Journal of Hepatocellular Carcinoma

Dovepress
Taylor & Francis Group

Open Access Full Text Article

REVIEW

Postoperative Adjuvant Transcatheter Arterial Chemoembolization (TACE) for Hepatocellular Carcinoma: Patient Selection and Clinical Predictors of Therapeutic Benefit

Jiayin Chen*, Zhuochao Li*, Xun Qi

Key Laboratory of DiagnosticImaging and Interventional Radiology of Liaoning Province, Department of Interventional Therapy, The First Hospital of China Medical University, Shenyang, 110001, People's Republic of China

*These authors contributed equally to this work

Correspondence: Xun Qi, Key Laboratory of DiagnosticImaging and Interventional Radiology of Liaoning Province, Department of Interventional Therapy, The First Hospital of China Medical University, Shenyang, 110001, People's Republic of China, Email qixun716@hotmail.com

Abstract: Hepatocellular carcinoma (HCC) ranks among the top five cancers in terms of both incidence and mortality. Although surgical resection is the first-line treatment for HCC, the significant rate of postoperative recurrence has a severe impact on patient prognosis; therefore, adjuvant therapy is crucial for preventing recurrence. Transarterial chemoembolization (TACE), as a widely used minimally invasive interventional procedure, has become the standard treatment for patients with advanced HCC who are ineligible for surgery. In clinical practice, postoperative adjuvant TACE is frequently used to improve patient prognosis and reduce the risk of recurrence. However, the clinical value of adjuvant TACE remains controversial, and the patient population likely to benefit from it has not yet been clearly defined. This review synthesizes evidence from relevant studies to identify patient subgroups most likely to benefit from postoperative adjuvant TACE and to evaluate clinical and molecular predictors of treatment response. A search of the PubMed (January 2010 to May 2025) was conducted to include clinical studies focusing on postoperative adjuvant TACE with overall survival (OS) and disease-free survival (DFS) as outcomes. Consistent evidence suggests that subgroups likely to benefit include patients with microvascular invasion, low-grade portal vein tumor thrombus, and tumors ≥5 cm. Patients with hepatitis B virus associated HCC and localized biliary duct tumor thrombus may benefit, but require enhanced monitoring or combination therapy; patients with advanced portal vein tumor thrombus and poor liver function do not benefit and may even be at risk. Potential predictive biomarkers include Cbx4, Ki67, and serum GGT levels, although the quality of evidence varies. These findings support a more individualized approach to adjuvant TACE but also underscore the need for prospective validation.

Keywords: hepatocellular carcinoma, adjuvant therapy, transcatheter arterial chemoembolization, patient selection, predictive factors

Introduction

Data from 2022 indicate that liver cancer continues to rank sixth in incidence and third in mortality worldwide. Globally, over 40% of new liver cancer diagnoses and related deaths occur in China, highlighting the country's disproportionate share of this disease's burden.[1] Surgical resection remains a cornerstone of liver cancer treatment and is recognized as the first-line treatment method in all guidelines. In the management of HCC, liver resection remains the standard of care for individuals without underlying cirrhosis.[2] Following surgical resection, a significant challenge persists, as more than half of liver cancer patients may develop recurrent or metastatic disease, with figures ranging from 50% to 70%. Consequently, the reduction of postoperative recurrence and metastasis via adjuvant therapy stands as a crucial determinant for enhancing surgical outcome.[3]

https://doi.org/10.2147/JHC.S601849
Received: 6 February 2026
Accepted: 17 April 2026
Published: 1 May 2026

Postoperative recurrence factors are critical for determining the necessity of adjuvant therapy. Major clinical guidelines, including those from EASL and NCCN, delineate several established high-risk indicators for postoperative HCC recurrence, such as major vascular invasion, satellite nodules, tumors exceeding 5 cm in diameter, and microvascular invasion.[3,4] The 2025 EASL Clinical Practice Guidelines on the management of hepatocellular carcinoma further emphasize that adjuvant TACE may be considered as a potential therapeutic option for HCC patients with high-risk recurrence factors (microvascular invasion, solitary tumor ≥5 cm, low-grade portal vein tumor thrombus) after curative resection, while noting that the evidence for its efficacy is mainly derived from retrospective cohort studies and lacks support from large-scale randomized controlled trials.[3] The Barcelona Clinic Liver Cancer (BCLC) staging system recommends individualized adjuvant therapy decisions for post-resection HCC patients: for BCLC 0/A stage patients with high-risk features, adjuvant TACE is a reasonable choice to reduce recurrence risk, while for patients with advanced portal vein tumor thrombus (Vp4) or poor liver function, adjuvant TACE is not recommended due to limited benefit and potential hepatotoxicity.[5] Additionally, both guidelines highlight the urgent need for high-quality prospective studies to validate the efficacy of adjuvant TACE and define the optimal beneficiary population. Furthermore, the presence of underlying liver disease, notably viral hepatitis or cirrhosis, is also recognized as a significant contributing risk factor.[6]

Currently, adjuvant treatment methods for HCC after surgery include radiotherapy, transcatheter arterial chemotherapy, transcatheter arterial chemotherapy embolization, and local ablation therapy, with the aim of improving surgical efficacy and reducing the risk of recurrence. TACE can simultaneously release embolization agents and chemotherapy drugs, exerting dual tumor-suppressing effects: embolization agents block the main blood supply arteries to the liver tumor, causing ischemic necrosis of the tumor, while simultaneously releasing chemotherapy drugs to eliminate residual cancer cells.[7] Clinical evidence consistently demonstrates that TACE confers a survival benefit to inoperable HCC patients, while also functioning as an effective bridging strategy for those awaiting liver transplantation.[8] Multiple studies have demonstrated that postoperative adjuvant TACE can improve patient outcomes.[9–13] However there is also evidence suggesting that it does not consistently improve survival rates for all resected patients and may even increase the risk of early recurrence in specific subgroups. Consequently, the patient population that benefits from postoperative adjuvant TACE and the predictive factors for its efficacy remain unclear.[14,15]

Although several meta-analyses and systematic reviews on postoperative adjuvant TACE have been published in recent years, they all have significant limitations. First, most studies focus on overall efficacy and lack deeper subgroup stratification. Second, differing inclusion criteria across studies lead to heterogeneity in results. Third, few studies incorporate predictive analyses that integrate molecular biomarkers with clinical factors. Finally, literature searches generally stopped in 2023, omitting key studies on TACE combined with immunotherapy or targeted therapy, and there is a lack of standardized evidence grading and clinical decision-making guidelines. With the rapid development of precision oncology and emerging systemic therapies, there is an urgent need for an updated review to comprehensively synthesize existing evidence, clarify subgroup-specific efficacy, and provide actionable clinical algorithms. However, there remains a lack of systematic organization and integration regarding the systematic classification of patient subgroups benefiting from postoperative adjuvant TACE for HCC and the associated predictive factors.

This review is a narrative review aimed at synthesizing existing evidence to identify patient subgroups that may benefit from adjuvant TACE following liver cancer resection, summarizing clinical and molecular predictive factors, and discussing the role of TACE in the current landscape of immunotherapy and targeted therapy, thereby providing a clinical decision-making framework for personalized treatment. The main content structure of this review is shown in Figure 1.

