Endocrine and Hemodynamic Changes during Liver Surgery in Patients with Compensated Liver Cirrhosis

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The purpose of this study was to determine hormonal levels in compensated liver cirrhotic patients under general anesthesia before and after liver surgery. We measured plasma norepinephrine, epinephrine, arginine vasopressin, and aldosterone levels and renin activity in non-cirrhotic and compensated cirrhotic patients undergoing liver resection after induction of anesthesia but before skin incision and after the end of operation but before discontinuation of nitrous oxide. We simultaneously measured hemodynamic variables. Plasma levels of norepinephrine ($P < 0.001$), epinephrine ($P < 0.001$), arginine vasopressin ($P < 0.05$), renin ($P < 0.05$) and aldosterone ($P < 0.001$) significantly increased after completion of surgery compared with those before incision in both groups. There was a significant positive correlation between plasma renin and aldosterone ($r=0.56$, $P < 0.01$) levels in non-cirrhotics, but no correlation was observed in cirrhotics; and there was a significant positive correlation between plasma norepinephrine and arginine vasopressin ($r=0.45$, $P < 0.05$) levels in non-cirrhotics, but no correlation in cirrhotics. Cardiac index and arterial pressure increased after the end of operation ($P < 0.05$). This increase after the operation was the same between cirrhotic and non-cirrhotic groups. There were no changes in heart rate, mean pulmonary arterial pressure, and pulmonary capillary wedge pressure after the end of operation. We conclude that hemodynamic and endocrinological changes were similar between compensated cirrhotic patients and non-cirrhotic patients during liver surgery. Endocrine changes might partly explain the hemodynamic changes during surgery. (Key words: hormones, surgery, liver, sympathetic nervous system, catecholamine, liver, cirrhosis)

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In liver cirrhosis, hyperstimulation of sympathetic tone is observed[1,2]. The non-osmotic release of arginine vasopressin and the stimulation of the renin-angiotensin-aldosterone system occur under the activation of the sympathetic nervous system in liver cirrhosis[1,3]. Degradation of aldosterone is reduced in liver disease as well, which further increases the

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Table 1. Patient characteristics

	Sex	Age (yr)	Body weight (kg)	Diagnosis	Operation
Non-cirrhotics					
1	M	50	77	Cholangioma	Extended right lobectomy
2	F	73	41	Hepatoma	Extended right lobectomy
3	F	67	49	Cholangioma	Left lobectomy
4	M	62	48	Cholangioma	Extended left lobectomy
5	M	62	55	Hepatoma	Extended right lobectomy
6	F	72	49	Liver cyst	Extended left lobectomy
7	F	57	50	Cholangioma	Extended right lobectomy
8	F	62	42	Hemangioma	Left lobectomy
9	M	58	65	Liver metastasis	Posterior inferior subsegmentectomy
10	F	59	44	Cholangioma	Extended left lobectomy
11	M	57	43	Cholangioma	Left lobectomy
12	M	59	54	Hepatoma	Right lobectomy
Mean		61.5	54.5		
± SE		1.9	3.2		
Compensated Cirrhotics					
1	M	52	58	Hepatoma	Posterior inferior subsegmentectomy
2	M	54	77	Hepatoma	Posterior inferior subsegmentectomy
3	M	62	48	Hepatoma	Lateral segmentectomy
4	M	59	60	Hepatoma	Posterior segmentectomy
5	M	46	57	Hepatoma	Left lobectomy
6	F	53	59	Hepatoma	Posterior segmentectomy
7	F	63	55	Hepatoma	Right lobectomy
8	M	54	48	Hepatoma	Wedge resection
9	M	30	65	Hepatoma	Right lobectomy
10	M	72	57	Hepatoma	Left lobectomy
11	F	54	55	Hepatoma	Lateral segmentectomy
Mean		54.4	58.1		
± SE		3.2	2.4		

