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Original Article

Clinical efficacy of precision liver resection for primary liver cancer

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Abstract: Aim: Precision liver resection is considered the gold standard in liver surgery. Therefore, optimizing the resection of lesions and minimizing unnecessary time of liver ischemia and hypoxia have become focal points. Methods: A total of 96 patients with primary liver cancer admitted to Cangzhou People's Hospital from January 2017 and December 2019 were included in this retrospective study, and divided into two groups according to the different surgical treatment, with 50 cases in the control group (conventional hepatic resection) and 46 cases in the observation group (precision liver resection). The surgical indicators, liver function, alpha-fetoprotein (AFP), complications, and three-year follow-up results were analyzed in the two groups. Results: The operation time, intraoperative bleeding, hospital stay, and time of anal venting in the observation group were shorter than those in the control group ($P<0.05$). One week after surgery, AST, TBiL, ALT, and γ-GT levels decreased in both groups, with more significant decreases in the observation group than those in the control group ($P<0.05$). PCT and hs-CRP levels in the observation group were significantly lower than those in the control group ($P<0.05$) observation. The incidences of pleural effusion, bile leak, abdominal infection, pulmonary infection, as well as the total complication rates in the observation group were lower in the observation group than those in the control group ($P<0.05$). The follow-up data revealed that the observation group exhibited a lower recurrence rate observationand higher survival rate than the control group within 3 years, but these differences were not significant ($P>0.05$). Conclusion: Precision liver resection can effectively treat primary liver cancer, reduce the incidence of complications, and promote patient recovery after surgery.

Keywords: Precision liver resection, primary liver cancer, clinical curative effect

Introduction

Primary liver cancer has become one of the most frequent malignant tumors in the world, threatening people's quality of life and having a high death rate [1]. China has a large population base and a big gap between the rich and the poor, resulting in many people affected by primary liver cancer. So far, the incidence of primary liver cancer in China has reached an average of 30.3 per 100,000 people, and the average number of deaths due to primary liver cancer is 140,000 per year [2, 3].

Surgery is one of the most important therapeutic means for primary liver cancer [4]. With the rapid development of medical imaging technology and surgical technology, especially the precise preoperative evaluation and fine surgical operation, the development and application of precise hepatic resection surgical concepts and techniques have received increasing attention in the clinic. Hepatic resection is currently the most efficient treatment for primary liver cancer. Lodewick first proposed the concept of precision hepatic resection based on the anatomic characteristics of the middle hepatic vein applied to the hepatic resection [5]. Medical experts found that, under the requirements of ultra-high precision and ultra-high efficiency, precision hepatic resection is a comprehensive and optimized application of modern scientific theories and techniques along with traditional surgical methods [6].

Precision liver resection is based on the anatomic characteristics of the liver, which centers on dissecting the area lacking vessels between

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liver lobular segments, while maximally preserving the remaining hepatic blood supply, blood outflow tracts, and biliary tracts under the precondition of complete resection of the lesions [7]. Precision liver surgery integrates high-resolution imaging, such as multidetector CT, high-field MRI, contrast-enhanced ultrasound, and IOUS to detect the minimal foci and to accurately assess the tumor stage [8, 9].

However, the definition and coverage of precision hepatectomy are internationally controversial. First, more studies are required to decide on the definition of precision hepatectomy, with the aim of better advancing its progress [10]. Second, although advanced science and technology have brought great convenience to clinical medicine, the development and use of new technologies require high-quality randomized controlled trials [11]. Third, patient screening is very important for precision hepatectomy, and its suitability should be considered for every individual patient. Individualized medicine requires clinicians to pay more attention to individual differences of patients, and therefore strict criteria and contraindications need to be established for the surgical techniques to ensure patient safety.

In this study, the clinical efficacy of conventional liver resection and precision liver resection in the treatment of liver carcinoma were analyzed and compared.

Methods and materials

Study design and participants

In this retrospective study, 96 consecutive patients with primary liver cancer who underwent liver resection in Cangzhou People's Hospital between January 2017 and December 2019 were included. This study was approved by the institutional review board of Cangzhou People's Hospital.

Inclusion and exclusion criteria

Inclusion criteria: (1) patients whose diagnosis and conditions met the relevant criteria in the 2011 version of the diagnostic and therapeutic standard of primary liver cancer [12], and postoperative pathologic result was confirmed to be primary hepatocellular carcinoma; (2) patients with Liver Function Child-Pugh score Grade A or B; (3) patients without preoperative TACE, systemic chemotherapy, or targeted therapies; (4) patients who were resected for fewer than 4 liver segments; (5) patients with complete clinical data.