Populations That May Gain Benefits from Postoperative Adjuvant TACE

Hepatocellular Carcinoma with Microvascular Invasion

Microvascular invasion (MVI) is described as the existence of tumor emboli in the portal vein, large cystic vessels, or vascular spaces that are lined with endothelial cells.[16] MVI is described as "a cancer cell nest consisting of more than 50 cells in the endothelial vascular lumen under a microscope".[17] Studies have shown that MVI is an independent risk factor for postoperative recurrence of HCC.[18,19] Evidence suggests that microvascular invasion negatively affects prognosis in individuals with solitary small HCC lesions.[20] Given the prevalence of MVI in roughly 15–60% of HCC cases,[21,22] its

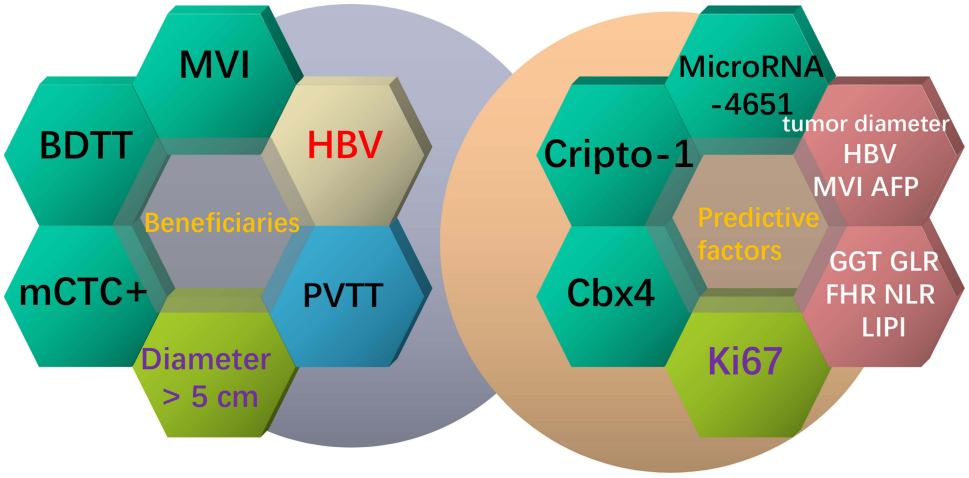

Figure 1 Article structure diagram.

management has become a major research priority aimed at lowering recurrence and improving survival.In recent years, postoperative TACE has shown significant therapeutic effect in patients with HCC with MVI, effectively improving the survival rate of patients. Ye et al and Wang et al conducted single-center retrospective studies with follow-up periods of 3 and 5 years, respectively. The results of both studies indicated that, compared with liver resection alone, postoperative adjuvant TACE significantly improved disease-free survival (DFS) and overall survival (OS) in patients with HCC complicated by MVI; however, these two studies may be subject to selection bias.[23,24] Qian et al, Luo et al,and Xiang et alall conducted multicenter retrospective studies with follow-up periods of 3–5 years and the results consistently showed that for patients with MVI, adjuvant TACE significantly prolonged DFS and OS, whereas in MVI-negative patients, adjuvant TACE did not demonstrate significant survival benefits. Furthermore, all three studies employed propensity score matching to minimize confounding factors and selection bias.[25–27] Mo et al and Chen et al conducted systematic reviews and meta-analyses, incorporating a large number of high-quality retrospective studies; the results consistently indicated that postoperative adjuvant TACE can prolong survival in patients with MVI.[28,29] High-quality randomized controlled trials are scarce. Wei et al conducted a single-center randomized controlled trial, confirming that postoperative TACE offers significant clinical benefits for patients with MVI, and this benefit is particularly pronounced in HCC patients who underwent liver resection for a solitary tumor ≥5 cm with MVI; this result is consistent with the prospective study by Qi et al However, the small sample size, single-center design, and lack of blinding limit the generalizability of the results.[30,31] Although a large number of high-quality retrospective studies have confirmed the efficacy of postoperative TACE in MVI-positive HCC patients, no large-scale, multicenter randomized controlled trials have been published to date, and there remains no unified clinical consensus on the efficacy of postoperative TACE. For example, Wang et al found that, MVI-positive HCC patients were found to derive greater prognostic benefit from postoperative radiotherapy than from adjuvant TACE.[32] Research has demonstrated that the survival advantage offered by adjuvant TACE for MVI-positive HCC varies according to clinical circumstances. It is effective for patients beyond the Milan criteria but does not translate to a comparable benefit for those within them.[33] At the same time, while the study by Mo et al demonstrated that postoperative TACE improves RFS and OS in patients with MVI, its subgroup analysis revealed that in the specific subgroup of patients with "multiple nodules," postoperative TACE did not significantly improve survival outcomes (P = 0.23). These findings suggest that adjuvant postoperative TACE may not be the optimal choice for patients with MVI and multiple tumors.[28] These controversial findings suggest that the efficacy of adjuvant TACE for MVI-positive HCC is closely related to patient selection and cannot be generalized to all MVI-positive populations. With advances in precision oncology, patients with MVI-positive HCC who have failed post-operative adjuvant TACE can receive TACE combined with systemic therapy to achieve survival benefits. A randomized controlled trial by Fan et al demonstrated that clinical outcomes with TACE combined with sorafenib were superior to those with TACE alone; therefore, combination therapy should be adopted for patients with MVI-positive intermediate-

https://doi.org/10.2147/JHC.S601849

Table 1 Results of TACE+SR versus SR Alone in Patients with MVI-Positive HCC

References	Time	Number of HCC Patients with MVI-Positive Receiving Different Treatments		1/3/5-Year OS (%)			1/3/5-Year DFS (%)		
		SR+TACE	SR	SR+TACE	SR	P	SR+TACE	SR	P
Luo et al[26]	2018-2021	620	620	96/82/NR	89/67/NR	0.001	88/61/NR	70/51/NR	0.001
Xiang et al[27]	2013-2019	109	137	81.7/47.2/26.1	/67.3/35.618.5	0.023	42/27.2/17.8	31.8/18.2/8.7	0.009
Ye et al[23]	2012-2015	86	174	92.7/73.1/NR	81.3/58.8/NR	0.019	72.1/54.9/NR	52/33.7/NR	0.002
Wang et al[24]	2010-2014	44	84	100/80.1/73.6	87.8/62.7/47.7	0.005	68.2/38.6/26.3	45.2/25/20.7	0.038
Qi et al[31]	2012-2014	91	109	96.6/89.2/NR	89.6/76.5/NR	0.030	64.1/24.4/NR	46.1/16.7/NR	0.077
Wang et al[33]	2004-2015	103	73	96/74/61	79/56/39	0.006	68/35/30	52/27/13	0.026

Abbreviations: SR, Surgical resection; TACE, Transcatheter arterial chemoembolization; OS, Overall survival; DFS, Disease-free survival; NR, Not reported.

Table 2 Quality Assessment of Key Studies on Adjuvant TACE for MVI-Positive HCC

Study	Year	Study Design	Sample Size (TACE/Surgery)	Follow-Up Duration	Key Outcomes	Evidence Strength	Limitations
Ye et al[23]	2017	Retrospective	86/174	3 years	Improved DFS and OS	Moderate	Single-center, selection bias
Wang et al[24]	2018	Retrospective	44/84	5 years	Improved DFS and OS	Moderate	Single-center, selection bias
Qian et al[25]	2024	Multicenter retrospective	192/192	5 years	Improved DFS and OS	Moderate-high	Retrospective design
Luo et al[26]	2023	Multicenter retrospective	620/620	3 years	Improved DFS and OS	Moderate-high	Retrospective design
Xiang et al[27]	2024	Multicenter retrospective	109/137	5 years	Improved DFS and OS	Moderate-high	Small sample size Retrospective design
Qi et al[31]	2019	Prospective study	91/109	3 years	Improved DFS and OS	Moderate	Small sample size Residual confounding
Wei et al[30]	2018	Randomized clinical trial	125/125	5 years	Improved median OS and DFS	Moderate-high	Small sample size Single-center

stage HCC who have relapsed after liver resection.[34] Another multicenter retrospective study, which employed propensity score matching, showed that in HCC patients with MVI, adjuvant TACE combined with targeted therapy or targeted immunotherapy significantly improved DFS.[35] These studies suggest that combination therapy can overcome the limitations of TACE, particularly in high-risk MVI patients; however, large-scale randomized controlled trials are still needed to confirm these findings. In summary, we recommend adjuvant TACE for patients with MVI-positive HCC, with moderate evidence strength; for high-risk MVI patients, combination therapy is recommended. Results of TACE plus SR versus SR alone in patients with MVI-positive HCC are shown in Table 1. Quality assessment of key studies on adjuvant TACE for MVI-positive HCC is shown in Table 2.

