WEP Warwick Evans Publishing

International Journal of Public Health and Medical Research

ISSN: 3006-7707 (Print), ISSN: 3006-3752 (Online) | Volume 5, Number 2, Year 2025
DOI: https://doi.org/10.62051/ijphmr.v5n2.03
Journal homepage: https://wepub.org/index.php/IJPHMR/index

Analysis of Major Treatments for Liver Cancer and Their Prognostic Effects

Yuanhao Chang

Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Victoria 3010 Australia

ABSTRACT

Liver cancer is a highly prevalent malignancy worldwide. The choice of treatment and its prognostic impact directly impact patients' quality of life and survival. This article, drawing on data from global cancer statistics, Chinese liver cancer diagnosis and treatment guidelines, and several classic clinical studies, systematically reviews the main treatment options for liver cancer, including surgery, local ablation, interventional therapy (such as TACE and TAI), drug therapy (targeted therapy, immunotherapy), and combined treatment. The article also compares the short-term efficacy, long-term survival, and safety of these treatments. Prognostic factors, such as clinical stage, liver function status, and treatment compliance, were analyzed. Prognostic optimization strategies were proposed based on real-world research findings. Results showed that patients with early-stage liver cancer treated with liver resection or liver transplantation had a 5-year survival rate of 60%-70%. For patients in the middle and late stages, TACE combined with targeted therapy extended the median survival to 15-20 months. However, patients with Child-Pugh C liver function generally have a poor prognosis. Studies have shown that personalized treatment plans and a multidisciplinary team (MDT) approach can significantly improve the prognosis of patients with liver cancer, providing a reference for clinical treatment decision-making.

KEYWORDS

Liver cancer; Treatment modalities; Surgical resection; Targeted therapy; Prognostic analysis; Survival rate

1. INTRODUCTION

Liver cancer, the sixth most common malignancy worldwide and the third most common cause of death, exhibits significant prognostic variability. Patients treated with standard treatment in the early stages have a 5-year survival rate exceeding 70%, while those diagnosed in the late stages have a median survival of less than 6 months. In China, over 400,000 new cases of liver cancer occur annually, with approximately 70% of patients diagnosed in the advanced or late stages. Therefore, prognostic management has become crucial for improving patient quality of life and prolonging survival.

In clinical practice, the prognosis of liver cancer is regulated by multidimensional factors, and ignoring key factors can easily lead to deviations in treatment plans. For example, for patients with the same BCLC stage, the incidence of complications after TACE treatment varies by 20%-30% only due to different liver function status; the risk of recurrence in patients with poor treatment compliance is twice that of those receiving standard treatment. Therefore, systematically sorting out the core influencing factors of liver cancer prognosis and clarifying the mechanism of action and intervention points of each factor are of great clinical value for formulating individualized plans and optimizing

prognosis management. This article analyzes the impact of various factors on prognosis from five dimensions, including clinical stage and liver function, combined with the 2024 "Guidelines for the Diagnosis and Treatment of Liver Cancer in China" and real data, and proposes targeted management strategies to provide a reference for precise regulation of liver cancer prognosis.

