Hepatic arterial and portal venous oxygen content and extraction in liver cirrhosis

Sezai S, Sakurabayashi S, Yamamoto Y, Morita T, Hirano M, Oka H. Hepatic arterial and portal venous oxygen content and extraction in liver cirrhosis.
Liver 1993: 13: 31–35. © Munksgaard 1993

Abstract: We examined the oxygen content in the hepatic arterial, hepatic venous and portal venous blood to evaluate the oxygen supply to the liver and hepatic oxygen extraction in cirrhosis. The arterial-portal venous difference of the oxygen content was within the normal range in cirrhosis patients, although the oxygen content of the hepatic artery and portal vein was lower than in the control patients. The hepatic venous oxygen content was normal in the cirrhosis patients. The oxygen tension and saturation were always higher in the splenic vein than in the other branches of the portal system. Oxygen was supplied chiefly by the hepatic artery, and arterial oxygen extraction was normal in cirrhosis. In addition, there was no change in arterial extraction during oxygen inhalation by cirrhosis patients. Portal venous oxygen extraction was decreased in cirrhosis and was increased by oxygen inhalation. These findings indicate the autoregulation of hepatic oxygen through a mutual relationship between the hepatic arterial and the portovenous oxygen supply.

Shuichi Sezai, Shin Sakurabayashi, Yoshihiro Yamamoto, Toshikazu Morita, Masanori Hirano and Hiroshi Oka

Division of Gastroenterology, Tokyo Metropolitan Police Hospital, Tokyo, Japan

Key words: hepatic oxygen extraction – liver cirrhosis – oxygen content

S. Sezai, Division of Gastroenterology, Tokyo Metropolitan Police Hospital, 2-10-41 Fujimi, Chiyoda-ku, Tokyo, Japan

Received 3 March, accepted for publication 16 October 1992

In an attempt to evaluate the pathophysiology of liver disease, hepatic blood flow has been measured in a variety of ways (1–4). However, these studies did not provide sufficient information regarding the relative contribution of blood flow in the portal vein and hepatic artery. The hepatic circulation has two inflow sources (the hepatic artery and the portal vein) and one outflow tract (the hepatic vein). The hepatic artery supplied more oxygen to the liver than the portal vein (5, 6), and in humans the hepatic artery has been shown to supply 35% of the blood flow and 50% of the oxygen during surgery. Although the liver generally receives about 75% of its blood flow from the portal vein (7), this situation may be modified in patients with liver cirrhosis (4, 5). It has been suggested that relative ischemia and hypoxia may contribute to alcoholic liver damage and the development of cirrhosis (1, 6, 8). To clarify the role of these factors, we evaluated the hepatic hemodynamic response to changes in oxygen supply and determined the effects of oxygen inhalation.

Patients and methods

We selected 28 patients with cirrhosis (17 men and 11 women) in whom the diagnosis was confirmed by liver biopsy. Their ages ranged from 37 to 74 years (mean age: 59 years; weight: 56 ± 9 kg).

The liver disease was due to hepatitis C virus in 12 patients, was cryptogenic in nine (antibody against hepatitis C virus was not determined) and was caused by alcohol in seven. All the alcoholic patients abstained from drinking for at least 4 weeks before the study. According to Child's classification, there were 12 class A, 8 class B, and 8 class C patients. The control group consisted of five men and four women (five patients with asymptomatic primary biliary cirrhosis, two with idiopathic portal hypertension, one with metastatic liver tumor and one with chronic pancreatitis; mean age: 53 years, weight: 54 ± 11 kg). Written informed consent was obtained from each patient before the study.

Portal venous flow was measured with a duplex ultrasound system (an electronic sector scanner and a pulsed Doppler flowmeter) according to the method of Kawasaki et al. (9). The direction of flow was confirmed to be hepatopetal by percutaneous transhepatic portography (PTP) (10) in all of the patients studied. A blood sample was collected from the portal vein during PTP, followed by sampling from the splenic vein, the superior mesenteric vein (SMV), and the inferior mesenteric vein (IMV). Arterial blood was taken from the femoral artery instead of the hepatic artery (HA). The hepatic venous specimen was collected during hepatic venography through a catheter placed in

the middle hepatic vein. Blood samples were obtained from the portal vein, HA, and hepatic vein simultaneously.