Hepatocellular Carcinoma with Low-Grade Portal Vein Tumor Thrombus

The unique biological behavior of HCC cells and the complex vascular architecture of the liver predispose the disease to intrahepatic metastasis. One of the key ways is that the tumor invades the portal vein system, which may eventually lead to the formation of portal vein tumor thrombus (PVTT), with an incidence rate as high as 44%–62.2%.[36,37] Currently, two widely used PVTT grading systems are the Japanese Vp classification and the Cheng classification.[38,39] Vp

classification: Vp0: Portal vein is free of tumor thrombus. Vp1: Denotes tumor thrombus exclusively within peripheral portal vein branches. It is characterized by thrombus presence distal to the second-order branches, which themselves remain uninvolved. Vp2: Cancer thrombi extend to the second-level hepatic segment portal vein branches, occurring in the second-level portal vein branches. Vp3: Cancer thrombi extend to the first-level hepatic lobe portal vein branches, occurring in the left and right portal vein branches. Vp4: Cancer thrombi involve the main trunk or extend beyond the hepatic hilum, occurring in the main portal vein trunk or above. Cheng classification: Type I: Cancer thrombi invade the hepatic lobe or portal vein branches of the liver. Type II: Cancer emboli invade the left and right branches of the portal vein. Type III: Tumor thrombi extend to the main portal vein. Type IV: The disease progression reaches the superior mesenteric vein. HCC patients complicated by PVTT have been reported to survive longer following surgical resection, as indicated in studies by Kim et al[40] The median survival period in the surgical group was 2.87 years, while that in the non-surgical group was 1.1 years ($P < 0.001$). Subgroup analysis showed that surgical resection did not prolong OS in patients with PVTT graded as Vp4 compared to non-surgical treatmentThis finding concurs with the results of a systematic analysis encompassing 29 studies conducted across the United States, Europe, and East Asia.[41] A national investigation demonstrated a survival advantage for HCC patients complicated by PVTT following surgical resection, the long-term survival cohort (≥3 years post-surgery) exhibited a higher proportion of individuals with Cheng type I or II PVTT compared to the non-long-term survival group.[42] Zhang et al discovered that the optimal therapeutic approach for HCC associated with PVTT is determined by the specific type of PVTT, and surgical resection might be more appropriate for cases of Type I or Type II PVTT.[43] Yang et al reported that surgery serves as the initial therapeutic option for HCC cases complicated with Vp1-Vp3 PVTT.[44] However, the postoperative recurrence rate of PVTT can reach up to 56.9%.[45] Thus, postoperative adjuvant treatment represents an essential component of care. Xu et al conducted a multicenter retrospective study with a 5-year follow-up, which demonstrated that postoperative adjuvant TACE is an effective treatment for patients with PVTT, helping to reduce the early recurrence rate and improve OS, and is suitable for patients with Vp1–Vp3. This study featured a large sample size and standardized follow-up, and utilized propensity score matching to exclude confounding factors and selection bias.[46] Similarly, a retrospective study by Liu et al included HCC patients with combined Type I and Type II PVTT. The results showed that PVTT patients with HCC who received adjuvant TACE after surgery had a significant survival advantage, indicating that this intervention helps achieve more favorable clinical outcomes. Among the 246 patients who did not relapse within one month postoperatively, the adjuvant TACE group showed significant superiority over the control group in terms of both OS and RFS. However, this study had a smaller sample size, and its level of evidence was lower than that of Xu's study.[47] A retrospective study by Liu et al performed multivariate Cox regression analysis on surgical patients with HCC and Type I, II, or III PVTT. The results indicated that as the extent of PVTT infiltration increased, patients who received postoperative adjuvant TACE achieved more significant protective benefits, with a corresponding reduction in the risk of death.[48] Zhou et al conducted a randomized trial comparing drug-eluting bead transarterial chemoembolization (DEB-TACE) with conventional TACE in patients with Vp1–Vp3, showing that DEB-TACE achieved higher 2-year OS and lower rates of hepatotoxicity. This is the first randomized controlled trial focusing on the PVTT subgroup, providing moderate-to-high-quality evidence supporting TACE; however, the follow-up period was relatively short.[49] While adjuvant TACE after surgery markedly improves survival outcomes in PVTT patients where thrombus is at a more peripheral stage, this benefit does not appear to translate into a comparable survival advantage for those with main trunk involvement.[50,51] Several studies have even shown that adjuvant TACE may increase the risk of liver failure and early recurrence in patients with Vp4 PVTT, which stands in sharp contrast to the favorable outcomes observed in Vp1-Vp3 subgroups.[49,50] Meanwhile, a study by Yuan et al suggests that for HCC patients with PVTT, relying solely on postoperative adjuvant TACE is not the optimal approach; instead, it should be combined with systemic therapy (such as targeted therapy or immunotherapy) or a multidisciplinary comprehensive treatment plan.[52] The core reason for this discrepancy lies in the distinct anatomical and pathophysiological characteristics between early and advanced PVTT. For patients with Vp1–Vp3, tumor thrombi are confined to peripheral or lobar portal vein branches, and the main portal vein trunk remains patent, ensuring adequate hepatic perfusion. Adjuvant TACE can specifically embolize the blood supply to residual tumors without significantly affecting overall hepatic circulation, thereby eliminating microscopic residual lesions while maintaining stable liver function. In contrast, Vp4 PVTT invades the main portal vein, leading to pre-

Table 3 Quality Assessment of Key Studies on Adjuvant TACE for Low-Grade PVTT

Study	Year	Study Design	Sample Size (TACE/ Surgery)	Follow-Up Duration	Key Outcomes	Evidence Strength	Limitations
Xu et al[46]	2023	Multicenter retrospective	369/380	5 years	Reduced early recurrence, improved OS	Moderate-high	Retrospective design
Liu et al[47]	2020	Retrospective	90/196	3 years	Improved DFS and OS	Moderate	Single-center, selection bias
Liu et al[48]	2018	Retrospective	232/232	5 years	Adjuvant TACE was associated with a lower risk of death	Moderate	Single-center, Retrospective design
Zhou et al[49]	2024	Randomized clinical trial	154	3 years	Improved median OS and DFS	Moderate-high	Small sample size

existing portal hypertension and impaired hepatic perfusion, and often affects liver function due to cirrhosis. TACE-induced arterial embolization further disrupts the liver's dual blood supply, resulting in severe hepatocyte ischemia and hypoxia, which significantly increases the risk of postoperative liver failure. Furthermore, Vp4 PVTT typically indicates more aggressive tumor behavior and a higher likelihood of systemic metastasis. As a localized therapy, TACE alone cannot address distant micrometastases, resulting in limited long-term efficacy. The study by Yuan et al further supports this view: for patients with PVTT and high metastatic potential, the combination of TACE (local control) and systemic therapy (inhibition of distant metastasis) can complement each other's advantages, better aligning with the treatment philosophy for advanced HCC. This also explains why single-agent adjuvant TACE is ineffective in patients with advanced PVTT and highlights the importance of personalized and comprehensive treatment strategies. A multicenter retrospective study with a 3-year follow-up period evaluated the efficacy and safety of immunotherapy combined with TACE versus immunotherapy alone in patients with advanced HCC complicated by PVTT. The study found that the median OS and PFS in the combination therapy group were significantly superior to those in the monotherapy group, and were identified as independent predictors of improved survival, with particularly pronounced benefits observed in patients with high-grade PVTT.[53] The study concluded that TACE combined with immune-targeted therapy is a safe and effective treatment option for these patients. Another retrospective study focused on patients with HCC and PVTT. The study compared the efficacy and safety of TACE combined with hepatic arterial infusion chemotherapy and immunosuppressants versus TACE alone. The results showed that the efficacy of combination therapy was significantly superior to that of TACE alone; subgroup analysis indicated that patients with high-grade PVTT benefited more from combination therapy, whereas TACE alone had limited efficacy in this patient group.[52] Results from a multicenter randomized controlled trial by Lu et al demonstrated that the placement of radioactive metal stents prolonged survival in patients with Vp4-PVTT compared to TACE combined with sorafenib.[54] Therefore, we strongly recommend adjuvant TACE for HCC patients with low-grade PVTT (Vp1–Vp3/Cheng I–II). Due to its superior efficacy and safety profile, DEB-TACE is more effective than conventional TACE. For high-grade PVTT, adjuvant TACE alone yields poor results; combination therapy (such as TACE + targeted therapy + immunotherapy) should be considered, or, if feasible, the placement of a radioactive metal stent. Quality assessment of key studies on adjuvant TACE for low-grade PVTT is shown in Table 3.

