Surgical Treatment for Hepatocellular Carcinoma

Dr. Man-hei Shiu MBBS(HK) FRCS(Eng) DipAmerBdSurg FHKAM(Surgery)
Honorary Consultant, Hong Kong Sanatorium & Hospital

Surgical resection is the principal method of treatment for hepatocellular carcinoma (HCC) presenting in a resectable part of the liver. The technique of liver resection for cancer first developed in the 1950's. Even though Francis Glisson clearly described the internal anatomy of the liver in the 17th century (Fig. 1), technical challenges confront the hepatic surgeon today as they did 50 years ago. The complex arterial and portal blood supply, hepatic venous network and branching bile-ducts demand accuracy and extreme care in surgical dissection. Errors in surgical judgement and technique can lead to sudden intra-operative haemorrhage, or postoperative liver failure, often with fatal consequences in the past. Today, surgical resection of HCC can be performed with marked improvement in safety, thanks to recent advances in radiological imaging, surgical instrumentation and surgical technique.

Radiological imaging of the liver

Of utmost importance to the surgical treatment of HCC is radiological imaging. Modern computerised tomography (CT) or magnetic resonance imaging (MRI) can clearly visualise the size and exact position of the tumour, and its relation to adjacent major blood vessels. Images can be viewed in multiple planes or in 3-dimensions (3D), permitting the surgeon to plan the resection with accuracy. Intra-operative ultrasound examination of the liver is routinely used in liver resection. The surgeon directly maps the tumour in relation to adjacent blood vessels, and accurately plots the plane of dissection through the liver. When a large portion of the liver such as 65-70% needs to be resected, as in right hemi-hepatectomy, the concern has always been whether the remaining left lobe of the liver is large enough to allow regeneration and functional recovery. CT volumetric measurement of the liver can now be performed as an aid to assessment. The measured volume of the left lobe, and its proportion relative to the total liver volume (minus the tumour), provide important quantitative information. Fig 2 shows a large HCC of the right lobe which had been judged to be too risky to resect. Despite advanced age and coexisting cardiac disease, the patient’s liver function tests results were adequate. CT volumetry showed that the left lobe had 31% of the liver’s functional mass. Right hemi-hepatectomy was successfully performed with recovery and discharge of the patient 9 days after resection.

Selection criteria for resection of HCC

Three questions arise when radiological imaging has shown a potentially respectable HCC. First, has the tumour spread...
to the lungs or other intra-abdominal locations? This needs to be ruled out, usually by CT of the abdomen and lungs. Second, do some other HCC foci exist in the liver? When doubt exists, additional imaging studies by high-contrast multiple-phase CT or MRI can be done. To add further diagnostic accuracy, positron emission CT fusion tomography (PET-CT) can be performed to look for metastatic disease and other foci of HCC. PET-CT is best done using 11-C-acetate, which has high affinity for HCC, in addition to the standard 18-Fluorine-deoxyglucose radioisotope. Third, is the patient medically fit enough to undergo the required liver resection? Advanced age, cardiac, pulmonary or other systemic medical disease should seldom be contraindications to resection of HCC, provided an internal medicine specialist can evaluate and prepare the patient before surgery. More important to recovery is the magnitude of liver resection and the expected functional reserve of the remaining liver after partial resection. This is important because most of the patients have hepatitis B or C associated liver cirrhosis or chronic active hepatitis. In addition to the CT volumetry of the remnant liver mass, a number of biochemical functional testing methods are used in this assessment. In the Child-Pugh classification, abnormality of the blood bilirubin, albumin, or prothrombin index, and presence of ascites or encephalopathy serve as indicators of hepatic functional deficiency. Major liver resection such as right hemi-hepatectomy can be safely done when none of these abnormalities are present (Child class A), but only minor resections of one or two segments are safe if one or more abnormalities exist (Child B or C).

