Original Article

DOI: 10.5582/bst.2018.01194

Impact of three-dimensional visualization technology on surgical strategies in complex hepatic cancer

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Summary **Surgical resection is still the mainstay of treatment for primary liver cancer (PLC). It is unclear whether three-dimensional visualization (3DV) preoperative evaluation and simulated liver resection would affect the surgical strategies and improve the R0 resection rates of patients with complex PLC when compared with the 2D evaluation using computed tomography or magnetic resonance imaging. In the study, patients with complex PLC who were subjected to laparotomy underwent both 2D and 3DV evaluation before operation. A comparison between the 2D and 3DV evaluation was compared with the gold standard of laparotomy findings. In this study, of 335 patients with complex PLC, 71 were assessed to have resectable tumors. 2D and 3DV assessments determined 63 and 71 patients to have resectable PLC, respectively. At laparotomy 69 of the 71 patients were found to have resectable PLC, but 2 patients were found to be unresectable because of detection of metastatic lesions on laparotomy, which were not detected either by 2D or 3DV preoperative evaluation. The accuracy, false positive and false negative rates of the 2D and the 3DV preoperative assessments in determining tumor resectability were 85.9%, 2.8%, 11.3%, and 97.2% ($p < 0.05$), 2.8%, 0%, respectively. The 3DV and 2D preoperative evaluation revealed 17 and 13 patients with vascular anomalies, respectively. There were 4 patients with major vascular anomalies not detected by 2D evaluation, whose surgical strategies were modified by 3DV evaluation. These results suggested 3DV preoperative assessment could lead to better in evaluating tumor resectability, with potential benefit in the modification of surgical strategy for patients with complex PLC.**

Keywords: Three-dimensional visualization, complex hepatic cancer, surgical strategy, vascular anomaly

1. Introduction

Primary liver cancer (PLC) poses a serious threat to global health (*1-3*). Partial hepatectomy is still considered as the curative treatment of choice for PLC in many centers (*4*). PLC which is close to, or even has invaded the bifurcation of the main portal vein or the hepatico-caval junction, or is centrally located (in liver segments 4, 5, 8) which is associated with major intrahepatic vascular anomalies is defined as complex PLC in this study. It is difficult to treat these lesions with resectional surgery and there is a high inherent risk of postoperative complications (*5,6*). Accurate preoperative assessment is important for safe surgery in these patients.

The conventional preoperation assessment of tumor resectability is conventionally based on two-

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dimensional (2D) medical imagings using ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI). These imaging techniques pose difficulty in accurately assessing and planning liver resectional surgery in borderline resectable liver tumors which are commonly found in complex liver tumors (*7-9*). Three-dimensional visualization (3DV) technology emerged more than 10 years ago, providing an alternative technique for diagnosis and surgical planning of PLC. A number of international groups have successfully developed 3DV technology and applied it in hepatobiliary and pancreatic operations (*10-13*). A recent report from Japan underlined the practicality of virtual hepatectomy, based on 3D image reconstruction, for surgical planning and performance of living donor liver transplantation and hepatectomy for hepatocellular carcinoma and colorectal liver metastases (*14*). Our group has also developed a new 3DV abdominal imaging system (software copyright No. 2008SR18798). This system has been used in the preoperative planning for hepatocellular carcinoma (*7*), intrahepatic calculi (*15*) and hilar cholangiocarcinoma (*16*). The present study aimed to discuss the difference between the 3DV and 2D preoperative evaluation and the possible impact of 3DV technology on the surgical strategy for complex PLC.

2. Patients and Methods

2.1. *Study Design*

Of 441 patients with complex PLC treated at the Department of Hepatobiliary Surgery of Zhujiang Hospital, Southern Medical University, from January 2008 to January 2017, 335 patients were included in this study. According to the different surgical strategies, patients who underwent laparotomy were selected in the study. The inclusion criteria were *i*) PLC which included hepatocellular carcinoma, intrahepatic cholangiocarcinoma and hepatoblastoma; *ii*) complex liver tumor; *iii*) PLC > 3.0 cm, and any PLC which was not considered to be suitable for radiofrequency ablation in our center; *iv*) no extra-hepatic metastasis; and *v*) preoperative liver function of Child-Pugh Class A or B. The exclusion criteria were: *i*) benign liver tumors; *ii*) metastatic liver cancer; and *iii*) concurrent or history of other malignant tumors.