Hepatocellular Carcinoma with a Diameter of ≥5 cm

Generally speaking, the size of a tumor often influences its staging and the patient's prognosis. For small tumor lesions, surgical resection can typically achieve a cure. However, as tumor volume grows, the difficulty of attaining a complete resection is heightened, thereby creating a significant clinical propensity for disease recurrence after surgery. According to the latest EASL clinical practice guidelines for HCC, resection is advised as the primary therapeutic approach for individuals presenting with a solitary tumor exceeding 5 cm and preserved hepatic function.[4] Studies have shown that tumor size, tumor number, and treatment modality are significant factors influencing DFS in HCC patients.[55] Other

studies have confirmed that large tumors are an independent risk factor for initial extrahepatic recurrence.[56] Mo et al found that preoperative TACE does not improve the prognosis of HCC patients with tumor diameters ≥5 cm.[57] Therefore, for HCC patients with large tumor volumes or multiple tumors, postoperative adjuvant therapy can be considered to prevent postoperative recurrence and improve patient survival rates. Substantial evidence support the use of adjuvant TACE following surgery for HCC patients presenting with tumor sizes exceeding 5 cm. A retrospective analysis revealed that adjuvant TACE following surgery can enhance outcomes in HCC patients exhibiting risk factors for residual disease. Within this cohort, a tumor diameter exceeding 5 cm was recognized as one such predictive factor.[58] The retrospective study results from Feng and Gao et al both indicated that patients with tumor diameters exceeding 5 cm had notable prognostic improvements after postoperative TACE, whereas for those with tumor diameters smaller than 5 cm, no significant difference was observed between postoperative TACE and surgery alone. Both studies had relatively large sample sizes, and both used propensity score matching to eliminate the influence of selection bias and confounding factors on the results; however, due to the limitations of their retrospective designs, the evidence is of moderate quality.[59,60] According to the results of a 5-year retrospective follow-up study by Wang et al, postoperative adjuvant TACE provides a safe and valuable adjuvant treatment option for patients with large-volume HCC, helping to improve postoperative DFS and OS. This study was also free of selection bias and confounding factors.[61] A subgroup analysis from Qi et al's prospective study indicated that the benefits of adjuvant TACE in improving DFS and OS were more pronounced in patients with tumor diameters exceeding 5 cm or those with a multinodular morphology.[31] A single-center randomized controlled trial confirmed that adjuvant TACE provided greater benefits in patients with HCC who had a solitary tumor diameter ≥5 cm and were classified as MVI.[30] However, for patients with HCC tumors greater than 5 cm, evidence from a number of studies points to limited long-term advantage from adjuvant TACE following surgery. Liang et al further confirmed through a systematic review and meta-analysis that adjuvant TACE did not significantly improve 5-year OS in patients with HCC larger than 5 cm, which may be related to the high rate of distant metastasis in this population and the limitations of TACE as a local treatment.[62] Peng et al also found that, after propensity score matching, adjuvant TACE did not provide a significant survival benefit in patients with resectable large HCC tumors, suggesting that it should be used in combination with other high-risk factors (such as MVI and PVTT) in patients with tumors ≥5 cm.[63] Studies have shown that while adjuvant TACE after surgery may theoretically help reduce the risk of recurrence, its long-term survival benefits are limited. Specifically, for patients with tumors larger than 5 cm and no microvascular invasion (MVI), adjuvant TACE alone did not significantly improve survival rates.[25] Systematic reviews further indicate that relying solely on TACE makes it difficult to completely eradicate large tumor cells; meta-analyses add that, in the overall patient population, adjuvant TACE does not significantly improve OS, and benefits may only be observed in specific high-risk subgroups (such as those with vascular invasion).[64] The differences in outcomes are primarily attributed to patient selection and tumor biological characteristics. In patients with high-risk factors such as MVI, PVTT, or incomplete surgical margins, adjuvant TACE can eliminate local residual disease and reduce the risk of intrahepatic recurrence; however, in patients without these high-risk factors, a large tumor volume alone does not necessarily indicate a high risk of local residual disease, and TACE is unable to address distant micrometastases. Furthermore, tumor heterogeneity further exacerbates these differences: well-differentiated, low-grade large tumors may benefit from local control, whereas highly aggressive tumors are prone to early systemic dissemination, making it difficult for adjuvant TACE to achieve long-term efficacy in such cases. A retrospective analysis showed that, for patients with multinodular or large (>5 cm) HCC, the combination of TACE with targeted and immunotherapy was superior to single-agent transarterial chemoembolization combined with targeted therapy in terms of prolonging PFS and OS, and the treatment was well-tolerated.[65] Therefore, we recommend adjuvant TACE for large HCC (≥5 cm) with high-risk factors (MVI, PVTT, incomplete resection), supported by moderate evidence of short- to mid-term DFS improvement, though the long-term OS benefit is limited. For large HCC without high-risk factors, TACE is not recommended. In cases of unresectable large tumors, a combination of TACE with immunotherapy and targeted therapy is advised. Quality assessment of key studies on adjuvant TACE for HCC with tumor diameter ≥5 cm is shown in Table 4.

Table 4 Quality Assessment of Key Studies on Adjuvant TACE for HCC with Tumor Diameter ≥5 cm

Study	Year	Study Design	Sample Size (TACE/ Surgery)	Follow-Up Duration	Key Outcomes	Evidence Strength	Limitations
Fabian et al[58]	2024	Retrospective	101	3 years	A tumour diameter greater than ≥ 5 cm has been identified as one of the predictive factors Improved OS	Moderate-low	Single-center Retrospective design
Feng et al[59]	2023	Retrospective	153/336	5 years	Adjuvant TACE is effective only in patients with high-risk factors	Moderate	Single-center Retrospective design
Gao et al[60]	2024	Retrospective	70/227	5 years	Adjuvant TACE is particularly effective for patients with multiple tumours or large tumours	Moderate	Single-center, Retrospective design
Wei et al[30]	2018	Randomized clinical trial	125/125	5 years	Improved median OS and DFS	Moderate-high	Small sample size Single-center

Hepatocellular Carcinoma with Hepatitis B

Globally, chronic hepatitis B virus (HBV) infection persists as a leading etiological factor for liver disease, accounting for a substantial portion of both morbidity and mortality. The most recent World Health Organization (WHO) report (2024) indicates that around 254 million people globally are affected by chronic HBV infection, leading to about 1.1 million fatalities each year.The vast majority of these fatalities are attributable to HBV-related complications, primarily liver cirrhosis and HCC.[66] HBV infection is a significant risk factor for HCC, with over 80% of liver cancer patients in China testing positive for HBV.[67] A retrospective study found that the recurrence rate among liver cancer patients without HBV infection was significantly lower than that among those with HBV infection.[68] Huang and He et alnoted that persistently high viral load during surgery is the primary mechanism for postoperative recurrence in HCC patients, and viral load acts as a valuable prognostic indicator for HBV-related HCC.[69,70] This is consistent with the conclusions of three large-scale prospective studies.[71,72] There are various treatment options for HCC with HBV coinfection, such as surgical resection, antiviral therapy, and TACE. After balancing long-term benefits, costs, side effects, and potential treatment risks of antiviral therapy and TACE, postoperative TACE remains one of the most cost-effective options for preventing recurrence.[73] A retrospective study by Yan et al enrolled 120 HCC patients with HBV infection, randomly assigning them to four groups: a control group, an antiviral therapy group, a TACE group, and a combination therapy group. The results showed that postoperative TACE prolonged DFS in all patients, regardless of whether it was combined with antiviral therapy (P=0.015); therefore, postoperative TACE can prevent early recurrence of HCC.[74] Through an analysis of 432 HBV-positive HCC patients, a retrospective study by Tu et al established a prognostic model showing that, compared with surgery alone, postoperative combined TACE significantly improved 1-year, 3-year, and 5-year OS.[75] The findings of Zhu et al indicated that patients receiving combined antiviral therapy and TACE had significantly better OS and DFS than those receiving TACE alone.[76] A retrospective cohort study showed that among HBV-positive patients, those with tumor diameters greater than 5 cm or accompanied by microvascular invasion constituted the subgroup deriving the greatest benefit from adjuvant TACE. These patients have an extremely high risk of postoperative recurrence, and TACE can effectively eliminate residual micrometastases. This study had a large sample size and balanced baseline characteristics, resulting in a high level of evidence.[77] A previous prospective randomized controlled trial indicated that postoperative TACE significantly reduces tumor recurrence and prolongs OS and DFS in patients with intermediate- to high-risk HBV-associated hepatocellular carcinoma.[78] In the randomized controlled trial by Li et al, results showed that postoperative adjuvant TACE improves survival rates in HBV-positive HCC patients compared to surgery alone.[79] However, some studies suggest that postoperative TACE is not beneficial for all patients with HBV-related HCC. For example, in patients with active HBV replication or impaired liver function (Child-Pugh B/C grade), adjuvant