plasma aldosterone[4,5]. Thus, liver function might be important, in part, to determine hormonal response to various stimuli. Stress induced elevations of catecholamines, arginine vasopressin and aldosterone are observed in surgical intervention[6–9]. Because basal sympathetic tone might be more activated in liver cirrhotic patients than in non-cirrhotic patients, surgical stimuli might have a profound effect on endocrine response in cirrhotic patients. Because patients with compensated liver cirrhosis are operated on frequently, we are interested in hormonal changes in patients with compensated liver cirrhosis. However, there have been only a few reports quantifying the endocrine responses associated with liver surgery. The purpose of this study was to determine hormonal levels in compensated liver cirrhotic patients under general anesthesia before and after liver surgery.

Patients and Methods

Twenty three oriental patients undergoing liver resection were studied.

Table 2. Preoperative laboratory data

	Non-cirrhotics (n=12)	Compensated Cirrhotics (n=11)
Albumin ($g \cdot dl^{-1}$)	3.90 ± 0.10	3.56 ± 0.08*
Prothrombin time (sec)	11.5 ± 0.2	11.9 ± 0.2
Hepaplastin test (%)	95.8 ± 4.7	78.6 ± 3.9
Choline esterase (ΔpH)	0.78 ± 0.04	0.68 ± 0.07
GOT ($u \cdot l^{-1}$)	41.0 ± 7.4	59.8 ± 7.9
GPT ($u \cdot l^{-1}$)	41.4 ± 9.1	72.1 ± 11.8
Total bilirubin ($mg \cdot dl^{-1}$)	0.69 ± 0.12	0.61 ± 0.07
ICGR15 (%)	7.9 ± 0.9	13.5 ± 1.3**
BUN ($mg \cdot dl^{-1}$)	12.1 ± 1.1	13.0 ± 1.2
Serum creatinine ($mg \cdot dl^{-1}$)	0.8 ± 0.06	0.9 ± 0.05
Creatinine clearance ($ml \cdot min^{-1}$)	90.1 ± 7.3	80.5 ± 8.6

Abbreviations; ICGR15, retention rate of indocyanine green (ICG) in plasma at 15 min after injection of ICG; GOT, glutamic oxaloacetic transaminase; GPT, glutamic pyruvic transaminase; BUN, blood urea nitrogen.

*$P < 0.05$, **$P < 0.01$, significantly different from the values of non-cirrhotics

Twelve were non-cirrhotic patients (six men and six women, aged 50–73 yr). Eleven were compensated cirrhotic patients (eight men and three women, aged 30–72 yr). The clinical and laboratory findings are summarized in tables 1 and 2. Cirrhosis was comfirmed by histological examination of the liver specimen obtained during surgery. Patients were premedicated with diazepam (10 mg intramuscularly) or hydroxyzine (50 mg intramuscularly), and atropine sulfate (0.5 mg subcutaneously) 60 min and 30 min before induction of anesthesia, respectively. Anesthesia was induced with 4–5 $mg \cdot kg^{-1}$ thiopental, 0.1–0.4 mg fentanyl and 5–7.5 mg droperidol, followed by 0.1 $mg \cdot kg^{-1}$ pancuronium with 50–65% nitrous oxide in oxygen. The trachea was intubated orally and anesthesia was maintained with 50–65% nitrous oxide in oxygen supplemented with enflurane on occasion plus fentanyl 0.1–0.2 mg iv every 45–90 min after commencement of surgery. The total dose of fentanyl during operation was 0.78 ± 0.06 mg (mean ± SE) in non-cirrhotic patients and 0.73 ± 0.07 mg in compensated cirrhotic patients with no significant difference between groups. The radial artery was cannulated for continuous measurement of arterial blood pressure and for blood sampling. A flow-directed pulmonary artery catheter was inserted via the right internal jugular vein into the pulmonary artery. Cardiac output was measured by the thermodilution method. Pulmonary capillary wedge pressure (PCWP) and right atrial pressure were measured using the mid-chest as external zero reference. Crystalloid solution (half saline or lactated Ringer's solution or 1:1 mixture of both) was infused from immediately before induction of anesthesia at a rate of 301 ± 23 $ml \cdot hr^{-1}$ (mean ± SE, range 161–433 $ml \cdot hr^{-1}$) in non-cirrhotic patients and 318 ± 27 $ml \cdot hr^{-1}$ (range 231–486 $ml \cdot hr^{-1}$) in compensated cirrhotic pa-