This study was approved by the Ethics Committee of Zhujiang Hospital, Southern Medical University (No. 2012-GDYK-001).

2.2. *Preoperative evaluation*

2.2.1. *Routine investigations*

The routine investigations included abdominal CT, complete blood count, liver and renal function tests, coagulation profile, and tumor markers (AFP, CA 19.9, CEA and CA 125). Magnetic resonance imaging was also carried out in some patients.

2.2.2. *2D preoperative evaluation*

For all the patients with a complex hepatic cancer, a 2D preoperative evaluation was performed by a team of hepatic surgeons using patients' clinical data and conventional CT/MRI scan images. A resection line was drawn according to the anatomic marks, such as the hepatic veins, portal veins and gallbladder fossa. The volume of the residual functional liver was calculated manually.

2.2.3. *3D preoperative evaluation*

The same team of liver surgeons also went on to do the 3DV reconstruction. 3DV reconstruction: The enhanced thin-slice CT data were collected using a Philips Brilliance 64-multislice spiral CT scanner. The setting of scanning parameters: conventional supine position was chosen for plain scan from head to foot. The range was from the top of diaphragm to the inferior margin of the liver. The scanning condition was 120 kV and 250 mAs. The detector combinations were 0.625×64, the slice thickness was 5mm, the interval was 5mm and the screw pitch was 0.984. The time for one revolution of bulb tube was 0.5 s. The delayed scan of arterial phase was 20-25 s and the delayed scan of portal phase was 50-55 s. These image data were put into CT postprocessing workstation after the scan. Then the CT data were transferred to the 3DV software for 3D reconstruction: *i*) for organ reconstruction; the region-growing method (*17*) was used to perform a 3D reconstruction of the liver, tumor, pancreas and spleen; *ii*) for vascular reconstruction: the segmentation based on threshold method (*18*) was used to perform a 3D reconstruction of the portal vein, hepatic artery and hepatic vein. The anatomy and variations of the portal vein, hepatic artery and hepatic vein were classified using Cheng's Standard (*19*), Michel's Standard (*20*), and Nakamura's Standard (*21*), respectively.

Simulated Surgery: Using the information obtained from the 3D reconstruction, which included tumor size, tumor location, proximity and relation of the tumor to its surrounding major blood vessels, and in line with the principle of R0 resection with preservation of adequate non-tumorous liver parenchyma in a cirrhotic patient, the residual liver functional ratio should be greater than 40% (*22*). After segmentation of the 3DV liver model and simulated surgery were performed using the built-in software, the volumes of the entire liver, tumor, resected liver and residual functional liver were calculated.

2.3. *Choice of surgical strategy*

Patients with complex PLC accepted the operation according to the comprehensive preoperative assessment and agreement of Multidisciplinary Treatment group of Zhujiang Hospital. Preoperative assessment included complete blood count, liver and renal function tests, coagulation profile and tumor markers (AFP, CA 19.9, CEA and CA 125). Information of tumor location, size and number obtained from CT or MRI was also important to preoperative assessment. A surgical strategy and a surgical plan were made by the team, based on whether a R0 resection could be carried out safely. The volume of the residual functional liver was calculated and the surgical strategy decision was recorded.

2.4. *Statistics*

Continuous data were expressed as median and range while categorical data were expressed as numerical numbers or as ratios. Continuous data were evaluated using the Mann-Whitney *U* test, and the categorized data were compared using the Chi square test. All statistical tests were 2-sided. A $p < 0.05$ was considered to be statistically significant. The statistical analysis was performed using SPSS software (version 21.0; SPSS, Chicago, IL).

3. Results

3.1. *Clinical characteristics of patients who underwent laparotomy*

After comprehensive preoperative evaluation, 71 patients underwent laparotomy, and 65 (91.5%) patients were male. Of the 71 patients, 65 (91.5%) patients had hepatitis and 58 (81.7%) patients had liver cirrhosis. The preoperative liver functional status was Child-Pugh grade A (65 patients, 91.5%) and grade B (6 patients, 8.5%). The median size of liver tumors was 8.1cm (range from 4.0 to 17.3 cm). There were 54 (76.1%) patients with a single tumor, while 17 (23.9%) patients had multiple tumors. The pathological results showed 67 patients (94.4%) had hepatocellular carcinoma, 3 patients (3, 4.2%) had intrahepatic cholangiocarcinoma, and 1 patient (1.4%) had hepatoblastoma. Of the 71 patients, 17 patients (23.9%) had vascular anomalies (Table 1).

