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Hepatectomy for Hepatocellular Carcinoma: Toward Zero Hospital Deaths

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Objective

The authors report on the surgical techniques and protocol for perioperative care that have yielded a zero hospital mortality rate in 110 consecutive patients undergoing hepatectomy for hepatocellular carcinoma (HCC). The hepatectomy results are analyzed with the aim of further reducing the postoperative morbidity rate.

Summary Background Data

In recent years, hepatectomy has been performed with a mortality rate of <10% in patients with HCC, but a zero hospital mortality rate in a large patient series has never been reported. At Queen Mary Hospital, Hong Kong, the surgical techniques and perioperative management in hepatectomy for HCC have evolved yearly into a final standardized protocol that reduced the hospital mortality rate from 28% in 1989 to 0% in 1996 and 1997.

Methods

Surgical techniques were designed to reduce intraoperative blood loss, blood transfusion, and ischemic injury to the liver remnant in hepatectomy. Postoperative care was focused on preservation and promotion of liver function by providing adequate tissue oxygenation and immediate postoperative nutritional support that consisted of branched-chain amino acid-enriched solution, low-dose dextrose, medium-chain triglycerides, and phosphate. The pre-, intra-, and postoperative data were collected prospectively and analyzed each year to assess the influence of the evolving surgical techniques and perioperative care on outcome.

Results

Of 330 patients undergoing hepatectomy for HCC, underlying cirrhosis and chronic hepatitis were present in 161 (49%) and 108 (33%) patients, respectively. There were no significant changes in the patient characteristics throughout the 9-year period, but there were significant reductions in intraoperative blood loss and blood transfusion requirements. From 1994 to 1997, the median blood transfusion requirement was 0 ml, and 64% of the patients did not require a blood transfusion. The postoperative morbidity rate remained the same throughout the study period. Complications in the patients operated on during 1996 and 1997 were primarily wound infections; the potentially fatal complications seen in the early years, such as subphrenic sepsis, biliary leakage, and hepatic coma, were absent. By univariate analysis, the volume of blood loss, volume of blood transfusions, and operation time were correlated positively with postoperative morbidity rates in 1996 and 1997. Stepwise logistic regression analysis revealed that the operation time was the only parameter that correlated significantly with the postoperative morbidity rate.

Conclusion

With appropriate surgical techniques and perioperative management to preserve function of the liver remnant, hepatectomy for HCC can be performed without hospital deaths. To improve surgical outcome further, strategies to reduce the operation time are being investigated.

Over the past two decades, hepatectomy has evolved from a rough, hasty, and bloody procedure to a refined, deliberate, and relatively bloodless operation. The operative mortality rate in hepatectomy for patients with cirrhosis has decreased from 58%, reported in Foster and Berman's survey in 1977,[1] to <10%, reported in many recent series.[2–7] However, a zero hospital mortality rate in a large patient series has never been reported. During the last 9 years at Queen Mary Hospital, the surgical techniques and perioperative care for hepatectomy have evolved into a standardized protocol. During the last 25 months of the study period, the hospital mortality rate in 110 consecutive patients was zero. In this report, the surgical techniques, perioperative management, and results of hepatectomy for hepatocellular

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carcinoma (HCC) are reviewed with the goal of further improving outcome.

PATIENTS AND METHODS

Between 1989 and 1997, 330 of 554 hepatic resections carried out by the Department of Surgery of the University of Hong Kong at Queen Mary Hospital were for HCC. All data were collected prospectively by a single research assistant.

Preoperative Management

Hepatic function assessment, including the Pugh et al[8] modification of Child's hepatic function classification system and the indocyanine green (ICG) clearance test, was performed after the HCC was considered resectable as shown by ultrasonography, computed tomography, or arteriography. During the period 1989 to 1993, the decision for laparotomy was based mainly on the Child's classification. After the ICG clearance safety limit for patients undergoing major hepatectomy was reported in 1995,[9] the selection of patients for hepatectomy was based largely on the results of ICG clearance tests rather than on Child's hepatic functional classifications.

On the day before surgery, the patient was given a light meal, and in the evening the bowel was washed out with a Phospho-soda buffered oral saline laxative (Fleet; CB Fleet Co., Inc. Lynchburg, VA). Bowel washout was performed in case *en bloc* resection of the HCC with the colon was required. Antibiotic coverage was by broad-spectrum cephalosporin (cefotaxime 2 g) administered at the induction of general anesthesia.

Surgical Techniques

Surgery was performed through a bilateral subcostal incision with an upward midline extension. Thoracic extension was required in 30 patients because the HCC in the right lobe was large. Eighteen patients who underwent segmentectomy for tumors in the right posterior segments were placed in a lateral position, and a subcostal incision was made with a thoracic extension in the seventh intercostal space.

