Abstract  

Objective The purpose of this study was to investigate the clinical value of hepatic segmental staining under intra-operative ultrasonography guidance in anatomic segment 8 (S8) segmentectomy. 

Method This was a retrospective study of 31 patients with hepatocellular carcinoma (HCC) whose lesions were located in S8. Under intra-operative ultrasonography guidance, the hepatic portal vein branch of S8 was dyed and then the resection line was marked with an electric knife on the stained area of the liver surface, in preparation for the anatomic S8 segmentectomy. The liver section exposed the right hepatic vein, the middle hepatic vein trunk side wall and the hepatic pedicle of S8. 

Results The average operation time of 31 cases of anatomic S8 segmentectomy was (230±76) min, the average surgical blood loss was (305±235) ml, the incidence of post-operative complications was 26% (8/31), average post-operative hospitalization time was (13±3) d, with a 1-year recurrence rate of 19% (6/31) and a 1-year survival rate of 94% (29/31). 

Conclusion Under the guidance of intra-operative ultrasonography, hepatic segmental staining can improve the precision of an anatomic S8 segmentectomy, maximally reducing the post-operative complications and improving the safety of liver resection. 

Keywords Intra-Operative Ultrasonography, Hepatocellular Carcinoma, Hepatic Segmental Staining, Anatomic S8 Segmentectomy

1. Introduction 

Hepatocellular carcinoma (HCC) is considered the fifth most common cancer in the world and the third most common cause of cancer-related mortality [1]. Although more common in Asia and Africa, the incidence of HCC is increasing in the Western world [2]. 

Hepatic resection is now established as the preferred therapeutic option for HCC [3]. However, a high incidence of post-operative recurrence - with a 3-year recurrence rate of up to 60% - remains a serious problem [4]. Anatomic resection, which was originally introduced by Makuuchi et al. [5], is the systematic removal of a hepatic segment confined by tumour-bearing portal tributaries. Because of the high likelihood of the cancer cells from HCC spreading through the portal venous system, anatomic resection is especially effective in the eradication of the intrahepatic metastases of HCC [6, 7].
Precise anatomic liver resection in some segment is always among the most difficult hepatobiliary surgeries, such as S8 segmentectomy. The purpose of this study was to investigate the clinical value of hepatic segmental staining under intra-operative ultrasonography guidance and evaluate the outcome of 31 cases of S8 segmentectomy of HCC with respect to the long-term results.

2. Materials and Methods

**Common Data** 31 patients with HCC underwent precise anatomic S8 segmentectomy at our hospital from October 2009 to August 2011, adopting hepatic segmental staining under intra-operative ultrasonography guidance. They subjects consisted of 26 male and five female patients, aged from 34 to 68, with an average age of 56 years. The liver function of 28 patients fell into the Child-Pugh A category, while the remaining three were Child-Pugh B7. The Indocyanine Green retention rate at fifteen minutes was 15%, at an average of 16.5% (3.6-28.4). Among the patients, 28 were also diagnosed with hepatocirrhosis (Table1). The surgical specimens were diagnosed as HCC pathologically.

**Pre-operative Evaluation** All the patients preserved normal cardiopulmonary function, without tumour metastasis and operation contraindication. Liver ultrasound CT scan or MRI parallel imaging and contrast-enhanced MRI were performed to visualize the liver anatomy, vascular and bile duct variation and their adjacent relationships with the tumour. An anatomic sketch of the tumour location was drawn. The concise sizes of the liver segments and anticipated excision parts were figured out according to 2D CT images in the PACS system. Accordingly, the anatomic S8 segmentectomy operation plan was formulated.

**Anaesthesia Management** Under routine anaesthetic induction, tracheal cannula and venous combined anaesthesia were implemented. During the operation, the indexes such as heart rhythm, artery blood pressure, CVP, pulmonary blood pressure, pulmonary capillary wedge pressure, blood gas analysis, biochemistry and coagulation function were monitored; the haemodynamics and the relative stability of the acid-base balance were both maintained; moreover, the central venous pressure was maintained at 5 cm H₂O (1 cm H₂O =0.098 kPa), usually at 3 cm H₂O or so when freeing the liver.