Exclusion criteria: (1) patients with unresectable liver cancer; (2) patients with concurrent cardiopulmonary diseases; (3) patients who had already received surgery or systemic chemotherapy, TACE, or targeted therapy; (4) patients with tumors in other parts of the body; (5) patients with concurrent serious infections; (6) patients with missing follow-up data.

Surgical procedures

The control group included 50 patients who underwent conventional hepatic resection. The procedure involved tracheal intubation under general anesthesia, an epigastric herringbone incision for layer-by-layer abdomen opening, and cutting off the hepatic round ligament, sickle ligament, and right and left hepatic ligaments sequentially. The Pringle method was applied to block the first hepatic portal after the clamping, followed by scraping and suctioning to quickly detach the liver tissue. Residual blood vessels in the liver section were ligated, and liver trauma was sutured.

The observation group consisted of 46 patients who underwent precision liver resection. After successful general anesthesia, an oblique incision under the right costal margin or a reverse "L" incision was made. Intraoperative blood flow to the liver was either not blocked or selectively blocked in the resected segment. Surgical energy instruments were delicately used to cut the liver, securely ligating any encountered ducts (>1 mm in diameter) during the hepatic resection process. Without suturing the liver section, a routine placement of an abdominal drainage tube was performed in the postoperative period. Intraoperative central venous pressure was lowered to control intraoperative bleeding. Specific methods: the patient assumed a supine position after general anesthesia, with the right internal jugular vein punctured for tube placement while monitoring CVP. Simultaneously, efforts were made to maintain arterial systolic pressure above 90 mmHg and urine output exceeding 25 mL/h, thus significantly reducing intraoperative bleeding while ensuring blood perfusion to the organs. A clear operative field is highly advantageous for the manipulation of liver section ducts and the precise determination of the scope of liver resection. Precise hepatic resection uses the middle hepatic vein as an important anatomical landmark. The localization method of Glisson entails intrathecal puncture injection of melphalan in the pre-resected liver segment. Intraoperatively, the Glisson sheath of the pre-resected liver segment was punctured and injected with melphalan under direct vision. After staining, the corresponding Glisson sheath was ligated. This approach allowed the pre-resected liver segments to remain stained for an extended period, thus improving the accuracy of the resected liver section.

After awakening from anesthesia, the patients were transferred to the ward, where close observation was maintained for changes in vital signs and abdominal drainage. Additionally, the 24-hour in and out volume was recorded. After surgery, various treatments were implemented, including anti-inflammatory, hepatoprotective interventions, enzyme-lowering medications, anti-yellowing agents, hemostasis procedures, protection of gastrointestinal mucosa, replenishment of water and electrolytes, correction of hypoproteinemia, blood transfusion, and nutritional support. Regular reviews included blood routine, liver and kidney function, electrolytes, and coagulation function. According to the patient's postoperative recovery and the occurrence of complications, blood gas analysis, chest X-ray, abdominal CT and other examinations were carried out when necessary. No gastrointestinal decompression tubes were left in place before surgery, and abdominal drains and urinary catheters were removed as early as possible after surgery. Incisions were changed regularly, early mobilization activities were encouraged, and attention was paid to prevention of pneumonia and deep vein thrombosis of the lower limbs.

Outcome measures

The primary outcomes were surgical indicators, including the amount of intraoperative bleeding, duration of surgery, postoperative drainage, and postoperative hospital stay. The secondary outcomes included liver function indicators, inflammation indicators, and AFP levels. Before and one week after the operation, 6 ml of fasting venous blood was collected from all patients and centrifuged to obtain the supernatant. Beckman DXC800 automatic biochemistry analyzer (United States) was used to test the liver function indexes, encompassing aspartate aminotransferase (AST), glutamate aminotransferase (ALT), total bilirubin (TBIL), and γ-glutamyl transferase (γ-GT). The inflammation indicators included procalcitonin (PCT), immunoglobin G (IgG), and high-sensitivity C-reactive protein (hs-CRP). We also recorded the patients' postoperative complications, including abdominal fluid, bile leak, and pleural effusion.

Follow-up duration

Totally 96 patients received regularly postoperative follow-up. The follow-up deadline was set on January 2017 or the time of death. Survival time was defined as the time from admission to death or the end of follow-up. All patients were followed up at 3-month intervals for the 3 years. The median follow-up period was 30.81 months.