Intraoperative ultrasonography was performed routinely to detect tumor invasion into the major branches of the portal or hepatic veins or any lesion in the contralateral lobe. This also allowed us to mark the line of parenchymal transection on the liver surface in the cases of segmentectomy[10] to obtain the optimal tumor-free margin and to avoid a major hepatic vein at the transection plane. In extended right hepatectomy cases, in which the middle hepatic vein had to be resected with the tumor, the exact position of the middle hepatic vein joining the left hepatic vein or inferior vena cava was noted to avoid injury to the left hepatic vein during parenchymal transection. Intraoperative ultrasonography was repeated during parenchymal transection to define the spatial relationship of the transection plane to the tumor so that the transection plane did not approach the tumor.

For right and left hepatectomy, cholecystectomy, if not already done, was performed. To detect bile leakage after hepatectomy, the cystic duct was cannulated and methylene blue was injected into the common bile duct. It was also used before extended left hepatectomy or left trisegmentectomy for operative cholangiography to identify aberrant anatomic arrangements of the right hepatic duct in relation to the left hepatic duct. The ipsilateral branch of the hepatic artery and the portal vein were dissected at the liver hilum and divided between ligatures. For left hepatectomy, the left portal vein was ligated and divided distal to the branches supplying the caudate, unless the caudate lobe had to be resected together with the left liver. The hepatic duct was not routinely isolated at the liver hilum because such a procedure can denude the ductal wall from the glissonian sheath, making suturing or ligation of the divided end of the hepatic duct risky. The hepatic duct was ligated or sutured with the surrounding glissonian sheath while exposed during liver transection.

Mobilization of the tumor-containing liver lobe and extrahepatic control of the hepatic vein were carried out in the standard manner.[11] If the left hepatic vein joined the middle hepatic vein intrahepatically, extrahepatic control of the left hepatic vein was not attempted in a left hepatectomy. For right hepatectomy or lobectomy, the paracaval portion of the caudate lobe was separated completely from the inferior vena cava by dividing many small branches of the hepatic veins to obtain a wider tumor-free margin and better posterior control during parenchymal transection. Exposure of the space between the inferior vena cava and paracaval portion of the caudate lobe was facilitated by tilting the operating table to the left, lifting the left subcostal wound with a self-retaining retractor to allow space for liver rotation, and illuminating the field with a headlamp. During rotation of the liver toward the left side, the left lobe was monitored for any darkening, because twisting of the vascular inflow pedicle can occur. In that situation, rotation of the liver was interrupted momentarily to allow reperfusion of the liver. To expose and encircle the right hepatic vein, the inferior vena cava ligament or a sheath of liver tissue covering the right side of the inferior vena cava had to be divided. The separation plane between the right hepatic vein and the inferior vena cava ligament was best approached from the cranial aspect of the right hepatic vein. When the right hepatic vein stump in the inferior vena cava was sutured, the right liver was not rotated but instead was pulled caudally. This maneuver allowed adequate exposure of the stump, especially if the paracaval portion of the caudate lobe had been detached completely from the inferior vena cava and the vascular clamp controlling the stump was rotated gently in a clockwise direction.

In 34 patients with particularly large right liver tumors,

Figure 1. Computed tomography scan showing the direction of division of liver parenchyma in the anterior approach for a large right lobe tumor. PV, portal vein; IVC, inferior vena cava.

the right liver was not rotated because forceful mobilization can disseminate the tumor, avulse the hepatic vein, or twist the inflow and outflow vascular pedicles. In these patients, parenchymal transection was performed from the anterior surface of the liver down to the inferior vena cava without premobilization of the liver and extrahepatic control of the right hepatic vein (anterior approach)[12,13] (Figs. 1 through 4).

During the period 1989 to 1992, parenchymal transection was done in 48 patients using a combination of the crushing clamp and finger fracture methods. In the subsequent period, an ultrasonic dissector was used routinely for parenchymal transection. During transection of the liver near the liver hilum, the ultrasonic dissector was used minimally to avoid thermal injury to the hepatic duct. Injury to the hepatic duct was also avoided by using fine sutures instead of diathermy coagulation to control bleeding around the duct. During parenchymal transection, the intermittent Pringle maneuver (clamping of the portal vein and hepatic artery for 15 to 20 minutes and release of the clamp for a 5-minute interval) was applied in 131 patients. The Pringle maneuver was not employed in 199 patients.

