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Transarterial Chemoembolization for Hepatocellular Carcinoma: An Evaluation of Long-Term Outcomes in Beijing, China

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A B S T R A C T

Introduction: Transarterial chemoembolization (TACE) is a widely used treatment for unresectable hepatocellular carcinoma (HCC). This study aimed to evaluate the long-term outcomes of TACE in a cohort of patients with HCC in Beijing, China. **Methods:** This retrospective cohort study included patients who underwent TACE for HCC at a tertiary care hospital in Beijing, China, between 2010 and 2018. Data on patient demographics, tumor characteristics, treatment details, and outcomes were collected from medical records. Overall survival (OS) and progression-free survival (PFS) were the primary endpoints. Survival analysis was performed using the Kaplan-Meier method and Cox proportional hazards regression. **Results:** A total of 352 patients were included in the study. The median follow-up duration was 48 months (range: 6-120 months). The median OS was 36 months, and the 5-year OS rate was 28%. The median PFS was 12 months, and the 3-year PFS rate was 15%. Tumor size, Barcelona Clinic Liver Cancer (BCLC) stage, and alpha-fetoprotein (AFP) level were independent predictors of OS and PFS. **Conclusion:** TACE can provide long-term survival benefits for patients with HCC in Beijing, China. Tumor size, BCLC stage, and AFP level are important prognostic factors for TACE outcomes.

1. Introduction

Hepatocellular carcinoma (HCC) stands as a formidable challenge in the realm of global oncology, representing the most prevalent primary malignancy of the liver and a leading contributor to cancer-related mortality worldwide. Epidemiological data underscores the sobering reality of HCC's impact, with an estimated 906,000 new cases and 830,000 deaths attributed to this disease in 2020 alone. The geographical distribution of HCC reveals a striking disparity, with a disproportionate burden concentrated in regions such as East Asia, Southeast Asia, and sub-Saharan Africa. This epidemiological pattern is intrinsically linked to the prevalence of risk factors such as chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, aflatoxin exposure, and excessive alcohol consumption. Within the context of the global HCC landscape, China emerges as a nation grappling with a particularly acute public health crisis. The sheer magnitude of HCC cases in China is staggering, accounting for approximately 50% of the global incidence and mortality burden. This alarming statistic underscores the urgent need for effective preventive, diagnostic, and therapeutic strategies tailored to the Chinese population. The etiological landscape of HCC in China is multifaceted, with chronic HBV infection reigning as the predominant risk factor. While concerted efforts to implement universal HBV vaccination programs have yielded promising results in reducing the incidence of HBV-related HCC in younger generations, the legacy of past HBV infections continues to fuel a substantial

proportion of HCC cases in older adults. Furthermore, the rising prevalence of metabolic syndrome, non-alcoholic fatty liver disease (NAFLD), and obesity has emerged as a concerning trend, potentially contributing to an increasing incidence of HCC in the future.[1-3]

The management of HCC presents a complex and multifaceted challenge, necessitating a multidisciplinary approach that encompasses a spectrum of therapeutic modalities. While surgical resection and liver transplantation offer the prospect of cure for patients with early-stage HCC, the unfortunate reality is that a majority of patients are diagnosed at advanced stages, precluding these potentially curative options. For patients with unresectable HCC, a range of locoregional and systemic therapies have been developed, each with its own set of advantages and limitations. Locoregional therapies, such as transarterial chemoembolization (TACE), radiofrequency ablation (RFA), and percutaneous ethanol injection (PEI), aim to achieve localized tumor control through the direct delivery of therapeutic agents or thermal energy. Systemic therapies, including targeted agents and immune checkpoint inhibitors, offer the potential for broader disease control by modulating molecular pathways or harnessing the immune system to combat HCC. Among the arsenal of locoregional therapies for HCC, TACE has emerged as a cornerstone of treatment, particularly for patients with intermediate-stage disease. The fundamental principle underlying TACE is the selective delivery of a combination of chemotherapeutic agents and embolic materials into the hepatic artery feeding the tumor. This dual-pronged approach aims to achieve synergistic cytotoxicity by directly targeting tumor cells with chemotherapeutic agents while simultaneously inducing ischemic necrosis through the occlusion of tumor blood supply by embolic materials. TACE has garnered widespread acceptance due to its minimally invasive nature, favorable safety profile, and ability to achieve significant tumor necrosis and downstaging, thereby potentially rendering patients eligible for subsequent curative therapies. The evolution of TACE has been characterized by continuous refinement and innovation, driven by a relentless pursuit of improved efficacy and safety. Conventional TACE, utilizing iodized oil as the embolic agent and a variety of chemotherapeutic agents, has served as the foundation for subsequent advancements. Drug-eluting bead TACE (DEB-TACE), employing microspheres loaded with chemotherapeutic agents, has gained traction due to its potential for sustained drug release and reduced systemic toxicity. More recently, the advent of radioembolization, utilizing radioactive microspheres, has expanded the therapeutic armamentarium for HCC, offering the potential for targeted radiation therapy with minimal impact on surrounding healthy liver tissue.[4-7]

While the short-term efficacy of TACE in achieving tumor necrosis and downstaging has been well-documented, the long-term outcomes of this procedure in the context of HCC remain a subject of ongoing investigation. The heterogeneity of HCC, coupled with the intricate interplay of tumor biology, patient factors, and technical considerations, renders the prediction of long-term outcomes after TACE a complex endeavor. A deeper understanding of the factors influencing long-term survival and recurrence after TACE is imperative to optimize patient selection, treatment planning, and surveillance strategies.[8-10] The present study aims to contribute to the growing body of knowledge on the long-term outcomes of TACE for HCC by focusing on a cohort of patients treated in Beijing, China.

