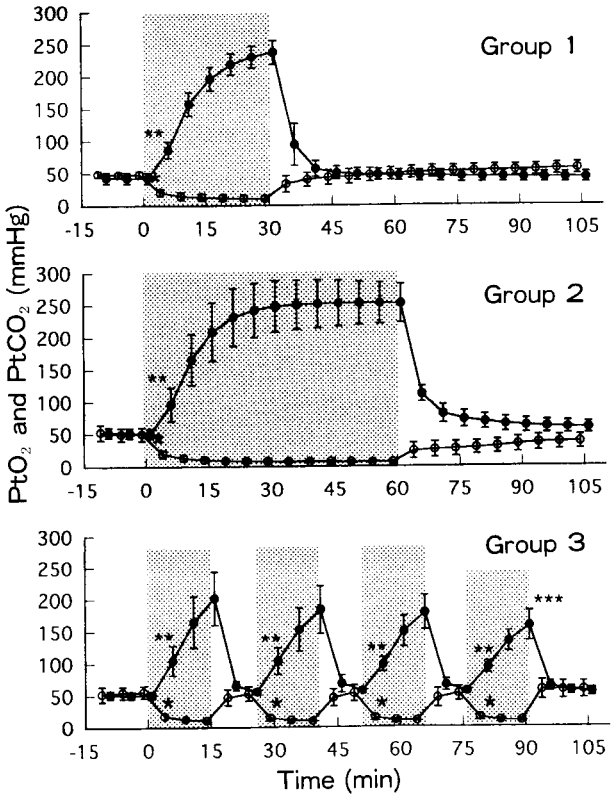

Fig. 2 Transits of PtO_2 and $PtCO_2$ during ischemia. Open and closed circles indicate PtO_2 and $PtCO_2$, respectively, in each group. Shaded areas indicate the ischemic periods. Bars indicate SDs. $*P < 0.05$ and $**P < 0.01$ compared to each value before ischemia, $***P < 0.05$ compared to the peak value in the 1st ischemic period.

ischemia. PtO_2 significantly decreased from 48.5 ± 4.8, 50.0 ± 10.5, and 54.7 ± 9.2 mmHg before ischemia to 14.2 ± 5.6, 13.3 ± 4.5, and 12.3 ± 2.9 mmHg 10 min after induction of ischemia in groups 1, 2 and 3, respectively ($P < 0.01$ for each) (Fig. 2). Thereafter, it did not change significantly until the end of ischemia, and there was no difference among the groups. On the other hand,

Table 2 Data for CAS and CAT

Variables	Case	Group 1	Group 2	Group 3
CAS	1	4190	8892	1910
	2	3371	11827	1468
	3	3389	14024	1828
	4	4274	13174	4574
	5	3444	9229	4311
	6	3654	12409	298
Mean		3720.3	11592.5*	2398.2
SD		409.8	2098.3	1687.2
CAT	1	18	38	13
(min)	2	13	47	7
	3	17	47	11
	4	17	47	21
	5	14	44	24
	6	15	49	2
Mean		15.7	45.3*	13.0
SD		2.0	3.9	8.3

$*P < 0.01$ compared to each corresponding value in groups 1 and 3. CAS: critically anaerobic score; CAT: critically anaerobic time.

$PtCO_2$ significantly increased soon after induction of ischemia, initially exhibiting an acute elevation in all groups (Fig. 2). That is, $PtCO_2$ elevated from 42.3 ± 8.9, 50.7 ± 7.9, and 51.2 ± 5.2 mmHg before ischemia to 196.5 ± 18.2, 209.0 ± 45.1, and 201.5 ± 41.6 mmHg after 15 min in groups 1, 2 and 3, respectively ($P < 0.01$ for each). Thereafter, in groups 1 and 2, the magnitude of the increase was gradually decelerated (Fig. 2-top and middle), and in group 2, $PtCO_2$ plateaued after 30 min (Fig. 2-middle). In group 3, the peak $PtCO_2$ in the 1st, 2nd, 3rd and 4th ischemia was 201.5 ± 41.6, 184.2 ± 36.9, 179.0 ± 26.7 and 158.2 ± 23.3 mmHg, respectively, gradually decreasing as the number of times of ischemia increased. Consequently, the peak $PtCO_2$ in the 4th ischemia was significantly lower than not only that in the 1st ischemia but also those in other two groups ($P <$