Table 5 Quality Assessment of Key Studies on Adjuvant TACE for HBV-Related HCC

Study	Year	Study Design	Sample Size (TACE/ Surgery)	Follow-Up Duration	Key Outcomes	Evidence Strength	Limitations
Yan et al[74]	2013	Retrospective	120	3 years	Reduced early recurrence, improved OS	Moderate-low	Single-center Retrospective design
Tu et al[75]	2023	Retrospective	432	5 years	Improved DFS and OS	Moderate	Single-center Retrospective design
Zhu et al[76]	2015	Retrospective	118/176	5 years	Improved DFS and OS	Moderate	Single-center Retrospective design
Li et al[77]	2024	Retrospective	1488	5 years	Improved median OS and DFS	Moderate-high	Retrospective design
Wang et al[78]	2018	Randomized clinical trial	140/140	5 years	Reduced early recurrence, improved median OS and DFS	Moderate-high	Small sample size

TACE not only fails to improve survival rates but may also increase the risk of liver failure; moreover, the hepatotoxicity associated with postoperative TACE is particularly pronounced in patients with active HBV replication.[80] This is primarily because the chemotherapeutic agents used in TACE can directly suppress the body's immune function, disrupting the immune balance and thereby inducing HBV reactivation. Reactivated HBV further invades and damages hepatocytes, triggering acute hepatitis and, in severe cases, leading to irreversible liver failure; Additionally, TACE blocks blood supply to the liver, causing ischemia and hypoxia in normal liver tissue. In patients with active HBV replication, hepatocytes are already in a state of chronic inflammation and damage due to long-term viral infection; the ischemia-reperfusion injury and chemotoxicity induced by TACE further exacerbate hepatocyte necrosis, ultimately leading to liver failure.[81,82] A 2023 retrospective study further confirmed that, in terms of recurrence rates and survival, postoperative TACE offers no significant advantage over surgery alone for patients with low viral loads and good liver function.[83] The key factors driving this difference lie in the liver's ability to tolerate TACE and the extent of viral replication: moderate- to high-risk patients (high viral load, mild liver dysfunction) may benefit from TACE's anti-recurrence effects under the protection of antiviral therapy; whereas in patients with active viral replication or poor liver function, whose hepatocytes are already damaged, TACE's chemoembolization may further exacerbate liver injury, thereby offsetting the therapeutic benefits. Furthermore, patients with low viral loads and good liver function have a lower risk of recurrence due to residual localized lesions; therefore, they cannot fully utilize the local therapeutic advantages of TACE. Currently, researchers have utilized Cox regression models to establish risk scoring models or nomograms based on risk predictive factors to guide decision-making for postoperative TACE in HBV-related HCC patients and predict tumor recurrence following postoperative TACE.[75,80,83] In summary, we recommend adjuvant TACE for patients with HBV-related HCC who have moderate-to-high viral loads (HBV-DNA $>10^4$ IU/mL) and Child-Pugh A liver function; the evidence for this is moderate-to-high. Concurrent use of antiviral medications is an essential measure to reduce the risk of HBV reactivation. TACE is not recommended for patients with low viral load, good liver function, active HBV replication, or Child-Pugh A liver function. Quality assessment of key studies on adjuvant TACE for HBV-related HCC is shown in Table 5.

Hepatocellular Carcinoma with Bile Duct Cancer Embolism

The occurrence of HCC with concurrent bile duct tumor thrombus (BDTT) is infrequent in clinical settings, reported rates falling within a range of 0.5% to 12.9%.[84] BDTT is characterized by malignant thrombus formation inside the biliary tract subsequent to tumor infiltration. Such thrombi can extend distally, potentially causing obstruction of the extrahepatic bile ducts. When the tumor extends into the proximal bile duct, pieces may break off and travel downstream. This process may precipitate bleeding, cause partial or complete bile duct blockage, and induce obstructive jaundice. Once this occurs, the patient's condition will deteriorate rapidly, and without timely treatment, death may result from liver failure.[85] Studies indicate that the development of BDTT in HCC portends a worse clinical outcome than cases where it is absent.[86] For HCC patients presenting with BDTT and preserved liver function, surgical resection is generally considered the treatment of choice in

clinical settings, and is capable of yielding satisfactory clinical results.[87] Retrospective analysis has shown that patients with HCC and extrahepatic BDTT can achieve favorable long-term survival following extrahepatic bile duct-preserving hepatectomy.[88] Adjuvant treatments, including postoperative TACE, radiotherapy, antiviral therapy, and targeted immunotherapy, may further enhance survival outcomes for HCC patients diagnosed with BDTT.[4,89] This investigation focuses on assessing whether adjuvant TACE following surgery improves clinical outcomes in HCC cases complicated by BDTT. In a retrospective clinical study, Luo et al examined 184 patients with HCC complicated by BDTT; the results indicated that curative hepatectomy combined with BDTT resection and TACE is the optimal treatment regimen for these patients.[90] This study had a small sample size and was conducted at a single center, resulting in a low level of evidence. In another retrospective analysis, Chen et al confirmed that both OS and DFS were lower in the group receiving surgery alone compared to the cohort that received adjuvant TACE postoperatively. This study had a moderate sample size, with no selection bias or confounding factors, and the evidence was of moderate quality.[91] Additionally, a case report described a patient with PVTT and BDTT. Following radical resection, the patient underwent postoperative TACE. Postoperative follow-up revealed a decrease in alpha-fetoprotein levels and resolution of jaundice. Although residual lesions were detected during the one-month postoperative follow-up, no significant recurrence was observed.[85] Huang et al found through propensity score matching analysis that HCC patients with BDTT who received adjuvant TACE after surgery had significantly better short-term recurrence rates and overall survival rates than those who did not receive TACE, and that adjuvant TACE was an independent protective factor for improved prognosis.[92] Nevertheless, only a few investigations have been conducted to date examining how postoperative TACE affects survival outcomes in BDTT-associated HCC. The therapeutic value of post-operative TACE in HCC cases complicated by BDTT is still subject to considerable controversy. Some studies have found that TACE does not improve OS in patients with severe BDTT (involving the common bile duct) or mixed biliary obstruction; more seriously, in patients who undergo extrahepatic cholangiectomy and choledochojejunostomy, postoperative TACE significantly increases the risk of complications such as liver abscesses.[93] The primary reasons for these differences in treatment outcomes are the extent of BDTT and the surgical approach: for patients with localized BDTT (confined to the intrahepatic bile ducts) who are candidates for complete surgical resection, adjuvant TACE can eliminate residual lesions and reduce recurrence; for patients with severe BDTT or biliary obstruction, bile stasis causes hepatocyte damage, and adjuvant TACE may further impair hepatocytes, increasing the risk of complications. Furthermore, in patients who have undergone biliary-enteric anastomosis, changes in biliary drainage occur; inflammation induced by TACE can trigger infection, rendering adjuvant TACE ineffective or even harmful. Although BDTT increases the difficulty of surgery, surgical resection can still significantly prolong patient survival when performed during an appropriate surgical window (when jaundice is controlled and liver function is good). Adjuvant TACE is recommended for patients with localized intrahepatic thrombosis and those undergoing total surgical resection for BDTT. However, TACE is not recommended for patients with severe BDTT or those who have undergone choledochoenterostomy, due to limited efficacy and an increased risk of complications. Quality assessment of key studies on adjuvant TACE for HCC with BDTT is shown in Table 6.