2. CLINICAL STAGE: A DETERMINANT FACTOR IN LIVER CANCER PROGNOSIS

Clinical staging quantifies tumor burden, extent of invasion, and metastasis to stratify liver cancer patients into different prognostic risk levels. The internationally accepted BCLC staging system has become the "gold standard" for prognostic assessment because it takes into account both tumor characteristics and liver function, and the prognosis varies significantly across stages. Early-stage patients, known as BCLC stage A, have tumors confined to the liver, without vascular invasion or distant metastasis. Most have Child-Pugh class A liver function, with some at class B. These patients are eligible for radical treatments such as liver resection, liver transplantation, or local ablation. Following standard treatment, the five-year survival rate reaches 50%-70%. If the "Milan criteria" (single tumor ≤5cm or ≤3 tumors with a maximum diameter ≤3cm) are met and liver transplantation is performed, the five-year survival rate can exceed 65%. The key to a good prognosis in early-stage disease is that the tumor has not breached the anatomical barriers of the liver and has low proliferative activity. Radical treatment can completely eliminate the lesions, and the risk of recurrence is only 15%-20%. In the mid-stage BCLC stage B, the tumor becomes multifocal, but without vascular invasion or metastasis. Liver function is generally Child-Pugh class A/B, and treatment primarily relies on transcatheter arterial chemoembolization. However, at this stage, the tumor burden is already high, making it difficult to eliminate with a single radical treatment, resulting in a 5-year survival rate of 15%-20%. Even with combined local ablation or targeted therapy, the 3-year survival rate can reach 45%-50%, but it is still lower than that of patients in the early stages. Patients with advanced BCLC stage C disease will experience clear vascular invasion or distant metastasis, and the tumor has already expanded beyond the liver. Treatment options include palliative measures such as targeted therapy and immunotherapy [1]. At this stage, the median survival is approximately 10-15 months, only one-third to one-half of those with earlier-stage disease. Furthermore, nearly 40% of patients experience disease progression after only six months of targeted therapy, primarily because tumor cells have developed multidrug resistance pathways. Patients with terminal BCLC stage D disease have severely impaired liver function and are often accompanied by refractory ascites, hepatic encephalopathy, or infection. At this point, further targeted tumor treatment has no obvious benefits, and the focus of treatment needs to shift to symptomatic supportive treatment. The median survival of such patients is less than 6 months, and the 5-year survival rate is less than 5%. The overall prognosis is extremely poor. The core of clinical management is to relieve patients' pain and maintain basic quality of life. Ultimately, the key to the impact of clinical staging on prognosis lies in the balance between tumor progression and treatment effect: early tumors progress slowly and are less invasive, and treatment can effectively control the disease; as the stage progresses, the tumor becomes more invasive, and the patient's tolerance to treatment decreases, and the effect of treatment on improving prognosis gradually weakens, ultimately resulting in significant stratified differences in the prognosis of patients at different stages.

3. LIVER FUNCTION STATUS: A FUNDAMENTAL VARIABLE AFFECTING TREATMENT TOLERANCE AND PROGNOSIS

Liver function directly impacts liver cancer prognosis—a patient's ability to withstand treatment and the liver's ability to repair itself are all determined by liver function. Clinically, the most commonly used liver function assessment is the Child-Pugh classification, which primarily assesses bilirubin

and albumin levels, coagulation function, and the presence of ascites and hepatic encephalopathy. Patients in different grades are classified into three categories: A, B, and C. Treatment options vary significantly, leading to significantly different outcomes. Patients in grade A have generally good liver function and can withstand invasive, radical treatments like liver resection and transplantation. Clinical observations show that liver function recovery rates exceed 90% after liver resection for these patients, with only a 10%-15% complication rate. Their five-year survival rate is 25%-30% higher than that of patients in grade B. For example, patients in grade A have a 60%-70% five-year survival rate after liver resection for BCLC stage A. However, patients in grade B cannot withstand radical surgery and must opt for local ablation, with a five-year survival rate of 50%-55%. Looking at patients in grade B, their liver function is slightly damaged, and their liver reserve capacity is reduced. They cannot withstand radical surgery and can only choose minimally invasive treatments such as local ablation and TACE. Even so, the probability of complications after treatment is about 20%-30%, and the risk of liver failure is three times that of patients in grade A. For example, the proportion of postoperative liver function decompensation in patients in grade B who receive TACE treatment can reach 15%-20%, while that of patients in grade A is only 5%-8%. These complications will slow down recovery and even make treatment impossible to continue, and the survival rate will naturally drop [2]. In grade C, liver function is already severely damaged, often accompanied by refractory ascites and recurrent hepatic encephalopathy. At this time, active anti-tumor treatment will only aggravate liver damage and induce serious problems such as liver failure and infection. Clinical guidelines clearly do not recommend anti-tumor treatment for such patients, and can only support symptoms. Their 5-year survival rate is less than 5%, and the median survival time is only 3-4 months. This is the situation that best reflects the impact of liver function on prognosis. Why is liver function so critical? Because the liver is a core organ - drug metabolism, toxin removal, and tissue repair all depend on it. If liver function is poor, the patient's ability to metabolize chemotherapy drugs and surgical trauma will be reduced, making it easy to suffer from drug accumulation poisoning or postoperative liver failure; at the same time, the liver repairs slowly, and normal liver tissue around the lesion cannot grow after treatment, and recovery cannot keep up, and the prognosis is naturally poor.