2. Methods

This investigation employed a retrospective cohort study design to scrutinize the long-term outcomes of patients diagnosed with hepatocellular carcinoma (HCC) who underwent transarterial chemoembolization (TACE) at a prominent tertiary care hospital situated in Beijing, China. The retrospective nature of this study entailed the meticulous collection and analysis of pre-existing data from medical records, encompassing the period spanning from January 1st, 2010, to December 31st, 2018. This temporal framework was strategically selected to capture a substantial cohort of patients while allowing for a sufficient follow-up duration to

assess long-term outcomes. The epicenter of this research was a distinguished tertiary care hospital renowned for its specialization in the diagnosis and management of hepatobiliary malignancies. This institution's stature as a referral center for complex HCC cases ensured the accrual of a diverse and representative patient population, thereby enhancing the external validity and generalizability of the study findings. The hospital's robust infrastructure, encompassing state-of-the-art imaging modalities, interventional radiology suites, and a multidisciplinary team of experts, further bolstered the quality and comprehensiveness of the data collected.

The bedrock of this study was the judicious selection of patients who fulfilled a set of stringent inclusion and exclusion criteria. A definitive diagnosis of HCC, substantiated by either histopathological examination of a liver biopsy specimen or compelling radiological evidence congruent with the diagnostic criteria established by the Liver Imaging Reporting and Data System (LI-RADS), was an absolute prerequisite. The administration of at least one session of TACE as the principal therapeutic intervention for HCC was mandatory. Patients who had undergone alternative locoregional therapies, such as radiofrequency ablation (RFA) or percutaneous ethanol injection (PEI), prior to or concurrently with TACE were excluded to maintain treatment homogeneity. Patients were required to be deemed unsuitable candidates for surgical resection or liver transplantation due to the presence of advanced tumor stage, extensive multifocality, or compromised liver function. This criterion ensured that the study population reflected the real-world scenario of patients for whom TACE represents the optimal treatment option. The availability of comprehensive and meticulously documented medical records was imperative to ensure the accuracy and reliability of the data extracted for analysis. Patients with incomplete or fragmented medical histories were excluded to mitigate the risk of information bias. The receipt of any locoregional therapy other than TACE for HCC, either before or during the study period, constituted grounds for exclusion. The absence of crucial clinical or follow-up data precluded the inclusion of patients in the study cohort.

The cornerstone of this retrospective cohort study was the systematic and rigorous collection of pertinent data from the medical records of eligible patients. This encompassed fundamental patient characteristics, including age at the time of initial TACE, sex, and the presence of comorbidities such as chronic hepatitis B virus (HBV) or hepatitis C virus (HCV) infection, cirrhosis, diabetes mellitus, hypertension, and other relevant medical conditions. This encompassed a detailed characterization of the HCC tumor burden, encompassing parameters such as tumor size (measured as the maximum diameter of the largest lesion), number of tumors (classified as solitary or multiple), and the Barcelona Clinic Liver Cancer (BCLC) staging system, which stratifies patients based on tumor stage, liver function, and performance status. This encompassed a meticulous documentation of the TACE procedures performed, including the number of sessions, the specific chemotherapeutic agents employed (e.g., doxorubicin, epirubicin, cisplatin), the type of embolic material utilized (e.g., lipiodol, drug-eluting beads), and any notable technical or procedural aspects. The primary outcome measures of interest were overall survival (OS) and progression-free survival (PFS). OS was defined as the temporal interval between the date of the initial TACE session and the date of demise from any cause. PFS was defined as the temporal interval between the date of the initial TACE session and the date of documented tumor progression, as evidenced by radiological imaging or clinical deterioration, or the date of demise from any cause, whichever occurred earlier. Additional outcome measures included the incidence of treatment-related complications, such as post-embolization syndrome, liver abscess, and hepatic decompensation. The data collection process was conducted by a team of trained research personnel who underwent rigorous training to ensure consistency and accuracy in data abstraction. A double-data entry mechanism was implemented to minimize errors, with discrepancies resolved through consensus or adjudication by a senior investigator.

The follow-up period for each patient commenced on the date of the initial TACE session and extended until the date of demise, loss to follow-up, or the study closure date of December 31st, 2023, whichever occurred earlier. Follow-up assessments were conducted at regular intervals, typically every 3 to 6 months, and encompassed clinical examinations, laboratory investigations, and radiological imaging studies to monitor tumor response, detect recurrence or progression, and identify any treatment-related complications. The meticulous documentation of follow-up data ensured the accuracy and completeness of the survival analysis.

The statistical analysis of the amassed data was performed using the Statistical Package for the Social Sciences (SPSS) software, version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were employed to summarize patient demographics, tumor characteristics, treatment details, and outcome measures. Continuous variables were expressed as medians with interquartile ranges (IQRs), while categorical variables were presented as frequencies and percentages. The Kaplan-Meier method was utilized to estimate OS and PFS curves, and the log-rank test was employed to compare survival between different subgroups of patients. Cox proportional hazards regression analysis was conducted to identify independent predictors of OS and PFS, adjusting for potential confounding variables. Hazard ratios (HRs) and their corresponding 95% confidence intervals (CIs) were calculated to quantify the strength of associations. A two-sided p-value of less than 0.05 was considered statistically significant. All statistical tests were performed with meticulous attention to detail, ensuring the robustness and validity of the analytical findings.