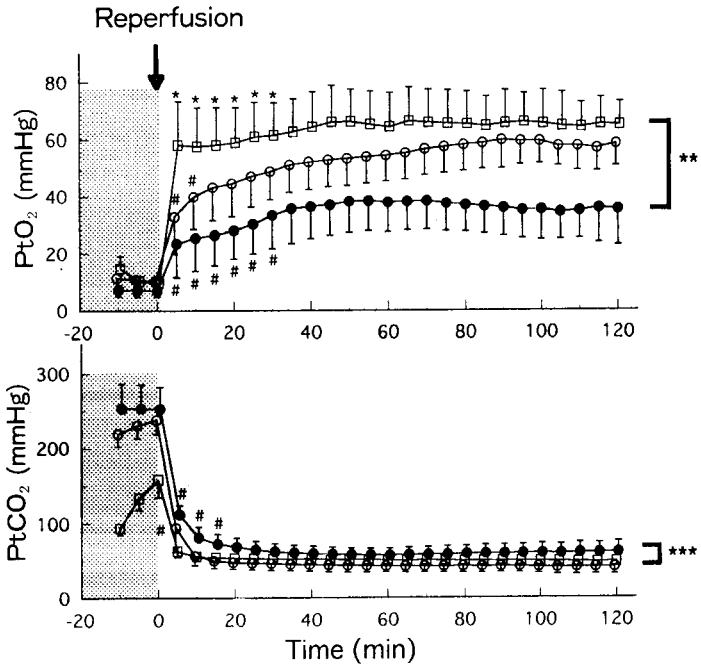

Fig. 3 Transits of PtO_2 and $PtCO_2$ after reperfusion. Open and closed circles, and open squares indicate the values in groups 1, 2 and 3, respectively. Shaded areas indicate the ischemic periods. Bars indicate one-side SDs for simplicity. $^{\#}P < 0.05$ compared to each control value before ischemia. $^{*}P < 0.05$ compared to each corresponding value in group 1. $^{**}P < 0.01$ between groups 2 and 3 throughout reperfusion. $^{***}P < 0.05$ between groups 1 and 2 throughout reperfusion.

Table 3 Serial changes of tissue blood flow (ml/min/100g)

Group	Before ischemia	After 5min of reperfusion	After 2h of reperfusion
1	38.88 ± 5.02	31.07 ± 11.18	38.70 ± 5.18
2	42.38 ± 4.95	30.77 ± 12.49	25.10 ± 9.34*
3	44.50 ± 7.61	43.67 ± 7.97	43.07 ± 4.10

$^{*}P < 0.01$ compared to each corresponding value in groups 1 and 3.

Table 4 Changes of serum GOT (IU/l)

Group	Before ischemia	After 2h of reperfusion
1	75.0 ± 80.1	421.7 ± 305.9*
2	99.8 ± 96.9	2345.0 ± 2158.4*#
3	100.8 ± 59.1	280.8 ± 180.2*

$^{*}P < 0.05$ compared to each corresponding value before ischemia. $^{\#}P < 0.05$ compared to each corresponding value in groups 1 and 3.

0.05 for each) (Fig. 2-bottom).

The CA point, and CAS and CAT. The CA point was observed 12.7 ± 2.9 (range, 6–22) min after induction of ischemia, and the majority (78%) were between 10 and 16min. The data for the CAS and CAT in three groups are presented (Table 2), showing that both CAS and CAT were statistically largest in group 2 ($P < 0.01$ for each). There was, however, no difference in these indices between groups 1 and 3.

Serial changes of PtO_2 and $PtCO_2$ after reperfusion. After 5min from the beginning of reperfusion, PtO_2 significantly increased from 10.2 ± 4.4, 6.8 ± 2.0, and 9.5 ± 1.4mmHg at the end of ischemia to 32.8 ± 12.9, 23.5 ± 12.0, and 58.0 ± 15.1mmHg in groups 1, 2 and 3, respectively ($P < 0.01$ for each) (Fig. 3-top). However, the values in groups 1 and 2 were significantly lower than each control value before ischemia (32.8 ± 12.9 *vs* 48.5 ± 4.8, and 23.5 ± 12.0 *vs* 50.0 ± 10.5mmHg, respectively; $P < 0.05$ for each), and the difference disappeared after 10 and 30min of reperfusion in groups 1 and 2, respectively. Throughout reperfusion, PtO_2 was always highest in group 3 and lowest in group 2, but the difference between groups 1 and 3 disappeared after 30min of reperfusion.