tients. Sodium intake was controlled at 33.5 ± 3.7 mEq·hr^{-1} (range 14.5–49.4 mEq·hr^{-1}) in non-cirrhotic patients and 32.6 ± 2.7 mEq·hr^{-1} (range 20.8–45.9 mEq·hr^{-1}) in compensated cirrhotic patients. There were no significant differences in mean values between two groups in terms of fluid infusion and sodium load. Urine was collected throughout the operation and urinary sodium excretion rates (amount of sodium excreted in urine per hour) were calculated. Mechanical ventilation maintained Pa_{O_2} over 100 mmHg, Pa_{CO_2} at 30–40 mmHg and pH at 7.30–7.45. The systolic blood pressure was maintained over 100 mmHg throughout the operation.

Blood sampling for measurement of plasma norepinephrine, epinephrine, arginine vasopressin, renin and aldosterone were performed: 1) before incision, that is 30 min after induction of anesthesia but before commencement of surgery; 2) end of operation, that is before discontinuation of nitrous oxide but 10 min after the completion of surgery. At the same time the hemodynamic measurements including heart rate, mean arterial pressure, cardiac index, mean pulmonary arterial pressure and PCWP were performed. Arterial blood for measurement of plasma norepinephrine, epinephrine, arginine vasopressin, renin and aldosterone was collected in plastic syringes, centrifuged immediately in a glass test tube containing EDTA-2Na and plasma was stored at −20°C until assay. Norepinephrine and epinephrine were analyzed by high performance liquid chromatography (HPLC). The intraassay coefficients of variation were 3.0% for norepinephrine and 3.8% for epinephrine. Aldosterone and arginine vasopressin were analyzed by radioimmunoassay. The intraassay coefficients of variation were 10.8% for aldosterone and 7.2% for arginine vasopressin. Renin activity was analyzed by radioimmunoassay, and the intraassay coefficient of variation was 5.8%.

Statistical Analysis

The data were expressed as mean ± standard error (S.E.). Data were analyzed statistically by a two-way analysis of variance (ANOVA) to assess the effect of operation and the presence of compensated liver cirrhosis. Student's t test was used to assess preoperative data between two groups and to assess the difference in the urinary sodium excretion rate between compensated cirrhotics and non-cirrhotics during surgery. Linear regression analysis was used to detect whether there were correlation between two hormones, and correlation between urinary sodium excretion rate and sodium load or arginine vasopressin levels or aldosterone levels in each group. A P value of < 0.05 was considered to indicate a statistically significant difference.

Results

The cirrhotic patients were well-compensated as evidenced by the average prothrombin time not different from non-cirrhotics (table 2). Albumin was significantly different. Retention rate of indocyanine green (ICG) in plasma at 15 min after injection of ICG was significantly high in compensated cirrhotics and hepaplastin test was significantly low in compensated cirrhotics. The duration of anesthesia was 481 ± 53 min in non-cirrhotics and 357 ± 31 min in compensated cirrhotics without a significant difference between two groups. Blood loss in non-cirrhotics was 2,473 ± 268 gram and 135 ± 16% of blood loss was replaced by combination of volume expander, fresh frozen plasma and blood transfusion under the guide of PCWP to maintain the baseline values, so that there were no changes in the PCWP throughout the operation. Blood loss in compensated cirrhotics was 2,147 ±

Table 3. Plasma levels of norepinephrine, epinephrine, arginine vasopressin, aldosterone and renin activity and Hemodynamic parameters

