

Original Paper

Principle of perioperative management for hepatic resection and education for young surgeons

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Running title: Plan and education of hepatectomy

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ABSTRACT.

Background/Aims: An expert technique and special anatomical or physiological knowledge are needed in the field of hepatic surgery compared to other abdominal surgeries. The establishment of basic policy and operative techniques for hepatectomy, and stepwise training for young hepatic surgeons are necessary.

Methodology: We scheduled hepatic resection based on the indocyanine green retention rate at 15 minutes and volumetric analysis. Limited resection or preoperative portal vein embolization was often performed.

Results: Between 1994 and December 2005, 338 hepatectomy were performed. Operative procedures included limited or segmental resection in 215 and hemihepatectomy or more extended hepatectomy in 123. Hyperbilirubinemia or hepatic failure after hepatectomy was observed in 15 (4%) and hospital death in 10 (3%). Although death from hepatic failure was observed in 9 of 152 (6%) between 1994 and 1999, the mortality rate has been improved since 2000 (1 of 186 (0.5%)). Senior residents start training with step by step hepatectomy from partial resection to sectionectomy. Hemi-hepatectomy for normal liver is finally permitted after technical consolidation. More complicated hepatectomy must be performed by experienced teaching surgeons.

Conclusions: Competent operative techniques under experienced surgeons and the achievement of safe resection at each stage are our educational policy for hepatectomy.

Key Words: liver resection, protocol, education, post-hepatectomy complications, hemihepatectomy.

Abbreviations: hepatocellular carcinomas (HCC), indocyanine green retention rate at 15 min (ICG R15), computed tomography (CT), liver activity at 15 minutes by heart plus liver activity at 15 minutes: LHL15 (^{99m}Tc -GSA), hyaluronic acid (HA), portal vein embolization (PVE)

INTRODUCTION

An expert technique and special anatomical or physiological knowledge are needed in the field of hepatic surgery, different from other abdominal surgeries. The techniques of liver resection improved in the 1990's and, therefore, morbidity and mortality rates were dramatically decreased (1). Nowadays, hepatic resection is safely performed worldwide (2-5). Systematic liver resection can also be undergone even in cirrhotic patients or patients with obstructive jaundice by various pretreatment modalities such as a portal vein embolization technique to reduce the resected liver volume or postoperative management (6-9). At present, many surgeons can perform liver resections including hemihepatectomy with appropriate training from experienced liver surgeons. Therefore, the establishment of basic policy and operative techniques for hepatectomy at each institute, and stepwise training for young hepatic surgeons are necessary.

In this report, we present our strategy, operative techniques and results of liver resection between 1994 and June 2006. Furthermore, we discuss our policy to educate young liver surgeons to perform major hepatectomy.

METHODOLOGY

Patients

The subjects were 358 consecutive patients with liver diseases who underwent hepatectomy in the Division of Surgical Oncology, Department of Translational Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences between January 1994 and June 2006. They included 232 men and 126 women with a mean age of 60 ± 12 years (\pm SD, range, 21-80 years). The liver diseases warranting hepatic resection included hepatocellular carcinomas (HCC) in 131 patients, metastatic liver carcinomas in 143, intrahepatic cholangiocarcinoma in

26, gall bladder carcinomas in 18, hilar bile duct carcinomas in 23 and benign liver diseases in 17. The background liver diseases included chronic viral liver diseases in 120 patients with cirrhosis in 53 (caused by hepatitis B virus in 68, hepatitis C virus in 46, and both viruses in 6), obstructive jaundice in 22 patients and normal liver in 216.

In our hospital, the volume of liver to be resected is estimated before surgery based on the results of the indocyanine green retention rate at 15 min (ICG R15) using Takasaki's formula (10). The liver volume, excluding the tumor (cm^3), is measured by computed tomography (CT) volumetry (6). Furthermore, our previous studies clarified that the hepatic uptake ratio of $^{99\text{m}}\text{Tc}$ -GSA (liver activity at 15 minutes by heart plus liver activity at 15 minutes: LHL15) and serum hyaluronic acid (HA) level were useful liver functional tests to predict postoperative complications and outcomes (11-14). When discrepancies between these tests were observed, the operative indication according to matching 2 of 3 parameters of ICGR15, LHL15, and HA level was applied at this stage.