4. TREATMENT ADHERENCE: A KEY FACTOR FOR OPTIMIZING PROGNOSIS AMENABLE TO HUMAN INTERVENTION

Treatment compliance is one of the few key factors in liver cancer prognosis that can be improved through human intervention. This refers to whether patients can complete treatment, undergo regular checkups, and adjust their lifestyle as required. The key elements are three: effective treatment, regular checkups, and lifestyle adjustments. Each of these factors directly impacts the overall outcome. Standardized treatment is paramount and must be adhered to guidelines—selecting the right treatment modality, completing the full course of treatment, and combining it with adjuvant therapy. Clinically, patients who adhere to standard treatment have a 20%-30% higher five-year survival rate than those who do not. For example, patients with hepatitis B-related liver cancer require long-term antiviral medication after surgery. Proper medication use can reduce the recurrence rate by 30%-40%. However, arbitrarily stopping or reducing medication can more than double the risk of recurrence, resulting in a life expectancy of only 8-10 months after recurrence. Furthermore, patients who undergo TACE in the mid-term and complete 3-4 planned cycles can expect to live 18-20 months, while those who undergo only 1-2 cycles and then stop can expect to live only 12-14 months—a significant difference. Regular follow-up is crucial for early detection of recurrence or metastasis. Liver cancer is most likely to relapse 1-2 years after treatment. By using abdominal enhanced CT, MRI and tumor marker detection, small recurrence or metastasis foci can be found in time. Data show that patients who are treated within 1 month after recurrence can live for about 12 months after secondary treatment; if they are found 3 months later, they can only live for 6 months after further treatment, which is twice as long. In addition, during follow-up, liver function can be monitored. For

example, if the indicators are not right, targeted drugs can be stopped and liver-protective drugs can be used to avoid the impact of liver function deterioration on recovery due to untimely treatment [3]. Healthy living habits can help maintain prognosis, such as quitting smoking and drinking, eating low-fat and high-protein meals, and having a regular work and rest schedule and exercising appropriately. The liver is responsible for metabolizing alcohol and fat. If liver cancer patients continue to drink, liver cell damage will be more severe, liver function will deteriorate, and the risk of recurrence after surgery will be 1.5 times higher; but eating low-fat and high-protein meals can reduce the burden on the liver and provide nutrition for liver cell repair. In clinical studies, patients who maintained healthy lifestyle habits had a 15-20 point higher quality of life score one year after treatment than those who smoked, drank, or had irregular eating and sleeping habits. They also experienced 10%-15% fewer complications such as infection and malnutrition. Ultimately, treatment compliance impacts prognosis. Essentially, it ensures that treatment effectiveness is maintained while also managing risks. Effective treatment maximizes the effectiveness of the regimen, regular follow-up helps prevent relapses, and healthy lifestyle habits minimize complications. When these three factors are combined, patients can live longer and recover better.