When a potentially respectable HCC fails to meet these criteria, alternative treatments are available. For example, if the left liver lobe is deemed too small for right hemi-hepatectomy, catheter embolisation of the right portal vein can be performed to induce atrophy of the right lobe and hypertrophy of the left, allowing successful resection after a period of 6-8 weeks. Hepatic arterial chemo-embolisation, Yttrium-90 microsphere injection and systemic chemotherapy have also been used with modest success in shrinking a massive tumour, to the extent that subsequent resection can be achieved.

For the patient with poor functional reserve (Child class C), radiofrequency ablation (RFA) of HCC is now often preferred to surgical resection. The radiofrequency probe can be inserted percutaneously, or if necessary due to anatomical reasons, by laparoscopy or open surgery. It is ideally suited to the treatment of tumours of 4.0cm diameter or less. RFA is less prone to complications of haemorrhage and liver failure in these patients. RFA can also be employed at the same time as surgical resection for the patient with more than one HCC. For example, a large HCC in the right lobe can be surgically resected, and a second HCC in the left lobe is subjected to RFA rather than resection, to minimise further loss of liver substance.

Technical advances in liver resection

Before embarking on liver resection, the modern liver surgical team must have a precise mapping for surgical navigation through the liver, based on preoperative scans and direct intra-operative ultrasound examination. To achieve resection, the liver substance must be safely divided along the pre-determined, carefully mapped plane(s). While standard surgical tools, such as scalpel, scissors, clamps and electro-cautery can be used, the numerous large and fragile blood vessels deep inside the liver are often difficult to dissect, visualise and control. Modern high-frequency ultrasonic suction-aspiration dissectors can help divide the liver substance, separating and bringing into clear view these blood vessels. The harmonic knife and similar devices can divide the blood vessels as well as liver substance with minimal bleeding (Fig. 3). These technological advances have enabled safer, more precise liver resections to be performed. Intra-operative blood loss is minimised, resulting in less need for blood transfusion. Limitation of blood loss and avoidance of transfusion are important developments in the surgical resection of HCC. As in the surgical treatment of colon and gastric cancer, blood transfusion may have a deleterious effect on survival after resection of HCC. Today, most major liver resections can be performed without need for blood transfusion. In a consecutive series of 106 liver resections for HCC performed from 1992 to 2004 at the author’s institution, the median number of units of blood transfusion during the most recent 5-years period was zero, as compared with a median number of 3 units transfused during the earlier years (1992-1997).

Surgical morbidity and mortality versus safety of liver resection

Resection of HCC has for decades incurred an operative mortality rate of over 10%, in some series over 20% in past decades. Many of these deaths were due to haemorrhage and liver failure. The risk of minor liver resection such as wedge or single segment resection is relatively small. The risk increases in proportion to the amount of liver substance removed. Thus right hemi-hepatectomy incurs a higher risk than left hemi-hepatectomy, especially when the liver’s reserve functional capacity is limited, as in many patients with cirrhosis. Proper pre-operative assessment and selection of patients for surgery have helped to reduce these risks. Furthermore, advancements in anaesthesiology, critical care, surgical technology and peri-operative surgical care during the last decade have contributed to the safety of liver resection. Today most institutions in Hong Kong and elsewhere report an operative mortality of 0% to 3%. Postoperative morbidity is encountered in up to 30% of
patients after major liver resection, comparable to other types of major upper abdominal surgery. Wound or intra-abdominal infection and cardio-pulmonary complications often develop. The most serious complication is liver failure. When this occurs, active measures must be taken to promote regeneration of the remaining liver. Nutritional support with infusion of branched-chain aminoacids, and close attention to acid-base and electrolyte derangements, such as hypo-phosphataemia, can avert progressive metabolic failure and death. A majority of the patients are discharged after 7 to 10 days after liver resection. Prolonged hospitalisation is needed for the occasional patient who develops serious organ-system derangements.

