Surgical treatment for HCC – Special reference to anatomical resection

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1. Introduction

I would like to express my sincere gratitude for the invitation extended to me as one of the lecturers for the festschrift in honor of Professor Renzo Dionigi.

Naturally, as surgeons, we strive hard every day, handling difficult operations, to save lives. However, with the rise in awareness of patient rights, we are ever more often made to defend ourselves in court. Therefore, the completion of a full-term professorship may be another proof of Professor Dionigi's clinical excellence. While also being fortunate enough to retire safely six years ago at the age of 60 from professorship at the University of Tokyo, I am still full of strength and zeal to carry on as an active surgeon, so that I find myself in the operating room three times a week leading the HPB and Organ Transplantation Department of the Japanese Red Cross Medical Center in liver resection and living donor liver transplant operations, hoping that the younger generation of surgeons will learn what they can from my performances.

The basic of surgical treatment for cancer is to remove the tumor en bloc from as far away from the malignant tumor itself. Gastrointestinal cancer will require accurate and meticulous lymph node dissection. In Japan, the late Dr. Tamaki Kajitani had initiated lymph node dissection for gastric cancer in the late 1940s. At that time, most surgeons were skeptical to the idea. However, 25 to 30 years later, lymph node dissection is acknowledged as being one of the effective surgical procedures for improving long term survival in patients with gastric cancer.

2. Biological characteristics and treatment options for hepatocellular carcinoma

Hepatocellular carcinoma (HCC) infiltrates portal venous branches and tumor cells are carried into the peripheral portal venous branches generating intrahepatic metastases. Another form of infiltration into the portal vein is tumor thrombus. Unlike in the case of gastric cancer, lymph node metastasis is an indication for dismal prognosis and of end-stage condition for HCC patients. Furthermore, non-cancerous livers of patients with HCC in general are cirrhotic or fibrotic to a degree that a wide parenchymal resection may induce grievous consequences. Therefore, a surgical procedure which minimizes the volume of non-cancerous liver to be resected and raises the curability as an optimal treatment choice is required. A surgical procedure tailored to cater these two seemingly contradicting requirements is systematic segment/subsegment anatomical resection (AR).

3. Systematic segment/subsegment anatomical resection

In most cases, ligating the portal pedicle within the targeted segment/subsegment from porta hepatis is difficult, and it is required to be ligated at a point inside the liver parenchyma. Intraoperative ultrasound (IOUS) scanning of the liver surface will provide a crude demarcation line of segment/subsegment on the liver surface, but an accurate identification is still difficult to achieve. In this method, the tumor-bearing portal pedicle is punctured, and dye is injected under IOUS guidance. The stained area is carefully marked with electrocautery. Transection is carried out from the liver surface, gradually proceeding towards the portal pedicle. Hepatic vein thicker than 5 mm in diameter is preserved, and transection is carried out alongside the vessel. For example, total S8 segmentectomy should clearly and lengthily expose the cutting edge of 2 to 3 portal pedicles of S8, right paramedian portal trunk stemming from such portal pedicles, and the main trunks of the right hepatic vein (RHV) and the middle hepatic vein (MHV).
4. Other anatomical resections

Conventionally, liver transections have been carried out by ways of avoiding exposing the hepatic veins in cases of sectoriectomies and hemihepatectomies. For example, in right hemihepatectomy, a demarcation line will appear along the main portal fissure by ligating the arterial and portal branches at porta hepatitis, and transection of the liver has been carried out some 5 mm to 1 cm right of the demarcation line to the right of the vena cava so as not to expose the MHV. However, in order to accomplish total eradication of intrahepatic metastases of HCC, complete exposure of the right side wall of the MHV is necessary. Similarly, in the right lateral sectoricotomy of the liver, the main trunk of the RHV must be exposed on the transection plane, and in right paramedian sectoricotomy, RHV and MHV must both be well exposed.

The author considers that accurate transection along the sectorial demarcation and complete exposure of the hepatic veins are uncompromising requirements for any segment/subsegment liver resection to be called an AR.