Table 6 Quality Assessment of Key Studies on Adjuvant TACE for HCC with BDTT

Study	Year	Study Design	Sample Size (TACE/ Surgery)	Follow-Up Duration	Key Outcomes	Evidence Strength	Limitations
Luo et al[90]	2009	Retrospective	184	3 years	Radical hepatectomy combined with BDTT resection and TACE is the optimal treatment regimen	Moderate-low	Single-center Retrospective design Small sample size
Chen et a.[91]	2022	Retrospective	134/174	5 years	Improved DFS and OS	Moderate	Single-center Retrospective design
Anh et al[85]	2024	Case Report	–	–	Improved DFS and OS	Moderate	Case study
Huang et al[92]	2020	Retrospective	61/48	3 years	Reduced early recurrence, improved OS	Moderate	Small sample size Retrospective design

Hepatocellular Carcinoma with Positive Mesenchymal Circulating Tumor Cells

In 1896, scientists from Australia were the first to identify a class of cells in the blood of patients with metastatic cancer that bore morphological similarity to tumor cells; these were subsequently designated as circulating tumor cells (CTCs). CTCs originate from the primary tumor or metastatic sites and are considered precursors to tumor metastasis and recurrence.[94] Studies demonstrate that postoperative detection of mesenchymal CTCs (mCTCs) in the bloodstream is independently associated with early tumor recurrence after curative HCC resection and could function as a promising prognostic indicator.[95,96] This is primarily because CTCs originating from the primary tumor participate in the hematogenous spread of HCC, leading to extrahepatic and intrahepatic recurrence. This review has elaborated on the substantial survival advantages that postoperative adjuvant TACE can offer to a subset of HCC patients. Therefore, determining the potential of adjuvant TACE to extend survival in HCC patients with positive mCTC status merits further investigation. This is an area that requires further exploration. A retrospective study by Zhang et al involving 261 patients with HCC showed that, compared with patients who received surgery alone, those with mCTC-positive disease who underwent postoperative TACE treatment had significantly improved RFS and OS (P=0.004, P=0.045). An analysis of 102 mCTC-positive HCC patients showed that, compared with patients who underwent surgery alone, those who received adjuvant TACE therapy postoperatively had a significantly lower mCTC positivity rate (46.4% vs. 88.4%, P=0.031).[96] This single-center study had a small sample size and a short follow-up period, resulting in low-quality evidence. Due to the low incidence of this disease, no other studies have been published to date, and it remains to be determined whether postoperative TACE can improve the prognosis of these patients. More robust clinical trials are needed to clearly evaluate the therapeutic efficacy of postoperative TACE for mCTC-positive HCC. Therefore, adjuvant TACE may improve outcomes for patients with mCTC-positive; however, the evidence is limited and of low quality, and further exploration through large-scale clinical trials is still needed.

Predictors of Clinical Benefit from Postoperative Adjuvant TACE Treatment for Hepatocellular Carcinoma

The predictive factors for clinical benefit from postoperative adjuvant TACE treatment for hepatocellular carcinoma are shown in Table 7.

Chromobox 4 (Cbx4)

Cbx4, which belongs to the CBX protein family, functions as a distinctive Polycomb group (PcG) protein. By participating in essential biological processes, it plays a role in cancer progression and cell cycle modulation. As a core component of the Polycomb group (PcG) family, polycomb repressive complex 1 (PRC1) acts as a key regulatory complex responsible for chromatin modification and transcriptional repression[108] Cbx4 expression is notably upregulated in hepatocellular carcinoma tissues. High Cbx4 expression also shows connections to several negative prognostic factors, for instance, heightened AFP, enlarged tumor size, inferior differentiation grade, and progressed TNM stage.[109] Increased levels of Cbx4 are linked to poorer OS outcomes in individuals with HCC.[110] Cbx4 has been found to promote angiogenesis and metastasis in HCC via the acetylation of hypoxia-inducible factor 1α, according to recent research.[111] Additional research confirms that Cbx4 promotes vascular endothelial growth factor (VEGF) upregulation in hypoxic HCC cellular environments. In parallel, significant associations have been identified between Cbx4 expression, VEGF levels, and markers of angiogenesis in clinical HCC tissue samples.[112] Jiao et al carried out a retrospective investigation involving 727 HCC patients, who either received postoperative TACE or did not undergo the treatment. For patients with elevated Cbx4 expression, TACE was associated with a marked extension in OS. In the low-expression population, however, no such prolongation of survival was demonstrated.[111] Consequently, Cbx4 might be considered a candidate indicator for anticipating therapeutic outcomes from postoperative TACE.

https://doi.org/10.2147/JHC.S601849

Table 7 Predictive Indicators for the Efficacy of TACE Treatment After Surgery

Indicator	References	Number of Patients in the TACE/ Control Group		1/2/3/5-Year OS (%)		Median/1/3/5-Year DFS (%)	
		High Expression	Low Expression	High Expression TACE+SR High Expression SR	Low Expression TACE+SR Low Expression SR	High Expression TACE+SR High Expression SR	Low Expression TACE+SR Low Expression SR
Ki67	Zhao et al[97]	38/37	45/46	97.5/85/79.5/NR 79.1/48.8/42.9/NR P=0.001	91.7/83.3/74.3/NR 91.7/88.9/71.4/NR P=0.89	80/77.5/69.2/NR 53.5/39.5/32.6/NR P<0.001	63.9/55.6/42.9/NR 83.3/63.9/55.6/NR P=0.279
MicroRNA-4651	Zhang et al[98]	NR	NR	High expressionTACE (-):MST:8 months;MRT:6 months High expressionTACE (+):MST:23 months;MRT:15 months Low expressionTACE (-):MST:34 months;MRT:24 months Low expressionTACE (+):MST:29 months;MRT:26 months			
Cripto-1	Li et al[99]	NR	NR	Median OS:36.5 months/NR/NR/NR/40.9 Median OS:22.5 months/NR/NR//NR/28.1	NR		
NLR≥2.5	Feng et al[100]	84/45	82/40	97.4/87.2/76.9/NR 82.2/62.2/50.8/NR	95.2/80.9/78.4/NR 92.5/80/67.3/NR	74.4/71.8/59/NR 57.8/40/28.9/NR	73.8/61.7/59.2/NR 87.5/69.5/59.1/NR

References	Indicator	OS		P
		HR	95% CI	
Hu et al[80]	Increase in liver function grading≥2	1.264	1.063–1.502	0.008
	Thrombocytopenia<100	0.659	0.461–0.941	0.022
	Tumor diameter≥5cm	1.67	1.101–2.534	0.016
	MVI	1.36	1.029–1.798	0.031
	Increased serum HBV viral load	1.612	1.179–2.205	0.003
	Increase in liver function grading≥1	1.48	0.93–2.36	0.033
	Serum HBV viral load>104	1.71	1.13–2.59	0.012
	Tumor size≥5cm	1.75	1.15–2.65	0.008
	MVI	1.53	0.99–2.36	0.008
Gu et al[101]	TNM (III)	0.547	0.346–0.865	0.015
	Tumor size (>5 cm)	0.593	0.389–0.905	0.025
	Tumor number (>1)	0.403	0.195–0.835	0.034
	Preoperative AFP (>100 ng/mL)	0.585	0.367–0.932	0.037
	HBV positive	0.557	0.377–0.822	0.007
	Spleen diameter (≥110 mm)	0.533	0.332–0.855	0.019
	ALP (>95U/l)	0.566	0.360–0.890	0.024
	MONO(>0.4×10^9/l)	0.437	0.272–0.702	0.003

Liu et al[102]	GGT (>80U/L)	3.249	1.946–5.425	<0.001	
Zhao et al[103]	GLR (≥30.39)	1	0.14–0.6	0.001	
	AFP (≥400)	1	0.31–0.84	0.008	
	MVI	1	1.96–8.17	<0.001	
Chen et al[104]	FHR (>23)	3.338	1.810–6.157	<0.001	
Xia et al[105]	AHR (>0.94)	Univariable analysis:6.376	2.584–15.735	<0.001	
		Multivariable analysis:6.698	2.561–17.519	<0.001	
	IRE	2.204	0.990–4.906	0.053	
		2.800	1.186–6.608	0.019	
	PTC	0.314	0.135–0.732	0.007	
		0.401	0.166–0.965	0.041	
Liang et al[106]	LIPI	4.018	1.716–9.408	0.001	
		2.205	1.416–3.434	<0.001	

References	**1/3/5-year OS (%)**			**1/3/5-year DFS (%)**			**Recurrence rate/Mortality rate (%)**		
	Early-stage TACE	**Delayed TACE**	**P**	**Early-stage TACE**	**Delayed TACE**	**P**	**Early-stage TACE**	**Delayed TACE**	**P**
Sun et al[107]	94.5/79.8/65.4	93.4/66.7/51.2	NR	72.1/48.8/37.7	59.4/37.5/26.1	NR	52.72/29.41	70.75/46.23	<0.01
Gu et al[101]	2-year survival rate 88.7	2-year survival rate 78	0.021	NR			20.8	40.8	0.006