In this cohort, we performed limited resection in 132 patients, segmental resection or sectorectomy in 95, hemihepatectomy in 96, and extended hemihepatectomy in 35. Persistent ascites or pleural effusion (defined as massive ascites unresponsive to diuretics for more than 2 weeks) in 98 patients; hepatic failure (defined by total bilirubin of >3 mg/dl on postoperative day [POD] 28 or postoperative death without other cause) in 15 patients, and intra-abdominal infection in 12 patients. Ten patients (2%) died of hepatic failure within 30 days. The study design was approved by the Ethics Review Board of our University.

Operative procedure

The J-shape incision for laparotomy was basically performed for liver resections, whereas the thoracoabdominal approach by oblique incision was often applied for liver resections in the posterior sector and segment 8 to shorten the length of incision and the operation time

(Figure 1) (15). Prior to transection of hepatic parenchyma, isolation or dividing of main hepatic hilar vessels and dividing of hepatic veins in the resected liver were performed to reduce intraoperative bleeding and operative risks. Transection of parenchyma was undergone by combining the clash clamping fracture technique (16) and ultrasonic dissecting apparatus (CUSA) under intermittent occlusion of hepatic in-flow for 15 minutes with release for 5 minutes by the so-called Pringle's maneuver (17). For resection of HCC or cholangiocarcinoma, systematic removal of a liver segment confined by portal branches and hepatic vein was basically performed (18); however, limited resection (8) was applied for patients with poor hepatic functional reserve. When Pringle's maneuver was difficult because of severe intra-operative adhesion or poor hemostasis such as cirrhotic liver, special dissecting devices such as an ultrasonic coagulation and cutting machine (SonoSurg, Olympus, Tokyo) (19) or TissueLink's dissecting sealer DS3.0 with radio-frequency energy (Tissue Link Medical Inc., Dover, NH, USA) (20) were used for resection.

Evaluated parameters

Clinical data, conventional liver functions and surgical data were analyzed. ICG was injected intravenously at a dose of 0.5 mg /kg body weight and the 15-minute retention rate was measured using a photopiece applied to the fingertip (RK-1000, Sumitomo Electric, Tokyo, Japan) without blood sampling (21, 22). Patients received 3 mg (185 MBq) of ^{99m}Tc -GSA (Nihon Medi-Physics, Nishinomiya, Japan) as a bolus dose into the antecubital vein. The hepatic uptake ratio of ^{99m}Tc -GSA (LHL15) was calculated after injection of ^{99m}Tc -GSA. (11). Peripheral blood samples for HA level were collected from every patient early in the morning in a stable condition during hospitalization. Blood samples were centrifuged at 3000 rpm for 15 min, and serum was stored at -80°C (13, 14). HA was assayed using the sandwich binding protein assay by SRL, Inc. (Tokyo). The normal value of serum HA determined by the

laboratory data of SRL, Inc. is <50 ng/ml. We used the Liver Damage Grade of ICGR15 instead of encephalopathy for five parameters of Child-Pugh classification of the Liver Cancer Study Group of Japan in 2000 (23).

Technique of portal vein embolization and evaluation

Preoperative portal vein embolization (PVE) was undergone in 28 patients. The two approaches to the right portal vein were direct catheterization of the ileocolic vein (n=15) and percutaneous transhepatic puncture (n=13) (7, 24). The substances used for embolization in our series included 1 g of absorbable gelatin sponge powder (Gelfoam[®]; Upjohn, Kalamazoo, MI) and 5,000 units (5 ml) of liquid thrombin (Sankyou Co., Tokyo) mixed in contrast media. Permanent embolization materials were not used.¹⁷ Embolization was completed when the entire right portal vein was totally occluded. At 14 days after PVE, the hepatic volumes of the non-embolized lobe and embolized lobe (lobe to be resected) were reassessed by CT volumetry. Surgical resection of the liver was performed at 21 days after PVE.

Statistical analysis

Continuous data are expressed as the mean \pm SD. Data from different groups were compared using one-way analysis of variance (ANOVA) and examined by the Mann-Whitney U-test. Categorical data were compared by the Chi-square test. Differences between groups were analyzed by Fisher's exact test or Scheffé's multiple comparison test. Correlations between two parameters were examined by calculating Pearson's correlation coefficient. A two-tailed *P* value < 0.05 was considered significant. Statistical analyses were performed using STATISTICA[™] software (StatSoft, Tulsa, OK).

RESULTS

Postoperative Hepatic Complications and patient outcomes

Although the incidence of intraabdominal long-term ascites and infection or other systemic complications was not different between the early period (1994 to 2000) and the latest period (2001 to May 2006), the incidence of hospital death due to hepatic failure in the latest period (0/176; 0%) was significantly lower than that in the early period (10/182; 5%) ($p=0.005$). After induction of PVE, 25 patients with liver diseases underwent right hemi-hepatectomy. By comparing the results in patients who underwent right hepatectomy without PVE technique, the incidences of postoperative complications and hospital death due to liver failure were similar between groups (**Table 1**).