5. Tips for achieving accurate anatomical resection

5.1. Knacks to obtain reliable staining on the liver surface

There are several tricks available to obtain deep staining of the liver surface. First and foremost, is to be well experienced in IOUS. Start by accumulating diagnostic ultrasound training from the body surface, then proceed to acquire experience in IOUS.2 Second is the experience in ultrasound guided puncture.2 The author is able to puncture portal pedicles without the use of puncture adapters, however, these are available for novices. Ultrasound guided puncture training begins from accumulating experience in suction of abscess, pleural effusions and ascites, then in biopsies of little tumors and biliary drainages.3 What one should always keep in mind is to maintain the tip of the needle in view. In order to deeply stain the liver surface, the blood flow of the hepatic artery should be cut off at the porta hepatitis before injecting the dye into the portal vein.4 Check for replaced hepatic artery and aberrant hepatic artery. If portal venous pressure is low, staining of the liver surface will not be achieved or will only partly be achieved if the portal venous flow is blocked by pressing the hepatic vein.5 Pressing the liver surface too hard with the probe will also impede satisfactory staining of the liver surface. Fibrin glue applied on the liver surface after the first resection may also interfere with satisfactory staining at the following operations if it has formed a thick layer.6

5.2. Preventing bleeding from the liver parenchyma during liver transection

What we must first bear in mind is sufficient administration of muscle relaxant, and the second is strict water control. Exceeding 7 ml/kg/h will significantly increase the amount of bleeding. In patients with liver cirrhosis, administration of 4~4.5 ml/kg/h is recommended.3 Obviously, fresh-frozen plasma (FFP) will have to be administered, therefore the amount of Na in the intravenous infusion (IV) will have to be cut down and adjusted accordingly. Generally, Na concentration diluted to half the normal saline level is used.3

Inflow vascular occlusion to the liver is also an important issue. In general, Pringle maneuver or selective inflow vascular occlusion is employed.4 At Pringle maneuver, 15-minute occlusion and 5-minute reperfusion is repeated. After the fourth 15-minute occlusion, 10-minute reperfusion is carried out. The reason for the prolonged reperfusion time comes from the data acquired through experiments using pigs, showing gradual reduction of oxygen saturation in liver cells. At selective inflow vascular occlusion, arterial portal taping at the porta hepatitis is necessary. However, the procedure will avert congestion of the gastrointestinal tract and will allow repetition of 30-minute occlusion with only 5-minute reperfusion. Liver as an organ is tolerant to such ischemia procedures, but to further the ischemic tolerance, 100 mg hydrocortisone sodium phosphate is injected 30 minutes before the liver transection, and for preconditioning purpose, the first occlusion is kept to 10 minutes.

5.3. Measures to safely expose hepatic vein

To safely isolate the hepatic vein, maintaining low portal venous pressure as recommended in the previous subsection, and securing good operative view are imperative. The liver is caged inside the ribs. Therefore, the view of the cranial side of the liver is especially hard to maintain. Most major bleedings during liver resections are said to occur where hepatic venous flow streams into the inferior vena cava. Resections of this area, especially total resection of S7 or S8, should be carried out with J-shape incision. Resect the costal arch at the 9th intercostal space, intercostal muscles to the vertebra from the upper border of the 10th rib, pull the right costal arch cranially by Kent retractor5 (Takasago Medical Industry Co., Tokyo, Japan), and a full view of the right side of the confluence area of the hepatic vein and the inferior vena cava can be obtained at a right angle. Thoracotomy is therefore much recommended. Furthermore, the danger of air embolism induced by gasping caused at major bleeding due to insufficient light anesthetic depth which may lead to death can be prevented by thoracotomy.