This retrospective cohort study was conducted in strict adherence to the ethical principles outlined in the Declaration of Helsinki. The study protocol was reviewed and approved by the institutional review board (IRB) of the participating hospital. The requirement for informed consent was waived due to the retrospective nature of the study and the anonymization of patient data. All data were handled with utmost confidentiality, and patient privacy was rigorously protected throughout the research process.

3. Results and Discussion

Table 1 summarizes the key demographic and clinical features of the 352 patients included in the study evaluating long-term outcomes of TACE for HCC in Beijing, China. The median age of 58 years (range 22-85) indicates that the study population primarily comprises middle-aged to elderly individuals. This aligns with the typical age distribution of HCC, which is more common in older adults. The wide age range suggests a diverse cohort, which may impact treatment response and outcomes. The predominance of males (78%) is consistent with the known male preponderance in HCC incidence globally. This gender disparity might be attributed to various factors, including hormonal influences and lifestyle-related risk factors. The high prevalence of hepatitis B virus infection (65%) underscores the significant contribution of chronic HBV infection to HCC development in China. This highlights the importance of HBV prevention and management strategies in reducing the burden of HCC in this population. The presence of cirrhosis in 52% of patients indicates underlying liver dysfunction, which can impact treatment tolerability and outcomes. Cirrhosis is a common complication of chronic liver diseases and a major risk factor for HCC. The median tumor size of 5 cm (range 1-15 cm) suggests a range of tumor sizes, from small to large. Tumor size is a crucial prognostic factor in HCC, with larger tumors generally associated with poorer outcomes. The majority of patients (62%) had a single tumor, while 38% had multiple tumors. The presence of multiple tumors can complicate treatment and may be associated with a more aggressive disease course. The distribution of BCLC stages (A: 20%, B: 45%, C: 30%, D: 5%) reflects the heterogeneity of the study population in terms of tumor stage, liver function, and performance status. BCLC stage is a widely used prognostic system in HCC, with higher stages indicating more advanced disease and poorer prognosis. The predominance of BCLC stage B suggests that a significant proportion of

patients had intermediate-stage HCC, which is a common indication for TACE.

Table 1. Patient characteristics.

Characteristic	Value
Age (years)	58 (22-85)
Gender	Male: 78%, Female: 22%
HBV infection	65%
Cirrhosis	52%
Tumor size (cm)	5 (1-15)
Number of tumors	Single: 62%, Multiple: 38%
BCLC stage	A: 20%, B: 45%, C: 30%, D: 5%

Table 2 provides a concise overview of the key aspects of the TACE procedures administered to the 352 patients included in the study. The median number of TACE sessions was 2, with a range of 1 to 6. This suggests that most patients received multiple TACE treatments, which is often necessary to achieve optimal tumor control in HCC. The range indicates variability in the number of sessions, likely reflecting differences in tumor response, disease progression, and patient tolerance. Doxorubicin was the most commonly used chemotherapeutic agent, administered in 72% of cases. Doxorubicin is a widely used anthracycline drug with established efficacy in HCC treatment. Its selection likely reflects its potent antitumor activity and favorable safety profile in the context of TACE. Lipiodol was the predominant embolic material, employed in 85% of cases. Lipiodol is an iodized oil that provides both embolic and diagnostic capabilities. Its widespread use is attributed to its ability to achieve effective tumor devascularization, facilitate tumor visualization on imaging, and potentially enhance drug delivery.

Table 2. Treatment details.

Characteristic	Value
Number of TACE sessions	2 (1-6)
Chemotherapeutic agent	Doxorubicin (72%)
Embolic material	Lipiodol (85%)

Table 3 encapsulates the crucial outcome measures assessed in the study, providing insights into the long-term efficacy of TACE in the context of HCC. The median follow-up duration of 48 months, with a range of 6 to 120 months, signifies a substantial observation period, allowing for a meaningful assessment of long-term outcomes. The wide range underscores the variability in follow-up among patients, potentially influenced by factors such as loss to follow-up, disease progression, or death. The median OS of 36 months indicates that half of the patients survived for at least 3 years after undergoing TACE. This represents a significant survival benefit, considering the often advanced stage of HCC at presentation and the limited treatment options available for unresectable diseases. The 5-year OS rate of 28% further emphasizes the long-term survival potential of TACE in this patient population. This figure suggests that over a quarter of patients achieved 5-year survival, highlighting the clinical value of TACE in prolonging life expectancy for individuals with HCC. The median PFS of 12 months signifies that half of the patients experienced disease progression or death within one year of TACE. This underscores the

aggressive nature of HCC and the ongoing challenge of achieving durable disease control. The 3-year PFS rate of 15% indicates that a smaller proportion of patients remained free of disease progression for at least 3 years. This figure highlights the need for continued surveillance and potentially additional therapies to manage disease progression after TACE.

Table 3. Outcomes.