Two patients were found to have unresectable tumors on laparotomy, as the metastatic lesions were not detected on preoperative CT or MRI. The other 69 patients underwent the following operations successfully: right hemihepatectomy (*n* = 17, 24.6%), resection of segments 6 and 7 + part of segments 5 and 8 (*n* = 9, 13.0%), right hemihepatectomy + resection of segment 1 (*n* = 1, 1.5%), right hemihepatectomy+ partial resection of segment 4 (*n* = 1, 1.5%), resection of segments 4, 5 and 8 (*n* = 2, 2.9%), resection of segments 5, 6 and 7 (*n* = 5, 7.2%), resection of segments 5 and 6 (*n* = 4, 5.8%), resection of segments 6 and 7 (*n* = 8, 11.6%), resection of segments 5 and 8 (*n* = 3, 4.4%), resection of segments 6 and 8 (*n* = 1, 1.5%), resection of segments 7 and 8 (*n* = 3, 4.4%), resection of segments 4 and 7 (*n* = 1, 1.5%), resection of segments 2, 3 and 4 (*n* = 4, 5.8%), resection of segments 2, 3, 4, 5 and 8 (*n* = 1, 1.5%), resection of segments 2, 3, 4 and 8 (*n* = 2, 2.9%), resection of segments 2, 3 and 8 (*n* = 1, 1.5%), resection of segments 2 and 5 (*n* = 1, 1.5%), resection of segment 5 (*n* = 1, 1.5%), resection of segment 7 (*n* = 2 cases, 2.9%) and resection of segment 8 (*n* = 2, 2.9%).

Table 1. Clinical characteristics of 71 patients with resectable complex hepatic cancer

Items	*n* or median (range)
Age, yrs	44 (13-74)
Sex (Male/Female)	65/6
Hepatitis status	
Hepatitis B	60
Hepatitis C	2
Hepatitis B+C	2
Hepatitis E	1
Negative	6
Cirrhosis	58
Liver functional status	
Child-Pugh Grade A	65
Child-Pugh Grade B	6
AFP > 400 (μg/L, n)	26
AFP < 400 (μg/L, n)	45
HBV-DNA < 500 (copy/mL)	16
HBV-DNA > 500 (copy/mL)	46
Tumor size (cm)†	8.1 (4.0-17.3)
Tumor number	
Single	54
Multiple	17
Pathology	
HCC	67
ICC	3
Hepatoblastoma	1
Vascular variation	
PV	6
HA	5
HV	1
PV +HA	3
PV +HA+HV	2

AFP, alpha fetal protein; HA, hepatic artery; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HV, hepatic vein; ICC, intrahepatic cholangiocarcinoma; PV, portal vein. †Tumor size was determined by CT imaging and defined as the largest diameter (in single tumor) and the sum of the largest diameters (in multiple tumors).

3.2. *Comparison of preoperative evaluation and the actual surgery in tumor resectability*

Of the 71 patients, 2D preoperative evaluation predicted 63 patients to have resectable and 8 patients to have unresectable tumors. The corresponding numbers predicted by 3DV preoperative evaluation were 71 and 0. At the operation, 69 patients underwent R0 resection but 2 patients were found to have unresectable lesions because of detection of metastatic lesions on laparotomy which were not detected either by 2D preoperative