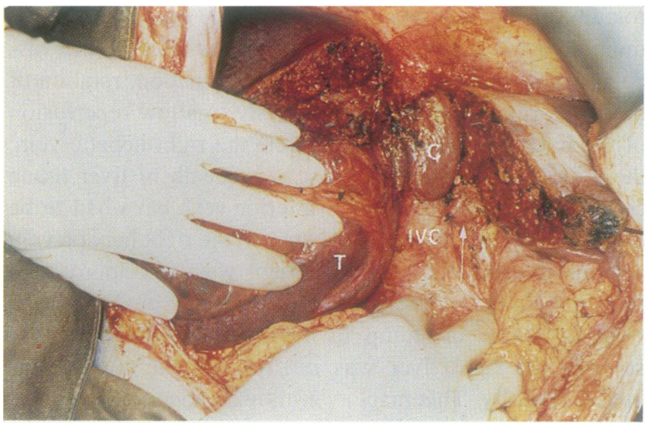

Figure 2. Anterior approach. Intraoperative photograph showing completion of transection of right portal pedicle (*long arrow*) and liver parenchyma down to the caudate lobe (C). The caudate lobe was exposed after division of the middle hepatic vein. IVC, inferior vena cava; T, tumor.

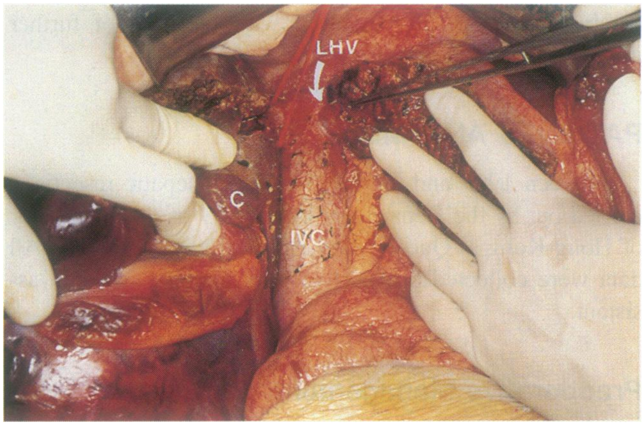

Figure 3. Anterior approach. Intraoperative photograph showing complete separation of the caudate lobe (C) from the inferior vena cava (IVC). The forcep points to the suture line of the middle hepatic vein. The red vascular sling encircled the right hepatic vein. LHV, left hepatic vein.

After parenchymal transection, methylene blue was injected into the bile duct through the cystic duct cannula to detect bile leakage. If the cystic duct had not been cannulated, a piece of clean swab was applied firmly to the transection surface and the liver was squeezed gently to detect bile leakage. The leak, if present, was closed with 5-0 sutures. The falciform ligament was reconstructed for right hepatectomy or lobectomy to prevent the left lobe from falling into the right subphrenic space, which would cause torsion of the left hepatic vein. The cut surface of the liver was covered as best possible with the greater omentum. A

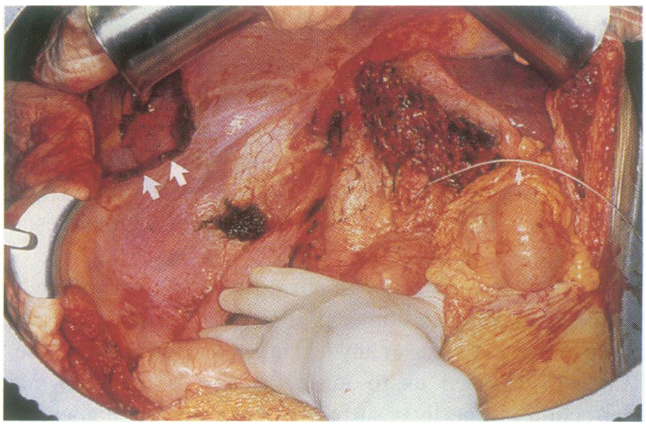

Figure 4. Anterior approach. Intraoperative photograph showing completion of hepatectomy and the appearance of the right subphrenic cavity after delivery of the specimen. The cut surface of the liver was completely dry. A cannula (*short arrow*) was inserted into the cystic duct and was used for checking bile leakage by methylene blue injection. In this case, a thoracic extension was added and the diaphragm was incised (*double arrows*). With the division of the diaphragm, additional space was available for mobilization of the tumor.