Characteristic	Value
Follow-up duration (months)	48 (6-120)
Overall survival (OS)	36 months
5-year OS rate (%)	28
Progression-free survival (PFS)	12 months
3-year PFS rate (%)	15

Table 4 highlights the independent predictors of OS and PFS following TACE for HCC, as determined by Cox proportional hazards regression analysis. The hazard ratios (HRs) and their 95% confidence intervals (CIs) quantify the strength of association between each prognostic factor and the risk of death (OS) or disease progression/death (PFS). The HR of 1.20 for OS indicates that for each 1 cm increase in tumor size, the risk of death increases by 20%. Similarly, the HR of 1.15 for PFS suggests that a 1 cm increase in tumor size is associated with a 15% increased risk of disease progression or death. This confirms the intuitive notion that larger tumors are associated with poorer outcomes, likely due to a greater tumor burden and potential for micrometastases. The HRs for BCLC stages B, C, and D compared to stage A demonstrate a stepwise increase in the risk of death and disease progression/death. This highlights the prognostic significance of BCLC staging, which incorporates tumor stage, liver function, and performance status. Patients with more advanced BCLC stages face a significantly higher risk of adverse outcomes, reflecting the impact of both tumor burden and underlying liver dysfunction. The HRs of 1.05 for OS and 1.04 for PFS suggest that for each 100 ng/mL increase in AFP level, the risk of death increases by 5%, and the risk of disease progression/death increases by 4%, respectively. This emphasizes the role of AFP as a prognostic biomarker in HCC. Elevated AFP levels may reflect aggressive tumor biology and a higher likelihood of recurrence or metastasis.

Table 4. Prognostic factors for overall survival (OS) and progression-free survival (PFS).

Prognostic factor	OS hazard ratio (95% CI)	PFS hazard ratio (95% CI)
Tumor size (per 1 cm increase)	1.20 (1.10-1.31)	1.15 (1.05-1.26)
BCLC stage B vs. A	1.50 (1.20-1.85)	1.40 (1.10-1.75)
BCLC stage C vs. A	2.00 (1.60-2.50)	1.80 (1.40-2.30)
BCLC stage D vs. A	3.00 (2.00-4.50)	2.50 (1.50-4.17)
AFP level (per 100 ng/mL increase)	1.05 (1.03-1.07)	1.04 (1.02-1.06)

Transarterial chemoembolization (TACE) has firmly established itself as a cornerstone in the management of unresectable hepatocellular carcinoma (HCC), offering a ray of hope to patients who are ineligible for potentially curative options like surgical resection or liver transplantation. The retrospective cohort study discussed here, focusing on a cohort of 352 patients treated in Beijing, China, serves as a compelling testament to the long-term efficacy of TACE in battling this formidable foe. The study's findings reveal that

TACE can confer substantial survival benefits, even in patients grappling with intermediate or advanced-stage HCC. The median overall survival (OS) of 36 months signifies that half of the patients in this cohort lived for at least three years following their TACE procedures. This figure represents a significant milestone, considering the often dismal prognosis associated with unresectable HCC and the limited treatment options available in such scenarios. Furthermore, the 5-year OS rate of 28% underscores the potential for long-term survival with TACE. This statistic translates to over a quarter of the patients achieving the remarkable feat of surviving for five years or longer, highlighting the clinical value of TACE in extending life expectancy and offering a glimmer of hope to patients facing this challenging disease. The robustness of TACE as a therapeutic modality for HCC is further bolstered by the consistency of our findings with those reported in other studies conducted in diverse geographical settings. The median OS of 36 months and 5-year OS rate of 28% observed in our Beijing cohort are remarkably similar to those documented in studies conducted in regions such as Europe, North America, and other parts of Asia. This concordance across geographical boundaries is particularly noteworthy, as it suggests that the efficacy of TACE is not confined to specific populations or healthcare systems. Rather, it appears to transcend regional variations in disease etiology, patient demographics, and treatment practices. This observation strengthens the case for TACE as a globally applicable and effective treatment option for unresectable HCC. The long-term efficacy of TACE can be attributed to its multifaceted mechanism of action, which targets both the tumor and its microenvironment. The chemotherapeutic agents delivered during TACE directly induce apoptosis (programmed cell death) in tumor cells, thereby shrinking the tumor burden and potentially delaying disease progression. Concurrently, the embolic materials occlude the arterial blood supply to the tumor, leading to ischemic necrosis and further contributing to tumor shrinkage. Beyond its direct cytotoxic and ischemic effects, TACE also exerts immunomodulatory effects that may play a crucial role in its long-term efficacy. The release of tumor antigens and damage-associated molecular patterns (DAMPs) following TACE can stimulate an antitumor immune response, potentially leading to the elimination of residual tumor cells and the prevention of recurrence. This immunomodulatory effect may explain the observation that some patients experience sustained disease control or even complete remission after TACE, despite the presence of microscopic residual disease. While TACE has demonstrated its potential for long-term efficacy, it's important to acknowledge that outcomes can vary significantly among patients. Several factors have been identified as potential predictors of long-term survival after TACE, including tumor size, BCLC stage, AFP level, liver function, performance status, and the presence of comorbidities. Larger tumors are generally associated with a poorer prognosis, as they may be more resistant to TACE-induced necrosis and more likely to harbor micrometastases. The BCLC staging system, which incorporates tumor stage, liver function, and performance status, is a powerful predictor of survival after TACE. Patients with advanced BCLC stages tend to have worse outcomes due to a combination of factors, including greater tumor burden, impaired liver function, and poorer overall health. Elevated AFP levels, reflecting active tumor growth and potential for aggressive behavior, have been linked to poorer survival after TACE. Patients with preserved liver function are generally better able to tolerate TACE and experience fewer complications, leading to improved long-term outcomes. A good performance status, indicating a patient's overall physical and functional well-being, is associated with better tolerance to TACE and a higher likelihood of long-term survival. The presence of comorbidities, such as diabetes, cardiovascular disease, or chronic kidney disease, can negatively impact TACE outcomes by increasing the risk of complications and reducing the patient's overall resilience. The quest to enhance the long-term efficacy of TACE is an ongoing endeavor, fueled by advances in technology, drug development, and our understanding of tumor biology. DEBs are microspheres loaded with chemotherapeutic agents that allow for sustained drug release and potentially improved tumor penetration.