Statistical analyses

SPSS 20.0 software (Chicago SPSS Co., Ltd.) was used for statistical analysis. Continuous variables were expressed as mean ± standard deviation, and independent samples t-test was used for comparison between groups. The counted data were expressed as ratios, and Fisher's exact probability or chi-square test was used for comparison between groups. The survival of patients was analyzed by Kaplan-Meier method and compared using log-rank test. A $P<0.05$ was considered a significant difference.

Results

Clinical characteristics

There were no significant differences between the two groups in terms of body mass index, cirrhosis, age, tumor diameter, Child-Pugh grade, TNM stage, CNLC stage, pathologic type, hypertension, stroke, distance between the lesion margins, and coronary heart disease ($P>0.05$) (**Table 1**).

Comparison of surgical indicators between the two groups

As shown in the **Table 2**, the operation time, intraoperative bleeding, hospital stay, and time of anal venting were significantly shorter in the

Table 1. Comparison of demographic data and clinical characteristics of two groups

Indicator	Observation group (n = 46)	Control group (n = 50)	χ^2/t	P
Age (years)	56.25±12.34	55.98±12.61	0.049	0.958
Body mass index	20.32±2.39	20.87±3.34	0.088	0.546
Sex			0.480	0.384
Male	27	28		
Female	19	22		
Cirrhosis			0.370	0.545
Yes	26	21		
No	20	29		
Tumor diameter (cm)	7.59±1.98	7.61±2.10	0.146	0.885
Child-Pugh grading (n)			0.273	0.605
Grade A	37	43		
Grade B	9	7		
TNM stage (n)			0.508	0.469
Stage I	33	41		
Stage II	13	9		
CNLC staging (n)			0.048	0.828
Stage I	30	35		
Stage II	16	15		
Pathological type (n)			0.304	0.593
Hepatocellular carcinoma	38	43		
Bile duct cell carcinoma	8	7		
Hypertension	5	10	0.709	0.423
Stroke	7	8	0.336	0.567
Coronary heart disease	6	7	0.382	0.537
Distance between the lesion margins	5.59±0.98	6.61±1.10	0.046	0.985

Note: TNM: Tumor Node Metastasis.

Table 2. Comparison of surgical indicators between the two groups

Indicator	Observation group (n = 46)	Control group (n = 50)	χ^2/t	P
Operating time (min)	91.27±7.87	98.49±8.30	-4.389	0.003
Intraoperative bleeding (mL)	220.69±10.21	248.94±12.29	-12.319	0.001
Anal venting time (h)	72.22±7.40	81.33±7.50	-6.019	0.004
Length of hospital stay (days)	9.29±1.26	11.42±1.34	-8.071	0.002

observation group than in the control group (P<0.05).

Comparison of liver function and AFP between the two groups

Before surgery, there were no significant differences in the levels of AST, TBiL, ALT, γ-GT, and AFP between the two groups (P>0.05). One week after the surgery, the levels of AST, TBiL, ALT and γ-GT markedly decreased in both groups, with more significant decreases in the observation group (P<0.05). However, no significant difference was observed in AFP between the two groups one week after the surgery (P>0.05) (**Table 3**).

Comparison of incidence of complications between the two groups

The incidences of pleural effusion, bile leak, abdominal infection, pulmonary infection, as well as the total complications rates in the observation group were significantly lower than those in the control group, with significant differences (P<0.05), as shown in **Table 4.**

Table 3. Comparison of liver function and AFP between the two groups

Indicator	Time	Observation group (n = 46)	Control group (n = 50)	χ^2/t	P
AST (U/L)	Before surgery	58.90±7.73	58.70±7.91	0.153	0.883
	1 week after surgery	34.30±6.41	41.96±6.80	4.829	0.001
TBIL (U/L)	Before surgery	31.83±5.86	32.15±5.63	-0.182	0.853
	1 week after surgery	14.57±5.20	17.34±5.12	2.983	0.002
ALT (U/L)	Before surgery	46.80±4.93	45.71±5.09	1.063	0.288
	1 week after surgery	26.84±5.34	32.93±5.39	5.323	0.002
γ-GT (U/L)	Before surgery	68.73±5.82	68.62±6.12	0.049	0.963
	1 week after surgery	30.42±6.02	39.22±6.12	7.548	0.001
AFP	Before surgery	224.87±12.34	212.67±10.38	1.664	0.889
	1 week after surgery	80.34±9.89	89.34±8.98	2.784	0.324

Note: AST: Aspartate transaminase; TBIL: Total Bilirubin; ALT: Alanine transaminase; γ-GT: γ-glutamyl transpeptidase; AFP: Alpha-fetoprotein.