	Before incision		End of operation	
	Non-Cirrhotics	Compensated Cirrhotics	Non-Cirrhotics	Compensated Cirrhotics
Norepinephrine ($ng \cdot ml^{-1}$)	0.19 ± 0.04	0.18 ± 0.04	0.52 ± 0.10**	0.56 ± 0.24**
Epinephrine ($ng \cdot ml^{-1}$)	0.04 ± 0.02	0.02 ± 0.004	0.37 ± 0.13*	0.23 ± 0.10*
Arginine Vasopressin ($pg \cdot ml^{-1}$)	7.16 ± 1.57	5.53 ± 1.0	13.3 ± 1.93*	13.0 ± 2.70*
Aldosterone ($pg \cdot ml^{-1}$)	62.2 ± 6.2	60.3 ± 8.68	241.8 ± 24.7**	218.0 ± 38.2**
Renin ($ng \cdot ml^{-1} \cdot hr^{-1}$)	1.65 ± 0.35	2.36 ± 0.52	3.35 ± 0.83*	3.43 ± 0.87*
MAP (mmHg)	101 ± 4.2	88 ± 6.3	109 ± 3.7*	104 ± 4.7*
Heart Rate (min^{-1})	92 ± 4.6	79 ± 5.5#	101 ± 3.4	87 ± 6.0#
C.I. ($liter \cdot min^{-1} \cdot m^{-2}$)	3.61 ± 0.49	3.41 ± 0.21	4.10 ± 0.32*	4.37 ± 0.29*
MPAP (mmHg)	12.8 ± 0.9	11.6 ± 1.0	14.4 ± 1.5	14.4 ± 1.0
PCWP (mmHg)	5.5 ± 0.9	5.3 ± 0.7	5.4 ± 1.0	6.5 ± 0.9

Values are mean ± SE, MAP, mean arterial pressure; C.I., cardiac index; MPAP, mean pulmonary arterial pressure PCWP, pulmonary capillary wedge pressure.

*$P < 0.05$ compared to the values before incision (two-way ANOVA)

**$P < 0.001$ compared to the values before incision (two-way ANOVA)

# $P < 0.05$ compared to the values in non-cirrhotics (two-way ANOVA)

412 gram and 116 ± 11% of blood loss was replaced by the same manner with non-cirrhotics. There were no differences in blood loss and replaced volume between compensated cirrhotics and non-cirrhotics. Urine volume was 95 ± 10 $ml \cdot hr^{-1}$ in non-cirrhotics and 84 ± 5 $ml \cdot hr^{-1}$ in compensated cirrhotics with no significant difference between the groups.

Endocrine Changes

The results of norepinephrine, epinephrine, arginine vasopressin, renin and aldosterone are shown in table 3. The values before incision were within the normal range in both cirrhotic and non-cirrhotic patients. There were significant increases in norepinephrine ($P < 0.001$), epinephrine ($P < 0.05$), arginine vasopressin ($P < 0.05$), renin ($P < 0.05$) and aldosterone ($P < 0.001$) after operation in both cirrhotic and non-cirrhotic patients. However, there was no inter-group difference in the changes of these hormones after operation. There was a significant positive correlation between plasma renin activities and aldosterone levels (fig. 1) in non-cirrhotic patients ($r=0.56$, $P < 0.01$), but no correlation in compensated cirrhotic patients. There was a significant positive correlation between plasma norepinephrine and arginine vasopressin levels (fig. 2) in non-cirrhotics ($r=0.45$, $P < 0.05$), but no correlation in compensated cirrhotics. Plasma aldosterone and arginine vasopressin levels were not related to urinary sodium excretion rate in either compensated cirrhotic or non-cirrhotic patients. There was a positive correlation between sodium load and urinary sodium excretion rate in compensated cirrhotic patients ($r=0.71$, $P < 0.05$), but no correlation in non-cirrhotics (fig. 3). There was no correlation between urinary sodium excretion rate during operation and the plasma aldosterone levels at the end of operation.

