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Analysis of Survival Rate and Influencing Factors in Surgical Treatment of Primary Hepatocellular Carcinoma

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Abstract: Objective: To study the survival rate of patients with primary hepatocellular carcinoma (HCC) undergoing clinical surgical treatment and various influencing factors, with the aim of further improving the survival rate of primary HCC patients. Methods: Sixty patients with primary hepatocellular carcinoma who underwent liver cancer resection surgery between January 2020 and December 2022 in our hospital were selected. A retrospective analysis was conducted on the patients' clinical characteristics (family medical history, alpha-fetoprotein levels, degree of liver cirrhosis, vascular invasion), treatment methods (surgical techniques, adjunctive therapies), and prognosis. The survival rate of patients and the influencing factors on the postoperative survival rate were analyzed. Results: There was a statistically significant difference in the five-year survival rate comparisons between different liver cirrhosis statuses, tumor sizes, preoperative alpha-fetoprotein levels, vascular invasion statuses, adjunctive treatment methods, and family medical histories ($P < 0.05$). Comparisons between different genders, ages, tumor locations, tumor pathological types, hepatitis B surface antigens, Child-Pugh classifications of liver function, tumor numbers, and methods of liver cancer resection showed no statistically significant differences ($P > 0.05$). Liver cirrhosis, tumor size ≥ 5cm, preoperative alpha-fetoprotein level > 400ng/ml, change in alpha-fetoprotein levels pre-and post-surgery, vascular invasion, adjunctive treatment methods, and PLC family medical history are independent factors influencing the survival rate of surgical treatment in primary HCC patients. Conclusion: There are several factors affecting the postoperative survival rate of primary HCC patients. Clinicians need to take a comprehensive approach. For high-risk patients, regular follow-ups are necessary, coupled with early diagnosis and treatment, to improve the prognosis. This approach is worth promoting.

Keywords: Primary Hepatocellular Carcinoma; Survival Rate; Independent Risk Factors.

1. Introduction

Primary liver cancer is one of the most common malignant tumors both domestically and internationally. The incidence of this disease is increasing year by year. According to relevant research findings, the incidence rate of primary liver cancer in China has reached approximately 80 per 100,000 people. The mortality rate of this disease is second only to lung cancer, posing a serious threat to patients' life safety. From the perspective of pathological histological classification, primary liver cancer can be divided into three types: hepatocellular carcinoma, intrahepatic bile duct carcinoma, and hepatocellular-cholangiocarcinoma. The most common type of primary liver cancer is hepatocellular carcinoma, followed by intrahepatic bile duct carcinoma and mixed-cell type liver cancer. The occurrence of primary liver cancer is influenced by multiple factors. Both domestic and international studies have found that factors such as viral hepatitis, liver cirrhosis, genetics, environment, obesity, and alcohol consumption are closely related to the development of this disease. The interaction of genetic factors and other factors plays a significant role in the occurrence of primary liver cancer. Since the 1970s, the maturity of techniques such as B-ultrasound, CT, MRI, and angiography has greatly improved the diagnostic accuracy of primary liver cancer, and there are also a variety of treatment methods available. Currently, clinical treatments include surgical and non-surgical approaches. However, surgical treatment, specifically liver cancer resection surgery, is the primary surgical procedure for patients with primary liver cancer. This method can improve patients' quality of life and prognosis [1,2]. However, due to the unique characteristics of liver cancer, it often lacks obvious clinical symptoms in the early stages, leading to most patients being diagnosed in the middle or late stages of the disease. This results in missed opportunities for optimal surgical treatment. Furthermore, a significant proportion of liver cancer patients in China have coexisting conditions such as hepatitis B and liver cirrhosis, which can impair liver reserve function. After undergoing resection surgery, the regenerative capacity of the remaining liver is affected, making liver function failure a major cause of postoperative mortality. According to relevant statistics, the recurrence rate of liver cancer patients within five years after surgical resection exceeds 60%. Therefore, enhanced screening for high-risk populations of this type is of great significance. Currently, there is no unified standard for the prognosis assessment of liver cancer patients. Various factors can impact the prognosis of liver cancer, including host factors, treatment factors, and tumor factors. Host factors include gender, age, liver function, viral hepatitis, and other conditions. Tumor factors encompass pathological characteristics of the tumor lesions, such as tumor volume, number of lesions, tumor encapsulation, and pathological histological grading. Treatment factors include the surgical approach, intraoperative blood transfusion, and pre- and post-operative adjuvant treatment. Both domestically and