Fourteen of the 28 patients with cirrhosis received 100% oxygen at 2 l/min via nasal prongs for 20 min following the initial blood sampling. We then repeated blood sampling and determined pH, carbon dioxide tension (PCO_2), base excess (BE), oxygen tension (PO_2), and oxygen saturation (SO_2) by the standard electrode method using the Hill-equation (ABL-300; Radiometer Trading Co., Ltd., Denmark). The oxygen content of each sample was calculated from the PO_2, SO_2, and hemoglobin level (Hb) and was expressed in terms of vol% according to the following formula (11):

$$\text{vol\%} = 1.34 \times SO_2/100 \times Hb + 0.0031 \times PO_2$$

The hepatic arterial oxygen extraction coefficient (HA Ext) and the portal venous coefficient (PV Ext) were defined in terms of the oxygen content in the hepatic artery (OHA), the hepatic vein (OHV), and the portal vein (OPV) as follows:

$$\text{HA Ext} = (\text{OHA}-\text{OHV})/\text{OHA} \times 100\,(\%)$$
$$\text{PV Ext} = (\text{OPV}-\text{OHV})/\text{OPV} \times 100\,(\%)$$

Statistical analysis was performed using Student's *t*-test; $p < 0.05$ was considered significant.

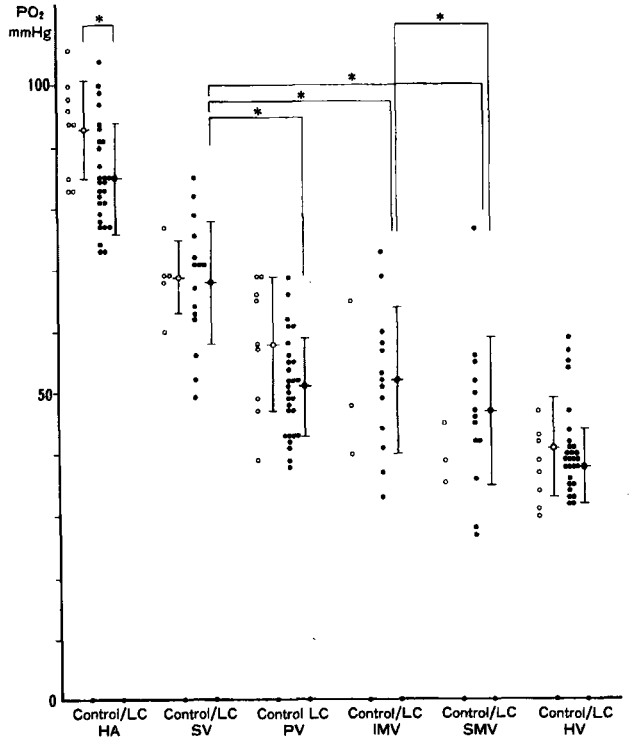

Fig. 1. Oxygen tension in the hepatic artery (HA), hepatic vein (HV), and portal vein (PV) and its main branches (SV, IMV, and SMV). Closed circles show the liver cirrhosis patients (LC) and open circles show the control patients. *$p < 0.05$, values are the mean ± S.D.

Table 1. Oxygen saturation in the hepatic artery (HA), hepatic vein (HV), and portal vein (PV) and its main branches – splenic vein (SV), inferior mesenteric vein (IMV) and superior mesenteric vein (SMV)

	HA	SV	PV	IMV	SMV	HV
Control (n=9) %	96±1	92±1[a]	85±7[a,b]	80 (n=3)	72 (n=3)	70±7
LC (n=28) %	95±1	90±5[a]	83±6[a,b]	79±10[a,b] (n=13)	77±9[a,b] (n=13)	74±7

[a] $P < 0.05$, oxygen saturation in HA compared to that in SV, PV, IMV, and SMV.