On the other hand, $PtCO_2$ significantly decreased from 237.7 ± 18.4, 252.7 ± 29.8, 158.2 ± 23.3mmHg at the end of ischemia to 94.5 ± 32.3, 112.0 ± 12.0, and 63.2 ± 8.0mmHg after 5min of reperfusion in groups 1, 2 and 3, respectively ($P < 0.01$ for each) (Fig. 3-bottom). It was, however, significantly higher than each control value before ischemia in groups 1 and 2 ($P < 0.01$ for each), and the difference disappeared after 15 and 30min of reperfusion in groups 1 and 2, respectively. Further-

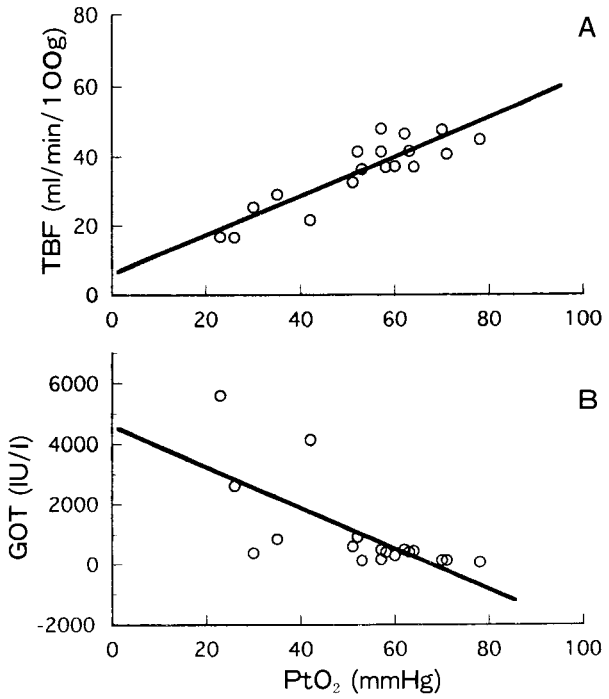

Fig. 4 Correlations of PtO_2 with tissue blood floor (TBF) (**A**) and GOT (**B**). **A**: $Y = 6.039 + 0.559X$, $r = 0.88$ ($P < 0.0001$); **B**: $Y = 4515.1 - 66.16X$, $r = -0.68$ ($P = 0.0018$).

more, the $PtCO_2$ in group 2 was higher than those in the other two groups throughout reperfusion; only the difference from group 1 was significant ($P < 0.05$).

Changes of TBF. Before ischemia, there was no difference with TBF among the groups (Table 3). The TBF volume after 5 min of reperfusion was smaller than each control value before ischemia in groups 1 and 2, but the difference was not statistically significant in either group. On the other hand, in group 3, it was not reduced, being larger than those in the other two groups; this difference was not significant either. After 2 h of reperfusion, however, the TBF volume recovered to the value before ischemia in group 1, whereas it did not in group 2. As a consequence, the TBF volume at this time point was significantly smaller in group 2 than in groups 1 and 3 ($P < 0.01$ for each).

Changes of GOT. The changes of serum GOT levels showed no difference between groups before ischemia (Table 4). After 2 h of reperfusion, however, it increased significantly to 421.7 ± 305.9, 2345.0 ± 2158.4, and 280.8 ± 180.2 IU/l in groups 1, 2 and 3, respectively ($P < 0.05$ for each). The value in group 2 was strikingly higher than those in groups 1 and 3 ($P < 0.05$ for each), whereas there was no difference between groups 1 and 3.

Correlations of PtO_2 with TBF and GOT. It was observed after 2 h of reperfusion that the PtO_2 significantly correlated proportionally with the TBF volume ($r = 0.88$, $P < 0.0001$; Fig. 4-top). A significant negative correlation was also observed between PtO_2 and the serum GOT level measured at the same time point ($r = -0.68$, $P = 0.0018$; Fig. 4-bottom). There was not, however, any significant correlation between $PtCO_2$ and these variables.

