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***Retrospective Study***

**Effectiveness of surgical resection for complicated liver cancer and its influencing factors: A retrospective study**

Yu J *et al*. Surgical resection of complicated liver cancer

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**Abstract**

BACKGROUND

Surgical resection is the preferred method for patients with complex liver cancer. But the tumor is in a special position, the surgery is highly risky, postoperative complications can easily occur, and the prognosis is not ideal.

AIM

To investigate the effectiveness of surgical resection for complex liver cancer and its influencing factors.

METHODS

Fifty-seven patients who had complicated liver cancer and underwent surgical resection at our hospital from August 2015 to August 2016 were enrolled in this study. All patients were followed for three years, and their postoperative complications, survival, and factors that impacted their survival were analyzed.

RESULTS

The total incidence of postoperative complications was 45.61%, and the incidence of pleural effusion was the highest at 28.07%. There were no correlations between the 2-year and 3-year survival rates and sex, age, and HbsAg of the patients (*P* > 0.05). In terms of pathological parameters, the 2-year and 3-year survival rates were significantly different according to the presence of a tumor capsule, degree of liver cirrhosis, satellite or focal lesions, hepatic vein thrombosis, portal vein tumor thrombus, and intraoperative blood loss (*P* < 0.05).

CONCLUSION

The effectiveness of surgical resection for complex hepatocellular carcinoma may be affected by factors such as the presence of a tumor capsule, cirrhosis degree, satellite or focal lesions, hepatic vein embolization, portal vein tumor thrombus, and intraoperative blood loss. Therefore, these factors should be controlled and prevented during surgery to help improve patient survival after surgery.

**Key words****:** Complicated liver cancer; Surgical resection; Survival rate; Complications

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**Core tip:** Complex hepatocellular carcinoma surgery is difficult for hepatobiliary surgeons. We aimed to find some factors that affect postoperative survival rate through these cases, so as to improve the surgeons' understanding of the surgery and the patients' survival rate.

**INTRODUCTION**

On a global scale, liver cancer is a malignant disease with a high prevalence and mortality. Approximately 1 to 4 million people die each year from this disease, of which Chinese patients account for approximately 43.7%[1,2]. The development of liver cancer is related to *Aspergillus flavus*, viruses, hepatitis, cirrhosis, *etc.*[3,4]. Although various new treatment models have been introduced with the development of new medical technology and the survival rate of patients has improved, surgical resection is still the preferred method for patients with complex liver cancer. Because the tumor is in a special position, the surgery is highly risky, postoperative complications can easily occur, and the prognosis is not ideal. Therefore, in the process of completely resecting the lesion and retaining residual liver function, accelerating the rehabilitation process and improving prognosis have become an in-depth area of study in the medical community. To improve the surgical effect and patient prognosis, we must first identify the relevant influencing factors and then develop targeted prevention and control measures. This study was based on these points and is reported below.

**MATERIALS AND METHODS**

***General information***

A total of 57 patients with complicated liver cancer who underwent surgical resection at our hospital from August 2015 to August 2016 were enrolled. The patients comprised 21 female patients and 36 male patients, aged between 64 years and 29 years old. The mean age was 43.26 ± 5.81 years old, and there were 30 HbsAg-positive patients and 27 HbsAg-negative patients.

The inclusion criteria were as follows: Diagnosis based on a combination of clinical symptoms, laboratory parameters, pathological examination, imaging examination, *etc.*; preoperative liver function was Child-Pugh grade A or B; and consistent indications for surgical resection, without extensive extrahepatic metastasis, and without residual tumor.

The exclusion criteria were as follows: Surgical contraindications; small liver cancer or large liver cancer, with tumor diameters less than 10 cm; tumors not completely resected intraoperatively; residual cancer; inability to cooperate with the follow-up; and communication disorders or mental disorders.

This study was approved by the hospital ethics committee. Both the patient and family were aware of the study and voluntarily signed written agreements.

***Methods***

All patients underwent hepatectomy or partial hepatectomy according to their actual condition. The lesions were removed first, and then the liver function recovery indicators were considered. The need for adjuvant therapy was considered. If there was no exact recurrence, hepatic arterial infusion chemotherapy was performed. The intraoperative bleeding control methods included 23 cases of selective hepatic blood flow occlusion and 34 cases of selective hepatic blood flow occlusion. The treatment of the cross-section and hepatic margins are follows: 2 cases of bioadhesive, 36 cases of suture closures, and 19 cases of electrocautery.