internationally, there have been numerous studies on the factors influencing the prognosis of liver cancer [3,4]. If only single-factor analysis is conducted without considering the interactions between prognostic factors, it can lead to significant bias in the prognosis factors. Therefore, this study aims to analyze the survival rate and influencing factors of primary liver cancer patients who underwent liver cancer resection surgery, based on a selection of 60 cases treated at our hospital from January 2020 to December 2022.

1.1. Materials and Methods

1.1.1. General Information

From January 2020 to December 2022, our institution treated 60 patients with primary hepatocellular carcinoma (HCC) requiring hepatectomy. Of these, 38 were male and 22 were female, aged between 30-80 years, with an average age of (55.68±12.46) years. Tumor sizes ranged from 2.0-13.8 cm with an average size of (7.36±1.19) cm. According to the Child-Pugh liver function classification: 42 patients were Grade A and 18 patients were Grade B. Surgical resection types included: 12 patients with hemi-hepatectomy (either left or right lobe removal), 31 patients with lobectomy (right posterior, right anterior, left medial, left lateral lobes), 9 patients with segmental resection (segments V, VI, VII, VIII or combinations thereof), and 8 patients had local resections [5,6].

Inclusion criteria:

1) All patients were diagnosed and staged according to the criteria for primary HCC.

2) Patients experiencing their first onset of the disease, who hadn't undergone minimally invasive or conservative treatments pre-surgery, and were pathologically confirmed as having primary HCC after surgery.

3) Complete clinical data.

4) Patients informed of this study and agreed to participate.

Exclusion criteria:

1) Patients with associated cardiovascular diseases, endocrine diseases, or other underlying conditions.

2) Severe liver function abnormalities, or the presence of jaundice or ascites.

3) Presence of distant metastasis.

4) Patients with malignant tumors in other systems.

1.1.2. Methods

A retrospective analysis was conducted on the 60 patients, considering factors such as family medical history, alpha-fetoprotein (AFP) levels, degree of liver cirrhosis, and vascular invasion. Treatment methods (surgical techniques and adjunct treatments) and prognosis were also assessed. Vascular invasion was diagnosed based on imaging or postoperative pathological examinations, specifically the presence of tumor thrombus in the portal or hepatic veins. The degree of liver cirrhosis was based on postoperative pathological examination. An AFP level of 400ng/ml was set as the threshold, and changes in AFP levels pre- and post-surgery were recorded. Surgical interventions were classified into four categories based on the extent of resection: hemi-hepatectomy, lobectomy, segmental resection, and local resection. Adjunctive therapies primarily included: intraoperative implantation of fluorouracil implants, postoperative prophylactic hepatic artery embolization chemotherapy, or a combination of the two treatments [7,8].

1.1.3. Follow-Up

Patients were followed up for one year, either by phone or through home visits. The survival rate of the patients was recorded, and independent risk factors affecting the prognosis were analyzed.

1.1.4. Statistical Analysis

The SPSS 20.0 statistical analysis software was used. Count data were presented as percentages and analyzed with the $\chi 2$ test. Measurement data were expressed as mean ± standard deviation and analyzed using the t-test. A P-value of less than 0.05 indicated statistically significant differences [9, 10].

1.2. Results

1.2.1. Follow-Up Findings

Comparisons of five-year survival rates based on the presence or absence of liver cirrhosis, tumor size, preoperative alpha-fetoprotein (AFP) levels, presence or absence of vascular invasion, adjunctive treatment methods, and family medical history showed statistically significant differences ($P<0.05$). Comparisons based on gender, age, tumor location, tumor pathological type, hepatitis B surface antigen status, Child-Pugh liver function grading, number of tumors, and hepatectomy methods showed no statistically significant differences ($P>0.05$). Refer to Table 1 for details [11,12].

1.2.2. Independent Risk Factors for Prognosis

The presence of cirrhosis, tumor size ≥5cm, preoperative alpha-fetoprotein (AFP) level >400ng/ml, changes in AFP levels before and after surgery, vascular invasion, the method of adjuvant treatment, and family medical history are independent influencing factors for the survival rate of patients with primary liver cancer undergoing surgical treatment, as shown in Table 2.