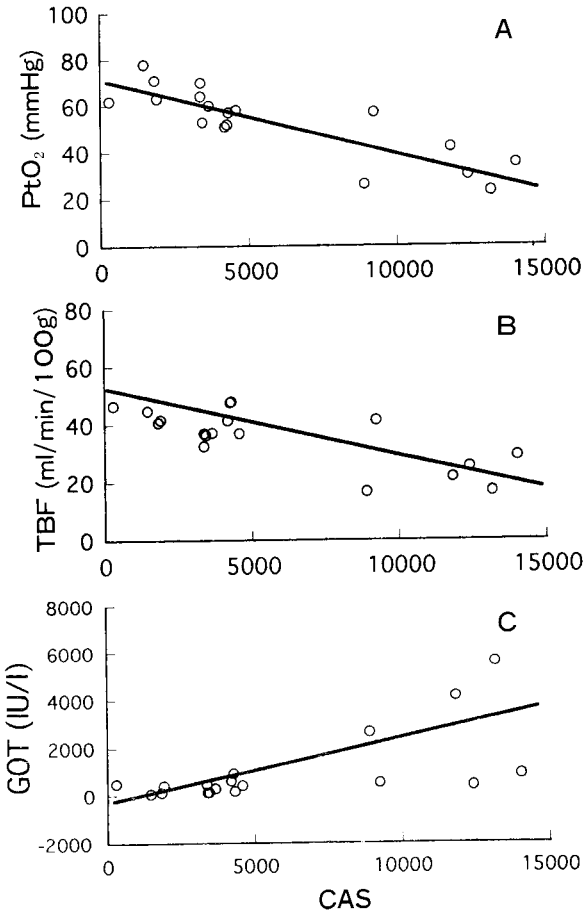

Fig. 5 Correlations of CAS with PtO_2 (**A**), TBF (**B**) and GOT (**C**). **A**: $Y = 70.86 - 0.003X$, $r = -0.85$ ($P < 0.0001$); **B**: $Y = 45.84 - 0.002X$, $r = -0.77$ ($P = 0.0002$); **C**: $Y = -274.4 + 0.219X$, $r = 0.63$ ($P = 0.0049$). CAS, TBF: See legends to Figs 2 and 4.

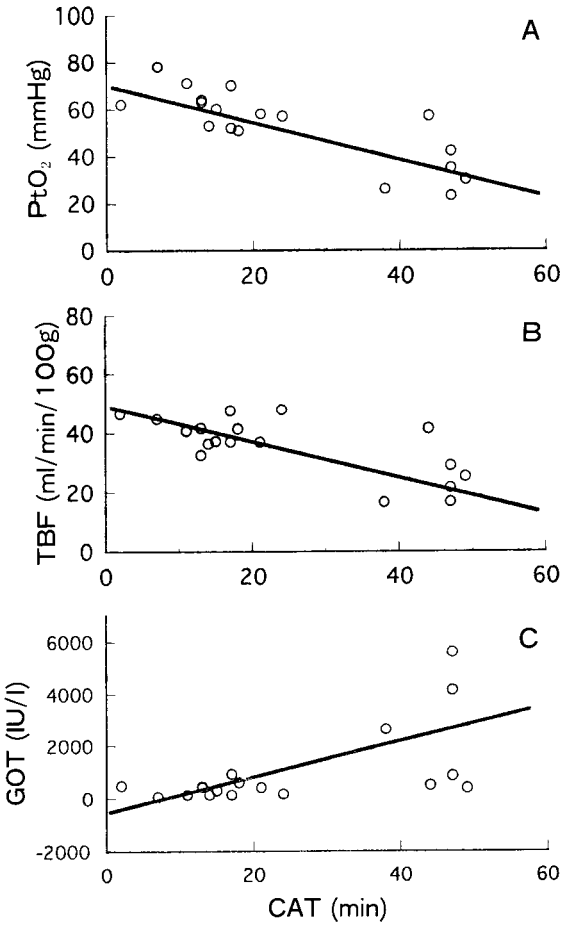

Fig. 6 Correlations of CAT with PtO_2, TBF and GOT. **A**: Y = 72.90 − 0.811X, r = − 0.82 ($P < 0.0001$); **B**: Y = 46.88 − 0.457X, r = − 0.73 ($P = 0.0007$); **C**: Y = − 401.9 + 57.5X, r = 0.60 ($P = 0.0089$). CAT: See Fig. 1.