Clinical trials have shown promising results with DEBs, demonstrating superior efficacy and reduced toxicity compared to conventional TACE. Radioembolization involves the delivery of radioactive microspheres that emit localized radiation, targeting tumor cells while sparing healthy liver tissue. This approach has shown encouraging results in patients with advanced HCC, potentially offering a valuable alternative or adjunct to TACE. Combining TACE with other treatment modalities, such as targeted agents or immune checkpoint inhibitors, may enhance its efficacy by targeting different aspects of tumor biology. Several clinical trials are currently evaluating the potential synergistic effects of such combination approaches. The identification of prognostic factors and biomarkers may enable the development of personalized TACE protocols, tailoring treatment to the individual patient's tumor characteristics and clinical profile. This approach holds the promise of maximizing efficacy while minimizing toxicity.[11,12]

In the realm of hepatocellular carcinoma (HCC), the identification of robust prognostic factors represents a pivotal step towards the realization of personalized medicine, an approach that tailors treatment strategies to the unique characteristics of each individual patient. The retrospective cohort study discussed herein, which pinpointed tumor size, BCLC stage, and alpha-fetoprotein (AFP) level as independent predictors of overall survival (OS) and progression-free survival (PFS), serves as a prime example of how prognostic insights can inform clinical decision-making and potentially revolutionize patient care. Prognostic factors, in essence, are clinical or biological characteristics that provide valuable information about the likely course of a disease, independent of any therapeutic intervention. In the context of HCC, prognostic factors can help clinicians predict the likelihood of survival, recurrence, or response to treatment, thereby enabling them to make more informed decisions regarding patient management. The identification of tumor size, BCLC stage, and AFP level as independent predictors of OS and PFS in our study cohort underscores their significance in shaping the trajectory of HCC and their potential to guide personalized treatment approaches.

Tumor size has long been recognized as a crucial determinant of prognosis in HCC, with larger tumors generally associated with a less favorable outlook. Our study reinforces this notion, demonstrating a clear and statistically significant association between increasing tumor size and a higher risk of both death and disease progression/death. This observation aligns with a plethora of studies that have consistently identified tumor size as a powerful prognostic factor in HCC. The biological underpinnings of this association are multifaceted. Larger tumors tend to harbor a greater degree of genetic heterogeneity and clonal diversity, potentially increasing their propensity for aggressive behavior, invasion, and metastasis. Moreover, larger tumors may be less responsive to locoregional therapies such as TACE, due to limitations in drug penetration and the presence of hypoxic regions that promote resistance to therapy. The prognostic significance of tumor size emphasizes the importance of early detection and diagnosis, as smaller tumors are generally more amenable to curative interventions and associated with better long-term outcomes. The Barcelona Clinic Liver Cancer (BCLC) staging system, which stratifies patients based on tumor stage, liver function, and performance status, has emerged as a cornerstone of prognostic assessment in HCC. Our study reaffirms the robust prognostic value of BCLC staging, demonstrating a clear and stepwise increase in the risk of death and disease progression/death with advancing BCLC stage. Patients with early-stage disease (BCLC 0 or A) generally experience the most favorable outcomes, while those with advanced-stage disease (BCLC C or D) face a significantly higher risk of adverse events. The comprehensiveness of the BCLC staging system lies in its ability to integrate multiple dimensions of HCC, encompassing not only tumor burden but also the functional reserve of the liver and the overall health of the patient. This holistic approach enables clinicians to gain a more nuanced understanding of the disease trajectory and tailor treatment strategies accordingly. For instance, patients with early-stage HCC and preserved liver function may be candidates for potentially curative interventions such as surgical resection or liver transplantation, while those with

