原 著

Significance of Systemic Inflammatory Response Syndrome After Hepatectomy

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Abstract

We evaluated whether systemic inflammatory response syndrome (SIRS) after hepatectomy should be a sign of poor outcome and what peri-operative factors were related to SIRS after hepatectomy. Sixty patients, who had elective hepatectomy and admitted to the ICU after tracheal extubation were divided into two groups according to whether they were diagnosed as SIRS within 12 hours after ICU admission or not. Organ dysfunction (central nervous system, cardiovascular system, pulmonary system, hepatic system, renal system, the intestine, or the hematology) was evaluated in the next morning, on the 3rd and 7th day after surgery and compared between the two groups. We compared the peri-operative factors including demographic data, anesthetic and surgical data, and ICU data between the two groups. Thirty-one patients were diagnosed as SIRS. In the next morning, 27 out of the 31 SIRS patients and 26 out of the 29 non-SIRS patients showed liver dysfunction. Three days after surgery, 25 SIRS patients and 25 non-SIRS patients still showed liver dysfunction while only two SIRS patients had liver dysfunction 7 days after surgery. The incidence of liver dysfunction was not significantly different between the groups. Dysfunction of other organs was not observed in both groups. All the patients were alive 28 days after surgery. A significantly lower incidence of preoperative liver cirrhosis was found in the SIRS patients. There were no significant differences in other peri-operative factors between the two groups. In conclusion, SIRS in the early phase of post-hepatectomy may not be a sign of poor outcome. Accordingly, it has little clinical significance and may rather be only a physiological response to hepatectomy. Preoperative liver cirrhosis may prevent such a response after hepatectomy.

Key Words : Systemic inflammatory response syndrome, Hepatectomy, Liver cirrhosis

Introduction

Systemic inflammatory response syndrome (SIRS) - like symptoms such as fever and tachycardia are usually observed after major surgery[1,2,3]. We also often encounter such symptoms in the patients after hepatectomy. Liver resection is a surgical procedure still associated with a higher morbidity and mortality than other major abdominal surgical procedures[3]. Accordingly, we hypothesized that SIRS could be a sign of poor outcome in these patients. However, as far as we know, the cause and significance of SIRS seen after hepatectomy has been still undetermined.

In this study, to test the hypothesis, we evaluated whether SIRS was observed especially in the early phase of hepatectomy and whether SIRS should be a sign of poor outcome after that. We also evaluated the

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peri-operative factors related to SIRS.

Patients and Methods

Between July 1997 and March 1999, Sixty patients, who underwent elective hepatectomy and admitted to the intensive care unit (ICU) after tracheal extubation at the end of surgery in the operating room (OR), were evaluated. We obtained institutional approval and informed consent from each patient. Selection of anesthesia methods was entrusted to the anesthesiologists in charge. In two patients who revealed platelet count of < 100,000/mm^3, epidural anesthesia was avoided. In other patients, a catheter for epidural anesthesia was inserted at the T 7/8 or 8/9 interspace and intermittent doses of 5 to 10 ml of 1.5 % lidocaine with 1/200,000 epinephrine were administered during surgery.

We divided the patients into two groups according to whether they were diagnosed as SIRS by the guideline of American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference[4] within 12 hours after ICU admission. The guideline defined SIRS as two or more of the following clinical manifestations: a) a body temperature of > 38℃ or < 36℃; b) a heart rate (HR) of > 90 beats/min; c) tachypnea as manifested by a respiratory rate of > 20 breaths/min or hyperventilation, as indicated by a $Paco_2$ of < 32 torr (<4.3 kPa); d) an alteration of the white blood cell (WBC) count of > 12,000 cells/mm^3 or the presence of 10 % immature neutrophils ("bands").

Organ dysfunction was evaluated in the next morning, on the 3rd and 7th day after surgery according to the criteria by Gando, et al[5]. Organ dysfunction was defined as follows: a) for the central nervous system, a progressive coma independent of direct cerebral insult and sedation, b) for the cardiovascular system, hemodynamics that need inotropic support; c) for the pulmonary system, a Ling Injury Score of ≥ 1.0; d) for the hepatic system, a serum bilirubin concentration of ≥ 5 mg/dL or AST and ALT concentrations of more than twice normal; e) for the renal system, oliguria of < 500 mL of urine / 24 hours or creatinine concentration of 2 ≥ mg/dL; f) for the intestine, stress ulcer requiring transfusion; g) for hematology, disseminated intravascular coagulation. Patient mortality was evaluated 28 days after admission to the ICU.