Correlations of CAS and CAT with PtO_2, TBF, and GOT. CAS showed a significant negative correlation with PtO_2 and the TBF (r = − 0.85, $P < 0.0001$, and r = − 0.77, $P = 0.0002$, respectively) and was proportional to the serum GOT level (r = 0.63, $P = 0.0049$). All values were determined after 2 h of reperfusion (Fig. 5). Similarly, there were significant correlations of the CAT with these variables (Fig. 6).

Discussion

As observed with the arterial blood pressure, the systemic hemodynamics was not significantly changed by the experimental procedure in this dog model. Therefore, other adverse influences on hepatic circulation and metabolism could be eliminated in this study.

PtO_2 sensitively reflects small changes in the tissue microcirculation and O_2 consumption. Therefore, monitoring PtO_2 is quite useful to assess the state of tissue perfusion and the balance between O_2 supply and demand. For this purpose, polarographic electrodes are used as a standard method of PtO_2 measurement. On the other hand, a mass spectrometer is also useful for continuous *in vivo* measurement of tissue, blood, and respiratory gas tensions. Furthermore, not only PtO_2 but also $PtCO_2$, argon gas and nitrogen gas tensions can be measured at the same time. This unique function is very useful to assess tissue perfusion and oxygen supply. There are many papers describing the measurement of gas tensions in brain tissue (17), myocardium (18), kidney (19), and skeletal muscles (15, 20), both experimentally and clinically. However, there have been very few studies in which $PtCO_2$ was used as an index of microcirculation and/or metabolism in liver tissue.

It is well known that PtO_2 decreases and $PtCO_2$ increases when ischemia is induced in an organ; the former was thought to be caused by O_2 consumption by tissue after cessation of the supply, and the latter was caused by the following three mechanisms: (a) cessation of CO_2 wash-out due to obliteration of circulation, (b) continuous CO_2 production by metabolism in the TCA-cycle as long as cells survive, either aerobic or anaerobic, and (c) buffering of H^+ by bicarbonate (8, 18); this was thought to be the major causes since there are a number of sources for H^+ production in ischemia, the most important of which is the breakdown of ATP (21). In addition, $PtCO_2$ accurately reflects the overall CO_2 pool in ischemic tissue because CO_2 can freely diffuse across the cell membrane. Therefore, continuous measurement of not only PtO_2 but also $PtCO_2$ in liver by mass spectrometry may provide very important information regarding intrahepatic microcirculation and anaerobic metabolism in a sequence of ischemia/reperfusion. In fact, PtO_2 decreased after induction of ischemia, initially rapidly and thereafter slowly, and then it leveled-off with a plateau pattern after approximately 10 min, indicating that oxygen consumption by tissue had ceased. Conversely, as seen in groups 1 and 2, $PtCO_2$ continuously increased for approximately 30 min after ischemia induction although the increasing magnitude gradually decelerat-

ed, and thereafter it plateaued in group 2. These observations suggest that the tissue metabolism is predominantly aerobic until the transit of PtO_2 reaches a plateau and is predominantly anaerobic thereafter, and that even the anaerobic metabolism must be frozen when $PtCO_2$ showed a plateau. This is because it is generally considered that the magnitude of the CO_2 production is proportional to that of anaerobic generation of high energy phosphates, upon which the tissue survival depends (21, 22). Consequently, the beginning of the significant deceleration of the magnitude of CO_2 production probably indicates that even anaerobic metabolism itself is becoming impossible, resulting in severe and irreversible cell damage. Therefore, based on the assumption that deceleration of less than 1/2 of the maximum increase in $PtCO_2$ for 1 min could be considered as really significant, we tried to evaluate the influence of the severely anaerobic state on the tissue microcirculation and damage after ischemia/reperfusion using the indices of CAS and CAT.

On the other hand, soon after commencement of reperfusion, O_2 supply and CO_2 wash-out are restored, and usually PtO_2 increases and $PtCO_2$ decreases, causing tissue metabolism to return from anaerobic to aerobic metabolism. However, when the ischemic time was long, the restoration would be delayed and incomplete. In fact, the recovery of PtO_2 and $PtCO_2$ was slowest in group 2, and the TBF volume was significantly depressed in this group, similar to the 'no-reflow phenomenon'. Sunakawa *et al.* (15) also reported that the shorter the ischemic time was, the faster PtO_2 and $PtCO_2$ returned to the pre-ischemia level.