Table 1. PREOPERATIVE AND PATHOLOGIC DATA

	1989 (n = 25)	1990 (n = 29)	1991 (n = 31)	1992 (n = 30)	1993 (n = 35)	1994 (n = 33)	1995 (n = 39)	1996 (n = 52)	1997 (n = 56)
Age (years)	57 (26–79)	51 (34–79)	56 (34–72)	56 (2–71)	51 (26–77)	57 (28–78)	51 (5–82)	52 (19–80)	55.5 (7–79)
Male:female	19:6	28:1	28:3	27:3	27:8	28:5	32:7	43:9	44:12
ICG% 15 min	12.6% (1.5%–34%)	8.9% (4.2%–39%)	11.5% (2.7%–50%)	13.7% (3%–33%)	9.9% (6%–24.5%)	9.5% (2.2%–35%)	11.4% (3.5%–37.6%)	8.15% (1.6%–67%)	11.6% (2.4%–56%)
Resectability	25/113 (22%)	29/124 (23%)	31/140 (22%)	30/116 (26%)	35/178 (20%)	33/178 (19%)	39/169 (23%)	52/223 (23%)	56/248 (23%)
Tumor size (cm)	9.5 (2.3–17)	10 (2–15.9)	8 (0.5–18)	9.5 (2.5–25)	9.0 (1–18)	6.5 (1.5–18)	5.7 (1.2–23)	7.0 (1–17)	5 (1.5–20.5)
TNM stage									
I	0	1	2	0	4	3	3	1	2
II	6	8	12	11	8	15	20	26	24
III	12	14	10	15	16	11	15	20	27
IVA	7	5	6	3	6	3	0	5	3
IVB	0	1	1	1	1	1	1	0	0
Normal liver	8 (32%)	6 (21%)	2 (6%)	4 (13%)	10 (29%)	9 (27%)	6 (16%)	11 (21%)	5 (9%)
Chronic hepatitis	4 (16%)	6 (21%)	7 (23%)	8 (27%)	12 (34%)	15 (46%)	13 (33%)	22 (42%)	21 (38%)
Cirrhosis	13 (52%)	17 (58%)	22 (71%)	18 (60%)	13 (37%)	9 (27%)	20 (51%)	19 (37%)	30 (54%)

ICG% 15 min: % retention of indocyanine green at 15 minutes after injection

closed vacuum suction drain was inserted into the subphrenic space away from the cut surface of the liver and liver hilum to avoid injury to these structures. More recently, when thoracotomy was performed, we used a 16F vacuum drain instead of a standard chest drain connected to an underwater sealed bottle.[14] Before wound closure, care was taken to ensure that the small bowel had not been displaced into the subphrenic cavity.

Postoperative Care

After surgery, the patients, particularly those with cirrhosis and major hepatectomy, were monitored in the intensive care unit with attention to fluid balance, oxygenation, and tissue perfusion. Mechanical ventilation was given to 190 (58%) patients. All patients were given albumin 50 g daily for 3 to 5 days and broad-spectrum antibiotics for 3 days. Parenteral nutrition consisting of branched-chain amino acid-enriched solution, low-dose dextrose, medium- and long-chain triglycerides, phosphate, and multivitamins was started immediately after hepatectomy in all patients with cirrhosis or major hepatectomy and was continued for 3 to 7 days by means of a central line inserted aseptically. Once parenteral nutrition was started, no other intravenous fluid was given, and central venous pressure was maintained as low as possible to avoid congestion of the liver remnant. Oral nutrition was encouraged once bowel sounds returned. An oral preparation of branched-chain amino acid-enriched solution (Aminoleban EN, Korea Otsuka Pharmaceutical Co., Ltd., Seoul, Korea) was given as a supplement to the usual diet.

An in-hospital death was defined as death during the period while the patient was in the hospital for the hepatectomy. All complications that affected the postoperative course were recorded. To assess the evolving surgical techniques and perioperative management, the data were compared year by year. Major hepatectomy was defined as resection of three or more liver segments, according to the Couinaud nomenclature.[15] Minor hepatectomy was defined as resection of two or fewer liver segments. In terms of anatomic region, the classification of hepatectomy was also made according to the Couinaud nomenclature.[15] All continuous variables were expressed as median (range) and compared between groups by the Mann–Whitney test. A chi square test was used to compare discrete variables. Stepwise logistic regression analysis was used to define factors that were related to postoperative complications. Discriminant analysis was used to define the cutoff value for significant parameters that could maximally separate patients with or without complications. Significance was defined as $p < 0.05$. All statistical calculations were made using SPSS/PC+ computer software (SPSS, Chicago, IL).

RESULTS

There was a steady increase in the number of new cases of HCC and hepatectomies over the 9 years under review (Table 1). Resectability remained the same. The patients for each year were comparable in terms of age, sex ratio, tumor size, TNM staging,[16] and ICG clearance test results. Underlying cirrhosis and chronic hepatitis were present in 161 (49%) and 108 (33%) patients, respectively.