Comparison of surgical records between surgeons

Table 2 shows comparisons of surgical records in 55 patients undergoing hepatic resection for these 2 years (June 2004 to June 2006) between surgeons including teaching staff (A: 18 years after graduation from medical college), senior fellow (B: 13 years), junior fellow (C: 10 years) and a resident (D: 5 years). In background liver diseases, surgeon A tended to perform hepatectomy for cirrhotic and icteric liver diseases compared to other surgeons ($p=0.088$). Surgeon A tended to perform major hepatectomy but this was not significantly different compared to other surgeons. The mean operating time for surgeon A was the longest, and was significantly longer than surgeon B. Mean occlusion time of hepatic in-flow using Pringle's maneuver was similar between surgeons but only the time by surgeon C was significantly longer than surgeon A. The amount of bleeding and red cell transfusion were not significantly different between surgeons. The incidence of hepatic complications after operation was not significantly different between surgeons.

Figure 2 shows the current protocol of step by step education in hepatic resection at our institute. Concerning laparoscopic hepatectomy, surgeons experienced in Step 3 could operate according to our policy.

DISCUSSION

Previous investigators have reported various risk factors associated with post-hepatectomy complications (e.g., liver failure, massive ascites and intra-abdominal infection), which were age (25), liver cirrhosis (26), steatosis (25), viral hepatitis status (25), portal pressure (27), hyperbilirubinemia (28), prothrombin activity (28, 29), remnant liver volume or hepatic resection rate (28, 30), and the volume of blood loss or transfusion (26). Usually, the surgeon carefully selects the extent or type of hepatectomy according to the above preoperative risk parameters and attempts to avoid excessive hepatectomy, bleeding and biliary leakage; however, there is always a fine balance between curability of the malignant tumor and the above risk factors in some patients. At present, however, liver surgery is safe and hepatic failure after partial hepatectomy has significantly decreased due to improved surgical techniques (1-5), surgical devices (19, 20) and perioperative management (24, 25, 27). Our results showed that hospital death by hepatic failure has not been observed in the past 5 years, different from the period between 1994 and 2000. From 1994 to 2003, hepatic surgeons did not change and the number and method of hepatectomy were similar between the early period and the past 5 years. This improvement in the mortality rate might be due to the competence in techniques and management of patients undergoing hepatic resection. Furthermore, the PVE technique has been applied in patients who needed right hepatectomy since 1997 (7, 24, 31). In our results, 25 patients needed PVE due to impaired liver function or excessive hepatic resection by comparing the functional liver reserve. By applying PVE, these patients might safely undergo right hepatectomy similar to patients who did not need PVE before right

hepatectomy. Introduction of the PVE technique allow us to extend the range of our hepatectomy and gives an insurance of safety after hepatectomy.

Education and specialist training in hepatic surgery are current topics, discussed at the Japanese Congress of the Japanese Association of Hepato-biliary Pancreas Surgery in 2006 (not published). Therefore, a comprehensive training system should be developed in the near future. We compared the surgical records of hepatectomy in surgeons with different experience to consider hepatectomy education. The most experienced teaching surgeon had the longest operating time, which was, however, due to more complicated major hepatectomy in patients with cirrhosis or obstructive jaundice. Although we applied Pringle's maneuver during hepatic transection, the mean occlusion time in the junior fellow was significantly longer. This surgeon performed segmental resection or sectorectomy not only in normal liver but also in cirrhotic liver. Inexperience in operative technique during transection might cause a longer occlusion time. In particular, as transection is more difficult and hepatic hemorrhage occurs more in cirrhotic liver compared to normal liver, the less experienced surgeon often took much longer for transection. From our results we considered that an important point in training younger surgeons is to improve the techniques of hepatic transection to shorten occlusion time and to achieve transection in the hard cirrhotic liver.