Furthermore, it was demonstrated that the PtO_2 measured after 2 h of reperfusion correlated proportionally with the TBF volume and inversely with the serum GOT level obtained at the same time point. However, there was no correlation between $PtCO_2$ and these variables. This means that the PtO_2 during reperfusion reflects the magnitude of the tissue microcirculatory disturbance and cell damage in ischemia/reperfusion. Additionally, it was observed after 2 h of reperfusion that not only CAS but also CAT was significantly correlated with the serum GOT level, PtO_2, and TBF volume. Therefore, it can be considered that CAT and CAS accurately predict the magnitude of tissue microcirculatory disturbance and cell damage after ischemia/reperfusion. Thus, the detection of the CA point is essential. It was not clear, however, how long liver ischemia could safely be continued after the $PtCO_2$ reached the CA point. This problem requires further study.

As a clinical implication, our observations in group 3 are very important since the procedure of intermittent short-term ischemia (23) is a common surgical technique to reduce blood loss during hepatectomy. In this group, both PtO_2 and $PtCO_2$ rapidly improved after starting reperfusion, and after 2 h of reperfusion the TBF volume was larger and the serum GOT level was lower than in the other two groups. Therefore, ischemic injury must be, least in this group, in spite of the fact that the total ischemic time was longer than that in group 1 and equivalent to that in group 2. Horiuchi *et al.* (24) have reported a similar observation, describing that the maximum period of ischemia without irreversible damage was 15 min in the rat liver. Our results also, particularly those with the indices of CAS and CAT, strongly suggested that intermittent short-term ischemia as of 15 min or less would be safe and beneficial in hepatic surgery. A careful analysis, however, of the transit of $PtCO_2$ in group 3 revealed a very important problem. That is, the peak $PtCO_2$ observed at each end of ischemia gradually decreased as the number of times of ischemia increased. The possibility that CO_2 wash-out through collateral circulation develops after repeated ischemia can be excluded since there are anatomically few collaterals in the dog liver. Alternatively the time point when the $PtCO_2$ reached the peak might be delayed because of deceleration of the $PtCO_2$ increasing speed or the peak value itself might become gradually lower as the number of times of ischemia increased. Although the reasons were not clear to us, the procedure of intermittent short-term ischemia may not have been completely free from ischemic tissue injury even though each ischemic time was short. Therefore, it should be elucidated in near future how many times such short-term ischemia can safely be repeated in the liver.

There were a few problems in this study. That is, an assumption was made regarding the way of determining the CA point, and additionally CAS and CAT in group 3 that were obtained simply by summing and solely the values in four periods of ischemia should not be equally weighed as those in other groups. However, we can say at least that the deceleration of the magnitude of the $PtCO_2$ increase will surely indicate some, critically severe phase of anaerobic metabolism resulting in irreversible ischemic tissue injury.

In conclusion the profiles of PtO_2 and $PtCO_2$ in ischemia/reperfusion could be clearly demonstrated by mass spectrometry. $PtCO_2$ appears to sufficiently indi-

cate the state of anaerobic tissue metabolism during ischemia, and PtO_2 after reperfusion may reflect the tissue microcirculatory disturbance and injury probably caused by ischemia/reperfusion. Therefore, continuous monitoring of not only PtO_2 but also $PtCO_2$ using a mass spectrometer is beneficial for hepatic surgery with ischemia.