During the study, the number of major hepatectomies decreased, whereas the number of minor hepatectomies increased (Table 2). However, major hepatectomies still constituted >60% of the cases in 1996 and 1997 (Table 3). The volume of intraoperative blood loss and volume of blood transfused decreased. In the last 4 years, the median

Table 2. INTRAOPERATIVE AND POSTOPERATIVE DATA

	1989 (n = 25)	1990 (n = 29)	1991 (n = 31)	1992 (n = 30)	1993 (n = 35)	1994 (n = 33)	1995 (n = 39)	1996 (n = 52)	1997 (n = 56)
Major hepatectomy	21 (84%)	21 (72%)	21 (68%)	20 (67%)	26 (74%)	26 (79%)	25 (64%)	33 (63%)	34 (61%)
Minor hepatectomy	4 (16%)	8 (28%)	10 (32%)	10 (33%)	9 (26%)	7 (21%)	14 (36%)	19 (37%)	22 (39%)
Thoracic extension	1	0	4	2	1	1	3	19	17
Blood loss (l)	2.25* (0.4–10.5)	2.0† (0.5–8.5)	2.5 (0.3–20)	3.5 (0.9–15)	1.6 (0.2–18)	1.5 (0.2–8)	1.5 (0.2–20)	1.65 (0.3–10)	1*† (0.2–7.5)
Blood transfusion (l)	1.46 (0–7.7)	1.3 (0–5.8)	1.62 (0–7.8)	1.8 (0–6.6)	0.9 (0–9.6)	0 (0–3)	0 (0–9.9)	0 (0–12.9)	0 (0–5.16)
Operation time (min)	300‡ (180–590)	337.5§ (195–540)	320 (210–600)	317.5 (180–590)	342.5 (110–630)	326 (140–675)	334 (105–780)	384 (120–610)	420‡§ (135–720)
Patients not requiring blood transfusion	1 (4%)	2 (7%)	1 (3%)	2 (6%)	10 (29%)	19 (58%)	26 (67%)	27 (52%)	43 (77%)
Length of hospital stay (days)	22 (2–89)	16 (8–128)	15 (9–72)	15 (8–46)	14 (2–130)	9.5 (4–41)	11 (7–76)	11 (8–28)	12.5 (5–66)
Complications	12 (48%)	16 (55%)	13 (42%)	12 (40%)	13 (37%)	10 (30%)	14 (36%)	18 (35%)	21 (38%)
Hospital deaths	7 (28%)	3 (10%)	4 (12%)	2 (6%)	2 (6%)	1 (3%)	2 (5%)	0 (0%)	0 (0%)

* p = 0.002, 1989 *vs.* 1997
† p = 0.0009, 1990 *vs.* 1997
‡ p = 0.022, 1989 *vs.* 1996
§ p = 0.02, 1989 *vs.* 1997

blood transfusion requirement was 0 ml, and 64% of the patients did not require blood transfusions. In 1997, only 13 patients (23%) received blood transfusions. The operation time was longer during the last 2 years of the study.

Table 3. TYPES OF HEPATECTOMY

	Period 1989–1995	Period 1996–1997
Major hepatectomy	160	67
Right hepatectomy	90 (7)	37 (3)
Extended right hepatectomy	29 (2)	7 (1)
Left hepatectomy	10 (1)	10
Extended left hepatectomy	11 (2)	3
Right lobectomy	19 (4)	9 (2)
Resection of segment 2, 3, 4, 5, 8	1	1
Minor hepatectomy	62	41
Left lobectomy	20	11
Segmentectomy of segment 1	2	0
2	1	1
3	4	1
4	6	3
5	4	2
6	4	3
7	2	5
8	4	1
4 & 5	3	0
4 & 8	1	0
5 & 6	6	7
6 & 7	3	5
7 & 8	2	1
5 & 8	0	1

( ) indicates concomitant resection of segment 1

The hospital stays decreased from a median of 22 days in 1989 to 11 days in 1995 and 1996 and 12.5 days in 1997 (see Table 2). The hospital mortality rate decreased from 28% in 1989 to 5% in 1995 and 0% in both 1996 and 1997. The causes of hospital deaths from 1989 to 1995 are listed in Table 4. From December 1995 to December 1997, there were no hospital deaths in the 110 consecutive patients undergoing hepatectomy for HCC. Despite a reduction in the hospital mortality rate, the postoperative morbidity rate remained approximately the same during the study period. However, comparison of the types and incidence of complications between the 1989 to 1995 period (hospital mortality rate of 9.5%) and the 1996 to 1997 period (hospital mortality rate of 0%) showed that there was a significant reduction in potentially fatal complications such as subphrenic abscess, biliary fistula, and hepatic coma; however, there was an increased incidence of wound infection during the latter period (see Table 4). The bacteria cultured from infected wounds during this period included *Staphylococcus aureus* (n = 5), *Pseudomonas aeruginosa* (n = 2), *Enterobacter* sp. (n = 1), *Proteus* sp. (n = 1), α-hemolytic streptococci (n = 1), and *Enterococcus* (n = 1).

