Intraperitoneal Septic Complications after Hepatectomy

KATSUHIKO YANAGA, M.D. TAKASHI KANEMATSU, M.D. KEIZO SUGIMACHI, M.D.
KENJI TAKENAKA, M.D.

One hundred forty-nine elective hepatic resections were performed during the 12 years from 1973 to 1984. Nineteen of these patients (12.8%) developed intraperitoneal septic complications after hepatectomy (IPSCH), of whom 13 died of liver failure. Perioperative variables associated with IPSCH were as follows: (1) right or extended right lobectomy, (2) age > 65, (3) operation time > 5 h, (4) blood loss at operation > 3000 g, and (5) postoperative bleeding, which required laparotomy for hemostasis. Improved outcome of IPSCH since 1981 coincided with the emergence of opportunistic pathogens. Survivors of IPSCH had been diagnosed earlier, all by culture of the subphrenic drainage, and all had a lower bilirubin level at the time of diagnosis. It is concluded that secure hemostasis and avoidance of tissue devitalization during hepatectomy are essential to reduce the incidence of IPSCH and that routine culture of the subphrenic drainage will improve the outcome of IPSCH.

From the Department of Surgery II, Faculty of Medicine, Kyushu University, Fukuoka, Japan

ALTHOUGH ELECTIVE hepatic resection is performed in the absence of any obvious bacterial contamination, postoperative intraperitoneal sepsis is not uncommon. Fortner et al.[1] in 1978 reported subphrenic abscess in 22 out of 108 patients (20.4%), and Thompson et al.[2] in 1983 reported intra-abdominal sepsis in 23 out of 138 patients (16.7%) after major hepatic resection. These intraperitoneal septic complications after hepatectomy (IPSCH) are some of the main causes of death after hepatic resection[2,3] and have been attributed to sloughing of devitalized tissue at the site of hepatic resection, large dead space after hepatectomy, and contamination through the drain or T-tube.[1-5] For these life-threatening complications, closed drainage of the subphrenic space has been advocated.[6] We investigated the risk factors related to IPSCH and assessed the effect of various perioperative variables on the outcome of IPSCH.

Address for correspondence: Katsuhiko Yanaga, M.D., Department of Surgery II, Faculty of Medicine, Kyushu University, Fukuoka 812, Japan.

Reprints requests: Katsuhiko Yanaga, M.D., Department of Surgery II, Faculty of Medicine, Kyushu University, Fukuoka 812, Japan.

Submitted for publication: September 18, 1985.

Patients and Methods

Charts of 162 patients who had undergone elective hepatic resection in the Second Department of Surgery at Kyushu University Hospital between 1973 and 1984 were reviewed. Of these, 13 patients were excluded from the study because of concomitant gastrointestinal procedures in 10, presence of subphrenic abscess at operation in one, postoperative ischemic perforation of the gallbladder in one, and postoperative mesenteric artery thrombosis in one. Among the 149 patients studied, indications for hepatectomy were neoplasia in all but five patients (96.6%), and liver cirrhosis was associated in 103 patients (69.1%). Hepatectomy performed consisted of extended right lobectomy in nine, right lobectomy in 28, left lobectomy in 13, segmentectomy in 21, and partial hepatectomy in 78 patients. Parenchymal dissection of the liver was performed in a blunt fashion with blunt-tipped scissors while a liver clamp was applied. Cut surface of the liver was drained with water-sealed silicone drains, 7 mm in diameter, in all but four patients (97.3%). Drains were removed when the drainage became serous and less than 100 ml per day, usually around the seventh postoperative day. All patients were given a regular dose of systemic antibiotics for about 7 days starting immediately after the operation. The antibiotics used were either cephalosporins alone (first-generation, mostly cephalothin or cephazolin, until late 1980 and then second- or third-generation, mostly cefmetazole, cefotaxime, or moxalactam, afterwards) or in combination with aminoglycosides, mostly tobramycin or dibekacin.