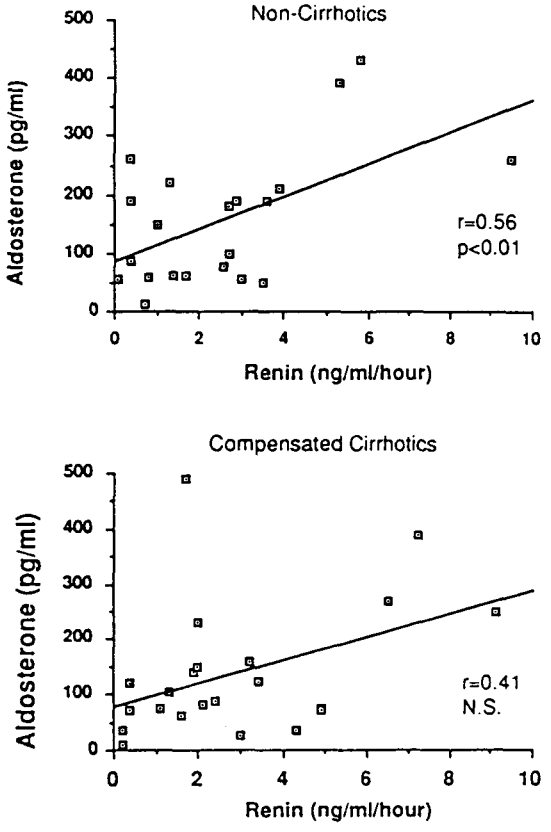

Fig. 1. Correlation between plasma renin activities and aldosterone levels.

There was a significant correlation between plasma renin activities and aldosterone levels in non-cirrhotic patients (upper panel; r=0.56, slope=27.9, intercept=85.5, $P < 0.05$.), whereas no significant correlation in compensated cirrhotics (lower panel; r=0.41, N.S.).

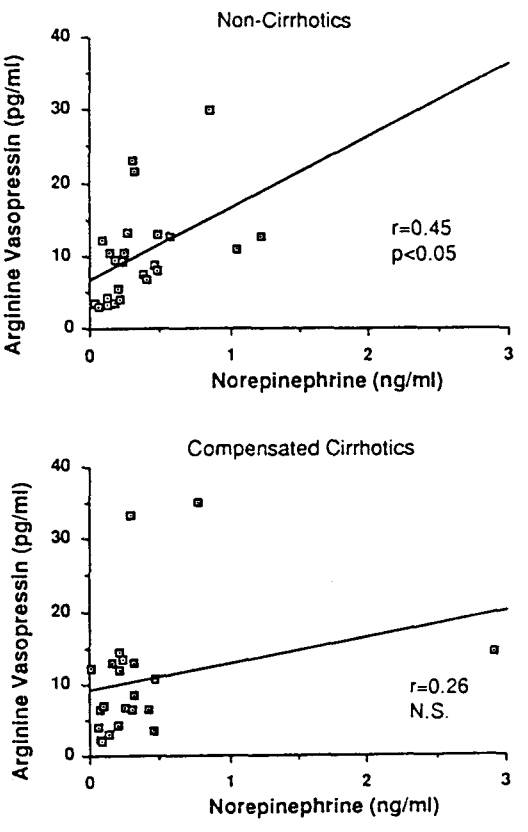

Fig. 2. Correlation between plasma norepinephrine and arginine vasopressin levels.

There was a significant correlation between plasma norepinephrine and arginine vasopressin levels in non-cirrhotic patients (upper panel) (r=0.45, slope=10.0, intercept=6.7, $P < 0.05$.), whereas no significant correlation in compensated cirrhotics (lower panel; r=0.26, N.S.).