Further analysis was done to define factors that could account for the postoperative complications during the 1996 to 1997 period. Comparison of preoperative data, operative data, and pathologic factors in patients with and without complications showed that the operation time, the volume of intraoperative blood loss, and the volume of transfused blood were related significantly to the occurrence of complications (Tables 5 and 6). Stepwise logistic regression analysis revealed operation time to be the only factor related to postoperative complications (coefficient = 0.148, p =

Table 4. COMPLICATIONS AND DEATHS

	Period 1989–1995 (n = 222)	Period 1996–1997 (n = 108)
Infectious complications		
Chest infection	28	11
Wound infection	11	14*
Subphrenic abscess	15 (3)	1*
Urinary tract infection	1	0
Biliary fistula	11	0*
Infected ascites	1 (1)	1
Empyema thoracis	1	0
Noninfectious complications		
Pleural effusion requiring tapping	31	6*
Wound dehiscence	4	3
Postoperative bleeding	6	0
Variceal bleeding	1	0
Peptic ulcer bleeding	5	0
Myocardial infarction	1 (1)	0
Intestinal obstruction	1	0
Hepatic coma	19 (14)	0*
Pericardial effusion	1 (1)	0
Superior mesenteric vein thrombosis	1 (1)	0
Ileocolic anastomotic leakage	0	1

* $p < 0.05$
( ) no. of patients dying of the complication

Table 5. CLINICAL AND OPERATIVE DATA OF PATIENTS WITH AND WITHOUT POSTOPERATIVE COMPLICATIONS IN 1996–1997

	With Complications (n = 39)	Without Complications (n = 69)
Age	53 (19–79)	52 (7–80)
Male:female	33:6	54:15
Concomitant medical disease	15	32
Cirrhosis	18	31
Chronic hepatitis	17	26
Blood loss (l)	1.5 (0.2–10)	1 (0.1–10)*
Blood transfusion (l)	0.3 (0–12.9)	0 (0–9)*
Fresh-frozen plasma infusion	0 (0–3)	0 (0–1.3)
Major hepatectomy	25	42
Minor hepatectomy	14	27
Operation time (min)	435 (135–720)	390 (120–600)*
Tumor size (cm)	6 (1.3–17)	6 (1.5–20.5)
Tumor stage I	1	2
II	22	28
III	14	33
IVA	2	6

* $p < 0.05$

0.023). By discriminant analysis, the operation time that maximally separated patients with and without complications was 409 minutes ($p = 0.02$).

DISCUSSION

In the past two decades, suboptimal preoperative liver function, massive intraoperative bleeding, postoperative septic complications, and hepatic failure were identified as the chain of events leading to hospital death in patients undergoing hepatectomy for HCC.[17,18] To improve the outcome of hepatectomy for HCC, our attention has been focused on preoperative evaluation of hepatic function to select patients with adequate hepatic functional reserve for hepatectomy; on surgical techniques to reduce intraoperative bleeding; on avoiding ischemic injury to the liver remnant and biliary leakage; and on promoting liver function in the postoperative period (Table 7).

Selection of patients for hepatectomy in the recent years of this study was based primarily on the results of ICG clearance tests. ICG clearance is a more refined criteria than Child's hepatic functional classification because even among patients with Child's A liver function, a wide range of ICG retention values are often seen,[19] and hospital deaths after hepatectomy have occurred.[20] Consistent with the findings of Yamanaka et al,[21] an ICG retention value <14% at 15 minutes was found in our previous study[9] as the safety limit for major hepatectomy and was adopted as a guideline in the selection of patients for major hepatectomy. However, firm criteria for minor hepatectomy selection based on ICG clearance have not been established.

The remnant liver volume is another important preoperative consideration. Resection of 60% to 70% of the non-

Table 6. LABORATORY DATA OF 1996–1997 SURGERY PATIENTS WITH AND WITHOUT POSTOPERATIVE COMPLICATIONS

	With Complications (n = 39)	Without Complications (n = 69)
Hemoglobin (g/l)	14.2 (9.7–19.9)	14.3 (7.4–16.6)
White blood cell × 10^9/l	6.4 (2.5–17.2)	6 (2.3–14.6)
Platelet × 10^9/l	154 (53–566)	167 (41–927)
Serum creatinine (μmol/l)	92 (66–113)	89 (43–183)
Serum total bilirubin (μmol/l)	11 (2–31)	11 (5–41)
Serum albumin (g/l)	41 (31–49)	42 (29–50)
Serum alkaline phosphatase (IU/l)	97 (52–155)	97 (55–2540)
Serum alanine aminotransferase (IU/l)	44 (13–152)	3 (8–207)
Serum aspartate aminotransferase (IU/l)	50 (20–283)	46 (16–246)
International normalized ratio	1 (0.9–1.2)	1 (0.9–1.5)
ICG% retention 15 min	9.3 (3–30.3)	11.4 (1.6–66.9)