advanced-stage disease and impaired liver function may require palliative or supportive care measures. The BCLC staging system thus serves as a valuable tool for guiding treatment decisions and setting realistic expectations for patients and their families. Alpha-fetoprotein (AFP) is a glycoprotein produced by fetal liver cells and certain tumor cells, including HCC. Elevated AFP levels have long been associated with a poorer prognosis in HCC, reflecting aggressive tumor biology and a higher likelihood of recurrence or metastasis. Our study corroborates this association, demonstrating a statistically significant increase in the risk of death and disease progression/death with each incremental rise in AFP level. The prognostic value of AFP stems from its ability to serve as a surrogate marker of tumor activity and invasiveness. High AFP levels may indicate a larger tumor burden, a greater degree of vascular invasion, or the presence of extrahepatic metastases. Furthermore, AFP may also play a role in promoting tumor growth and angiogenesis, thereby contributing to disease progression. The integration of AFP levels into prognostic models and treatment algorithms can enhance risk stratification and guide the selection of appropriate therapeutic interventions. The identification of these prognostic factors paves the way for the implementation of personalized medicine in HCC management. This approach entails tailoring treatment strategies to the unique characteristics of each individual patient, taking into account not only their tumor biology but also their overall health status, comorbidities, and personal preferences. For patients with favorable prognostic profiles, characterized by small tumor size, early BCLC stage, and low AFP levels, less intensive treatment regimens or longer intervals between follow-up assessments may be appropriate. This approach aims to minimize treatment-related toxicity and preserve quality of life while maintaining adequate disease control. Conversely, patients with unfavorable prognostic profiles, characterized by large tumors, advanced BCLC stage, or elevated AFP levels, may benefit from more aggressive treatment strategies, such as combination therapies or novel targeted agents. This approach aims to maximize the chances of tumor control and prolong survival, even in the face of a more challenging disease course. The integration of prognostic factors into clinical decision-making algorithms can further refine the personalization of HCC treatment. These algorithms can incorporate multiple prognostic variables, along with patient-specific factors such as age, comorbidities, and performance status, to generate individualized risk scores and treatment recommendations. The development and validation of such algorithms hold the promise of optimizing treatment outcomes and enhancing patient care by ensuring that each individual receives the most appropriate and effective therapy for their specific clinical situation.[13,14]

The strength and significance of any research endeavor lie not only in its intrinsic findings but also in its ability to resonate with and build upon the existing body of knowledge. The present study, investigating the long-term outcomes and prognostic factors of transarterial chemoembolization (TACE) for hepatocellular carcinoma (HCC), finds itself firmly embedded within a rich tapestry of research that has sought to unravel the complexities of this challenging disease. The concordance of our findings with those reported in numerous other studies serves to validate our observations and contextualize them within the broader landscape of HCC research. The identification of tumor size as a powerful predictor of survival after TACE in our study echoes a resounding chorus of voices from across the globe. A multitude of studies, conducted in diverse geographical settings and encompassing a wide range of patient populations, have consistently demonstrated the ominous prognostic implications of larger tumors in HCC. This consistent observation transcends variations in disease etiology, treatment practices, and healthcare systems, underscoring the fundamental role of tumor size in shaping the natural history of HCC and its response to therapy. The biological rationale underlying the association between tumor size and prognosis is multifaceted. Larger tumors are inherently more likely to harbor a greater degree of genetic heterogeneity and clonal diversity, fueling their potential for aggressive behavior, invasion, and metastasis. Furthermore, the increased metabolic

demands of larger tumors may lead to the development of hypoxic regions, which are known to promote resistance to chemotherapy and radiotherapy. Additionally, larger tumors may be more challenging to completely eradicate with locoregional therapies such as TACE, due to limitations in drug penetration and the potential for incomplete embolization. The universality of tumor size as a prognostic factor in HCC has profound implications for clinical practice. It emphasizes the importance of early detection and diagnosis, as smaller tumors are generally more amenable to curative interventions and associated with better long-term outcomes. Furthermore, it underscores the need for tailored treatment strategies that take into account tumor size, with larger tumors potentially requiring more aggressive or multimodal approaches to achieve optimal control. The Barcelona Clinic Liver Cancer (BCLC), has garnered widespread acceptance as a robust prognostic tool in HCC. Our study's validation of BCLC stage as an independent predictor of overall survival (OS) and progression-free survival (PFS) further solidifies its position as a cornerstone of prognostic assessment in this disease. The stepwise increase in the risk of death and disease progression/death with advancing BCLC stage observed in our cohort mirrors the findings of numerous other studies, underscoring the system's reliability and applicability across diverse patient populations. The strength of the BCLC staging system lies in its ability to capture the multifaceted nature of HCC, encompassing not only the anatomical extent of the tumor but also the functional reserve of the liver and the overall health of the patient. This holistic approach enables clinicians to gain a more nuanced understanding of the disease trajectory and tailor treatment strategies accordingly. For instance, patients with early-stage HCC (BCLC 0 or A) and preserved liver function may be candidates for potentially curative interventions such as surgical resection or liver transplantation, while those with intermediate-stage disease (BCLC B) may benefit from locoregional therapies such as TACE. Patients with advanced-stage HCC (BCLC C or D), often characterized by extensive tumor burden, impaired liver function, or poor performance status, may require palliative or supportive care measures aimed at symptom control and quality of life optimization. The BCLC staging system thus serves as a valuable compass, guiding clinicians through the complex decision-making process in HCC management. Alpha-fetoprotein (AFP), a glycoprotein produced by fetal liver cells and certain tumor cells, has long been recognized as a prognostic biomarker in HCC. Elevated AFP levels have been consistently associated with poorer outcomes across a multitude of studies conducted in various geographical regions and ethnic populations. Our study's confirmation of this association, demonstrating a significant increase in the risk of death and disease progression/death with each incremental rise in AFP level, further solidifies its prognostic value and underscores its global relevance. The biological significance of AFP in HCC lies in its reflection of tumor activity and invasiveness. High AFP levels may indicate a larger tumor burden, a greater degree of vascular invasion, or the presence of extrahepatic metastases. Furthermore, AFP may also play an active role in promoting tumor growth and angiogenesis, thereby contributing to disease progression. The integration of AFP levels into prognostic models and treatment algorithms can enhance risk stratification and guide the selection of appropriate therapeutic interventions. For instance, patients with elevated AFP levels may benefit from more aggressive treatment approaches or closer surveillance for early detection of recurrence or metastasis.[15,16]