From our results, our recent education protocol for hepatic resection in inexperienced surgeons is shown in **Figure 2**. The first steps (Steps 1 and 2) are to learn the basic procedures for preparing liver resection and to learn to assist the chief surgeon. Experience as a first assistant operator is important in training to learn to handle the liver and the intraoperative anatomy of the liver. In Step 3, the trainee can experience various hepatectomy methods step by step and this step should be repeated until the trainee clearly understands the intrahepatic vessels and liver segments. As shown in our results, hepatectomy for pre-cirrhotic or cirrhotic liver is more difficult and, therefore, hepatectomy for such liver has been considered as Step 4

in our protocol. The number of hepatectomy for training is set as 5 for each step. If trainees perform well, they can move to the next step after experiencing a few cases. On the other hand, if trainees perform poorly after experiencing 5 cases, they should continue the same step. Finally, trainees complete Step 4 and then they can perform hemi-hepatic resections. Recently, laparoscopic hepatectomy has been increasing rapidly (32). Subjects for laparoscopic surgery might be basically partial resection for a tumor located near surface of the liver, or left lateral sectorectomy. As these procedures are operations a) and b) in Step 3 and are not complicated, residents, fellows or even regular laparoscopic surgeons are permitted to perform such a hepatectomy.

In conclusion, good knowledge of basic anatomy and techniques is important in hepatectomy training but special techniques or devices are not necessary. Under instruction from experienced hepatic surgeons, the ability to perform operating procedures competently and to master safe hepatectomy procedures are of basic important to develop hepatic surgeons.

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Figure legends

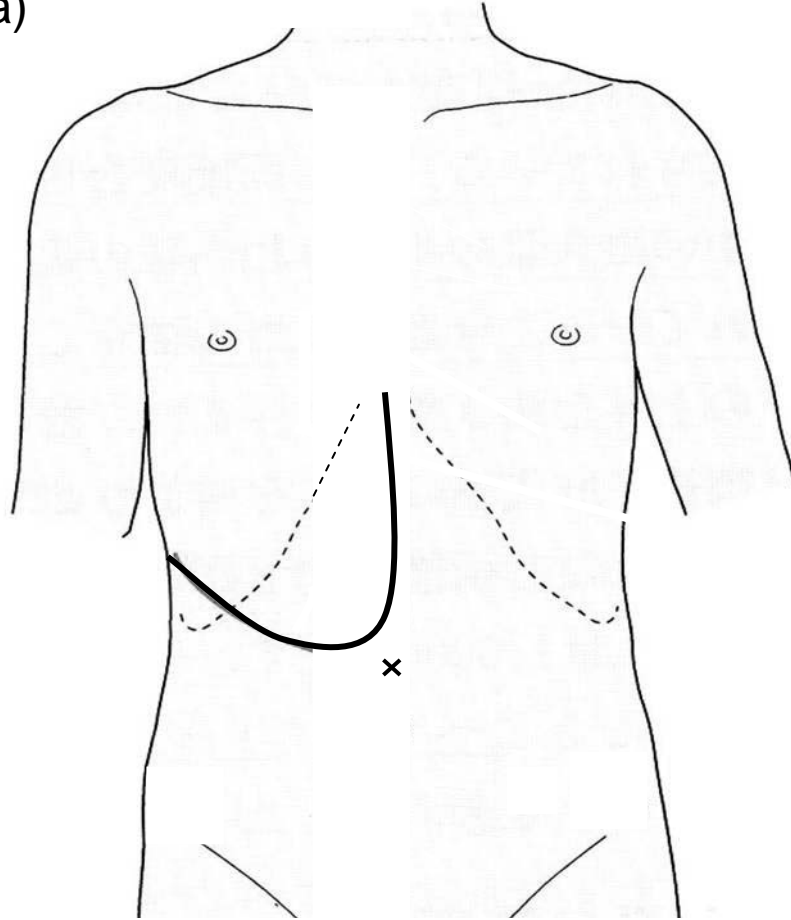
Figure 1. Scheme of two patterns of incision in hepatic surgery in our institute.

a) J-shape incision b) right oblique incision for thoracolaparotomy for right-side hepatectomy.

Figure 2. Education and training plan for hepatic surgeons at our institute.

Figure 1

a)



b)