References

1. Pringle JH: Notes on the arrest of hepatic hemorrhage due to trauma. Ann Surg (1908) **48**, 541-549.
2. Huguet C, Gavelli A, Chieco PA, Bona S, Harb J, Joseph JM, Jobard J, Gramaglia M and Lasserre M: Liver ischemia for hepatic resection: Where is the limit? Surgery (1992) **111**, 251-259.
3. Witte CL, Connell PN and Witte MH: Direct on-line monitoring of hepatic tissue oxygen tension: A new technique. J Surg Res (1976) **21**, 33 44.
4. Hartong JM, Dixon RS and Meyers TT: Use of an *in vivo* oxygen electrode to determine the effect of hemorrhagic shock on liver oxygen tension. Am J Surg (1977) **133**, 607-608.
5. Iseki J, Shibayama K, Ushiyama K, Wada T, Sudo K and Furuse A: Experimental study on intrahepatic gas tensions measured by mass spectrometry: Effect of temporary occlusion of the afferent hepatic circulation. Nippon Geka Gakkai Zasshi (1985) **86**, 304-318 (in Japanese).
6. Severinghaus JW and Bradley AF: Electrodes for blood pO_2 and pCO_2 determination. J Appl Physiol (1958) **13**, 515-520.
7. Brantigan JW, Gott VL and Martz MN: A Teflon membrane for measurement of blood and intramyocardial gas tensions by mass spectrometry. J Appl Physiol (1972) **32**, 276 282.
8. Khuri SF, Flaherty JT, O'Riordan JB, Pitt B, Brawley RK, Donahoo JS and Gott VL: Changes in intramyocardial ST segment voltage and gas tensions with regional myocardial ischemia in the dog. Circ Res (1975) **37**, 455-463.
9. MacGregor DC, Wilson GJ, Holness DE, Lixfeld W, Yasui H, Tanaka S, Silver MD and Gunstensen J: Intramyocardial carbon dioxide tension. J Thorac Cardiovasc Surg (1974) **68**, 101 107.
10. Kawamura E, Yamanaka N, Okamoto E, Tomoda F and Furukawa K: Response of plasma and tissue Endothelin-1 to liver ischemia and its implication in ischemia-reperfusion injury. Hepatology (1995) **21**, 1138 -1143.
11. Sugiyama S, Ishizaki M and Uchida H: Spinal epidural oxygen partial pressure and evoked spinal cord potential in relation to the severity of spinal ischemia during cross-clamping of thoracic aorta. Acta Med Okayama (1993) **47**, 369-376.
12. Brantigan JW, Gott VL and Vestal ML: A nonthrombogenic diffusion membrane for continuous *in vivo* measurement of blood gases by mass spectrometry. J Appl Physiol (1970) **28**, 375 377.
13. Kety SS and Schmidt CF: The determination of cerebral blood flow in man by the use of nitrous oxide in low concentrations. Am J Physiol (1945) **143**, 53-66.
14. Kawakami S, Yamane Y, Noishiki Y, Sasaki M and Komoto Y: Data processing of medical mass spectrometry: On the correction for thermal changes and response time. Rinsho Seiri (1975) **5**, 256-264 (in Japanese).
15. Sunakawa M, Kohmoto T and Komoto Y: Evaluation of tissue perfusion in ischemic legs of dogs by CO_2 clearance rate. Acta Med Okayama (1989) **43**, 47-54.
16. Kohmoto T: Local tissue perfusion determined by the clearance curve of tissue partial pressure of CO_2. Myakkangaku (1984) **24**, 1331-1337 (in Japanese).
17. Kawakami S, Sasaki M, Yamane Y, Noishiki Y and Komoto Y: The measurement of cerebral blood flow and metabolism in mongrel dogs by argon desaturation technique using medical mass spectrometer. Kokyuu to Junkan (1975) **23**, 609-614 (in Japanese).
18. Khuri SF, Kloner RA, Karaffa SA, Marston W, Taylor AD, Lai NJ, Tow DE and Barsamian EM: The significance of the late fall in myocardial pCO_2 and its relationship to myocardial pH after regional coronary occlusion in the dog. Circ Res (1985) **56**, 537 547.
19. Kasai T: Renal hemodynamic study during cardiopulmonary bypass. Nippon Kyoubu Geka Gakkai Zasshi (1976) **24**, 1533-1543 (in Japanese).
20. Komoto Y, Kawakami S, Kasai T and Yamane Y: A new approach in evaluating the hemodynamics of ischemic legs by mass spectrometry: A preliminary report. Angiology (1977) **28**, 568-577.
21. Kamiike W, Watanabe F, Hashimoto T, Tagawa K, Ikeda Y, Nakao K and Kawashima Y: Changes in cellular levels of ATP and its catabolites in ischemic rat liver. J Biochem (1982) **91**, 1349-1356.
22. Karwinski W, Farstad M, Ulvik R and Soreide O: Sixty-minute normothermic liver ischemia in rats. Transplantation (1991) **52**, 231-234.
23. Fuse A: Experimental studies on influences of intermittent hemihepatic vascular occlusion. Nippon Geka Gakkai Zasshi (1989) **90**, 863-873 (in Japanese).
24. Horiuchi T, Muraoka R, Tabo T, Uchinami M, Kimura N and Tanigawa N: Optimal cycles of hepatic ischemia and reperfusion for intermittent pedicle clamping during liver surgery. Arch Surg (1995) **130**, 754 758.

Received April 24, 1996; accepted July 25, 1996.