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The relationship of systemic hemodynamics and oxygen consumption to early allograft failure after liver transplantation

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Abstract. The early postoperative hemodynamic data of 88 patients who underwent primary liver transplantation between July 1989 and October 1990 at the University Health Center of Pittsburgh were analyzed to establish the relationship of systemic hemodynamics and oxygen consumption to perioperative allograft function. The 15 patients whose allografts failed within the 1st month following transplantation were designated as group 1, while 73 patients who retained adequate graft function constituted group 2. Although the cardiac index and oxygen delivery did not differ significantly between the groups, group 1 consistently demonstrated a lower mean arterial pressure, oxygen consumption, arteriovenous oxygen content difference, and arterial ketone body ratio. The etiology of reduced oxygen consumption in group 1 patients is speculative, but the data support the notion that oxygen consumption is a useful, predictive indicator for liver allograft function after transplantation.

Key words: Liver transplantation, oxygen consumption – Failure of liver transplantation, oxygen consumption – Oxygen consumption, liver transplantation failure

Introduction

Although orthotopic liver transplantation has become the preferred treament for many types of end-stage liver disease, the operation still has a significant perioperative morbidity and mortality [14]. The early mortality after liver transplantation has been reported to be caused by the use of grafts damaged by ischemia, as well as by massive operative hemorrhage, thrombosis of reconstituted homograft blood supply, intraoperative air embolism, unsuspected recipient abnormalities, etc. [14]. It has been reported that the rate of retransplantation needed as a result of graft failure in the first 3 postoperative months is 10%–20% [14].

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Dramatic hemodynamic changes and a decrease in oxygen consumption in the liver or systemic organs have been reported in nontransplant patients with severe liver damage, such as the end stage of liver cirrhosis and after major hepatectomy [8, 9, 12]. The severe hepatic dysfunction from early postoperative graft failure may cause changes in systemic hemodynamics and metabolism, especially oxygen consumption, that parallel the changes seen in the nontransplant patient with severe liver injury. However, there are few reports on the systemic hemodynamics or on overall oxygen consumption after liver transplantation [4]. The present study was carried out in order to evaluate oxygen delivery, oxygen consumption, and hemodynamic profiles after liver transplantation with special attention to the patients who developed perioperative graft failure.

Patients and methods

Five hundred and sixty-one primary liver transplantations, excluding patients who had undergone multiorgan transplantations, were performed between July 1989 and October 1990 at the University Health Center of Pittsburgh. One hundred and fourteen of these patients whose complete hemodynamic profiles were available within the first 48 h in the intensive care unit (ICU) were analyzed in this retrospective study. Twenty-eight patients whose core body temperature was lower than 36°C at the time of the measurement were then excluded. The remaining 86 patients included 47 males and 39 females whose ages ranged from 16.5 to 67.5 years (mean ± SD, 50.9 ± 12.2 years).

Fifteen grafts failed within the 1st month (group 1; Table 1). All except two cases had severe ischemic damage that was proved by biopsy. One patient had bile leakage from choledochocholedochostomy and died from sepsis on day 18. Another patient had hepatic arterial thrombosis and was retransplanted on day 10. These patients were excluded from this analysis. One patient had a positive crossmatch against donor lymphocytes and 73 patients had relatively adequate graft function (group 2).

A diagnosis of primary nonfunction was made if a graft never demonstrated evidence of initial function following transplantation. Clinical findings strongly associated with primary nonfunction included stage 4 coma, sluggish or no bile flow, progressive jaundice, uncorrectable coagulopathy, metabolic acidosis, and renal failure. The pathology of such grafts usually showed massive or submassive

Table 1. Thirteen patients with graft failure within the 1st month after liver transplantation. ReTx, Retransplantation; PNC, cirrhosis; B, HBsAg +; NANB, non-A non-B; E, alcoholic; PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis; PNF, primary nonfunction; IVC, infrahepatic cava