3. Operation Method and Key Technical Points

3.1 **Intra-operative ultrasonography inspection**

The laparotomy started from the inverted "L" font incision on the right upper quadrant. After successful liver freeing, the root of the second porta hepatis was scanned from top to bottom with a convex probe (Aloka UST - MC11-8731) to visualize the routes of both the middle and the right hepatic veins and their branches, the distributions of the anterior right lobe of the liver and its branches, and the segments of the portal vein branches of the posterior right lobe of the liver. The location and size of the tumour within the S8 as well as the presence of intrahepatic metastasis were detected. The stereoscopic relations within the tumour were noted, as well as the S8 vein and the portal vein branches, so as to compare with the pre-operative imaging results and confirm the diameter of the portal vein branch to be dyed and determine the needle insertion angle.

3.2 **S8 portal vein branch dyeing localization via puncture**

The S8 portal vein has two branches in common - the ventral branch (ventral branch - P8v) and the dorsal branch (dorsal branch - P8d) - but some have an additional lateral branch (lateral branch - P8l). In common cases, a 20 g PTCD needle or 20 g trocar are chosen for dyeing via puncture under intra-operative ultrasonography guidance and real-time monitoring. After injecting 4 ~ 6 ml or so of methylene blue into each branch, the liver surface dyed well. The cut line could then be marked according to the dyed area (Figure A).

3.3 **The first hepatic portal vein blood flow blocking**

Liver blood flow was occluded with Pringle. The general mode of Pringle is to block for 10 minutes, followed by opening for five minutes, then blocking for 15 minutes followed by opening for five minutes. This procedure is then repeated throughout the surgery.

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Table 1. Clinical Data of 31 Patients

<table>
<thead>
<tr>
<th>Gender (Male / Female)</th>
<th>26/5</th>
</tr>
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<tbody>
<tr>
<td>Hepatitis b antigen positive/ Hepatitis c antibody positive</td>
<td>29/1/0/1</td>
</tr>
<tr>
<td>Both positive/both negative Normal liver/hepatic fibrosis or chronic hepatitis/ cirrhosis Child-Pugh A/B</td>
<td>1/2/28</td>
</tr>
<tr>
<td>ICG-R15 (%)</td>
<td>16.5(3.6-28.4)</td>
</tr>
<tr>
<td>diameter of the tumour (cm)</td>
<td>2.8 (1.5-5.9)</td>
</tr>
<tr>
<td>Surgical blood loss (ml)</td>
<td>305±235</td>
</tr>
<tr>
<td>the incidence of post-operative complications (%)</td>
<td>26 (8/31)</td>
</tr>
<tr>
<td>average post-operative hospitalization time (d)</td>
<td>13±3</td>
</tr>
<tr>
<td>1-year recurrence rate (%)</td>
<td>19 (6/31)</td>
</tr>
<tr>
<td>1-year survival rate (%)</td>
<td>94 (29/31)</td>
</tr>
</tbody>
</table>
Figure 1 A shows sub-S8 hepatic segmental staining. B shows after S8 segmentectomy, residual liver exposing the left side of right hepatic vein, the right wall of the middle hepatic vein trunk and the Glisson root stump of S8, and C shows three dimensional anatomy sketch of the tumor in the live.

3.4 S8 or sub-S8 resection

The second porta hepatis was separated to expose the gap between the middle hepatic vein and the right hepatic vein, resected the staining hepatic segments along the marked line with an ultrasonic aspirator combined with an electrotome knife under intra-operative ultrasonography so as to fulfil the resections of S8 or sub-S. Afterwards, any residual liver wound should show on the left side of the right hepatic vein, the right wall of the middle hepatic vein trunk and parts of the front wall of the suprahepatic vena cava or the Glisson root stump of S8 or sub-S8 (Figure B).