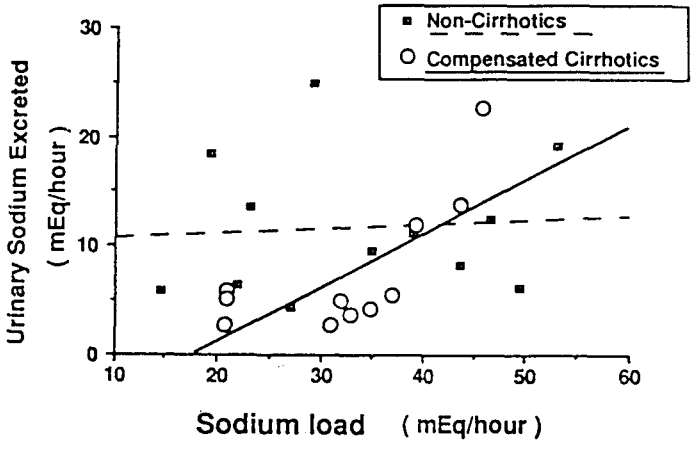

Fig. 3. Sodium load and urinary sodium excretion rate.

There was no significant correlation between the urinary sodium excreted and the sodium load in non-cirrhotic patients (n=12) whereas significant correlation in compensated cirrhotics (n=11) (r=0.71, slope=0.49, intercept=−8.4, $P < 0.05$).

Abbreviations: urinary sodium excreted, amount of sodium excreted in urine per hour ($mEq \cdot hr^{-1}$); sodium load, amount of sodium infused per hour ($mEq \cdot hr^{-1}$).

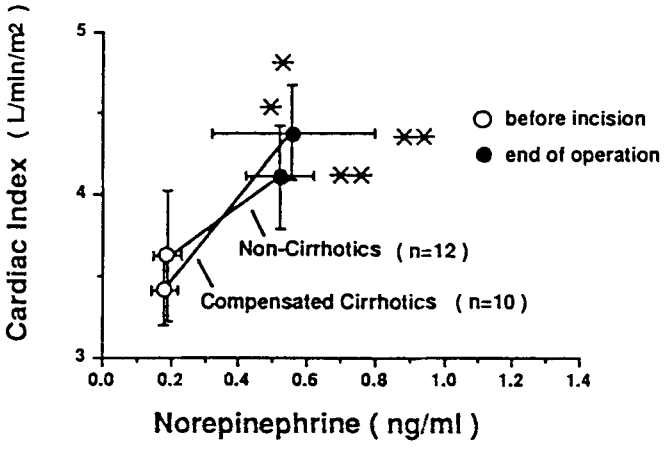

Fig. 4. Cardiac index and plasma norepinephrine levels.

There was a simultaneous increase in the values of cardiac index and plasma norepinephrine levels.

Abbreviations as in figure 1. Values are mean ± SE. (horizontal bar, norepinephrine; vertical bar, cardiac index) $*P < 0.05$, significantly different from the values of cardiac index before incision.

$**P < 0.001$, significantly different from the values of plasma norepinephrine levels before incision.

Changes of Hemodynamics

The results of hemodynamic parameters are shown in table 3. There were no differences in cardiac index, mean arterial pressure, mean pulmonary arterial pressure and pulmonary capillary wedge pressure between non-cirrhotic and compensated cirrhotic patients. There was a significant difference in the pre-incision heart rate between two groups ($P < 0.05$, ANOVA). Cardiac index and mean arterial pressure significantly increased after operation in both groups ($P < 0.05$, ANOVA). Simultaneous increase in the mean values of cardiac index and plasma norepinephrine was observed (fig. 4).

Discussion

We expected increased baseline values of norepinephrine, arginine vasopressin, renin and aldosterone in compensated cirrhotics compared with those in non-cirrhotics. But there were no differences in the baseline levels between the two groups probably due to the relative mildness of the disease in our compensated liver cirrhotic patients[2,5,10]. We speculate that sympathetic nervous system was not activated in the compensated cirrhotics in this study. Another possibility is that there was no difference in the sympathetic activity between two groups at least under the anesthesia used in this study. There have been many reports concerning the endocrine status of liver cirrhotics. Although increased production of renin and aldosterone and decreased degradation of these hormones have been reported generally in cirrhotics[10–12], the increase in plasma aldosterone level is a consequence of advanced stage of cirrhosis[5]. Plasma norepinephrine, arginine vasopressin, renin and aldosterone increase in the cirrhotic patients with impaired sodium excretion, but not in the cirrhotic patients with normal excretion[1]. Plasma norepinephrine levels are within normal range in patients with compensated cirrhosis, but the levels increase in patients with decompensated liver cirrhosis with ascites or former ascites[2,10]. Thus increased plasma concentration of norepinephrine in cirrhotics might be observed, but the level of norepinephrine is different according to the stages of cirrhosis. On the other hand plasma epinephrine levels reportedly are within the normal range in any stage of liver cirrhosis in the non-surgical state[1,2,10].