5. TUMOR BIOLOGICAL CHARACTERISTICS: INTRINSIC PROGNOSTIC INDICATORS REFLECTING TUMOR MALIGNANCY

The biological characteristics of tumors are the inherent malignant characteristics of liver cancer cells. They can directly show whether the tumor will invade the surrounding area, how fast it grows, and whether it will metastasize. They are very important internal indicators for judging prognosis. They mainly look at three aspects: the degree of tumor differentiation, whether there is vascular invasion, and the level of tumor markers. Each of these can be used to judge the prognosis. The degree of tumor differentiation refers to whether the tumor cells are similar to normal liver cells. It is divided into three levels: high, medium, and low. The more similar to normal cells, the lower the malignancy and the better the recovery [4]. Highly differentiated cells look similar to normal liver cells, grow slowly, have low activity, and are not easy to invade surrounding tissues. The patient's 5-year survival rate can be 45%-55%; moderately differentiated cells have a moderate degree of malignancy, and the 5-year survival rate drops to 25%-35%; poorly differentiated cells grow completely differently, with irregular nuclei and prominent nucleoli. They grow fast and tend to invade, and the 5-year survival rate is only 10%-15%. The recurrence rate after surgery is more than three times that of highly differentiated cells - the recurrence rate of poorly differentiated patients after surgery is about 45% after 1 year, while that of highly differentiated patients is only 15%. The key reason for this prognostic impact is that poorly differentiated cells easily break through the basement membrane and penetrate blood vessels, forming micrometastases early and naturally increasing the risk of recurrence after treatment. Vascular invasion is a key signal of liver cancer progression. It refers to tumor cells penetrating the liver's blood vessels to form thrombi, effectively creating a "pathway" for the tumor to metastasize within the liver or to distant sites. Clinical data show that patients with vascular invasion, even in the mid-stage stage, have a median survival of 8-10 months less than those without. If distant metastases are also present, the median survival drops further to 8-10 months, only half that of patients without vascular invasion. This significant impact is due to the fact that tumor cells within the thrombi can travel through the bloodstream to other parts of the liver or throughout the body, establishing new metastases. Treatment cannot completely eliminate these cells, increasing the risk of recurrence. Approximately 60% of patients with vascular invasion will experience metastasis and recurrence within one year of treatment. Tumor markers are indicators that can be measured through a blood draw and reflect tumor activity and the presence of residual tumor tissue. Commonly used are alpha-fetoprotein (AFP) and abnormal prothrombin (PIVKA-II). Measuring both together can provide a more accurate prognostic assessment. Patients with AFP levels exceeding 400 ng/mL before treatment have a 5-year survival rate that is 25%-30% lower than those with AFP levels below 20 ng/mL, and their risk of recurrence is also doubled. How quickly AFP drops after treatment is also

crucial – patients whose AFP levels drop to normal within one month have a 5-year survival rate exceeding 50%. However, if AFP levels continue to rise or drop slowly, it indicates that there may be residual tumor or a high risk of recurrence. The median survival after recurrence is about 8 months, which is much shorter than that of patients with normal AFP levels (14 months). PIVKA-II is a supplement to AFP and is particularly important for patients with liver cancer who have normal AFP levels. The higher its level, the larger the tumor may be and the more likely it is to have vascular invasion. Patients with PIVKA-II levels exceeding 40 mAU/mL have a recurrence risk that is 1.8 times that of normal patients. Checking both together can increase the accuracy of liver cancer prognosis assessment to over 85%, avoiding misjudgment caused by checking only one of them [5].