[b] Oxygen saturation in the SV versus the other main portal branches (*$p < 0.05$).

Results

The oxygen tension and saturation in the hepatic artery, hepatic vein, and portal vein are shown in Fig. 1 and Table 1.

The splenic vein levels of PO_2 and SO_2 were always higher than those in the other portovenous branches. In addition, PO_2 was higher in the IMV than in the SMV. The oxygen content did not differ significantly between the patients with alcoholic (n=7) and viral cirrhosis (n=12), with the mean values being 15.2±4.1 vs 15.2±1.9 vol% (hepatic artery), 13.2±3.2 vs 13.2±1.9 vol% (portal vein), and 11.9±3.4 vs 11.7±1.5 vol% (hepatic vein). The arterio-hepatic venous and porto-hepatic venous oxygen content differences were smaller in the patients with cirrhosis when compared to those in control patients (Fig. 2). No significant difference in the arterial-portal venous difference was observed between the two groups (cirrhosis patients: 1.9±1.0; controls: 1.8±1.1). Table 2 shows the parameters of hepatic hemodynamics in the two groups. The hepatic arterial blood oxygen content (vol%) was lower in the cirrhosis patients. The

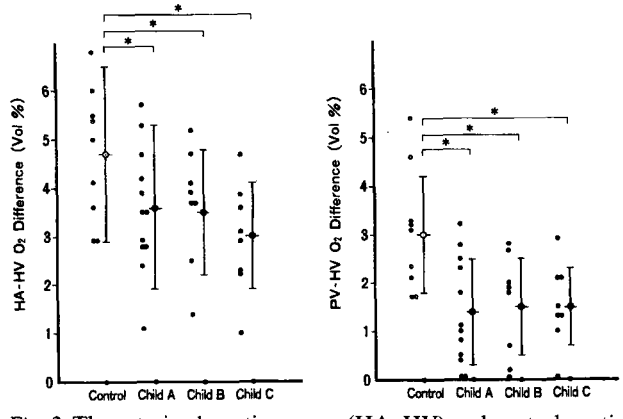

Fig. 2. The arterior-hepatic venous (HA–HV) and porto-hepatic venous (PV-HV) oxygen content differences were significantly lower in the cirrhosis patients (graded as Child's A, B, and C) when compared to the control patients. *$p < 0.05$, values are mean ± S.D.

portal venous vol% and extraction were lower in the cirrhosis group, while portal venous flow showed no difference between the two groups. The hemodynamic parameters of the hepatic venous system showed no significant difference between the two groups (Table 2).

The oxygen content before inhalation was as follows: 15.4±3.1 vol% (n=14) in the HA, 13.1±2.7 vol% in the portal vein, and 11.5±2.5 vol% in the hepatic vein. Hepatic arterial and portal venous extraction were 24.5±3.7% and 11.7±7.0, respectively (Fig. 3). The oxygen content after inhalation was 15.9±3.0 vol% in the HA, 14.2±2.4 vol% in the portal vein, and 11.8±2.7 vol% in the hepatic vein. The hepatic arterial oxygen extraction was not changed by inhalation (26.3±7.5%), but the portal extraction was increased (18.5±9.1%) (Fig. 3).

Oxygen inhalation significantly decreased the pH in the hepatic artery, portal vein, and hepatic vein (Table 3), but there was no change in PCO_2. The HCO_3 level was decreased in portal venous blood and the BE was decreased in all vessels (especially the portal vein), indicating enhanced production of lactic acid.