No.	Sex	Age (years)	Preoperative diagnosis	Cause of graft failure	Duration to graft failure (days)	Outcome
1	M	57	PNC-B	PNF	0	ReTx
2	F	55	PNC-NANB	PNF	1	ReTx
3	M	63	PNC-NANB	PNF, Acute rejection IVC clotted	2	ReTx
4	F	64	PNC-NANB	PNF	2	ReTx
5	M	66	PNC-NANB	PNF, subcapsular hematoma	2	ReTx
6	M	56	PNC-E	PNF	2	ReTx
7	M	53	PNC-NANB	PNF	3	ReTx
8	F	60	PBC	PNF	3	ReTx
9	F	56	PBC	PNF	6	ReTx
10	F	49	PBC	PNF	6	ReTx
11	M	63	PNC-E	PNF	12	ReTx
12	M	58	PNC-E	PNF	14	ReTx
13	M	52	PNC-B	PNF	16	Died

Table 2. Data on hemodynamics, oxygen supply and demand, arterial ketone body ratio (AKBR), and blood chemistry (mean ± SD). MAP, Mean arterial pressure; CI, cardiac index; SVR, systemic vascular resistance; DO_2, oxygen delivery; $\dot{V}O_2$, oxygen consumption; $AVDO_2$, arteriovenous oxygen content difference; O_2ER, oxygen extraction ratio; PT, prothrombin time; POD, postoperative day

	Group 1 ($n = 13$)	Group 2 ($n = 73$)	P value
Body temperature	36.8 ± 0.8	36.8 ± 0.6	NS
FiO_2	0.44 ± 0.18	0.44 ± 0.14	NS
PaO_2	116 ± 32	140 ± 61	NS
MAP	77.8 ± 21.3	94.2 ± 16.4	< 0.05
CI	4.83 ± 1.10	4.88 ± 1.29	NS
SVR	1195 ± 495	1454 ± 547	NS
DO_2	1128 ± 439	1324 ± 414	NS
$\dot{V}O_2$	112 ± 29	140 ± 35	< 0.01
$AVDO_2$	2.37 ± 0.65	2.97 ± 0.91	< 0.05
O_2ER	0.17 ± 0.05	0.20 ± 0.07	NS
AKBR (POD 1)	0.77 ± 0.26	1.37 ± 0.71	< 0.01
AKBR (POD 2)	0.69 ± 0.20	1.30 ± 0.58	< 0.01
BUN (POD 1)	32.2 ± 15.7	29.8 ± 20.3	NS
Creatinine (POD 1)	1.9 ± 1.9	1.5 ± 1.6	NS
PT (POD 1)	29.8 ± 16.8	16.4 ± 4.4	< 0.001
T. bilirubin (POD 1)	7.7 ± 4.1	5.8 ± 3.7	NS
SGOT (POD 1)	3708 ± 3664	1255 ± 1570	< 0.001

ischemic necrosis or severe cholestasis without evidence of rejection. The cause of graft failure in group 1 patients was, in all cases, related to primary nonfunction. One graft failed as a result of primary nonfunction in combination with acute cellular rejection within 2 days. Retransplantation was performed on 12 patients in group 1 0–14 days postoperatively (mean ± SD, 4.9 ± 4.1 days). In group 2, five grafts were lost on postoperative days 44–213 even though those grafts were working satisfactorily and the patients' liver function tests improved in the early postoperative periods.

The degree of illness of each patient, defined prospectively using the criteria for urgency used for the United Network for Organ Sharing (UNOS) distribution system [3], was similar in both groups. The technique of orthotopic liver transplantation has been described previously [13], and standard immunosuppression protocols, using steroids with either FK 506 or cyclosporin A, were followed [15, 16].

Variables measured

All measurements were made within 48 h post-transplantation.

Mean arterial pressure (MAP) was measured via an indwelling radial or femoral arterial catheter. Right atrial pressure (RAP) was assessed by means of a pulmonary artery catheter. Cardiac output (CO) was measured using the thermodilution method with a Cardiac Output Computer (COM-1, Edwards, Irvine, Calif.). Arterial and mixed venous blood samples were obtained for determination of hemoglobin concentration and gas tensions using a blood gas analyzer (ABL-4, Radiometer, Denmark).