Survival after resection and recurrence of HCC

The average 5-year survival rate after resection of HCC is approximately 36%, while the disease-free survival is 20% 6,7. Smaller tumours (diameter 5.0 cm or less) have a more favourable outcome compared to larger tumours (Fig. 4). The presence of tumour satellites or vascular invasion, and hepatic functional deterioration due to chronic hepatitis and cirrhosis also adversely influence the prognosis. Patients whose tumours measure 2.0 cm or smaller in size and show no evidence of vascular invasion have the best survival rate, as high as 75%. Most tumour recurrences occur within the remaining liver after resection. Repeat surgical resection or treatment by RFA can successfully control some of these recurrent tumours. In selected patients, total hepatectomy and liver transplantation may be a useful consideration.

Figure 4. Resection of a small hepatocellular carcinoma; the patient is surviving after 10 years.

Prevention of tumour recurrence after resection

The high frequency of tumour recurrence after resection of HCC prompts measures to reduce this risk. Adjuvant chemotherapy and/or radiotherapy, as is the currently recommended strategy for locally advanced breast, colon and lung cancer, have not shown much survival benefit for HCC. However, adjuvant intra-hepatic arterial injection of one single-dose of iodine-131-Lipiodol has shown a statistically significant improvement of the disease-free survival rate in a prospective randomised trial8.

Conclusions

Technological advances have made surgical resection of HCC a safe operation in carefully selected patients. Resection remains the gold standard of treatment against which other evolving local ablative methods such as RFA must be compared. The high frequency of tumour recurrence after resection necessitates continued research and development of new and better adjuvant therapies.

References

1. Glisson S. Anatomia Hepatis. Fig. 2, page 350, Amsterdam, 1659.

MCHK CME Programme Self-assessment Questions

Please read the article entitled "Surgical Treatment for Hepatocellular Carcinoma" by Dr. Man-hei Shiu and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded 1 CME credit under the Programme for returning completed answer sheet via fax (2865 0345) or by mail to the Federation Secretariat on or before 31 January 2005. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-5: Please select one best answer. Questions 6-10: Please answer T(True) or F(False).

1. In recent years, which of the following radiological imaging is seldom used in the management of hepatocellular carcinoma:-
   a) MRI/CT
   b) PET
   c) Intraoperative Ultrasound
   d) Angiogram
   e) Liver Scan
   2. Hepatic functional deficiency is best indicated by:-
      a) Serum bilirubin
      b) Serum albumin
3. Which of the following modality has not been used to treat hepatocellular carcinoma:
   a) Cryotherapy
   b) Radiofrequency
   c) Arterial chim-embolisation
   d) Laser Surgery
   e) Chemotherapy

4. The average 5 years survival rate after resection for hepatocellular carcinoma is approximately:
   a) 10%
   b) 15%
   c) 20%
   d) 35%
   e) 50%

5. The preferred curative treatment for early hepatocellular carcinoma is:
   a) Chemotherapy
   b) Radiofrequency
   c) Radiotherapy
   d) Intra-arterial injection of iodine-131-Lipiodol
   e) Surgical resection

6. Blood transfusion may have a deleterious effect on survival after resection of hepatocellular carcinoma.

7. Despite recent technical advances in liver resection, massive blood transfusions are often required for major liver resections.

8. Left hemihepatectomy incurs a higher risk than right hemihepatectomy.

9. The most serious complication after liver resection is liver failure.

10. Radiofrequency ablation (RFA) of hepatocellular carcinoma is ideally suited to the treatment of tumours of 4.0 cm diameter or less.

Answer Sheet for January 2005

Please return the completed answer sheet to the Federation Secretariat on or before 31 January 2005 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Surgical Treatment for Hepatocellular Carcinoma
Dr. Man-hei Shiu
MBBS(HK) FRCS(Eng) Dip.AmerBdSurg FHKAM(Surgery)
Honorary Consultant, Hong Kong Sanatorium & Hospital

1 2 3 4 5 6 7 8 9 10

Name: __________________________________________ HKID No. ___ ___ - ___ ___ ___ ___ X X (x)

Signature: ___________________________ Contact Tel No.: ________________________

Answers to December 2004 issue

Diagnosis and Management of Ischaemic Heart Disease
1 e  2 e  3 d  4 a  5 c
6 F  7 F  8 T  9 T  10 T