There was a significant positive correlation between sodium excretion rate and sodium load under the surgical state in compensated cirrhotic pa-

tients in this study (fig. 3). The figure clearly indicates that sodium retention is present in compensated cirrhotic patients. In cirrhotics with ascites, a very low sodium excretion is observed[11]. There was no correlation between urinary sodium excretion rate during operation and the plasma aldosterone levels at the end of operation. Generally plasma arginine vasopressin, and aldosterone levels and renin activity increase during operation, but the precise role of these hormones on salt and water metabolism during operation[7,13] and under cirrhotic state[1,10,14] is still unclear.

Pain or hemmorhage during surgery activates the sympathetic nervous system, and the plasma concentration of norepinephrine shows the degree of sympathetic nervous activity[1,10]. The non-osmotic release of arginine vasopressin and the stimulation of renin-angiotensin-aldosterone system occur under the activation of the sympathetic nervous system[1,3]. The degree of activation of the renin-angiotensin-aldosterone system in cirrhosis depends on the increase in systemic and renal sympathetic tone[1]. Thus activation of the sympathetic nervous system during surgery is partly important for the hormonal responses during surgery. We hypothesized that in compensated cirrhotics surgical stimuli provoke more accentuated hormonal response than in non-cirrhotics. But there was no significant difference between compensated cirrhotics and non-cirrhotics after liver surgery. These results suggest that the hormonal response of compensated liver cirrhotic patients to surgery might be similar to the response of non-cirrhotic patients. The difference between two groups in the hormonal study was lack of correlations between hormones (renin and aldosterone, norepinephrine and arginine vasopressin). We speculate that in compensated cirrhotic patients hormonal interaction might be impaired under anesthesia and surgery. Other possibilities are as follows. Renin angiotensin system is an important factor to promote the secretion of aldosterone in response to sodium depletion[15]. In compensated cirrhotics sodium depletion was unlikely compared to the control group (fig. 3), which might explain no significant correlation between renin and aldosterone levels in compensated cirrhotics. Since no significant correlation was observed between arginine vasopressin and plasma norepinephrine levels, non-osmotic secretion of arginine vasopressin by sympathetic stimulation was not apparent in compensated cirrhotics. Stimulation other than sympathetic activation might be more important to induce the secretion of arginine vasopressin in compensated cirrhotics. Again, because sodium retention was observed in compensated cirrhotics, hyperosmolality or intravascular volume change might mask the effect of sympathetic stimulation. Unfortunately, since we did not measure the osmolality or plasma volume, this explanation is only speculation.

Our data showed no difference in hemodynamics between compensated cirrhotics and non-cirrhotics probably because of the relative mildness of cirrhosis. Increased cardiac output and heart rate and decreased arterial blood pressure have been observed in decompensated cirrhotics[5,10]. The cardiac index and arterial blood pressure increased after the termination of surgery. The increase was partly explained by hormonal changes because the simultaneous increases in cardiac index and the plasma catecholamine levels were observed.