All patients were followed for 3 years, and the survival and postoperative complications were evaluated. The factors affecting survival rate were analyzed, including sex, age, HbsAg, and pathological parameters.

***Observation indicators***

The postoperative complications of all patients, including edema, abdominal infection, bile leakage, and pleural effusion, were recorded. The impact of sex, age, and HbsAg on postoperative survival was analyzed. The influence of pathological parameters on survival time after surgery was also analyzed. A logistic regression analysis of factors affecting the effectiveness of surgical resection was performed.

***Statistical analysis***

All the data were processed with SPSS 22.0 software. The data are described as percentages (%). The *χ2* test was used for comparisons. The influencing factors were analyzed by logistic regression analysis. *P* < 0.05 indicated that the difference between groups was statistically significant[5].

**RESULTS**

A total of 26 patients had different degrees of complications after surgery, with a total incidence of 45.61%. Two (3.51%) patients had ascites, two (3.51%) had abdominal infections, six (10.53%) had bile leakage, and sixteen (28.07%) had pleural effusion. The most common complication was pleural effusion, which required active prevention and intervention.

There were no significant differences in the 2-year or 3-year survival rate among patients with different sexes, age, and HbsAg expression (*P* > 0.05). Gender, age, and HbsAg were not related to the postoperative survival rate (Table 1).

***Analysis of effect of pathological parameters on postoperative survival time***

There were no significant differences in the 2-year or 3-year survival rates of patients with different preoperative liver function grades, tumor sizes, and intraoperative anesthesia durations (*P* > 0.05). The 2-year and 3-year survival rates were significantly different according to the presence of a tumor capsule, cirrhosis degree, satellite or focal lesions, hepatic vein thrombosis, portal vein tumor thrombus, and intraoperative blood loss (*P* < 0.05) (Table 2).

***Multivariate logistic analysis of factors influencing effects of surgical resection***

The presence of a tumor capsule, degree of cirrhosis, satellite or focal lesions, hepatic vein thrombosis, portal vein tumor thrombus, and intraoperative blood loss were risk factors for the effect of surgery (Table 3).

**DISCUSSION**

Primary liver cancer lacks typical symptoms at the beginning of the disease, but the disease develops rapidly[6]. Once the diagnosis is made, the disease is usually in the middle and late stages, and if it cannot be treated effectively in time, the estimated natural survival time is less than 3 mo[7]. However, the treatment of liver cancer has made great progress[8-11], and complex liver cancer patients can also receive effective treatment; the 5-year survival rate after surgery has increased to approximately 40%. However, surgery is associated with certain risks, which inevitably influence the surgical effect and prognosis[12]. Therefore, when choosing the surgical method, the patient's tolerance, pathological stage, clinical manifestation, *etc*. should be comprehensively considered[7]. During the operation, the tumor tissue should be completely removed, and the liver tissue should be preserved to the greatest extent to ensure its unaffected physiological function. In addition, it is necessary to understand the factors affecting the surgical effect and survival rate and carry out targeted management and control strategies[13,14].

In this study, the basic data and postoperative pathological parameters of 57 patients with complicated hepatic carcinoma who underwent surgical resection were analyzed. The total incidence of postoperative complications was 45.61%, of which edema, abdominal infection, bile leakage, and pleural effusion accounted for 3.51%, 3.51%, 10.53%, and 28.07%, respectively. Additionally, there was no significant difference in the 2-year or 3-year survival rate among patients with different sexes, ages, and HbsAg expression (*P* > 0.05). The above three factors were not correlated with the survival rate. Univariate analysis of the pathological parameters of all patients showed that there was no significant difference in survival rate among patients with different preoperative liver function grades, tumor sizes, and intraoperative anesthesia durations (*P* > 0.05). Logistic multivariate analysis was performed, and the results showed that the postoperative 2-year and 3-year survival rates were significantly different according to the presence of a tumor capsule, degree of liver cirrhosis, satellite or focal lesions, hepatic vein thrombosis, portal vein tumor thrombus, and intraoperative blood loss (*P* < 0.05). The surgical resection effect was not related to preoperative liver function grade, tumor size, or intraoperative anesthesia, but was related to the presence of a tumor capsule and no or mild cirrhosis. Patients with no satellite or focal lesions, no hepatic vein embolization, no portal vein embolization, and intraoperative blood loss ≤ 700 mL had a higher survival rate at 2 years and 3 years.