4. Results

No peri-operative mortality occurred in the 31 cases. The success rate of methylene blue dyeing was 100%, S8 excision cases 27, sub-S8 resection cases four, average porta hepatitis block time 65±40 min, average blocking blood flow time 5±3, average surgery time 230±76 min. Specimens from the tumour cut edge were pathologically negative. With the exception of two patients presenting multiple tumours, all of the other tumours were solitary. The tumour diameters were 1.5–5.9 cm, with an average of 2.8 cm. The average surgical blood loss was 305±235 ml. The incidence of post-operative complications was 26% (8/31), that is, eight cases. All eight cases suffered pleural effusion, which healed by diuresis or puncture drainage therapy. The post-operative hospitalization time was (13±3) d. 22 months after the surgery, the follow-up data showed that the 1-year recurrence rate and survival rate were 19% (6/31) and 94% (29/31), respectively.

5. Discussions

Since the 1990s, anatomic segmentectomy has been gradually established as the mainstream therapeutic option for HCC due to further research into the liver’s anatomy and the biological characteristics of HCC, as well as the improvement of liver blood flow blocking technology and surgical instruments. HCC is characterized by small intrahepatic diffuse lesions or small satellites around the single nodule, which may form intrahepatic metastasis along the Glisson sheath. Anatomic segmentectomy can thoroughly eradicate the lesions. It is commonly recognized that the treatment effect of anatomic segmentectomy is more effective than non-anatomic resection [7].

After the liver resection, the 5-year recurrence rate was up to 60% – 100%. The first year after the liver resection is a critical period when recurrence and metastasis peak. Studies have shown that the main reasons for recurrence are early intrahepatic metastasis and a later occurring multicentre. The portal venous tumour emboli and micrometastases are the main factors influencing the recurrence of early HCC [8, 9]. The intrahepatic metastasis mainly disseminated via the portal vein. In those cases where there was a tumour greater than 4 cm in diameter, and where there existed multiple tumour invasions or blood vessel or microvascular invasions, it is easy to find tumour microsatellite foci further from the primary tumour, greatly reducing the possibility of resection [10, 11]. In conventional non-anatomic resection, the resection is carried out at more than 1 cm distance from the tumour. However, the radical cure standard determines that no residual cancer, pathologically, is in the specimens from the cut edge. As opposed to the non-anatomic or local resection, anatomic segmentectomy regularly combines the liver surface mark and intra-operative ultrasound. The single segment, multiple segments and liver lobe resection meet the Couinaud section standards. It is commonly recognized that early tumour recurrence may be reduced or delayed by the standard practice of the complete eradication of the hepatic portal vein and its branches where the tumours are located [12-14]. Wakai, et al. reported that, compared to non-anatomic segmentectomy, anatomic segmentectomy (which is carried out under ultrasound guidance and
marked by intrahepatic portal vein) could dramatically reduce the recurrence of HCC during the T1 and T2 stages and raise the long-term survival rate [15].

Among the patients, 27 of the patients’ tumours were located in S8 and four in sub-S8. All of them had cirrhosis except for two, one preserved normal liver function, and the other suffered from chronic hepatitis B. Child - Pugh class A and class B7 presented as 28 cases and three cases respectively. ICG - R is 15%, at an average of 16.5%. The precise anatomical S8 and sub-S8 segmentectomy was adopted to ensure the maximum function of the residual liver.

In traditional hepatic resection, the first porta hepatitis was blocked to reduce intra-operative blood loss. Meanwhile, in anatomic segmentectomy the blood flow in the liver through the hepatic artery vein and the hepatic portal vein was temporarily interrupted, greatly reducing liver wound bleeding and allowing enough time for the surgery. It is difficult to define the cut edge accurately in the traditional hepatic resection. Although the middle and right hepatic veins can be scanned by intra-operative ultrasonography, they cannot act as an interface between areas. The strict regionalization method used is staining [5]. A combination of intra-operative ultrasonography with methylene blue dyeing does not only detect tumour invasion in other parts of the liver but also dye the selective portal vein blood vessel in confirming the scope of the anticipated resection liver lobe and segments, demonstrating many more advantages over the traditional method.