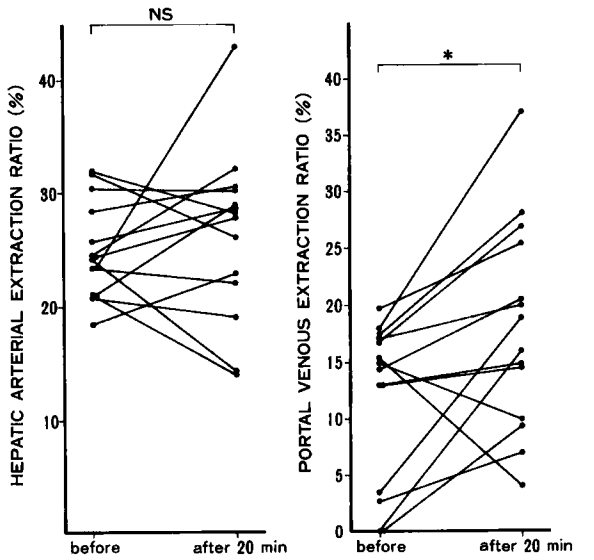

Fig. 3. Changes in the hepatic oxygen extraction ratio (left = hepatic arterial extraction; right = portal venous extraction) with oxygen inhalation. *p<0.05. NS: not significant.

Discussion

Many researchers have reported that alcoholic cirrhosis and noncirrhotic alcoholic liver disease are frequently associated with a decrease in arterial oxygen tension and saturation when compared with control patients (1, 3, 4, 12). Our study indicated that the oxygen content showed no difference whether the cause of cirrhosis was viral or alcoholic. Some other authors have reported that these two parameters of hepatic venous blood were normal (1) or increased in cirrhosis (4), and we found that the hepatic venous oxygen content showed no difference between the cirrhosis and control patients. The arterio-hepatic venous oxygen content difference was smaller in the cirrhosis patients than in the controls (Fig. 2). There are only a few reports concerning the oxygen content of portal blood in cirrhosis. Smythe et al. have reported that the mean arterio-portal venous oxygen difference in unanesthetized humans was 1.9 vol% (13).

In our present study, the difference was 1.9 vol%

Table 2. Blood gas data in the cirrhosis patients and controls

		Control (n=9)	LC (n=28)
HA	pH	7.36±0.13	7.40±0.56
	Vol%	17.2±2.0	15.0±2.5**
	PCO_2 (mmHg)	37±5	35±6
	BE (mm/l)	−1.7±2.5	−2.3±2.4
	HCO_3^- (mm/l)	24.0±5.6	22.2±3.0
	A ext (%)	28.3±9.0	22.5±7.3
PV	pH	7.29±0.17	7.38±0.48
	Vol%	15.5±36	13.0±2.2**
	PCO_2 (mmHg)	40±5	39±6
	BE (mm/l)	−1.8±3.0	−2.4±2.7
	HCO_3^- (mm/l)	22.9±2.8	22.2±2.7
	P ext (%)	19.4±8.7	10.6±6.9**
	Portal flow (ml/min)	694±141	710±438
	Portal flow (ml/min/kg)	13.1±2.5	13.1±7.1
HV	pH	7.31±0.71	7.39±0.51
	Vol%	12.2±2.5	11.6±2.1
	PCO_2 (mmHg)	39±4	37±7
	BE (mm/l)	−0.7±2.8	−2.1±3.3
	HCO_3^- (mm/l)	23.8±2.9	22.3±3.4

The hepatic artery (HA) and portal vein (PV) oxygen contents (Vol%) were decreased in the cirrhosis patients. Portal venous oxygen extraction (P ext) was lower in the cirrhosis patients than in the controls. **p<0.01, values are the mean±S.D. (HV: hepatic vein; A ext: hepatic arterial extraction; BE: base excess).