Table 7. IMPORTANT PERIOPERATIVE MEASURES FOR GOOD RESULT

Preoperative
- Evaluation of hepatic functional reserve by indocyanine green clearance test

Intraoperative
- Adequate exposure, thoracotomy if necessary
- Preservation of caudate lobe portal vein supply in left hepatectomy
- Avoidance of prolonged liver rotation
- Avoidance of dissection of hepatic duct during hilar dissection
- Cautious application of ultrasonic dissector
- Prompt hemostasis to avoid massive bleeding and hypoxic injury to the liver
- Checking for and suture of bile leakage sites by fine sutures
- Reconstruction of falciform ligament after right or extended right hepatectomy

Postoperative
- Mechanical ventilation and immediate parenteral nutritional support for patients with cirrhosis having major hepatectomy
- Early oral nutrition with branched-chain amino acid-enriched solution formula
- Avoidance of overloading of circulation

tumorous liver has been reported to be compatible with survival, even in patients with chronic liver disease.[22] Preoperative embolization of the ipsilateral branch of the portal vein feeding the tumor has been suggested to encourage hypertrophy of the contralateral liver lobe so that the liver remnant would represent >40% of the total liver volume.[22] However, an adequate liver remnant is not an absolute safeguard against postoperative liver failure because intraoperative massive bleeding and maneuvers that induce compressive or ischemic injury to the liver remnant can result in postoperative liver failure.

The surgical approach presented here focuses on avoiding massive bleeding and ischemic injury to the liver remnant. A generous incision is mandatory for adequate exposure. Excellent exposure of the liver can be achieved using a bilateral subcostal incision and a self-retaining retractor. The right liver can be mobilized and rotated to the wound surface if necessary. This maneuver is easy when the liver is soft and normal and the tumor is relatively small, but it is difficult for a small cirrhotic liver situated deeply inside the right subphrenic cavity and dangerous for a large right liver tumor because the space available for manipulation is limited. Forceful mobilization may cause laceration of a large right liver tumor or avulsion of the hepatic vein. With segmentectomy of segment 6, 7, or 8, prolonged rotation of the liver may lead to ischemic injury to the liver remnant because inflow and outflow vascular pedicles may become twisted. In such difficult situations, a thoracic extension to the subcostal wound or a J incision[23] can increase the space for mobilization of a large right liver tumor, and for segmentectomy of segment 6, 7, or 8, the liver transection plane would be perpendicular to the wound, especially with the patient placed in a lateral position. In the past, thoracotomy was considered harmful and unnecessary, but recent evidence indicates that patients undergoing segmentectomy for right liver tumors using a transthoracic[24] or thoracoabdominal approach[25] have equally favorable results. To reduce the pain associated with the chest drain and to allow early mobilization, a small vacuum drain may be useful.[14]

To avoid tearing of the inferior vena cava and right hepatic vein, as well as prolonged rotation of the liver during mobilization of a large right liver tumor, it might be possible to employ an anterior approach.[13] However, the anterior approach is potentially dangerous and should not be taken lightly by beginners because bleeding at the deeper plane of parenchymal transection can be difficult to control if the posterior surface of the liver was not previously mobilized. If the tumor had gained a collateral blood supply from the right diaphragm, congestion of the right liver tumor and diffuse bleeding from the transected liver surface are also observed after division of the right hepatic vein. Careful and gentle mobilization of the right liver aided by thoracotomy, adequate illumination of the field, and meticulous dissection in the space between the inferior vena cava and the back of the liver are our favored techniques for large right liver tumors, especially when teaching junior surgeons to perform the surgery. We reserve the anterior approach for patients with HCC invading the right or middle hepatic veins.

The major bleeding occurs during parenchymal transection, and the blood loss is proportional to the transection surface area.[26] Gentle and cautious application of an ultrasonic dissector with the Pringle maneuver can reduce the bleeding significantly.[26,27] However, use of an ultrasonic dissector is not entirely bloodless and it is time-consuming, but the Pringle maneuver must be limited to 120 minutes to avoid irreversible liver injury.[26] Establishment of a technique to transect the liver with the ultrasonic dissector without the Pringle maneuver is therefore critical, especially when a large transection area is involved. A technique for rapid parenchymal transection that does not cause excessive bleeding is still needed.