1.3. Discussion

Primary liver cancer is a malignant tumor with high incidence and mortality rates worldwide, and China is one of the primary regions for its occurrence. According to relevant literature, the number of new liver cancer cases in China has been steadily increasing. The incidence rate is significantly higher in males than in females. Primary liver cancer can occur at any age but is most commonly found in young and middle-aged individuals. There are multiple factors contributing to the development of primary liver cancer, including infectious factors, chemical exposures, individual lifestyles, environmental factors, and genetic factors. Currently, clinical consensus suggests a strong correlation between primary liver cancer and the hepatitis B virus (HBV). HBV is prevalent in China, and its sustained elevation has become a major factor in the development of liver cirrhosis and liver cancer. The exact mechanisms behind HBV-induced liver cancer are still a subject of debate. It is suggested that HBV DNA can integrate with the host liver cell chromosomes, leading to DNA deletions within some liver cell chromosomes. This integration can result in gene rearrangement, causing liver cell damage and a malignant cycle. This ultimately activates oncogenes, significantly reducing the activity of tumor suppressor genes, potentially leading to necrosis and the development of malignant tumors. In China, most liver cancer patients have a history of progression from hepatitis B and liver cirrhosis. Currently, there is an insufficient screening mechanism for high-risk factors related to hepatitis B and liver cirrhosis, which results in liver function impairment for many patients. Most patients are diagnosed in the middle to late stages of the disease, impacting their prognosis negatively [13,14].

Table 1. Follow-up Results

Influencing Factors		Number of Cases	5-Year Survival Rate (%)	X2	P
Gender	Male	38	15(39.5)	0.057	0.811
	Female	22	8(36.4)		
Age (years)	>50	25	10(40.0)	0.050	0.822
	≤50	35	13(37.1)		
Tumor Location	Left lobe	14	5(35.7)	0.003	0.955
	Right lobe	43	15(34.9)		
	Junction of left and right liver	3	1(33.3)		
Tumor Pathological Type	Hepatocellular carcinoma	53	21(39.6)	0.000	0.987
	Cholangiocellular carcinoma	5	2(40.0)		
	Hepatocellular and Cholangiocellular mix carcinoma	2	1(50.0)		
Hepatitis B Surface Antigen	Positive	47	20(42.6)	0.070	0.791
	Negative	13	5(38.5)		
Liver Function Child Grade	Grade A	46	16(34.8)	0.004	0.949
	Grade B	14	5(35.7)		
Presence of Cirrhosis	Yes	40	10(25.0)	5.275	0.022
	No	20	11(55.0)		
Tumor Volume (cm)	≥5cm	29	7(24.1)	5.884	0.015
	<5cm	31	17(54.8)		
Number of Tumors	Single	32	12(37.5)	0.020	0.887
	Multiple	28	11(39.3)		
Preoperative AFP Level (ng/ml)	>400	15	3(20.0)	3.863	0.049
	≤400	45	22(48.9)		
AFP Changes Pre- and Post-surgery	Both negative	26	16(61.5)	5.472	0.019
	Pre-pos, Post-neg	19	5(26.3)		
	Both positive	15	2(13.3)		
Method of Liver Cancer Resection	hemihepatectomy	12	4(33.3)	0.497	0.481
	segmental hepatectomy	31	14(45.2)		
	Liver lobectomy or local resection	17	6(35.3)		
presence or absence of vascular invasion	Yes	32	8(25.0)	4.019	0.045
	No	28	14(50.0)		
Adjuvant therapy	Intraoperative Fluorouracil Implantation	15	1(6.7)	4.935	0.026
	Preventive TACE	23	9(39.1)		
	Both	22	11(50.0)		
Family medical history	Yes	9	3(33.3)	8.663	0.003
	No	51	23(45.1)		