From the results of these determinations, the following values were calculated using standard formulas:

Cardiac index (CI; l/min per m^2) = cardiac output (CO; l/min)/body surface area (BSA; m^2)

Systemic vascular resistance (SVR; dyne sec kg/cm^5) = [mean arterial pressure (MAP; mm Hg) − right atrial pressure (RAP; mm Hg)] × 80/CI

Arterial oxygen content (CaO_2; unit) = hemoglobin × 1.39 × SaO_2 + 0.003 × PaO_2

Venous oxygen content (CvO_2; unit) = hemoglobin × 1.39 × SvO_2 + 0.003 × PvO_2

Arteriovenous oxygen content difference ($AVDO_2$) = $CaO_2 - CvO_2$

Oxygen extraction ratio (O_2ER; %) = $(CaO_2 - CvO_2)/CaO_2$

Oxygen delivery (DO_2; ml/min) = CI × CaO_2 × 10

Oxygen consumption ($\dot{V}O_2$; ml/min) = CI × $AVDO_2$

The arterial ketone body ratio (AKBR) was measured daily using the enzymatic method [6, 17] with a Ketorex Kit (Sanwa Chemical, Nagoya, Japan) and a KETO-340 semi-automatic spectrophotometer (Ihara-denshi, Kasugai, Japan).

Statistical analysis

Statistical comparison was carried out using Student's t-test. A P level less than 0.05 was considered to be significant.

Results

After primary orthotopic liver transplantation, the early hemodynamic pattern differed significantly between groups 1 and 2 (Table 2). Group 1 demonstrated a lower mean arterial pressure ($P < 0.01$) than group 2. The cardiac index and oxygen delivery in the two groups did not differ. Although there was no statistically significant difference, the systemic vascular resistance of group 1 tended to be lower than that of group 2. Oxygen consumption of group 1 was significantly lower than that of group 2 ($P < 0.01$), which was followed by a smaller arteriovenous oxygen content difference ($P < 0.05$; Fig. 1).

The arterial ketone body ratio of group 1 was significantly lower ($P < 0.01$) than that of group 2 on both the 1st and 2nd postoperative days (Table 2).

Group 1 showed significant hepatic dysfunctions on the 1st postoperative day that were indicated by a prolonged prothrombin time ($P < 0.001$) and elevated SGOT and SGPT ($P < 0.001$), respectively.

Discussion

Oxygen consumption has been shown to decrease in critically ill patients or cirrhotic patients with severe hepatic dysfunction [2, 5, 12]. In this study, the decrease in oxygen