As the background of the patients, we compared gender, age, height, body weight, body surface area, body mass index (BMI), and preoperative findings (Hypertension, Diabetes mellitus, Liver cirrhosis) between the groups. Liver cirrhosis was diagnosed through the pathological evaluation for resected liver. To evaluate the effect of anesthesia, we compared an anesthetic method (inhalation or intravenous), whether epidural anesthesia was used, and whether nitrous oxide was used. As other factors, times of operation and anesthesia, blood loss, water balance and volume of hepatic resection (above lobectomy or below segmental resection) were also evaluated.

At ICU admission, we analyzed arterial blood gas (pH, $Paco_2$, Pao_2, Base Excess. lactate, hemoglobin,) (ABL520, Radiometer, Copenhagen, Denmark). We also measured arterial blood pressure and central venous pressure (Component Monitoring System, Hewlett Packard, Boblingen, Germany). The degree of pain was evaluated using a 4-point rating scale: 1 = none, 2 = mild, 3 = moderate, and 4 = severe. The degree of conscious recovery was also evaluated using a 4 - point rating scale: 1 = no response, 2 = drowsy, 3 = sleepy, and 4 = clear. These estimations were carried out by ICU nurses who were blind to the patient profile. Acute Physiology and Chronic Health Evaluation (APACHE) II score and the duration of ICU stay were also compared between the two groups.

Data were compared using the unpaired t test (Student or Welch when the variance of two groups was not equal by F- test) or the chi- square test except for the following values. Pain and conscious recovery scores were compared by the Mann- Whitney U-test. Data are expressed as mean ± standard deviation (SD) and $p < 0.05$ was considered as statistically significant.

Results

Among 60 patients, 31 patients, who met two or more of the SIRS criteria within 12 hours after ICU admission, were diagnosed as SIRS (Table 1). The

Table 1 SIRS criteria being met

number of criteria being met	number of patients	items of criteria being met (numerals: patient number)
4 crteria	0	
3 crteria	8	8: B & H & W
2 crteria	23	15: B & H
		7: B & W
		1: H & W
1 criterion	26	22: B
		3: H
		1: W
0 criterion	3	

Four SIRS criteria according to the guideline of American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference(4):
1. Body temperature of $>38℃$ or $36℃$(B)
2. Heart rate of >90 beats/min(H)
3. White blood cell count of $>12{,}000$ cells/mm^3, <4000 cells/mm^3 or immature neutrophils >10 %(W)
4. Tachypnea as manifested by respiratory rate >20, or $PaCO_2<32$ torr(T)

Thirty-one patients who met more than 2 of the above criteria are diagnosed as SIRS.

numbers who met the SIRS criterion for body temperature were large in both SIRS (30 out of 31) and non-SIRS (22 out of 29) patients. All of them had a fever of more than 38℃. Namely, many patients had hyperthermia after hepatectomy regardless of diagnosis of SIRS. On the other hand, the numbers who met the SIRS criteria for HR and WBC count were small (3 and 1, respectively) in the non-SIRS patients. The numbers were significantly smaller compared to those in SIRS patients. Accordingly, whether the patients met criterion of HR and/or WBC count in addition to body temperature seemed to be the turning point for the diagnosis of SIRS. There were no patients who met the criterion of tachypnea in both groups.

In the next morning, 27 out of the 31 SIRS patients and 26 out of the 29 non-SIRS patients showed liver dysfunction according to Gando's criteria[5] ($p= 0.76$ in the prevalence of liver dysfunction between the groups). Three days after surgery, 25 out of the 31 SIRS patients and 25 out of the 29 non-SIRS patients still showed liver dysfunction[5] ($p= 0.56$) while only two SIRS patients had liver dysfunction 7 days after surgery ($p= 0.16$). Dysfunction of other organs including the central nervous system, the cardiovascular system, the pulmonary system, the renal system, the intestine, or the hematology was not seen in the next morning, on 3rd and 7th day after surgery in both groups. All the patients were alive 28 days after surgery.

Among the demographic data, the SIRS patients showed a significantly low incidence of preoperative liver cirrhosis ($p= 0.01$) (Table 2). There were no significant differences in the other representative data between the two groups (Table 2, 3, 4). There was no evidence that the number of non-SIRS patients who were treated by beta blockers or calcium channel blockers was more than that of SIRS patients.