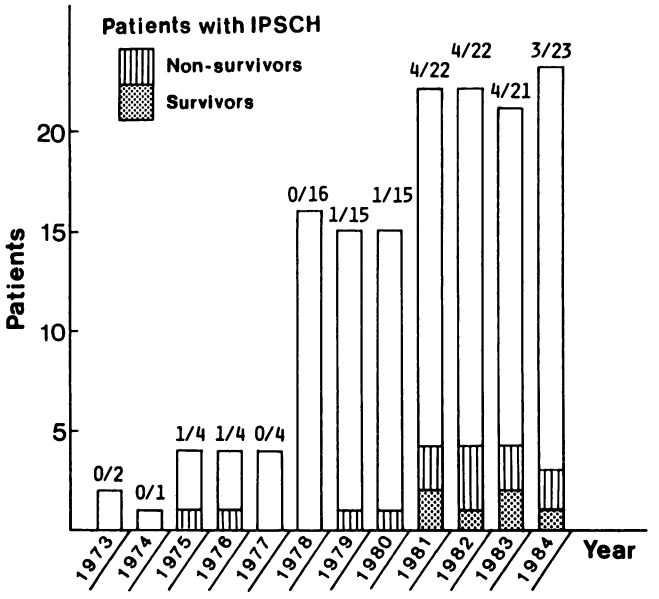

FIG. 1. Yearly distribution of the patients who underwent elective hepatic resection and the incidence of intraperitoneal septic complications after hepatectomy (IPSCH).

Out of the 149 patients, culture-proved IPSCH developed in 19, which consisted of right subphrenic abscess in 16 and peritonitis in three patients. The findings in patients with IPSCH were compared with those in 118 patients without IPSCH or 30-day operative mortality.

Statistical Analyses

Chi square, Student's t, and Mann-Whitney's U tests were used in the statistical evaluation of the clinical data.

Results

Yearly distribution of the patients who underwent elective hepatic resection and the incidence of IPSCH are shown in Figure 1. Although the incidence has not been reduced, six out of 15 patients (40%) survived IPSCH in the period 1981–1984.

As shown in Table 1, IPSCH occurred in 19 out of 149 patients (12.8%), and all these 19 had primary malignant neoplasms. Among the various types of hepatectomy performed, those who underwent right or extended right lobectomy had a significantly higher incidence of IPSCH ($p < 0.001$) (Table 2). When the patients with IPSCH were compared with control patients who neither had IPSCH nor 30-day operative mortality (Table 3), no difference was seen in sex, presence of associated liver cirrhosis, and preoperative laboratory data. Nevertheless, IPSCH occurred more frequently in those over 65 years old ($p < 0.02$), those whose operation time exceeded 5 hours ($p < 0.05$), those whose estimated blood loss at operation was over 3000 g ($p < 0.001$), and those who had postoperative hemorrhage that required laparotomy for hemostasis ($p < 0.001$).

TABLE 1. *Indications for Hepatic Resection and the Incidence of IPSCH*

Indications	Number of Patients: Total	Number of Patients: With IPSCH
Malignant		
Primary		
Hepatocellular carcinoma	125	18 (14.4%)
Cholangiocarcinoma	2	0
Mixed type	1	1 (100%)
Secondary	11	0
Benign		
Hemangioma	5	0
Cyst	3	0
Focal nodular hyperplasia	1	0
Intrahepatic cholelithiasis	1	0
Total	149	19 (12.8%)

IPSCH = intraperitoneal septic complications after hepatectomy.

Causative bacteria of IPSCH are listed in Table 4. In the period 1973–1980, five out of eight pathogens (62.5%) were coliform gram-negative rods, which sharply decreased to one out of 18 (5.6%) afterwards. Mixed infection was present in five patients. Among survivors of IPSCH, the causative bacteria was *Streptococcus fecalis* and alpha-hemolytic *Streptococcus* in one, *Staphylococcus epidermidis* in two, *Acinetobacter* in two, and *Clostridium* in one patient. The antibiotics administered after operation among the patients with IPSCH were as follows: in the period 1973–1980, first-generation cephalosporins alone in two and with aminoglycosides in three patients, and in the period 1981–1984, second- or third-generation cephalosporins alone in six, with aminoglycosides in seven and ampicillin alone in one patient.

Symptoms, signs, and laboratory findings of IPSCH were those of intraperitoneal abscesses or peritonitis in general, except for various degrees of cholestatic liver dys-

TABLE 2. *Incidence of IPSCH among Various Types of Hepatic Resection Performed*

Hepatectomy performed	Number of Patients: Total	Number of Patients: With IPSCH
Right lobectomy*	28	10 (35.7%)
Extended right lobectomy*	9	3 (33.3%)
Left lobectomy†	13	0
Segmentectomy†	21	1 (4.8%)
Partial hepatectomy†	78	5 (6.4%)
Total	149	19 (12.8%)

IPSCH = intraperitoneal septic complications after hepatectomy. $p < 0.001$ ($\chi^2 = 22.1$) when * and † are compared.