Abbreviations: SR, Surgical resection; TACE, Transcatheter arterial chemoembolization; OS, Overall survival; DFS, Disease-free survival; NR, Not reported; HR, Hazard Ratio; MST, Median Survival Time; MRT, Median Recurrence Time; AFP, Alpha-Fetoprotein; ALP, Alkaline Phosphatase; MONO, Monocyte; GLR, GGT-to-Lymphocyte Ratio; FHR, Ferritin-to-Hemoglobin Ratio; NLR, Neutrophil-to-lymphocyte ratio AHR, ALT-to-Hemoglobin Ratio; IRE, Indeterminate Rim Enhancement; PTC, Peritumoral Capsule.

https://doi.org/10.2147/JHC.S601849

Ki67

Ki67 is a protein found in the cell nucleus. It cannot be detected in cells in the resting phase (G0 phase). As a result, Ki67 is considered a marker of proliferative activity, and elevated expression levels show a significant relationship with disease prognosis across various malignant tumor types. Elevated Ki67 expression correlates independently with poorer prognosis and reduced survival rates in patients with HCC, as indicated by clinical reports.[113] Zhao et al carried out a retrospective investigation involving 180 HCC patients, and the results demonstrated that for HCC patients with high Ki67 expression, postoperative TACE was able to effectively lower the likelihood of tumor recurrence and extend OS.[97] However, Xu et al observed in their retrospective study that postoperative TACE appeared to provide benefits solely to patients with low or moderate Ki67 indices, and might not be advisable for those with high Ki67 indices.[114] Despite the discrepancy between these two studies, both imply that the extent of Ki67 expression could be a useful indicator in predicting response to adjuvant TACE after surgery.

MicroRNA-4651

MicroRNAs (miRNAs) represent a category of non-coding single-stranded RNAs transcribed from endogenous genes, and they have an approximate length of 22 nucleotides. These RNA molecules have the function of regulating target mRNAs. It has been reported that microRNAs have significant implications for the prognosis of HCC patients.[115] The microRNA-4651 gene encodes a small RNA molecule, microRNA-4651, which has been found to be present in HCC individuals who are positive for aflatoxin B1. It demonstrates potential for predicting the prognosis of aflatoxin B1-associated HCC.[116] Zhang et al reported in a retrospective investigation that microRNA-4651 overexpression potentiated the efficacy of postoperative TACE treatment in patients diagnosed with HCC. When microRNA-4651 expression is elevated, the implementation of postoperative TACE in HCC cases is associated with prolonged OS, reduced mortality, and decreased rates of tumor recurrence.[98] These findings suggest that microRNA-4651 is a valuable prognostic indicator for determining whether HCC patients require postoperative adjuvant TACE therapy and can also serve as one of the indicators for predicting the efficacy of postoperative TACE treatment.

Teratocarcinoma-Derived Growth Factor-1 (Cripto-1)

Cripto-1 exerts its oncogenic role by triggering epithelial-mesenchymal transition, a key mechanism that subsequently supports the invasive and migratory behaviors of cancer cells.; it also directly boosts cell proliferation, inhibits apoptosis, and enhances angiogenesis. It has been established in prior research that high expression of Cripto-1 indicates that HCC tumor cells exhibit invasive, proliferative, and migratory capabilities, leading to poor prognosis in HCC patients.[117] It was noted by Li et al that among HCC individuals with diminished Cripto-1 expression, postoperative TACE was linked to earlier disease recurrence and did not significantly improve OS when contrasted with those not treated with TACE. Conversely, individuals with high Cripto-1 expression exhibited enhanced OS following adjuvant TACE therapy.[99] The researchers also integrated Cripto-1 expression with high-risk recurrence factors to evaluate the response to adjuvant TACE in postoperative HCC patients. The results showed that among patients with high recurrence risk factors, individuals with low Cripto-1 expression gained no benefit from adjuvant TACE; in contrast, among those with high Cripto-1 expression, patients who received adjuvant TACE had a longer OS than those who did not. The results indicate that Cripto-1 expression could be useful in evaluating the clinical outcomes of diverse HCC patients following adjuvant TACE.

Gamma-Glutamyl Transferase (GGT)

GGT is one of the indicators of liver function tests, primarily involved in glutathione metabolism. Clinically, elevated GGT levels may indicate liver or biliary tract diseases in patients. Given its non-invasiveness and ease of acquisition, GGT has garnered significant attention in tumor prognosis.[118] Within the multivariate analytical framework developed by Liu et al, sustained high levels of gamma-glutamyl transferase (GGT) were correlated with increased mortality in advanced-stage HCC. Additionally, patients with low GGT levels exhibited notably higher 2-year survival rates in comparison to those with high GGT levels (P=0.001). The findings of the study suggest that, irrespective of factors

associated with the primary tumor, patients with high GGT levels have an unfavorable long-term prognosis. More importantly, postoperative adjuvant TACE decreased late mortality in individuals with high GGT levels.[119] Similarly, Ke et alnoted that the higher the GGT elevation in advanced HCC patients, the greater the benefit they derived from postoperative TACE.[118] Therefore, serum GGT levels can predict the effectiveness of TACE treatment in patients with HCC following surgery.

Gamma-Glutamyl Transferase to Lymphocyte Ratio (GLR)

Lymphocytes are crucial for tumor immunity in the human body. When high levels of lymphocytes are present around a tumor, it indicates a better prognosis. As discussed in Section 2.5, high levels of GGT indicate a poor prognosis for HCC. GLR is calculated using these two predictive factors and is able to comprehensively evaluate a patient's liver function and immune status. Therefore, a high GLR indicates severe liver dysfunction and impaired immune status.[103] In a multivariate analysis performed by Zhao et al, GLR emerged as a standalone factor in predicting HCC outcomes.[103] Moreover, in HCC patients treated with postoperative TACE, GLR independently predicts OS outcomes.

Ferritin-to-Hemoglobin Ratio (FHR)

Within the human body, ferritin primarily serves the function of store iron. It not only participates in the hematopoietic process but also regulates the function of the immune system. Serum ferritin levels can assess iron storage status and the body's overall nutritional status. Pathological studies have shown that free iron is a mechanism leading to tumorigenesis.[120] The liver is the primary site for the synthesis and storage of ferritin, and hepatocellular carcinoma cells can synthesize and secrete ferritin, leading to a significant elevation in serum ferritin levels.[121] Therefore, elevated serum ferritin levels indicate the progression of HCC. Studies reveal a higher prevalence of anemia among oncology patients, along with substantial shifts in hemoglobin measurements before and after treatment.[122] Chen et al observed that high FHR is linked to tumor progression and poorer OS, and postoperative adjuvant TACE can notably extend OS in HCC patients with high FHR.[104] Consequently, the FHR could function as a promising biomarker for predicting the efficacy of adjuvant TACE following HCC resection. Implementing TACE in postoperative patients with high FHR levels may significantly enhance their clinical outcomes.

Neutrophil-to-Lymphocyte Ratio (NLR)

Neutrophils, as the most abundant inflammatory cells, are a key component of the immunosuppressive microenvironment in HCC and are significantly related to HCC progression and immune escape.[123] Published reports have confirmed that NLR is a prognostic predictor for HCC, with higher NLR values being associated with poorer outcomes.[124,125] A meta-analysis by Li et al demonstrated that increased preoperative NLR predicts adverse clinical outcomes in HCC patients treated with TACE, highlighting its utility as an important prognostic assessment tool.[126] Additionally, Feng et al further observed that patients with lower preoperative NLR had a lower likelihood of benefiting from postoperative TACE, in contrast, the administration of TACE after surgery can lead to better prognosis in patients who present with increased preoperative NLR.[100] This indicates that NLR not only serves as a prognostic evaluation indicator for TACE treatment of HCC but also functions as a predictive factor for postoperative adjuvant TACE therapy.