Table 4. Comparison of the incidence of complications between the two groups

Indicator	Observation group (n = 46)	Control group (n = 50)	χ^2/t	P
Pleural effusion	2	3		
Biliary Leakage	1	2		
Abdominal Infection	1	2		
Pulmonary infection	0	1		
Total incidence (%)	4	8 (16.0%)	9.897	0.033

Table 5. Three-year recurrence and survival rates in the two groups

Indicator	Observation group (n = 46)	Control group (n = 50)	χ^2/t	P
Number of relapses	4	5	-	-
Recurrence rate (%)	8.7%	10%	3.456	0.113
Survival population	39	40	-	-

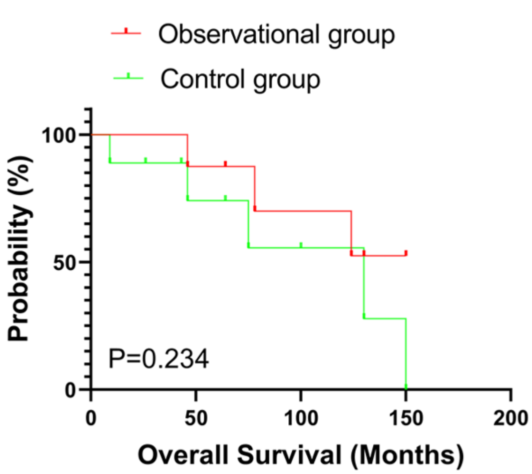

Figure 1. Kaplan Meier survival curves.

Three-year recurrence and survival rates in the two groups

Within three years of follow-up, the observation group demonstrated a lower recurrence rate and higher survival rate than the control group, but there were no significant differences (P>0.05) (**Table 5** and **Figure 1**).

Comparison of inflammation indicators between the two groups

Before surgery, there were no differences in PCT, hs-CRP, and IgG levels between the two groups (P>0.05). One week after the surgery, PCT, IgG and hs-CRP levels decreased in both groups, and significantly lower PCT and hs-CRP levels were observed in the observation group than in the control group (P<0.05) (**Figure 2**).

Discussion

In this study, we found the following advantages of phase precision hepatectomy. First, less surgical trauma: compared to conventional hepatectomy, which blocks blood flow entering the entire liver, precision hepatectomy only blocks the blood flow associated with the portal vein, which reduces ischemia-reperfusion damage to the residual liver. The non-contiguous hepatic injury layer effectively avoided the destruction of marginal tissues due to compression ischemia caused by tension suture. The data of this comparison showed that there