Table 3. Blood gas data before and after oxygen inhalation

		Before (9)	After (28)
HA	pH	7.406±0.548	7.378±0.378**
	PCO_2 (mmHg)	36.6±5.8	38.6±3.8
	HCO_3^- (mm/l)	22.6±2.2	22.4±1.8
	BE (mm/l)	−1.6±2.3	−2.3±2.1**
PV	pH	7.382±0.460	7.356±0.384*
	PCO_2 (mmHg)	40.4±5.7	40.9±5.5
	HCO_3^- (mm/l)	23.5±2.4	22.4±2.3**
	BE (mm/l)	−1.2±2.3	−2.7±2.3**
HV	pH	7.397±0.528	7.364±0.35**
	PCO_2 (mmHg)	38.2±6.6	40.1±5.2
	HCO_3^- (mm/l)	23.7±2.5	23.2±2.6
	BE (mm/l)	−0.7±2.5	−1.7±2.6**

(n=14, mean±SD)

HA: hepatic artery: PV: portal vein; HV: hepatic vein. *p<0.05, **p<0.01.

in the cirrhosis patients and 1.8 vol% in the controls, so the arterial-portal venous oxygen difference was quite similar in the two groups. However, the oxygen content of hepatic arterial and portal blood was different between the two groups. The oxygen content in the hepatic artery and portal vein was lower in the cirrhosis group, thus reducing the porto-hepatic venous difference in the oxygen content (Fig. 2). The oxygen content in the major branches of the portal system was highest in the splenic vein, while the oxygen content in the portal trunk was intermediate between the splenic and mesenteric venous levels. The oxygen content in the IMV vein was higher than that in the SMV. Both splenic and mesenteric blood flow have an influence on portal flow (14), and the oxygen supply to the liver is also partly determined by these veins.

Hepatic oxygen consumption is usually calculated using the Fick principle, but the results have differed markedly (4, 6, 8). To obtain the hepatic oxygen consumption, the hepatic blood flow and hepatic oxygen extraction ratio must be calculated according to the Fick principle. However, the reported values for these two factors vary markedly, and if they are simply multiplied to yield an answer the error will be compounded. Our current method of obtaining the extraction ratio has the following advantages: 1) because the procedure is performed under local anesthesia, we are able to assess the portal hemodynamics under more physiological conditions than in the case of procedures requiring general anesthesia, 2) the calculations are simple, 3) simultaneous blood collection from three vessels is possible, and 4) extraction ratios relative to the portal vein and hepatic artery can be determined separately.

Regarding the mutual relationship between these two vessels, an increase of blood flow in one vessel is thought to indicate a decrease of flow in the other (15), although same authors disagree with this proposition (16). Our present study showed that the hepatic artery plays a major role in oxygen supply to the liver when breathing room air and that oxygen inhalation increased supply by the portal vein. Therefore, the portal vein and the hepatic artery appeared to act synergistically to supply oxygen to the liver. This happened because the change in saturation was greater than the change in tension in the portal venous blood during oxygen inhalation, while it was smaller in arterial blood. Richardson & Withrington previously suggested that portal blood could be a source of oxygen for the liver (17). The increase of the portal venous oxygen content by oxygen inhalation was accompanied by increased portal flow and a decrease in portal venular resistance.

Gelman & Erast (11) administered oxygen to healthy dogs under general anesthesia and studied the changes in portal venous pH, CO_2 and oxygen content. They found no changes in pH and CO_2 along with the increase in oxygen content. The results obtained by Gelman differ from ours, since we found a decrease in portal venous pH due to metabolic acidosis caused by an increase of BE within the intestinal tract and an increase in lactic acid (1, 18). Lactate production is supposed to occur in an anaerobic environment, so this finding suggests that oxygen inhalation therapy may not be effective in chronic liver disease, even though hypoxia appears to aggravate the hepatic pathology. In contrast, there was no enhancement of hepatic BE during oxygen inhalation (Table 3), suggesting that oxygen metabolism in the liver differs from that in the intestinal tract under these circumstances.

Lastly, the relationship between SO_2 and PO_2 in this study, using the Hill-equation, shows a right shift of the oxyhemoglobin dissociation curve with a $P_{50}=32$ mmHg in liver cirrhosis (19, 20). Therefore, the figures for PO_2 and SO_2 must be modified; extraction coefficients, however, were considered not to be affected so much.