Bleeding will be observed more or less when exposing the hepatic vein, but it should not lead to any panicking. Ligate as many thin tributaries of the hepatic vein as possible. Hair-thin tributaries should be pulled out from the liver parenchyma in the direction of the hepatic venous wall with Cooley or Debakey forceps, which will prevent bleeding. If bleeding occurs from a minute hole, suture ligate usingatraumatic needle with a thread as thin as 4-0. The bleeding may be controlled by the operator holding up the bleeding point with his/her left hand from the dorsal side of the liver. When tackling the bleeding hepatic vein, the liver should be lifted up and the bleeding point approached from the longitudinally lateral side. The suction tube handled by the second assistant clearing the bleeding from the hepatic vein and any other fluids must be moved sideways from cranial to caudal direction. Since hepatic vein tributaries bifurcate at a narrow angle toward the caudal direction, if the suction tube is moved sideways toward the cranial direction, the bleeding will worsen because the bifurcation point will be torn by the tube.

6. Performance results of anatomical resection

During the 1990s to the beginning of 2000s, three papers have been published indicating AR’s superiority evaluated under univariate analysis as a prognostic factor for good long-term survival compared against non-anatomical resection (NAR).5~7 Imamura in his paper has also indicated under multivariate analysis AR to be a significant prognostic factor for good disease-free survival (DFS).8 In 2005, Hasegawa et al. for the first time in the world had indicated by way of multivariate analysis that AR is a significant prognostic factor for good overall survival (OS) and DFS.9 However, in 2007, Eguchi et al., comparing the survival of 2267 AR cases against 3514 limited resection cases in a nationwide survey in Japan, fell just short of a significant difference in OS (P=0.0529), although they did find a significant difference between the two groups in DFS.
Further to these results, in subsequent stratification analysis they reported significant differences in DFS between groups with different tumor diameters. In their study, groups with tumor diameters of $\leq 2$ cm and $> 5$ cm did not show significant difference in DFS, whereas 2–5 cm did (P = 0.0005). My speculation is that the $< 2$ cm group included less intrahepatic metastases cases, and the $> 5$ cm group included more advanced cancer cases thereby did not show significant DFS difference. Another possible explanation for the result is inadequate quality control of the operation.

Sixteen papers have been published from 1984 to 2010 comparing AR and NAR. Six concluded there to be no difference and 10 otherwise. However, to date, Hasegawa’s is the only paper able to report AR as a significant prognostic factor for both OS and DFS; results may rely on the study being a single center study with sufficiently large number of patients, a limited number of surgeons with highest surgical performance maintaining high-quality AR, and permitting long-term follow up.

7. Methods to identify inter-segmental/subsegmental plane in the liver

Up until quite recently, unlike on the liver surface, markers indicating segmental/subsegmental plane within the liver had been considered non-existent. The main trunk of the hepatic vein is indeed a demarcation line between segments. However, no other indicative markers are available on the transection plane. Demarcation plane of segments within the liver must be as irregular as the demarcation line on the liver surface, which is so obvious when you look at the corrosion casts. Methods such as ligating the portal vein or the portal pedicle near porta hepatitis and injecting dye had been tried. However, dye had spilled out from the damaged minute branches of the portal vein scratched on the transection plane, staining the other side of the liver parenchyma and ruining the effort. How we can identify this irregular inter-segmental/subsegmental demarcation plane, and transect the liver along it, has long been a problem we surgeons were challenged to solve.

So, the author has devised a method of tracing the thin hepatic vein near the liver surface all the way to the main trunk and exposing them on the surface, a method which could overcome the irregularity of the inter-segmental/subsegmental demarcation plane. In actuality, when transection is commenced at the stained demarcation line on the liver surface, a hepatic vein tributary of 1–1.5 mm in diameter appears just about 1 cm below the liver surface. As you follow the vessel deeper into the liver, naturally you will find the tributary confluent and eventually reach the main trunk of the right hepatic vein.

The entire length of the hepatic vein from its smaller tributaries near the liver surface to the main trunk. In order to be able to perform such surgery, one needs to be trained and to accumulate much experience in liver resection under the guidance of a skillful HPB surgeon who is able to carry out high-quality AR.

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References