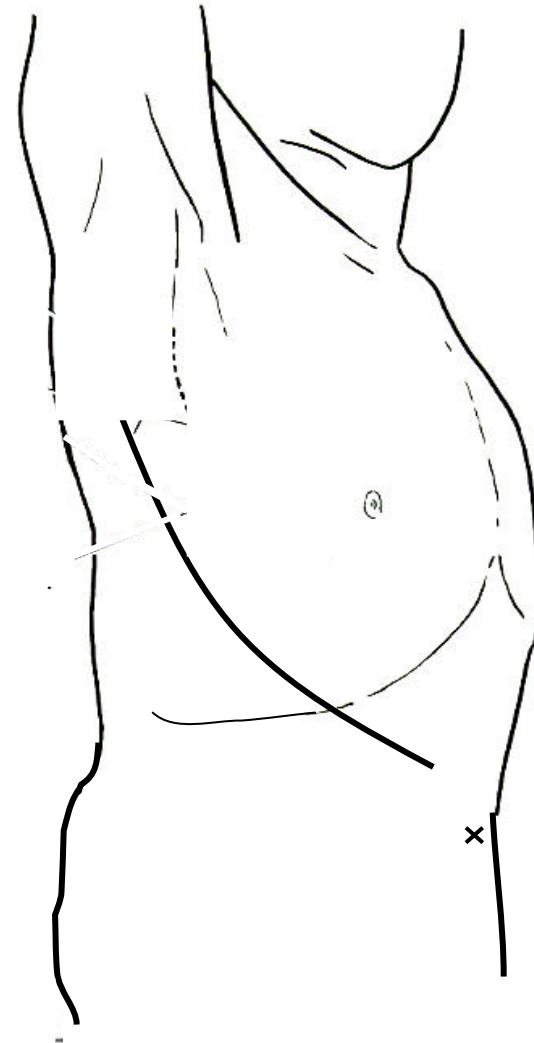


Figure 2

Education and plan for hepatic surgeons

Subjects: Surgeons who have trained in digestive surgery for over 5 years

Step 1: Thoracolaparotomy, Release and handling of liver, Intraoperative sonography, Isolation of hilar vessels, Encircling of major Glissons

Step 2: Handling of liver or ligation of intrahepatic vessels as a first assistant surgeon



Step 3: Training in hepatic resection as a chief surgeon

Experiences of 5 cases of each type of hepatectomy in the normal liver
in the order of a) partial resection, b) left lateral sectionectomy,
c) segmental resection and d) sectorectomy



Step 4: Step 3 training for patients with chronic viral hepatitis or cirrhosis



Step 5: Consolidation of techniques in Steps 3 and 4.

5 cases of hemihepatectomy without vascular anastomosis or intestinal reconstruction

- * Teaching staff or surgeons who have undergone Step 5

Hemihepatectomy or more with vascular anastomosis or intestinal reconstruction

- * Surgeons experienced in Step 3 can perform laparoscopic partial resection or left lateral sectionectomy

Table 1 Liver functions and patient outcomes after right hepatectomy between PVE and non-PVE groups

	PVE Group (n=25)	Non-PVE group (n=26)	P value
Background liver diseases			
Normal/CVLD / Jaundice	4 / 10 / 6	17 / 7 / 2	<0.01
Liver function			
ICGR15(%)	13.1±7.8	8.6±4.3	.035
LHL15	.946±.031	.934±.028	.355
Postoperative complications	8 (32%)	11 (52.4%)	.637
Hyperbilirubinemia(>3mg/dl)	3	1	
Uncontrolled ascites	6	8	
Bile leakage	2	3	.262
Intraabdominal infection	0	3	
Arrhythmia	0	1	
Sepsis	0	2	
Hospital death from liver failure	0 (0%)	1 (4%)	.992

PVE : portal vein embolization, CVLD: chronic viral liver disease, ICG: indocyanine green test, LHL15: hepatic uptake ratio of ^{99m}Tc-GSA

Table 2 Demographics, surgical records and patient outcomes after hepatectomy between surgeons

	Surgeon A (18 years) [§] (n=23)	Surgeon B (12 years) (n=20)	Surgeon C (10 years) (n=7)	Surgeon C (5 years) (n=5)
Background Liver Diseases				
Normal	8	16	3	4
CVLD	7	3	3	0
Cirrhosis	4	1	1	1
Jaundice	4	0	0	0
Hepatectomy				
Partial resection	7	12	2	4
Segmental resection	6	1	2	0
Sectorectomy	2	3	1	1
Hemihepatectomy or more	8	4	2	0
Mean operating time (minutes)	470	329*	397	410
Mean occlusion time (minutes)	41	44	48 [†]	41
Bleeding (ml)	1179	1083	932	1159
Red cell transfusion (ml)	497	258	339	482
Postoperative hepatic complications [‡]				
Yes	7	5	1	2
No	16	15	6	3

*: p<0.05 vs. Surgeon A, †: p<0.05 vs. Surgeon A

‡: Complications including uncontrolled ascites, liver failure, intraabdominal infection, postoperative hemorrhage or bile leakage

§ : years after graduation

CVLD: chronic viral liver diseases