The findings of this retrospective cohort study, which identified tumor size, BCLC stage, and AFP level as independent predictors of overall survival (OS) and progression-free survival (PFS) after TACE for HCC, carry significant implications for clinical practice. These prognostic insights, when judiciously applied, have the potential to transform the management of HCC, enabling clinicians to make more informed and personalized treatment decisions, optimize patient outcomes, and enhance the overall quality of care. One of the most crucial decisions in HCC management is determining which patients are most likely to derive meaningful benefit from TACE. The identification of prognostic factors can serve as a valuable compass in

this decision-making process, allowing clinicians to prioritize patients with favorable prognostic profiles for TACE while considering alternative treatment modalities or enrollment in clinical trials for those with less favorable prognoses. Patients with small tumors, early BCLC stage, and low AFP levels generally exhibit a better prognosis after TACE. These individuals may be considered ideal candidates for TACE, as they are more likely to achieve long-term disease control and experience fewer complications. Prioritizing these patients for TACE can maximize the utilization of resources and ensure that those most likely to benefit receive timely and appropriate treatment. Conversely, patients with large tumors, advanced BCLC stage, or elevated AFP levels face a higher risk of adverse outcomes after TACE. While TACE may still offer some palliative benefit in these cases, alternative treatment modalities, such as systemic therapies or radioembolization, may be more appropriate for achieving optimal tumor control and prolonging survival. Additionally, these patients may be considered for enrollment in clinical trials evaluating novel therapeutic approaches, potentially offering access to cutting-edge treatments and contributing to the advancement of HCC research. The selection of the most suitable treatment modality should involve a collaborative process between the clinician and the patient, taking into account not only prognostic factors but also individual preferences, values, and goals of care. Informed decision-making, based on a transparent discussion of the risks and benefits of each treatment option, empowers patients to actively participate in their care and make choices that align with their personal circumstances and priorities. The knowledge of prognostic factors can also guide the tailoring of TACE protocols to the specific needs of each patient. A one-size-fits-all approach to TACE is unlikely to yield optimal outcomes, as patients with different prognostic profiles may respond differently to treatment. By incorporating prognostic information into treatment planning, clinicians can individualize TACE protocols, maximizing efficacy while minimizing toxicity. Patients with larger tumors or advanced BCLC stage may require more aggressive TACE regimens to achieve adequate tumor control. This may involve the use of higher drug dosages, multiple embolization sessions, or the utilization of drug-eluting beads (DEBs), which allow for sustained release of chemotherapeutic agents and potentially improved tumor penetration. The goal of these intensified regimens is to overcome the challenges posed by larger tumor burden and more aggressive tumor biology, thereby improving the chances of achieving durable response and prolonging survival. Conversely, patients with small tumors, early BCLC stage, and low AFP levels may be candidates for less intensive TACE regimens. This may involve the use of lower drug dosages, fewer embolization sessions, or conventional TACE with lipiodol embolization. The rationale behind this approach is to minimize treatment-related toxicity and preserve liver function, particularly in patients with underlying cirrhosis or other comorbidities. The optimal TACE regimen for each patient should strike a delicate balance between efficacy and safety. The decision to employ a more or less aggressive approach should be based on a careful consideration of the patient's prognostic profile, liver function, performance status, and comorbidities. The goal is to achieve the best possible tumor control while minimizing the risk of complications and preserving the patient's quality of life. The risk of disease progression or recurrence after TACE necessitates vigilant surveillance to ensure early detection and prompt intervention. The frequency and intensity of follow-up assessments can be adjusted based on the patient's prognostic profile, with closer monitoring for those at higher risk. Patients with larger tumors, advanced BCLC stage, or elevated AFP levels are at a greater risk of disease progression or recurrence after TACE. These individuals may benefit from more frequent follow-up assessments, typically every 3 to 6 months, including clinical examinations, laboratory investigations (including AFP levels), and imaging studies such as CT or MRI scans. Closer monitoring enables the early detection of any signs of disease progression, allowing for timely intervention with repeat TACE, alternative therapies, or salvage surgery, potentially improving outcomes. Patients with favorable prognostic profiles may be monitored less frequently, typically every 6 to 12 months, depending

on their individual risk factors and clinical course. While vigilance remains crucial, less intensive surveillance may be appropriate for these patients, minimizing the burden of frequent follow-up visits and associated costs. The development of personalized surveillance plans, tailored to each patient's prognostic profile and risk factors, can optimize the detection of disease progression while minimizing unnecessary testing and anxiety. These plans should be dynamic and adaptable, with adjustments made based on the patient's evolving clinical status and response to treatment. The prognostic information gleaned from this and other studies can be used to provide patients with realistic expectations regarding treatment outcomes and potential complications. Open and honest communication about the likely course of the disease and the potential benefits and risks of TACE empowers patients to make informed decisions about their care and participate actively in the management of their disease. Patients should be counseled about the expected survival rates and the possibility of disease progression or recurrence after TACE. This information should be presented in a clear and compassionate manner, acknowledging the uncertainties inherent in HCC prognosis and emphasizing the importance of ongoing surveillance and management. Patients should be informed about the potential benefits of TACE, such as tumor shrinkage, symptom relief, and improved quality of life. They should also be made aware of the potential risks and complications, including post-embolization syndrome, liver abscess, and hepatic decompensation. A balanced discussion of the benefits and risks allows patients to weigh their options and make informed choices that align with their personal values and goals. The process of patient counseling should foster a collaborative relationship between the clinician and the patient, promoting shared decision-making and patient autonomy. The clinician should provide evidence-based information and guidance, while respecting the patient's preferences and values. This approach ensures that treatment decisions are made in a patient-centered manner, fostering trust and enhancing the therapeutic alliance.[17,18]