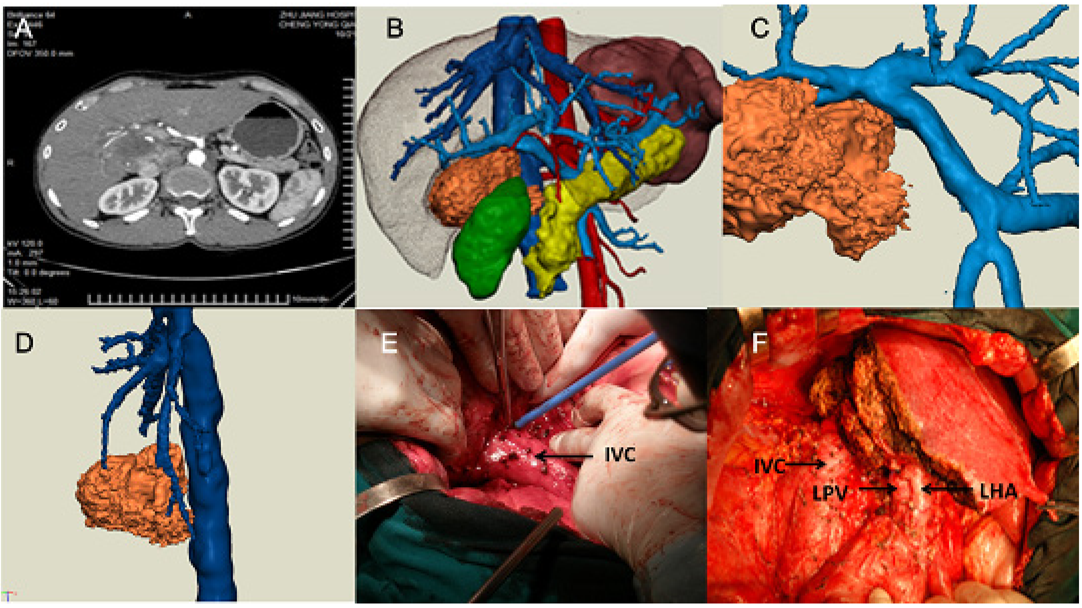

Figure 1. A 38-year-old man of HCC with a tumor located in segment 1. (A) CT showed that the tumor had probably invaded the portal vein (PV) and inferior vena cava. TACE was recommended. **(B, C, D)** 3D reconstruction demonstrated the spatial relationship between the tumor and surrounding tissues, such as the portal vein and inferior vena cava (IVC), without invasion of the PV and IVC. Surgical treatment was recommended as the treatment of choice. **(E, F)** Right hemihepatectomy and segment 1 resection were successfully performed. (LHA, left hepatic artery; LPV, left portal vein; TACE, transcatheter arterial chemoembolization.)

evaluation or 3DV preoperative evaluation.

Using the intraoperative findings as the gold standard, the accuracy, false positive and false negative rates of the 2D and 3DV preoperative evaluations for tumor resectability were 61/71 (85.9%), 2/71 (2.8%), 8/71 (11.3%), and 69/71 (97.2%), 2/71 (2.8%), 0/71 (0%), respectively. Comparing the 3DV preoperative evaluation with 2D evaluation, there was a significant difference in the accuracy rate (97.2% *vs*. 85.9%, p = 0.016) and the false negative rate (0% versus11.3%, p < 0.001). These results suggested significantly better prediction of the 3DV preoperative assessment in evaluating tumor resectability.

Eight patients who were predicted by 2D preoperative evaluation to have unresectable lesions due to tumor involvement of major vessels were determined to have resectable lesions on 3DV evaluation (Table 2, Figure 1). Of the 63 patients who were predicted by 2D preoperative evaluation to have resectable lesions, 13 cirrhotic patients were preoperatively assessed with future liver remnants to be less than 40% with a high chance of developing postoperative liver failure. After 3DV preoperative evaluation and simulation surgery, the surgical strategy was modified to a lesser extent of anatomical liver resection. These patients did not develop any postoperative liver failure (Table 3). Besides, in 2 patients, the extents of anatomical resection were extended from 2D preoperative evaluation to 3DV preoperative evaluation to allow for a R0 resection with an adequate resection margin. Two operations changed from segments 5 and 7 to resection of segments 5, 6 and 7; and right hemihepatectomy to right hemihepatectomy + segment 4, respectively.

3.3. *Preoperative evaluation of vascular anomalies and choice of surgical strategy*