Defining the precise resection boundaries is vital to carrying out the accurate anatomic S8 and sub-S8 segmentectomy. Intra-operative ultrasonography becomes the key technology in re-sectioning. Pre-surgery protocol involves accurately assessing the liver lesion range, predicting the residual liver volume and compensatory function, drawing the three dimensional anatomy sketch of the tumour in the liver (Figure C), and understanding the liver anatomy, blood vessels and bile duct variation and their adjacent relationships with the tumour. A miniature ultrasonic probe was used to detect the relationships between the tumour and the middle and right hepatic vein and the P8 branch, so that a three-dimensional stereogram could be rendered. A comparative analysis of the three-dimensional anatomy sketch before surgery, defining the resection boundary of S8 and sub-S8, was taken. Hepatic segmental staining in the guidance of intra-operative ultrasonography can improve the precision of an anatomic S8 segmentectomy. Under intra-operative ultrasonography guidance and real-time monitoring, after injecting about 4 - 6 ml methylene blue in each branch, the liver surface was well-dyed. Next, the liver parenchyma along the marked line in the dyed area was cut. The residual liver wound should show the left side of the right hepatic vein, the right wall of the middle hepatic vein trunk, and the Glisson root stump of S8 or sub-S8. Otherwise, it can only be called ‘S8 liver resection’.

No peri-operative mortality occurred in the 31 patients. All the patients adopted hepatic segmental staining in anatomic S8 segmentectomy under intra-operative ultrasonography, which was invented by Makuuchi. The success rate of methylene blue dyeing was 100%, with S8 dyeing cases at 27, sub-S8 at four, and average blood loss of 305±235 ml. The incidence of post-operative complication was 26% (8/31); all eight cases involved pleural effusion, which was treated with diuresis or puncture drainage therapy. The reason for pleural effusion was that the manipulations during or after the operation stimulate the diaphragm which near the top of S8. The post-operative hospitalization time was 13±3 d. The 1-year recurrence rate and the 1-year survival rate were 19% (6/31) and 94% (29/31) respectively. The long-term survival rate remains undetermined.

In our opinion, being familiar with intra-operative ultrasonography is essential for all surgeons in implementing accurate liver resection. When puncturing the S8 portal vein branch, we should fully free the liver to expose the puncture picture so as to facilitate the puncture. The whole length of the branches of the S8 portal veins should be exposed to ease the process of the puncture. The sequence of puncturing is from the central lateral to the peripheral side. After a successful puncture, methylene blue should be injected slowly to avoid refluxing. For multiple P8 branches, the puncture sequence is from the deep branch to the shallow branch. This prevents air from entering and affecting the operation. With liver biopsy staining for patients who do not suffer from cirrhosis, the dyeing duration of the anticipated resection liver segment is shorter due to the fast intrahepatic methylene blue metabolism, so it is necessary to mark the boundary of the target liver segment as soon as possible. Guiding with intra-operative ultrasonography, the liver parenchyma is freed, exposing the left side of the right hepatic vein, the right wall of the middle hepatic vein trunk, and part of the front wall of the suprahepatic vena cava or the Glisson root stump of the hepatic S8 or sub-S8. Hepatic venous drainage was largely responsible for liver bleeding. An ultrasonic aspirator combined with an electrotome knife to free the liver parenchyma accurately, and revealing the hepatic vein in the right branch helped to achieve minimal blood loss.

To reduce post-operative complications - such as pleural effusion in the operation - great care was taken to minimize the trauma to the diaphragm. Before closing the
abdominal cavity, we place the drainage tube appropriately and make sure the lead tube drainage is unobstructed after surgery. If there is pleural effusion, diuresis or puncture, drainage treatment is necessary in a timely manner.

We believe that the precise anatomic S8 segmentectomy under the guidance of intra-operative ultrasonography should be recognized and popularized for tumors located in S8. It does not only prevent vascular damage caused by freeing the porta hepatitis, but can also reduce intra-operative bleeding to minimize trauma and offer maximum protection.

6. References