Discussion

Liver resection is a surgical procedure still associated with a higher morbidity and mortality than other major abdominal surgical procedures[3]. Recent report indicated that 26 % of the 300 patients, who underwent hepatic resection for hepatocellular carcinoma, had postoperative complications including bleeding, infection and leakage[6]. The overall hospital mortality rate was 4 % in the study. Another recent report demonstrated that 22 % of the 478 patients without liver disease such as cirrhosis had postoperative complications after elective liver resection[7]. This study showed that the percentage of patients who had hepatic or renal failure was 1.2 or 0.7 %, respectively

Table 2 Patient demographic data

	SIRS patients (n=31)	Non-SIRS patients (n=29)	p value
Age (yr)	56±13	60±11	0.20
Gender (male/female)	21／10	22／7	0.49
Height (m)	1.6±0.1	1.6±0.1	0.85
Body weight (kg)	60±11	61±9	0.82
Area of body surface (m^2)	1.6±0.2	1.7±0.2	0.71
Body Mass Index (kg/m^2)	23.5±3.4	23.6±2.7	0.88
Preoperative findings			
Hypertension (Yes/No)	6／25	9／20	0.30
Diabetes mellitus (Yes/No)	8／23	9／20	0.65
Liver Cirrhosis (Yes/No)	6／25	15／14	0.01

Table 3 Intraoperative data

	SIRS patients (n=31)	Non-SIRS patients (n=29)	p value
Anesthesia			
inhalation / intravenous	30／1	28／1	0.96
epidural anestheisa (Yes/No)	31／0	27／2	0.14
nitrous oxide (Yes/No)	17／14	19／10	0.40
Time of operation (min)	430±168	394±138	0.36
Time of anesthesia (min)	518±173	482±135	0.38
Blood loss / BW (g/kg)	28.2±34.4	20.6±14.8	0.27
Water balance / BW (ml/kg)	46.6±35.4	39.0±18.6	0.30
Volume of resection (extended lobectomy・lobectomy/ segmetectomy・subsegmentectomy)	22／9	21／8	0.90

Table 4 ICU data

	SIRS patients (n=31)	Non-SIRS patients (n=29)	p value
At admission			
Arterial blood gas			
pH	7.37±0.05	7.38±0.04	0.42
$PaCO_2$ (mmHg)	42±4	42±6	0.74
PaO_2 (mmHg)	173±56	170±60	0.87
lactate (mmol/L)	4.3±2.2	3.4±2.0	0.09
Base Excess (mEq/L)	−1.4±2.9	−1.0±2.6	1.54
hemoglobin (g/dL)	10.7±1.5	10.8±1.5	0.76
Systolic arterial blood pressure (mmHg)	135±23	138±26	0.53
Central venous pressure (mmHg)	3.0±2.9	2.3±2.7	0.39
Degree of pain (median (range))	2 (1−4)	1.5 (1−4)	0.09
Degree of conscious recovery (median (range))	3 (2−4)	3 (1−4)	0.81
APACH II score	10±4	9±3	0.31
ICU stay (hours)	17±5	17±2	1.00

and that the mortality rate was 1 %. Thus, the morbidity and mortality rate in our study may be lower than those in these reports. This may be because we evaluated only the patients who could be extubated in the OR in order to exclude the factor whether the patients were intubated or extubated in the ICU. During the same period for investigation, we had 9 patients who could not be extubated in the OR. These

patients were in more severe condition. The point we would like to emphasize in our study, however, is that 52 % of the patients showed SIRS in the early phase of post-hepatectomy, even though these patients were not in so severe condition. In 272 consecutive patients who received elective common gastrointestinal surgery, SIRS that continued or reappeared after postoperative day 3 was indicated as an early sign of postoperative complications[8]. Accordingly, early symptoms of SIRS such as within 12 hours after surgery may not be a sign of poor outcome and may not be clinically important. Rather, it may be only a physiological response to hepatectomy.

Among the peri-operative factors, the incidence of SIRS in the patients without preoperative liver cirrhosis was significantly higher than that in patients with preoperative liver cirrhosis. Contrary to our expectation, however, levels of cytokines in normal condition[9] and also after hepatectomy[10,9] were reported to be higher in liver cirrhotic patients than those in non-cirrhotic patients. On the other hand, it was reported in liver cirrhotic patients that humoral inhibitors of hematopoietic progenitors existed and they caused leukopenia[11]. In the non-SIRS patients, the number who met the SIRS criterion for WBC count was significantly smaller than that in the SIRS patients. This may be because an increase in WBC count after hepatectomy was inhibited in liver cirrhotic patients. It is also well documented that liver cirrhotic patients have autonomic dysfunction[12]. The study with symptom-limited cardiopulmonary exercise testing in liver cirrhotic patients indicated that heart rate did not increase compared to the predicted values by the exercise[13]. These studies may indicate that tachycardia was prevented in the liver cirrhotic patients. Indeed, in our study, the number of the non-SIRS patients who indicated a heart rate over 90 b.p.m. was only three. Thus, liver cirrhotic patients might not meet the SIRS criteria for heart rate and WBC count although many of them had fever.

In conclusion, a comparable ratio of the patients had SIRS in the early phase of post-hepatectomy. SIRS in this period may not be a sign of poor outcome. Accordingly, it has little clinical significance and may rather be only a physiological response to hepatectomy. Preoperative liver cirrhosis may prevent such a response after hepatectomy.

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