TABLE 3. *Comparison of Perioperative Variables between Patients with IPSCH and Control**

Variables	Patients: With IPSCH (N = 19)	Patients: Control (N = 118)	p Value
Age	60.9 ± 7.7†	53.9 ± 10.5	<0.01‡
>65 years old	7 (36.8%)	16 (13.6%)	<0.02 (χ^2 = 6.35)
Sex (M:F)	17:2	84:34	NS
LC present	16 (84.2%)	78 (66.1%)	NS
Preoperative laboratory data			
ICG (%)	18.4 ± 7.4	19.0 ± 12.4	NS
Bilirubin (mg/dl)	0.8 ± 0.4	1.0 ± 0.5	NS
Albumin (g/dl)	3.5 ± 0.4	3.8 ± 0.5	NS
PT > control (sec)	1.5 ± 3.8	0.8 ± 1.7	NS
WBC ($\times 10^3/mm^3$)	5.65 ± 2.23	5.08 ± 1.62	NS
Operation time (h)	3.5 ± 1.3	2.9 ± 1.1	<0.05‡
>5 h	3 (15.8%)	5 (4.2%)	<0.05 (χ^2 = 3.97)
EBL ($\times 10^3$ g)	4.53 ± 2.89	2.32 ± 1.83	<0.02‡
>3000 g	13 (68.4%)	31 (26.3%)	<0.001 (χ^2 = 13.34)
Postoperative bleeding	5 (26.3%)	5 (4.2%)	<0.001 (χ^2 = 11.75)

IPSCH = intraperitoneal septic complications after hepatectomy; LC = liver cirrhosis; ICG = indocyanine green (normal 0–10%); EBL = estimated blood loss at operation; NS = not significant.

* No operative mortality or IPSCH.
† Mean ± SD.
‡ Student's t test.

function in all patients with mean (±SD) total (and direct) bilirubin of 9.6 ± 9.0 (6.5 ± 7.4) mg/dl and alkaline phosphatase of 154 ± 98 U/L (normal 30–110 U/L), and hepatic encephalopathy at the onset of IPSCH in three patients who had a fair preoperative liver function.

A definitive diagnosis of IPSCH was established by culture of the drainage from the subphrenic drain in nine, culture of the needle aspirate in eight, and positive bile culture with leakage of bile into the subphrenic cavity in two patients. Diagnosis in all six survivors was established by culture of the subphrenic drainage. Computed tomography (CT) and ultrasonography (US) were useful diagnostic aids by revealing subphrenic fluid collection but were diagnostic in only one patient.

Treatment and outcome of the patients with IPSCH are shown in Table 5. Treatment other than antibiotics given to the six survivors consisted of percutaneous drainage and irrigation in two, irrigation of the pre-existing drain in two, and none in two patients. All four patients treated by drainage but without irrigation died. The cause of death in the patients with IPSCH was progressive liver failure followed by multiple organ failure in all, and they

TABLE 4. *Causative Bacteria of IPSCH*

Causative Bacteria	1973–1980	1981–1984	Total
Aerobic			
Gram positive cocci	*2*	*11*	*13*
Staphylococcus aureus	1	1	2
Staphylococcus epidermidis	0	3 (2)	3 (2)
α-Hemolytic streptococcus	0	2 (1)	2 (1)
Streptococcus fecalis	1	5 (1)	6 (1)
Gram-negative rods	*6*	*5*	*11*
Escherichia coli	3	0	3
Klebsiella	1	1	2
Proteus	1	0	1
Pseudomonas	1	2	3
Acinetobacter	0	2 (2)	2 (2)
Anaerobic	*0*	*2*	*2*
Bacteroides	0	1	1
Clostridium	0	1 (1)	1 (1)

IPSCH = intraperitoneal septic complications after hepatectomy.
( ) = number of pathogens in patients who survived IPSCH.