According to the results of this study, it is necessary to comprehensively analyze the patient's tumor status before the operation and choose a reasonable surgical method[2,15]. The surgeon should also be familiar with the physiological anatomy of the liver. The nursing staff and the doctor should work together closely to reduce the volume of intraoperative blood loss[16]. This factor plays an important role in improving the surgical outcome of complicated liver cancer. In addition, during the operation, we must pay close attention to relevant factors and develop targeted intervention programs. The patients can benefit from the following recommendations: (1) The determination of the surgical incision position needs to account for the specific location of the patient's tumor to ensure a good surgical field and surgical environment and improve the accuracy of the surgery and the success rate of the surgery[17]; (2) the anatomy of the perihepatic ligament and the overall structure of the liver should be sufficiently retained to better control the amount of bleeding, and the scope of tumor resection and closure technique after resection should also be considered[18]; (3) to reduce the risk of the surgery, intraoperative bleeding should be actively prevented and controlled, the amount of bleeding should be recorded, and reasonable blood transfusions should be performed[19]; and (4) the prospective management of postoperative complications should be strengthened, the extent of preoperative blood circulation should be assessed, operative complications during surgery should be avoided, and targeted management after surgery should be performed to ensure that the patients can smoothly recover in the perioperative period, reduce the incidence of complications, and improve the safety and effectiveness of the surgery[20]. In addition, hemihepatic blood flow occlusion was applied in 23 cases in this study to stop bleeding and promoted the hematopoietic cell apoptosis of the hepatic resection. This is because of the susceptibility of the cells, and the defects of the bone marrow microenvironment, hematopoietic mass ischemia, lymphocytes, abnormal activation of monocytes, activation of other immunocompetent cells such as NK cells, bone marrow microenvironment, and hematopoietic cytoplasmic ischemia enhance apoptosis signals and attenuate anti-apoptotic signals[21,22].

In conclusion, the effectiveness of surgical resection for complicated liver cancer is affected by factors such as the presence of a tumor capsule, degree of liver cirrhosis, satellite or focal lesions, hepatic vein thrombosis, portal vein tumor thrombus, and intraoperative blood loss. Therefore, these factors should be controlled and prevented during surgery to improve the survival rate after surgery.

**Article Highlights**

***Research background***

Surgical resection is the preferred method for patients with complex liver cancer. But the tumor is in a special position, the surgery is highly risky, postoperative complications can easily occur, and the prognosis is not ideal.

***Research motivation***

To explore the safety and feasibility of complicated liver cancer surgery and improve the survival rate of patients.

***Research objectives***

To investigate the effectiveness of surgical resection for complex liver cancer and its influencing factors.

***Research methods***

Fifty-seven patients who had complicated liver cancer and underwent surgical resection at our hospital from August 2015 to August 2016 were enrolled in this study. All patients were followed for three years, and their postoperative complications, survival, and factors that impacted their survival were analyzed.

***Research results***

The total incidence of postoperative complications was 45.61%, and the incidence of pleural effusion was the highest at 28.07%. There were no correlations between the 2-year and 3-year survival rates and sex, age, and HbsAg of the patients (*P* > 0.05). In terms of pathological parameters, the 2-year survival rates and 3-year survival rates were significantly different according to the presence of a tumor capsule, degree of liver cirrhosis, satellite or foci lesions, hepatic vein thrombosis, portal vein tumor thrombus, and intraoperative blood loss (*P* < 0.05).

***Research conclusions***

The effectiveness of surgical resection for complex hepatocellular carcinoma may be affected by factors such as the presence of a tumor capsule, cirrhosis degree, satellite or focal lesions, hepatic vein embolization, portal vein tumor thrombus, and intraoperative blood loss. Therefore, these factors should be controlled and prevented during surgery to help improve patient survival after surgery.

***Research perspectives***

The influencing factors of complicated hepatocellular carcinoma surgery should be further explored to further improve patient survival after surgery.

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**Footnotes**

**Institutional review board statement:** This study was reviewed and approved by the Ethics Committee of the Shandong Provincial Qianfoshan Hospital, Shandong University.