All the compensated cirrhotics had hepatomas and all but two of the non-cirrhotics had other hepatic pathology. There is a low possibility that the difference of liver tumor might have effect on the results, because

there were no hormone producing tumor and there were no differences in endocrinological and hemodynamic values before incision between two groups. There might be differences in terms of the magnitude of the operative procedure, but there were no significant differences in the amount of blood loss and the duration of anesthesia between compensated cirrhotic and non-cirrhotic groups. In terms of the functional reserve of the remnant liver after liver resection, resectability of the impaired liver with cirrhosis is remarkably low[16]. Lobectomy or extended lobectomy were possible in non-cirrhotic patients, but segmentectomy or subsegmentectomy might be equivalent in compensated cirrhotics from the functional stand point of remnant liver.

We conclude that the increases in plasma norepinephrine, epinephrine, arginine vasopressin, renin and aldosterone levels during liver surgery were similar in compensated liver cirrhotic patients and in non-cirrhotic patients. Hormonal changes might partly explain the hemodynamic changes, but not sodium retention in compensated cirrhotic patients during liver surgery.

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References

1. Bichet D, Van Putten V, Schrier RW: Potential role of increased sympathetic activity in impaired sodium and water excretion in cirrhosis. N Eng J Med 307:1552–1557, 1982
2. Hasegawa M, Yamada S, Hirayama C: Fasting plasma caffeine level in cirrhotic patients: Relation to plasma levels of catecholamines and renin activity. Hepatology 10:973–977, 1989
3. Bichet D, Szatalowicz VL, Chaimovitz C, et al: Role of vasopressin in abnormal water excretion in cirrhotic patients. Ann Intern Med 96:413–417, 1982
4. Coppage W, Island D, Cooner AE: The metabolism of aldosterone in normal subjects and in patients with hepatic cirrhosis. J Clin Invest 41:1672–1679, 1962
5. Conn Ho, Atterbury CE: Cirrhosis, Disease of the Liver. Edited by Schiff L, Schiff ER. Philadelphia, Lippincott, 1987, pp. 725–864
6. Bormann BV, Weidler B, Dennhardt R, Sturm G, et al: Influence of epidural fentanyl on stress-induced elevation of plasma vasopressin (ADH) after surgery. Anesth Analg 62:727–732, 1983
7. Traynor C, Hall GM: Endocrine and metabolic changes during surgery: Anaesthetic implications. Br J Anaesth 53:153–160, 1981
8. Lehtinen AM, Fyhrquist F, Kivalo I: The effect of fentanyl on arginine vasopressin and cortisol secretion during anesthesia. Anesth Analg 63:25–30, 1984
9. Lange S, Boscoe MJ, Stanley TH, et al: Antidiuretic and growth hormone responses during coronary artery surgery with sufentanil-oxygen and alfentanil-oxygen anesthesia in man. Anesth Analg 61:434–438, 1982
10. Henriksen JH, Ring-Larsen H, Kanstrup IL, et al: Splanchnic and renal elimination and release of catecholamines in cirrhosis. Evidence of enhanced sympathetic nervous activity in patients with decompensated cirrhosis. Gut 25:1034–1043, 1984
11. Rosoff L, Williams J, Moult P, et al: Renal hemodynamics and the renin-angiotensin system in cirrhosis. Relationship to sodium retention. Dig Dis Sci 24:25–31, 1979
12. Bosch J, Arroyo V, Betriu A, et al: Hepatic hemodynamics and the renin-angiotensin-aldosterone system in cirrhosis. Gastroenterology 78:92–99, 1980
13. Kono K, Philbin DM, Coggins CH, et al: Renal function and stress response during halothane or fentanyl anesthesia. Anesth Analg 60:552–556, 1981

14. Epstein M, Pins DS, Schneider N, et al: Determinants of deranged sodium and water homeostasis in decompensated cirrhosis. J Lab Clin Med 87:822–839, 1976
15. Douglas WW: Polypeptides-angiotensin, plasma kinin, and others, The Pharmacological Basis of Therapeutics. Edited by Gilman AG, Goodman LS, Gilman A. New York, Macmillan, 1980, pp. 647–667
16. Mizumoto R, Kawarada Y, Yamawaki T, et al: Resectability and functional reserve of the liver with obstructive jaundice in dogs. Am J Surg 137:768–772, 1979