TABLE 5. *Treatment and the Outcome of Patients with IPSCH*

Treatment	Number: Survivors/Total
Survival drainage and SABT	0/1
Percutaneous drainage and SABT	2/9
(with irrigation)	(2/6)
Irrigation of the pre-existing drain and SABT	2/4
SABT alone	2/5*
Total	6/19 (31.6%)

IPSCH = intraperitoneal septic complications after hepatectomy; SABT = systemic antibiotic therapy.
* The pathogens of these two survivors were *Staphylococcus epidermidis* and *Acinetobacter*, respectively.

died 19 to 231 days (mean 57.2 days) after the hepatectomy.

When perioperative variables of the survivors and nonsurvivors were compared (Table 6), the diagnosis had been established earlier ($p < 0.05$) and the serum bilirubin level was lower ($p < 0.05$) in the survivors.

TABLE 6. *Comparative Data of Survivors and Nonsurvivors of IPSCH*

Variables	Survivors (N = 6)	Nonsurvivors (N = 13)
Age	58.8 ± 7.8*	61.8 ± 7.7
Sex (M:F)	6:0	11:2
LC present	5 (83.3%)	11 (84.6%)
Preoperative laboratory data		
ICG (%)	16.2 ± 7.5	19.4 ± 7.5
Bilirubin (mg/dl)	0.8 ± 0.4	0.8 ± 0.5
Albumin (g/dl)	3.7 ± 0.4	3.4 ± 0.3
PT > control (sec)	0.2 ± 0.9	2.1 ± 4.5
WBC ($\times 10^3/mm^3$)	5.72 ± 2.32	5.74 ± 2.58
Operation time (h)	3.3 ± 1.3	5.0 ± 3.2
EBL ($\times 10^3$ g)	3.57 ± 1.81	4.97 ± 3.23
#POD on diagnosis†	10.7 ± 2.9	18.3 ± 13.1
Laboratory data on diagnosis		
Bilirubin (mg/dl)†	3.3 ± 1.6	12.5 ± 9.6
ALP (U/L)	124 ± 37	168 ± 114
Albumin (g/dl)	3.7 ± 0.5	3.2 ± 0.5
WBC ($\times 10^3/mm^3$)	11.98 ± 7.79	15.36 ± 8.55

IPSCH = intraperitoneal septic complications after hepatectomy; ICG = indocyanine green (normal 0–10%); EBL = estimated blood loss at operation; #POD = number of postoperative day; ALP = alkaline phosphatase.

* Mean ± SD.

† $p < 0.05$ (Mann-Whitney's U test).

Discussion

In this series, IPSCH frequently followed right or extended right lobectomy, extensive bleeding, or a long operation and postoperative hemorrhage that required laparotomy for hemostasis. The incidence of IPSCH after right and extended right lobectomies was as high as that reported in the literature.[2,3] Hemoglobin and other proteinaceous substances are particularly noxious adjuvants of intraperitoneal infection,[7,8] and accumulation of blood, sloughed devitalized liver tissue, and bile[2,3,5] in the subphrenic dead space after hepatectomy therefore predisposes to the development of IPSCH by providing a favorable environment for the invasion and growth of the bacteria.

The liver is a solid organ with a rich blood perfusion, and securing hemostasis during parenchymal dissection, without devitalizing the cut surface, is not an easy task; this can only be achieved by individual ligation or clipping of the vascular structures before their division, since they retract into the liver parenchyma after transection.[5] In a recent animal experiment[9] and clinical report,[10] an ultrasonic scalpel was shown to decrease blood loss by giving excellent exposure of the intrahepatic blood vessels with little devitalization of the liver tissue. Although our experience of hepatectomy with the use of the ultrasonic scalpel is limited, its use in noncirrhotic liver seems promising.

Although laparotomy in cirrhotic patients carries a high risk of morbidity and mortality,[11] liver cirrhosis in our series was not a statistically significant risk factor of IPSCH. We believe that this relates to the fact that, in cirrhotic patients with poor hepatic functional reserve, we perform limited hepatic resection[12] rather than lobar or segmental resection in order to avoid postoperative liver failure due to over-resection.