References

1. Bendtsen F, Henriksen J H, Widding A, Winkler K. Hepatic venous oxygen content in alcoholic cirrhosis and non-cirrhotic alcoholic liver disease. *Liver* 1987: **7**: 176–181.
2. Bradley E L. Measurement of hepatic blood flow in man. *Surgery* 1974: **75**: 783–789.
3. Iturriaga H, Ugarte G, Israel Y. Hepatic vein oxygenation, liver blood flow, and the rate of ethanol metabolism in recently abstinent alcoholic patients. *Eur J Clin Invest* 1980: **10**: 211–218.
4. Cohn J K, Khatri I M, Groszmann R J, Kotelanski B. Hepatic blood flow in alcoholic liver disease measured by an indicator dilution technic. *Am J Med* 1972: **53**: 704–714.
5. Sherlock D S. The hepatic artery and hepatic veins: the liver in circulatory failure. In: Diseases of the liver and biliary system, 8th edn. Oxford, London: Blackwell Scientific Publications, 1989: 208–212.
6. Israel Y, Videla L, Berstein J. Liver hypermetabolic state after chronic ethanol consumption: hormonal interrelations and pathogenic implications. *Fed Proc* 1975: **34**: 2052–2059.
7. Womack N A, Peters R M. An investigation of the relationship between portal venous pressure and inferior vena caval and portal venous oxygen saturations. *Ann Surg* 1957: **146**: 691–699.
8. Gordon E R. Mitochondrial functions in an ethanol-induced fatty liver. *J Biol Chem* 1973: **248**: 8271–8280.
9. Kawasaki T, Moriyasu F, Kimura T et al. Hepatic function and portal hemodynamics in patients with liver cirrhosis. *Am J Gastroenterol* 1990: **85**: 1160–1164.
10. Lunderquist A. Transhepatic catheterization and obliteration of the coronary vein in patients with portal hypertension and esophageal varices. *New Engl J Med* 1974: **291**: 646–649.
11. Gelman S, Erast E A. Role of pH, PCO_2 and O_2 content

of portal blood in hepatic circulatory autoregulation. *Am J Physiol* 1977: **233**: E 255–262.
12. Wolfe J D, Tashkin D P, Holly F E, Brachman M B, Genoves M G. Hypoxemia of cirrhosis, detection of abnormal pulmonary vascular channels by a quantitative radionuclide method. *Am J Med* 1977: **63**: 746–754.
13. Smythe CMcC, Fitzpatrick H F, Blakemore A H. Studies of portal venous oxygen content in an anesthetized man. *J Clin Invest* 1951: **30**: 674.
14. Nishida O, Moriyasu F, Nakamura T et al. Interrelationship between splenic and superior mesenteric venous circulation manifested by transient splenic arterial occlusion using a balloon catheter. *Hepatology* 1987: **7**: 442–446.
15. Lindell B, Aronsen K F. Changes of cardiac output distribution after liver dearterialization in the rat. *Acta Chir Scand* 1977: **143**: 207–213.
16. Groszmann R J, Blei A T, Kniaz J L. Portal pressure reduction induced by partial mechanical obstruction of the superior mesenteric artery in the anesthetized dog. *Gastroenterology* 1978: **75**: 187–192.
17. Richardson P D, Withrington P G. Liver blood flow. Intrinsic and nervous control of liver blood flow. *Gastroenterology* 1981: **81**: 159–173.
18. Bihari D, Gimson A E S, Lindrige J, Williams R. Lactic acidosis in fulminant hepatic failure. *J Hepatol* 1985: **1**: 405–416.
19. Caldwell P R B, Fritts H W, Cournand A. Oxyhemoglobin dissociation curve in liver cirrhosis. *J Appl Physiol* 1965: **20**: 316–320.
20. Astrup J, Rorth M. Oxygen affinity of hemoglobin and red cell 2, 3 diphosphoglycerate in hepatic cirrhosis. *Scand J Clin Lab Invest* 1973: **31**: 311–317.