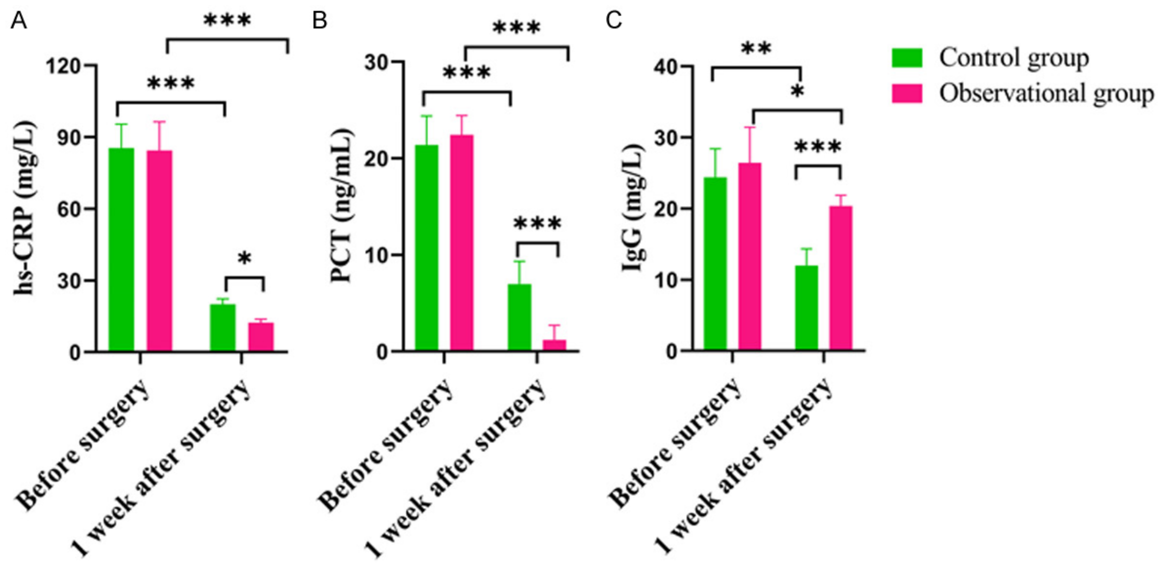

Figure 2. Comparison of inflammatory indicators between the two groups. A: hs-CRP; B: PCT; C: IgG. Note: PCT: procalcitonin; IgG: Immunoglobin G; hs-CRP: high-sensitivity C-reactive protein. *$P<0.05$ as compared with control group, **$P<0.01$ as compared with control group, ***$P<0.001$ as compared with control group.

was a significant difference between the observation group and the control group in terms of the indicators of surgical injuries. Second, a lower incidence of postoperative complications: the fine surgical procedure of precision hepatectomy allowed good exposure of the dissected liver parenchyma and provided good conditions for precise treatment of complex intrahepatic ducts, resulting in reduced intraoperative bleeding. Additionally, it allowed for clear exposure of the intrahepatic bile ducts and minimized damage to important inflow or outflow channels. This reduction in damage contributed to preserving the liver's functional capacity, mitigating potential negative impacts due to operational factors. Finally, the tumor-free principle: precise surgical operation avoids the probability of tumor dissemination in the liver tissue.

The results of this study showed that compared to the control group, the amount of intraoperative bleeding and blood transfusion was greatly reduced in the observation group, and the postoperative liver function was also significantly better than that in the observation group. This is because, compared to conventional liver resection, which involves the blockade of the entire hepatic blood flow, precision liver resection blocks only the collateral branch of the portal vein, which greatly restricts the bleeding caused by the surgical operation, avoids ischemia/reperfusion damage to the residual liver tissue, protects the surrounding normal liver tissue from damage, and preserves the functional volume of residual liver. Precision liver resection can protect the intrahepatic ducts due to fine dissection, reduce surgical bleeding, minimize trauma to the liver tissue, and preserve the volume and blood supply of the residual liver tissue. The removal perimeter required for precision hepatic resection is also more accurate than in conventional surgery. Intraoperatively, only the liver branch including the tumor and the portal vein is removed, and R0 resection can be maximized [13-16]. The analysis of this study indicates that it is feasible to choose precision liver resection for primary hepatocellular carcinoma cases, because it can greatly improve the recovery of liver function after surgery. Some studies have shown that the functional decline of residual liver tissue and various complications were greatly reduced after precision liver resection, which also suggests that precision liver resection facilitates better outcome of surgical operation and postoperative recovery.

Postoperative ALT and TBIL levels were significantly lower in the observation group compared with the control group. This is mainly due to the accurate imaging evaluation of the relationship between intrahepatic lesions and their surrounding tissues of the complex intrahepatic ductal system, the precise estimation of the residual liver volume, and the reasonable assessment of the reserved liver function before the surgery. These benefits allow the clinicians to carry out a fine liver parenchyma disconnection and hepatic section processing, which helps reduce the surgical damage to the liver tissues and lower the incidence of postoperative complications [17-20].

The results of our study showed that compared to conventional liver resection, precision liver resection had a better performance in decreasing postoperative complications such as bile leakage and postoperative bleeding. It was suggested that precision liver resection has a higher safety and is conducive to the rapid recovery of patients after the operation [21-24]. However, the data from the 3-year follow-up showed that there was no significant difference in the tumor recurrence and survival rates between the two groups. This result was considered to be closely related to an insufficient follow-up time of the present study, and therefore the postoperative recurrence and survival rates need to be further investigated through longer and more detailed follow-up visits [25-29].

The current study has several limitations. That is, this study was a retrospective analysis with a small sample size from a single-center cohort. Moreover, the research was conducted in a single institution. Further, only three years of postoperative follow-up was available. Therefore, the results of this study should be validated by multi-center international studies.

In conclusion, precision liver resection contributes to less surgical trauma, better recovery of postoperative liver function, and lower complication rate, compared to conventional liver resection, in patients with primary liver cancer, while the long-term efficacy still needs to be further studied.

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Disclosure of conflict of interest

None.

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