**Informed consent statement:** Informed consent was obtained from the patient.

**Conflict-of-interest statement:** Dr. Tian reports grants from the Medical Technology Innovation Plan of Jinan City (201805033), Key Research and Development Plan of Shandong Province (2016GSF201108), and Science and Technology Development Plan of Shandong Province (ZR2019MH116) during this study.

**Data sharing statement:** No additional data are available.

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**Table 1 Analysis of effect of sex, age, and HbsAg on postoperative survival time, *n* (%)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Factor** | | **Number of cases** | **Survival at 2 yr** | **Survival at 3 yr** | ***χ2*** | ***P*-value** |
| Sex | Female | 21 | 10 (47.62) | 9 (42.86) | 2.659 | 0.103 |
|  | Male | 36 | 17 (47.22) | 9 (25.00) |
| Age | > 50 years old | 23 | 8 (34.78) | 7 (30.43) | 3.141 | 0.076 |
|  | ≤ 50 years old | 34 | 19 (55.88) | 10 (29.41) |
| HbsAg | Negative | 27 | 11 (40.74) | 8 (29.63) | 0.870 | 0.351 |
|  | Positive | 30 | 12 (40.00) | 8 (26.67) |

**Table 2 Effect of pathological parameters on postoperative survival time, *n* (%)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Index** | | **Number of cases** | **Survival at 2 yr** | **Survival at 3 yr** | ***χ2*** | ***P*-value** |
| Preoperative liver function grade | A | 46 | 21 (45.65) | 12 (26.09) | 0.279 | 0.598 |
|  | B | 11 | 5 (45.45) | 2 (18.18) |
| Tumor size | < 15 cm | 54 | 29 (53.70) | 18 (33.33) | 0.978 | 0.323 |
|  | ≥ 15 cm | 3 | 1 (33.33) | 1 (33.33) |
| Tumor capsule | No | 21 | 6 (28.57) | 1 (4.76) | 24.532 | 0.000 |
|  | Yes | 36 | 20 (55.56) | 14 (38.89) |
| Degree of cirrhosis | No/mild | 40 | 25 (62.5) | 18 (45.00) | 48.714 | 0.000 |
|  | Moderate/ severe | 17 | 5 (29.41) | 2 (11.76) |
| Satellite or focal lesion | No | 33 | 17 (51.52) | 5 (15.15) | 26.057 | 0.000 |
|  | Yes | 24 | 0 (0.00) | 0 (0.00) |
| Hepatic vein thrombosis | No | 43 | 23 (53.49) | 17 (39.53) | 20.870 | 0.000 |
|  | Yes | 14 | 3 (11.43) | 2 (14.29) |
| Portal vein tumor thrombus | No | 40 | 37 (92.50) | 22 (55.00) | -431.863 | 0.000 |
|  | Yes | 17 | 1 (5.88) | 0 (0.00) |
| Intraoperative anesthesia duration | ≤ 3 h | 25 | 12 (48.00) | 8 (32.00) | 0.706 | 0.401 |
|  | > 3 h | 32 | 8 (25.00) | 7 (21.88) |
| Intraoperative blood loss | ≤ 700 mL | 42 | 35 (83.33) | 20 (47.62) | -40.353 | 0.001 |
|  | 700-2200 mL | 15 | 5 (33.33) | 4 (26.27) |

**Table 3 Multivariate logistic analysis of factors influencing effects of surgical resection, *n* (%)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Factor** | **Regression coefficient** | **Wald** | ***P*-value** | **Relative risk** | **OR (95%CI)** |
| Hepatoma capsule | -1.15 | 8.43 | 0.002 | 0.32 | 0.14-0.67 |
| Degree of cirrhosis | 1.43 | 4.167 | 0.05 | 4.3 | 1.03-16.23 |
| Satellite or focal lesion | 2.03 | 6.76 | 0.02 | 7.42 | 2.43-22.58 |
| Hepatic vein thrombosis | 0.42 | 0.73 | 0.037 | 1.53 | 0.56-3.95 |
| Portal vein tumor thrombus | 1.27 | 6.76 | 0.009 | 3.51 | 1.37-9.05 |
| Intraoperative blood loss | 0.002 | 3.94 | 0.045 | 1.03 | 1.00-1.02 |