It has been shown that lowering central venous pressure to <6 cm H_2O results in an almost bloodless field.[28] We were not able to validate this finding because our anesthesiologists were concerned about uncontrollable air emboli and preferred to maintain the central venous pressure at >10 cm H_2O in nearly all patients. Fortunately, cautious application of the ultrasonic dissector reduced blood loss, and more than half of the patients in our series in the last 4 years did not require blood transfusion. However, a longer operation time was required.

In the postoperative period, promotion of liver function was the goal. Restriction of intravenous fluid and lowering of central venous pressure to prevent congestion of the liver remnant,[29] and mechanical ventilation in the patients with cirrhosis to maintain adequate oxygenation and possibly to reduce pleural effusion,[30] were practiced. A recent study[31] suggested that supranormal oxygen delivery by mechanical ventilation and maintenance of a hyperdynamic state is beneficial in patients with cirrhosis undergoing partial hepatectomy. However, this treatment is labor-intensive, and the pulmonary artery catheter insertion needed for monitoring treatment is invasive. We consider that fluid retained by the patient with cirrhosis is difficult to eradicate, and restriction of intravenous fluid is more desirable. With fluid restriction during the postoperative period, routine measurement of central venous pressure may not be necessary, and the catheter used for measuring central venous pressure can be removed as soon as possible to avoid central line sepsis.

Parenteral nutrition was started immediately after surgery, which is the time when the patient most requires metabolic support.[12] In addition to providing nutrients and stimuli for liver regeneration,[32] a parenteral nutritional mixture can also serve as an efficient metabolic vehicle for resolving acute electrolyte and acid–base disturbances[33] and has been shown to prevent deterioration of liver function.[34] The contents of the parenteral nutritional mixture (*i.e.*, amino acids,[35,36] lipid emulsion,[37] and phosphate[38]) were selected to meet the metabolic needs of patients with cirrhosis. However, parenteral nutrition is expensive and potentially dangerous (*i.e.*, by overloading the circulation and inducing central line sepsis). Thus, in our series no other intravenous fluid was given, and oral feeding was encouraged once bowel function returned. Oral feeding is necessary for the maintenance of intestinal integrity, the prevention of bacterial translocation, the production of hormones, and the increased portal blood flow necessary for liver regeneration.[39,40] An oral preparation of branched-chain amino acid-enriched solution may be beneficial in patients with impaired hepatic function. Although the value of an oral preparation of branched-chain amino acid-enriched solution in the immediate postoperative period has not been documented, its use in patients with cirrhosis was found to be beneficial for improving liver function.[41,42]

With the refinements in surgical technique and perioperative care, we achieved a hospital mortality rate of zero in a patient series in which most of the patients had cirrhosis or underwent major hepatectomy. This achievement is not related only to the accumulated experience in a large-volume center[43] but is also the result of attention to fine details in every patient by the senior surgeons. Thus, potentially fatal complications such as biliary leakage, subphrenic abscess, and massive bleeding were reduced. In the postoperative period, monitoring and care of the patients with cirrhosis in the intensive care unit for 1 to 2 days is expensive but worthwhile, because unlike patients with normal liver function, patients with cirrhosis have little hepatic functional reserve, and their survival depends on vigilant postoperative care and support.

In the latter years of the study, the operation time was longer. This increase in duration resulted in part from teaching junior surgeons to do the hepatectomy. However, more minor hepatectomies were performed. Minor hepatectomy was designed to preserve the liver remnant volume and should not be regarded as a less serious procedure than a major hepatectomy, as the term implies. Resection of the middle segments (segment 4, 5, or 8) or the right posterior segments (segments 6 and 7) involves a much larger transection surface area and technical difficulty than a right or left hepatectomy.

In review, the only deficiency in the last 2 years was a high rate of wound infection, which could be related to the large number of patients with chronic liver disease; they might have been malnourished and immunodeficient.[44] However, the long operation time was also a factor, predisposing the wound to contamination and infection.[45] Contrary to two recent studies[25,46] that showed operation time to be one of many factors affecting the postoperative morbidity rate, the present study demonstrated operation time to be the *only* significant factor, thus highlighting the critical influence of operative stress imposed by the duration of general anesthesia. A prolonged operation time appears inevitable if a good result from hepatectomy for HCC is to be achieved, and was so noted in many recent series reported by experienced surgeons.[24,25,31,47] However, prolonged operation time is not always desirable—apart from the higher cost and the higher rate of wound infection, the patient is vulnerable to hypothermia. Hypothermia in turn leads to impairment of coagulation[48,49] and increased difficulty in hemostasis during liver transection. To reduce the operation time, practice in reducing the liver transection time or the development of equipment that is more efficient than the ultrasonic dissector is needed.

In conclusion, with this evolution in surgical technique and postoperative care toward preservation of liver remnant function, hepatectomy for HCC can be performed without hospital deaths. To improve outcome even further, measures to reduce operation time are being investigated.

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