IPSCH in this series always accompanied cholestatic liver dysfunction and often led to liver failure. Sepsis is a well-known cause of liver failure,[13–15] and rapid reduction of hepatic functional reserve caused by hepatectomy seems to predispose patients with IPSCH to postoperative liver failure. Since the prognosis of liver failure remains dismal, any delay in the diagnosis of IPSCH is morbid. However, a high incidence of nonspecific fever after hepatectomy,[2] resemblance of ISPCH to liver failure due to over-resection of the cirrhotic liver, and low yield of diagnostic findings on CT and US are all noncontributory events to the early detection of IPSCH. With the increasing awareness of IPSCH, we rely more on the culture of the subphrenic drainage for the early recognition of IPSCH. With this simple, low-cost, and noninvasive measure, a diagnosis of all survivors could be made when the serum bilirubin level was low. Periodic culture of the subphrenic drainage could well be considered as a routine test after right or extended right lobectomy.

The virulence of the pathogen did seem to have played a major role in the outcome of IPSCH. Opportunistic pathogens[16–18] were the causative bacteria in the majority of the survivors, and two survived without definitive drainage procedures. Since the improved outcome of IPSCH coincided with the emergence of the opportunistic pathogens and rather prolonged use of new-generation cephalosporins, alone or in combination with aminoglycosides in the postoperative period, we feel that a more refined use of prophylactic antibiotics as well as a secure hemostasis with minimal devitalization of the tissue during parenchymal dissection of the liver should reduce the incidence of IPSCH.

Acknowledgment

We thank M. Ohara for comments on the manuscript.

References

1. Fortner JG, Kim DK, Maclean BJ, et al. Major hepatic resection for neoplasia: personal experience in 108 patients. Ann Surg 1978; 188:363–371.
2. Thompson HH, Tompkins RK, Longmire WP Jr. Major hepatic resection: a 25-year experience. Ann Surg 1983; 197:375–388.
3. Iwatsuki S, Shaw BW Jr, Starzl TE. Experience with 150 liver resections. Ann Surg 1983; 197:247–253.
4. Lee NW, Wong J, Ong GB. The surgical management of primary carcinoma of the liver. World J Surg 1982; 6:66–75.
5. Foster JH, Berman MM. Liver resection: operative technique. *In* Foster JH, Berman MM, eds. Solid Liver Tumors. Philadelphia: WB Saunders, 1977; 255–303.
6. Fortner JG, Maclean BJ, Kim DK, et al. The seventies evolution in liver surgery for cancer. Cancer 1981; 47:2162–2166.
7. Condon RE, Malangoni MA. Peritonitis and intra-abdominal abscesses. *In* Schwartz SI, Shires GT, Spencer FC, Storer EH, eds. Principles of Surgery, 4th ed. New York: McGraw-Hill, 1984; 1391–1419.
8. Hau T, Simmons RL. Mechanisms of the adjuvant effect of hemoglobin in experimental peritonitis: III. The influence of hemoglobin on phagocytosis and intracellular killing by human granulocytes. Surgery 1980; 87:588–592.
9. Ottow RT, Barbieri SA, Sugarbaker PH, Wesley RA. Liver transection: a controlled study of four different techniques in pigs. Surgery 1985; 97:596–601.
10. Hodgson WJB, DelGuercio LRM. Preliminary experience in liver surgery using the ultrasonic scalpel. Surgery 1984; 95:230–234.
11. Garrison RN, Cryer HM, Howard DA, Polk HC. Clarification of risk factors for abdominal operations in patients with hepatic cirrhosis. Ann Surg 1984; 199:648–655.
12. Kanematsu T, Takenaka K, Matsumata T, et al. Limited hepatic resection effective for selected cirrhotic patients with primary liver cancer. Ann Surg 1984; 199:51–56.
13. Norton L, Moore G, Eiseman B. Liver failure in the postoperative patient: the role of sepsis and immunologic deficiency. Surgery 1975; 78:6–13.
14. Fry DE, Garrison RN, Heitsch RC, et al. Determinants of death in patients with intra-abdominal abscess. Surgery 1980; 88:517–523.
15. Zimmerman HJ, Fang M, Utili R, et al. Jaundice due to bacterial infection. Gastroenterology 1979; 77:362–374.
16. Dougherty SH. Role of enterococcus in intraabdominal sepsis. Am J Surg 1984; 148:308–312.
17. Burchard KW, Minor LB, Slotman GJ, Gann DS. Staphylococcus epidermidis sepsis in surgical patients. Arch Surg 1984; 119:96–100.
18. Jawetz E, Melnick JL, Adelberg EA. Miscellaneous pathogenic microorganisms. *In* Jawetz E, Melnick JL, Adelberg EA, eds. Reviews of Medical Microbiology. Los Altos: Lange, 1984; 284–290.