In the study, 3DV preoperative evaluation revealed 17 patients with vascular anomalies including the portal vein, hepatic artery or hepatic veins, while 2D preoperative evaluation detected 13 patients with vascular anomalies. There were 4 patients with major vascular anomalies who were not detected by 2D evaluation before operation. Figure 2 illustrates a patient with a 13.2 cm complex PLC in liver segments 5, 6, 7, 8 in a cirrhotic patient. The segment 4 portal vein arose from the right anterior sectional portal vein. 2D preoperative evaluation failed to identify this portal vein anomaly and right hemihepatectomy was planned. The future liver remnant was estimated to be 40.8%. Subsequent 3DV preoperative evaluation identified the portal vein anomaly. If right hemihepatectomy were to be carried out, the portal blood supply to segment 4 would have been damaged. Portal ischemia to segment 4 would decrease the actual future liver remnant to 21.4% and the chance of developing postoperative liver failure would be high. The subsequent surgical strategy was modified to extended right posterior sectionectomy (resection of liver segments 6, 7 and part of 5, 8) with preservation of the portal venous branch to liver segment 4. The remaining 3 patients included one patient with Cheng's type III portal vein whose surgical strategy was modified from right hemihepatectomy to resection of liver segments 6 and 7 plus part of segments 5 and 8 (*19*); one patient with Cheng's type II portal vein whose surgical strategy was modified from right hemihepatectomy to resection of liver segments

Table 2. The 8 patients of complex PLC performed laparotomy who were predicted to be unresectable by 2D evaluation

NO.	Sex	Age (years)	Tumor location (segment)	Tumor size (cm)	Hepatic cirrhosis	Major vessels close to tumor	Surgical strategy based on 2D evaluation	Surgical strategy based on 3DV evaluation	Actual surgery
1	Male	29	5/8	12.1	Yes	RHV+MHV+RPV	TACE	Right hemihepatectomy	Right hemihepatectomy
2	Female	50	5,7	7.0	Yes	RHV+RPPV	TACE	Resection of segments 5, 6 and 7	Resection of segments 5, 6 and 7
3	Male	33	8	8.1	Yes	RHV+RPV	TACE	Right hemihepatectomy	Right hemihepatectomy
4	Male	44	5,7	8.1	Yes	RHV+RPPV	TACE	Resection of segments 5, 6 and 7	Resection of segments 5, 6 and 7
5	Male	43	5/8	7.6	Yes	MHV+RPV	TACE	Resection of segments 5 and 8	Resection of segments 5 and 8
6	Male	38	1	8.0	Yes	RPV	TACE	Right hemihepatectomy+ resection of segment 1	Right hemihepatectomy+ resection of segment 1
7	Male	64	5/6/7/8	12.1	Yes	RHV + RPV	TACE	Right hemihepatectomy	Right hemihepatectomy
8	Female	13	6/7	12.6	Yes	RHV+RPV	TACE	Right hemihepatectomy	Right hemihepatectomy

MHV, Middle hepatic vein; RHV, Right hepatic vein; RPPV, Right posterior portal vein; RPV, Right portal vein; TACE: Transcatheter arterial chemoembolization.

Table 3. Clinical data for the 13 patients in whom the surgical strategy was modified

NO.	Sex	Age (years)	Tumor location (segment)	Tumor size (cm)	Hepatic cirrhosis	Vascular invasion	Surgical strategy based on 2D evaluation	Surgical strategy based on 3DV evaluation	Actual surgery
1	Male	69	5/8	9.3	Yes	RPV	RT	RH + partial resection of segment 4	RH + partial resection of segment 4
2	Male	28	5/6/7	12.7	Yes	RPPV	RH	Resection of segments 5, 6 and 7	Resection of segments 5, 6 and 7
3	Male	71	5/6/7	6.9	Yes	RPPV	RH	Resection of segments 5,6 and 7	Resection of segments 5,6 and 7
4	Male	39	5/6/7/8	5.4	Yes	RPPV	RH	Resection of segments 6 and 7 + part of segments 5 and 8	Resection of segments 6 and 7 + part of segments 5 and 8
5	Male	37	5/6/7/8	14.6	Yes	RHV	RH	Resection of segments 6 and 7 + part of segments 5 and 8	Resection of segments 6 and 7 + part of segments 5 and 8
6	Male	35	5/6/7/8	12.3	Yes	RHV + RPPV	RH	Resection of segments 6 and 7 + part of segments 5 and 8	Resection of segments 6 and 7 + part of segments 5 and 8
7	Male	43	5/6/7/8	12.3	Yes	RHV + RPPV	RH	Resection of segments 6 and 7 + part of segments 5 and 8	Resection of segments 6 and 7 + part of segments 5 and 8
8	Male	37	6, 8	8.5	Yes	RHV + RPPV	RH	Resection of segments 6 and 7 + part of segments V and 8	Resection of segments 6 and 7 + part of segments 5 and 8
9	Male	60	6/7/8	7.9	Yes	RHV + RPPV	RH	Resection of segments 6 and 7 + part of segments 5 and 8	Resection of segments 6 and 7 + part of segments 5 and 8
10	Male	49	7/8	10.4	Yes	RHV	RH	Resection of segments 6 and 7 + part of segments 5 and 8	Resection of segments 6 and 7 + part of segments 5 and 8
11	Male	24	5/6/7	7.3	Yes	RPPV	RH	Resection of segments 6 and 7 + part of segments 5 and 8	Resection of segments 6 and 7 + part of segments 5 and 8
12	Male	35	5/6/7/8	13.2	Yes	RHV + RPPV	RH	Resection of segments 6 and 7 + part of segments 5 and 8	Resection of segments 6 and 7 + part of segments 5 and 8
13	Male	34	6, 8	17.3	Yes	NO	RH	Resection of segments 6 and 8	Resection of segments 6 and 8