Table 2. Independent Risk Factors for Prognosis

Independent Risk Factor	Beta (β) Value	Wald Value	OR Value	95%CI	P-Value
Cirrhosis	1.566	8.004	0.805	0.293-0.490	<0.05
Tumor Size ≥5cm	0.480	4.544	0.474	0.311-0.591	<0.05
Preoperative AFP >400ng/ml	1.565	9.193	0.759	0.513-0.624	<0.05
Changes in AFP Before & After Surgery	1.136	8.384	0.579	0.325-0.470	<0.05
Vascular Invasion	1.556	4.011	0.769	0.691-0.813	<0.05
Method of Adjuvant Treatment	0.675	3.055	0.379	0.558-0.689	<0.05
Family Medical History	0.577	4.254	0.580	0.579-0.654	<0.05

To reduce the incidence and mortality rates of liver cancer, China has implemented a three-tier prevention program: primary prevention includes routine hepatitis B vaccination for newborns to reduce the chronic infection rate; secondary prevention involves early diagnosis and treatment through comprehensive screening; and tertiary prevention focuses on clinical diagnosis and treatment for liver cancer patients. There are various clinical treatment options for primary liver cancer, with liver cancer resection being a primary method. In recent years, clinical surgery has shifted from traditional extensive liver resection to precision liver resection, which reduces intraoperative blood loss, preserves the remaining liver's blood supply function, and minimizes complications. However, due to the elusive early symptoms of liver cancer, most patients are diagnosed in the middle or late stages of the disease, resulting in a high recurrence rate within five years after surgery, exceeding 60%. Postoperative recurrence is a significant factor affecting patient survival. This study found that several factors influence the prognosis of primary liver cancer patients. These include liver cirrhosis, tumor size ≥5cm, preoperative alpha-fetoprotein (AFP) levels > 400ng/ml, changes in AFP levels before and after surgery, vascular invasion, adjuvant treatment methods, and a family history of the disease. Liver cirrhosis is a major risk factor for the development of liver cancer, impacting treatment outcomes. Additionally, the severity of liver cirrhosis can affect patient survival and liver function after liver cancer radical surgery. Tumor formation is a gradual process, and tumor volume can effectively reflect the tumor's growth. Larger tumors are often associated with higher pathological grades, lower tumor differentiation, and poorer prognosis. Therefore, early diagnosis and scientific treatment are essential to improve the surgical rate of liver cancer and, consequently, patient prognosis. Serum alpha-fetoprotein

(AFP) levels are a key indicator for screening liver cancer patients. Elevated AFP levels are closely related to the severity of liver cancer. AFP is a glycoprotein secreted during embryonic development. In normal individuals, AFP levels are minimal. However, if liver cell carcinoma develops, hypomethylation reactions can trigger AFP expression, resulting in a positive AFP test. Approximately 7/10 liver cancer patients have positive AFP test results. AFP levels are used to evaluate liver cancer patients' prognosis and, in conjunction with imaging and pathology techniques, improve liver cancer diagnosis rates. Thus, elevated AFP levels in postoperative primary liver cancer patients indicate possible lesion metastasis, with significant implications for prognosis. Liver cancer patients often exhibit unique vascular characteristics, allowing cancer cells to invade the portal vein and hepatic vein progressively. Imaging or postoperative pathological diagnosis may reveal portal vein or hepatic vein tumor thrombosis, indicating potential intrahepatic metastasis. Family medical history can also affect patient prognosis, as those with a family history of liver cancer have a higher recurrence rate after surgery. Vascular invasion is a significant factor affecting postoperative survival in liver cancer patients. The unique vascular supply of liver cancer often results in a change in the route of metastasis to blood dissemination, primarily involving portal vein and hepatic vein invasion. Therefore, the presence of vascular invasion indicates a certain risk of intrahepatic metastasis. Vascular invasion includes macrovascular invasion and microvascular invasion. Macrovascular invasion can be detected in imaging studies, but microvascular invasion confirmation requires postoperative pathological examination. Microvascular invasion can lead to local invasion and distant metastasis, with progressive development into macrovascular invasion. Researchers have found that the prognosis of patients with macrovascular invasion is significantly worse than those with microvascular invasion. Therefore, evaluating liver cancer patients' prognosis effectively requires a combination of pathological examination results and immunohistochemical indicators, allowing for early management and prevention of microvascular invasion, ultimately improving postoperative survival rates [15].

In conclusion, there are multiple factors influencing the prognosis of primary liver cancer patients. In clinical practice, comprehensive consideration of independent risk factors is essential. Follow-up and timely treatment should be provided to improve patient prognosis.

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