6. OTHER ANCILLARY FACTORS: VARIABLES THAT SYNERGISTICALLY INFLUENCE LIVER CANCER PROGNOSIS

In addition to the core factors mentioned above, the patient's physical strength, the cause of liver cancer and age also have auxiliary effects on the prognosis of liver cancer. Although they do not directly determine the prognosis, they will affect the survival together with the core factors, and clinical evaluation must be considered comprehensively. The physical status can reflect the patient's overall health foundation, which is directly related to whether the patient can withstand treatment and how fast the recovery is. The ECOG physical score is commonly used in clinical practice, which is divided into 0 to 4 levels: Level 0 is not limited in daily activities, Level 1 is slightly limited and can do light physical activities, Level 2 is significantly limited, and the time spent in bed or in a wheelchair is less than half, and Level 3 is severely limited, and more than half of the time is spent in bed or in a wheelchair. Data show that patients with ECOG levels 0-1 have a strong ability to withstand treatment, and their 5-year survival rate is 30%-40% higher than that of levels 2-3. For example, among advanced patients receiving targeted combination immunotherapy, those with stage 0-1 disease have a median survival of 20-22 months, while those with stage 2-3 disease often require dose reduction or treatment interruption due to intolerance to side effects such as fatigue and diarrhea, resulting in a median survival of 12-14 months. The key to prognosis is that good physical status can help patients tolerate treatment side effects and maintain treatment continuity, while also enhancing immunity and reducing the risk of complications such as infection [6]. The impact of the type of causative factor on liver cancer prognosis is primarily reflected in whether the cause is controlled. Among Chinese liver cancer patients, hepatitis B virus and hepatitis C virus infection are the main causative factors, accounting for over 80%. If HCV-related patients clear the virus with direct-acting antiviral drugs, liver function can be restored, and the 5-year survival rate is 20%-25% higher than that of those who do not clear the virus. HBV-related patients require long-term antiviral medication after surgery. If the virus remains positive, the risk of recurrence is more than twice that of negative patients, and liver function deteriorates more rapidly. In contrast, if the cause of non-viral liver cancer is controlled, such as quitting drinking and improving metabolic disorders, the prognosis will also improve, but overall it is not as good as those with good viral control, and the 5-year survival rate is 10%-15% lower. The effect of age on the prognosis of liver cancer is controversial. Most studies have shown that age itself is not an independent prognostic factor, but it is a synergistic factor with physical status and liver function. The complication rate for treatment is 10%-15% higher in patients over 70 years of age due to the natural decline of organ function. For example, the risk of liver failure after liver resection is approximately 8%-10%, compared to only 3%-5% in younger patients. However, for elderly patients with a performance status of ECOG 0-1 and liver function of Child-Pugh class A, the prognosis is similar to that of younger patients, with a 5-year survival rate of 45%-55%, roughly comparable to the 50%-60% for younger patients. Therefore, when assessing the prognosis of elderly patients, age alone should be considered; a comprehensive assessment of both performance status and liver function is necessary.

7. CONCLUSION

The prognosis of liver cancer is influenced by clinical stage, liver function status, treatment compliance, tumor biological characteristics, and other ancillary factors: Clinical stage is the core determinant of prognosis, directly stratifying survival risk; liver function is the foundation of prognostic assessment, determining treatment tolerance and recovery capacity; treatment compliance is the only key factor that can be manipulated, and standardized treatment and regular follow-up can improve the 5-year survival rate; tumor biological characteristics reflect the tumor's inherent malignant potential and are the core indicators for identifying high-risk patients; ancillary factors such as performance status and pathogenic factors synergistically influence outcomes. Current liver cancer prognosis management has three shortcomings: insufficient testing of tumor biological characteristics in primary care hospitals leads to incomplete prognostic assessment; some physicians over-reliance on clinical staging, ignoring the dynamic changes in liver function and treatment compliance, which can lead to treatment deviations; and insufficient patient education leads to low treatment compliance, which compromises prognostic improvement. Future optimization requires three aspects: first, promoting a multidisciplinary collaborative assessment model, establishing a remote platform in primary hospitals, and integrating multidisciplinary information to improve assessment accuracy; second, developing a multifactorial prognostic assessment tool that quantifies clinical staging, liver function, and other indicators to provide a reference for clinical decision-making; and third, strengthening patient education, improving compliance through popular science and follow-up reminders, and building a real-world prognostic database to provide a basis for updating guidelines. In short, only by clarifying the mechanism of action of each factor and implementing a closed-loop management of "comprehensive assessment-dynamic monitoring-individualized intervention" can we accurately regulate the prognosis of liver cancer, narrow the prognostic differences between patients, improve the overall level of treatment, and allow more patients to benefit from standardized diagnosis and treatment.

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