RH, Right hemihepatectomy; RHV, Right hepatic vein; RPPV, Right posterior portal vein; RPV, Right portal vein; RT, Right trisegmentectomy.

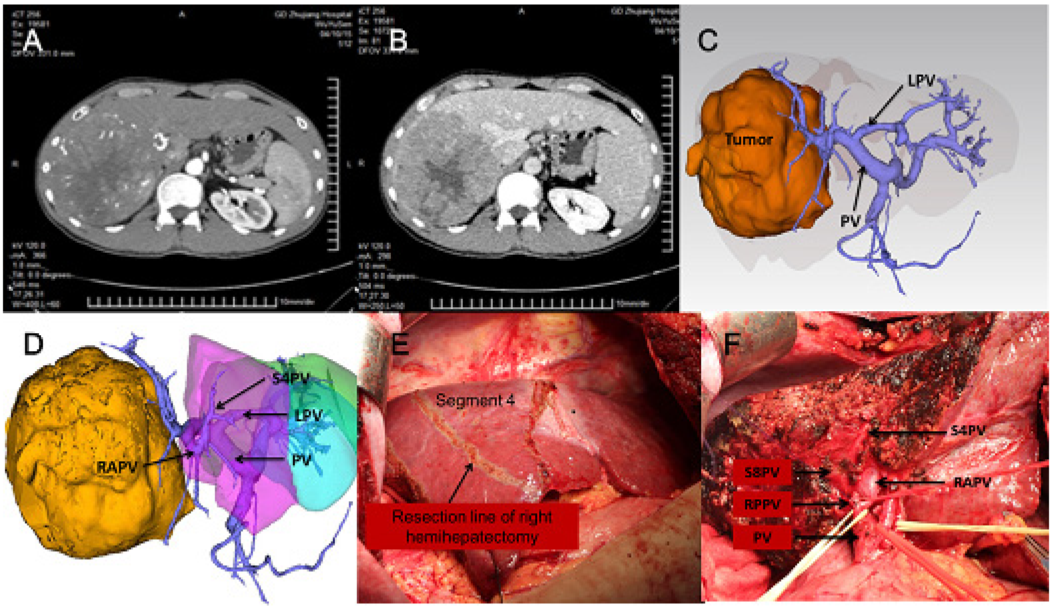

Figure 2. A 35-year-old man with hepatocellular carcinoma with the tumor located in segments 5/6/7/8. (A, B) Contrast-enhanced CT indicated that the tumor was close to the right portal vein (RPV) and had invaded the right posterior portal vein (RPPV). Right hemihepatectomy was recommended, and the residual liver volume ratio was 40.8%. **(C, D)** 3D reconstruction indicated that the tumor had only invaded the right posterior portal vein (RPPV), without invading the right anterior portal vein (RAPV). In addition, a variation of the portal vein of segment 4 (S4PV) was identified, with its origin coming from the RAPV. If the planned right hemihepatectomy was to be performed, according to the 2D CT assessment, the RPV would be ligated and resected, thus decreasing the venous blood supply to segment 4, with resulting ischemia to liver segment 4. The residual liver volume ratio would drop to 21.4% (subtracting the volume of segment 4). Finally, resection of segments 6 and 7 and partial resection of segments 5 and 8 were successfully performed **(E, F)**, with reservation of the portal supply to liver segment 4. (PV, portal vein; S8PV, portal vein of segment 8.)