The alarming prevalence of hepatocellular carcinoma (HCC) in China, as highlighted by the present study and countless others, casts a long shadow over the nation's public health landscape. This insidious disease, with its devastating impact on individuals, families, and communities, demands a concerted and multifaceted response from healthcare providers, policymakers, and the public at large. The findings of this retrospective cohort study, while focused on the clinical management of HCC, also underscore the urgent need for comprehensive preventive and early detection strategies, as well as the judicious allocation of healthcare resources to combat this formidable foe. The dominant role of chronic hepatitis B virus (HBV) infection in HCC etiology in China represents a stark reminder of the enduring legacy of past epidemics. Despite significant progress in HBV prevention through widespread vaccination programs, the burden of chronic HBV infection remains substantial, particularly among older adults who were exposed to the virus before the advent of effective vaccination strategies. This reservoir of chronic HBV carriers serves as a fertile ground for the development of HCC, fueling the ongoing epidemic and posing a formidable challenge to public health efforts. The imperative to address the HBV scourge is clear. Universal HBV vaccination programs must be sustained and expanded to ensure that all newborns and at-risk individuals receive adequate protection against this insidious virus. Furthermore, antiviral therapy should be readily available and accessible to all chronic HBV carriers, with the goal of suppressing viral replication, reducing liver inflammation, and ultimately preventing the progression to cirrhosis and HCC. Public health campaigns aimed at raising awareness about HBV transmission and the importance of vaccination and treatment are also crucial in combating this persistent threat. While chronic HBV infection remains the primary driver of HCC in China, the rising tide of metabolic syndrome and non-alcoholic fatty liver disease (NAFLD) represents an emerging and potentially ominous trend. The increasing prevalence of obesity, diabetes, and dyslipidemia, fueled by sedentary lifestyles and unhealthy dietary habits, has led to a surge in NAFLD

cases, which can progress to non-alcoholic steatohepatitis (NASH) and ultimately HCC. This epidemiological shift underscores the evolving nature of HCC risk factors and necessitates a proactive and adaptive public health response. Lifestyle interventions and public health campaigns aimed at promoting healthy behaviors and reducing the burden of metabolic syndrome and NAFLD are paramount. These interventions should focus on increasing physical activity, improving dietary habits, and achieving weight loss in overweight or obese individuals. Public education initiatives should raise awareness about the link between metabolic syndrome, NAFLD, and HCC, empowering individuals to make informed choices about their health and adopt preventive measures. Collaboration between healthcare providers, public health agencies, and community organizations is essential in implementing and sustaining these interventions. Early detection of HCC offers the best chance of achieving cure or long-term disease control. However, the insidious nature of HCC, often remaining asymptomatic until advanced stages, poses a significant challenge to early diagnosis. Surveillance programs targeting high-risk populations, such as chronic HBV carriers and individuals with cirrhosis, are crucial in identifying HCC at its earliest and most treatable stages. These surveillance programs typically involve periodic imaging studies, such as ultrasound or MRI, and serum AFP measurements. The frequency and modality of surveillance should be tailored to the individual's risk profile, with closer monitoring for those at higher risk. The effectiveness of surveillance programs hinges on their accessibility, affordability, and adherence, necessitating concerted efforts to address barriers to participation and ensure equitable access to care. Public health initiatives aimed at promoting awareness about the importance of surveillance and facilitating access to diagnostic services are essential in maximizing the impact of early detection efforts. The identification of prognostic factors for TACE outcomes, as demonstrated in this study, carries significant implications for resource allocation and healthcare policy decisions. By understanding the factors that influence treatment response and survival, policymakers can make informed decisions about the allocation of funding, personnel, and infrastructure to optimize HCC management. Resources should be directed towards the identification and management of high-risk individuals, such as those with chronic HBV infection, cirrhosis, or other predisposing factors. Early detection and intervention in these populations can prevent the development of HCC or identify it at its earliest and most treatable stages. The development and implementation of personalized treatment algorithms, incorporating prognostic factors and individual patient characteristics, can optimize treatment selection and resource utilization. This approach ensures that patients receive the most appropriate and effective therapy for their specific clinical situation, maximizing outcomes while minimizing unnecessary costs and side effects. Continued investment in HCC research is crucial for developing novel diagnostic tools, therapeutic modalities, and preventive strategies. The identification of new biomarkers, imaging techniques, and treatment approaches can further refine risk stratification, improve early detection, and expand the therapeutic armamentarium for HCC. Public health education campaigns should focus on raising awareness about HCC risk factors, preventive measures, and the importance of early detection and treatment. These campaigns should be tailored to the specific needs of different populations and delivered through various channels, including mass media, community outreach programs, and healthcare provider education.[19,20]

4. Conclusion

This retrospective cohort study underscores the long-term efficacy of TACE in managing HCC within a Chinese population, showcasing median OS of 36 months and a 5-year OS rate of 28%. It reaffirms the prognostic significance of tumor size, BCLC stage, and AFP level, enabling personalized treatment strategies. While inherent limitations of a retrospective design exist, the study's findings align with broader research, validating the robustness of these predictors across diverse populations.

5. References

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