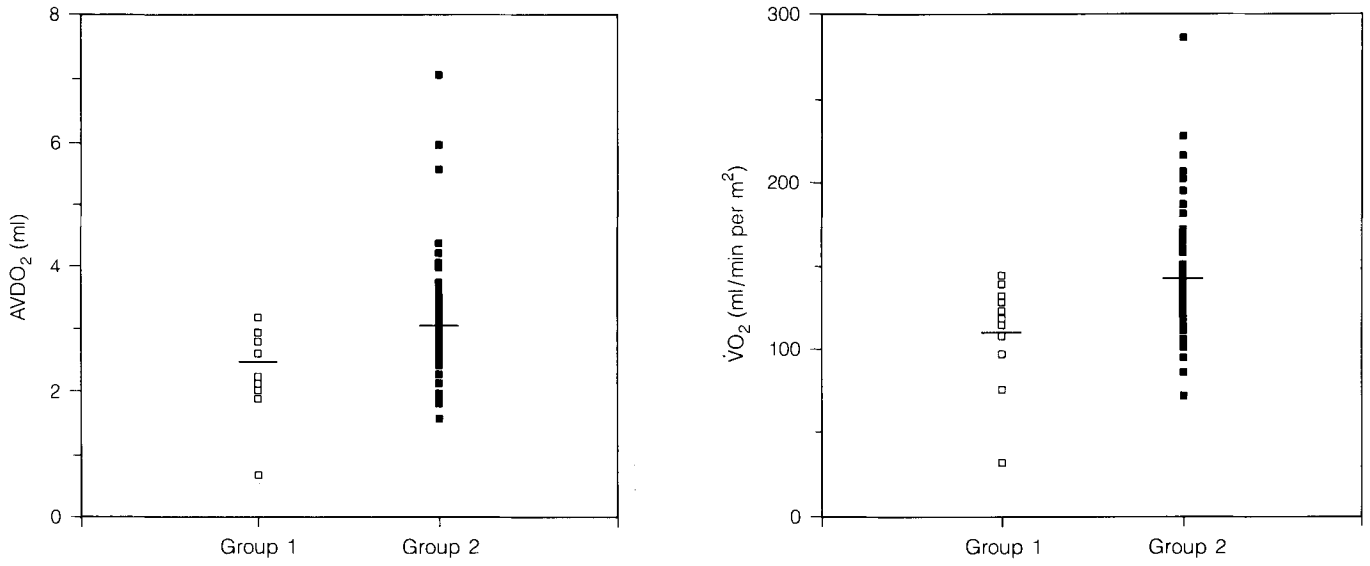

Fig. 1. Comparison of arteriovenous oxygen content difference ($AVDO_2$) and oxygen consumption ($\dot{V}O_2$) between group 1 (□) and group 2 (■) patients. $\dot{V}O_2$ in group 1 was significantly lower than that in group 2 ($P < 0.01$), which was followed by smaller $AVDO_2$ ($P < 0.05$)

consumption in group 1 (poor prognostic group) reflected severe liver damage and indicated their prognosis. The decrease in oxygen consumption and arteriovenous oxygen content difference in group 1 appears to have been caused by decreased oxygen consumption and the metabolism in the liver as well as in other vital organs, resulting from severe liver damage. The etiology of the decrease in oxygen consumption in the failed liver is considered to be the reduced hepatic arterial blood flow [11] and the decrease in the metabolism in the liver itself. The same high levels of cardiac index and oxygen delivery in patients in groups 1 and 2 indicate that the decrease in oxygen consumption in group 1 may not have been incurred by insufficient blood flow to the organs except the liver. Centrilobular hypoxia, mediated by enhanced hepatic consumption of oxygen, seems to be an important pathogenetic factor in ischemia-induced liver injury.

The arterial ketone body ratio (AKBR) has been reported to reflect postoperative hepatic function [10], allograft function, and survival after transplantation [1]. In the present study, a significant lower AKBR was demonstrated in group 1. The oxygen consumption was significantly correlated with the 1 st and 2 nd postoperative days' AKBR (Fig. 2). The data confirm that the decreased oxygen consumption in group 1 was associated with depressed hepatic metabolism.

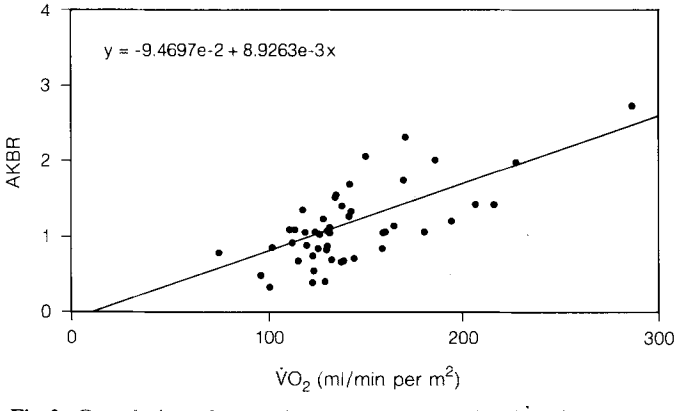

Fig. 2. Correlation of systemic oxygen consumption ($\dot{V}O_2$) and arterial ketone body ratio (AKBR). $\dot{V}O_2$ showed a significant correlation with the same day's AKBR values after primary liver transplantation ($r = 0.66$, $P < 0.001$)

Hypothermia results in a decreased metabolic rate and decreased oxygen consumption [7]. As a similar trend was evident in our patients, especially immediately after liver reperfusion, the oxygen consumption of those with hypothermia could not be analyzed, and we had to exclude those patients.

If a graft fails to function, the only recourse is retransplantation. A useful, predictive indicator is needed to evaluate the outcome of the graft at an early stage after liver transplantation. Oxygen consumption is one such useful indicator that predicts graft function. An increase in oxygen consumption in the phase immediately after liver transplantation is necessary in order for the liver graft to be successfully implanted.

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