5,6 and 7; and one patient with hepatic vein anomaly whose surgical strategy was modified from right hemihepatectomy without middle hepatic vein resection to right hemihepatectomy with middle hepatic vein resection.

4. Discussion

Liver resection is still the mainstay of treatment for PLC aiming at cure. The operative risk increases in patients with complex liver cancer which was initially defined by us as liver cancers which were close to, or even had invaded the bifurcation of the main portal vein or the hepatico-caval junction, or centrally located tumors (in liver segments 4, 5, 8) which were associated with major intrahepatic vascular anomalies involving the portal vein, hepatic artery or hepatic vein. 3D technology has been applied in many different fields (*7,23,24*). For these patients with complex PLC, it is crucial for the surgeons to have a very accurate preoperative assessment of the anatomy, and simulated surgery after 3D reconstruction helps tremendously in the planning of surgical strategies in these patients. Needless to mention that in cirrhotic patients, preoperative assessment and simulated surgery are even more important because the margin of safety in liver resection is low.

Preoperative 2D evaluation based on computed tomography or magnetic resonance is traditionally used by surgeons. This study showed that such an assessment for complex liver cancer is far from ideal, with an accuracy rate in determining surgical strategy only in 85.9% (61 of 71 patients). Our experience showed that 3DV preoperative evaluation for complex liver cancer allowed a more accurate preoperative evaluation of tumor resectability compared with the 2D preoperative evaluation. More importantly, some patients were assessed by 2D preoperative evaluation to be unresectable, but became resectable after 3D evaluation. Our findings are in agreement with the reports showing 3DV preoperative evaluation to be useful in different types of hepatobiliary surgeries (*7,14,16,25*).

Preoperative 3DV evaluation enables observation of the spatial relationship between the tumor with its surrounding structures by image amplification, rotation and transparency. It also enables addition or subtraction of the portal venous system, hepatic venous system and hepatic arterial system. Further advantages are its ability to allow segmentation of the liver, calculation of different parts of the liver volumes and simulated operations. It is not surprising that in this study the accuracy rate of the 3DV evaluation for complex liver cancer was 97.2% (69/71) when compared with the gold standard of the actual operations.

Assessment of the volume of the future liver remnant forms an important part of preoperative evaluation in preventing occurrence of postoperative liver failure (*26*). Mise *et al* suggested that 3DV technology can be used to accurately determine the volumes of all the individual liver segments and subsegments (*27*). We agree that not only would the volume of the future liver remnant be determined, but also the volumes of the tumorous and non-tumorous parts of the resected liver. Such an ability enabled us to determine the extent of liver resection in 13 cirrhotic patients with complex hepatic cancer without occurrence of postoperative liver failure (*28*).

Hepatic vascular anomaly is an important risk factor affecting safety of liver surgical procedures (*29*). It may be difficult to detect intrahepatic vascular anomalies using the conventional 2D computed tomography or magnetic resonance imaging sometimes. Inadvertent damage to major vascular anomalies can result in adverse consequences to patients (*29*). In our study, 3DV preoperative evaluation detected 4 patients with major vascular anomalies which were ignored by 2D preoperative evaluation, and according to these vascular anomalies, the surgical strategies determined by 2D preoperative evaluation were modified.

There are limitations of this study. First, the 3DV reconstruction models were based on the data obtained from computed tomography. The quality of the computed tomography would affect the quality of the 3DV reconstruction. Second, any small metastatic tumors which were not detected on computed tomography or magnetic resonance imaging could not be detected by the 3DV reconstruction models. Third, this is a single center study with a relatively small number of patients.

In conclusion, in our study, compared with the 2D preoperative evaluation, the 3DV preoperative assessment could be a better prediction in evaluating tumor resectability, and potential benefit in the modification of surgical strategy for patients with complex PLC.

Acknowledgements

This study was supported by grants from the National Natural Science Foundation of China under Grant (No.81627805); the National Key Research and Development Program of China (No.2016YFC0106500); the United Fund of National Natural Science Foundation of China and Government of Guangdong Province (No. U1401254); the Science and Technology Plan Project of Guangzhou (No. 201604020144; 201704020141); the National Natural Science Foundation of China (No.81601576); the Science and Technology Plan Project of Guangdong Province (No.2016A020220013); the National High Technology Research and Development Program of China (863 Program) (No.2012AA021105).

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(Received August 17, 2018; Revised October 9, 2018; Accepted October 31, 2018)