Lung Immune Prognosis Index (LIPI)

LIPI comprises the derived neutrophil-to-lymphocyte ratio and lactate dehydrogenase. The prognostic value of LIPI has recently been demonstrated for patients receiving immune checkpoint inhibitor therapy for cancer.[127] A prospective study established an effective cutoff point based on preoperative prognostic factors through multivariate analysis and validated it in a validation cohort.[106] The findings indicated that LIPI exhibited better predictive performance for HCC recurrence in comparison to other inflammatory biomarkers. It was also first proposed that preoperative LIPI may serve as a strong predictive factor for HCC patients who undergo postoperative TACE.

Timing of Postoperative Adjuvant TACE

While adjuvant TACE after surgery enhances outcomes for certain HCC patients, the optimal timing of TACE administration remains without established consensus. Several researchers recommend initiating TACE soon after surgery for HCC patients meeting the eligibility criteria for this treatment;[26] however, performing TACE too early after liver resection, when liver function has not yet recovered, may exacerbate the burden on the liver. Additionally, if postoperative infections are not fully controlled, complications such as liver failure may occur.[128,129] In their research, Sun et al applied logistic and Cox regression analyses to assess the effect of postoperative TACE timing on clinical outcomes. For HCC patients characterized by high-risk recurrence indicators, the study demonstrated that the postoperative timing of TACE independently influences prognosis. Earlier application of TACE was linked to substantially lower recurrence and fatality rates versus delayed administration. Significantly improved 1-, 3-, and 5-year DFS and OS were observed in patients receiving early TACE compared to those undergoing delayed TACE. The study recommended that patients undergo postoperative TACE approximately one month postoperatively.[107] Additional research confirmed that early TACE intervention (within 4-8 weeks post-resection) in HCC cases led to a reduction in postoperative recurrence and better survival rates.[102] Therefore, the optimal timing of postoperative TACE can predict its therapeutic efficacy.

Baseline Characteristics of Patients Prior to Postoperative Adjuvant TACE

Hu et al identified five risk factors closely linked to prognosis via multivariate Cox regression analysis: Pretreatment HBV load, platelet level, MVI presence, tumor dimension, and an increase by ≥2 points. Among these, a low platelet count was considered an independent risk indicator for postoperative TACE.[80] Despite the moderate survival benefit conferred by adjuvant TACE, factors such as vascular invasion and large tumor dimensions play a more dominant and potent role in predicting HCC prognosis. In two additional multivariate analyses, it was noted that increased Child-Pugh score, HBV levels, tumor diameter, and the presence of MVI are strongly correlated with predicting postoperative TACE prognosis.[83] Gu et al found that TNM stage (III), tumor size (>5 cm), tumor number (>1), preoperative AFP (>100 ng/mL), HBV positivity, and spleen diameter (≥110 mm) are important factors in predicting the efficacy of postoperative TACE. More importantly, in this study, spleen diameter was first identified as an important predictive factor, and elevated alkaline phosphatase and monocyte counts were first reported as risk factors for postoperative TACE outcomes.[101] In a multivariate regression analysis conducted by Xia et al, irregular rim-like enhancement in the arterial phase (IRE), peritumoral capsular enhancement (PTC), and the alanine transaminase-to-hemoglobin ratio (AHR) were identified as independent prognostic factors for OS following TACE.[105] All of these variables may function as prospective markers for predicting response to postoperative adjuvant TACE.

In summary, we believe that GGT and NLR, owing to their ease of acquisition, low cost and extensive validation in research, can serve as practical tools to guide decisions regarding adjuvant TACE at present; furthermore, key clinical parameters that directly influence treatment outcomes (timing of adjuvant TACE [1 month post-procedure], tumour diameter, HBV viral load), as well as pre-procedure AFP levels and spleen diameter, may also be used as references for comprehensive assessment. Although molecular biomarkers (Cbx4, Ki67, MicroRNA-4651, Crypto-1) and novel inflammatory markers (GLR, FHR) have demonstrated predictive value in preliminary studies, the evidence primarily stems from small-sample, single-centre retrospective studies, and testing standards remain inconsistent. Before these can be adopted as routine clinical biomarkers, validation through large-scale prospective studies is urgently required.

Limitations of Existing Evidence

Although numerous retrospective studies and meta-analyses suggest that adjuvant TACE after surgery may offer potential survival benefits for specific subgroups of HCC patients, the current evidence remains significantly limited, which constrains its clinical implementation and application. First, the study designs are limited; most existing evidence comes from retrospective cohort studies, which are prone to selection bias. High-quality, multicenter randomized controlled trials are extremely scarce, and existing randomized controlled trials often have small sample sizes and short follow-up

periods, resulting in low overall evidence strength. Second, there are significant differences in study designs. Definitions of high-risk factors, protocols for adjuvant postoperative TACE (chemotherapy drugs, embolization agents, treatment cycles), and follow-up criteria vary across studies, resulting in poor comparability and limited ability to synthesize findings. Third, there is a lack of standardization and external validation for biomarkers. For example, testing standards for predictive markers such as Cbx4 and Ki67 have not been unified, and relevant conclusions are often derived from single-center studies, making clinical translation challenging. Fourth, there is insufficient attention to the impact on liver function. Few existing studies systematically evaluate the influence of liver function status (Child-Pugh classification, HBV replication levels) on the efficacy of adjuvant TACE, and the risk of hepatotoxicity associated with TACE in patients with impaired liver function has not been fully validated. Fifth, combination therapy strategies remain unclear. There are few reports on the combined use of adjuvant TACE with emerging therapies such as immunotherapy and targeted therapy, and the optimal combination regimens and sequential treatment strategies have yet to be established. Fifth, the optimal combination therapy strategy remains unclear. Although there are numerous reports on the combined use of adjuvant TACE with emerging therapies such as immunotherapy and targeted therapy, the optimal combination regimens and sequential treatment strategies have yet to be established.

Summary

HCC treatment remains a complex and formidable challenge in clinical practice. The rate of tumor recurrence and distant metastasis at five years following surgery for HCC reaches 40% to 70%. To improve patients' quality of life, post-operative adjuvant therapy is often required. TACE, as one of the adjuvant therapy methods, has been widely applied in clinical practice. While numerous studies support the survival advantage of postoperative TACE in HCC, its appropriate use depends on careful evaluation of diverse patient-specific factors. Wang et al observed that postoperative TACE yielded greater clinical benefit for high-risk patients, characterized by conditions like diabetes or cirrhosis and a tumor size of at least 5 cm. However, patients with protective factors such as tumor encapsulation, anatomical liver resection, no severe surgical complications, and no blood transfusion can also benefit from postoperative TACE. This suggests that multiple factors should be considered when deciding on postoperative TACE.[130] We synthesized the existing evidence and conducted a stratified analysis to provide clear clinical recommendations and evidence grading. Patients with MVI, low-grade PVTT (Vp1–Vp3), tumors ≥5 cm, and high-risk factors (incomplete resection, satellite nodules) should receive postoperative adjuvant TACE, as it significantly reduces the rate of intrahepatic recurrence and improves DFS. For high-risk MVI-positive patients, combination therapy with immunotherapy and targeted therapy is recommended if liver function permits. Patients with HBV-related HCC who have a moderate-to-high viral load (HBV-DNA $>10^4$ IU/mL) or intrahepatic localized BDTT may benefit from adjuvant TACE, but must concurrently receive antiviral therapy or postoperative biliary drainage to reduce the risk of hepatotoxicity. For patients with Vp4-positive PVTT presenting with Child-Pugh B/C liver function, active HBV replication (HBV-DNA $>10^6$ IU/mL), or tumors ≥5 cm in diameter but without other high-risk factors, adjuvant TACE monotherapy should be avoided, as it does not prolong OS and may increase complication rates. It is recommended that Vp4-PVTT patients undergo TACE combined with immunotherapy or targeted therapy, and placement of a radioactive metal stent may be considered when feasible. Adjuvant TACE improves DFS in mCTC-positive patients, but this requires confirmation by large-scale prospective studies. Additionally, this review identifies several potential factors predictive of postoperative TACE treatment outcomes, including Cbx4, ki67, MicroRNA-4651, Cripto-1, and inflammatory indices (GGT, GLR, FHR, NLR), as well as clinical factors such as the optimal timing for postoperative TACE (1 month after surgery), preoperative AFP level, and spleen diameter. GGT and NLR have been well-validated as guides for decision-making regarding adjuvant TACE. The optimal timing for TACE (1 month post-surgery), tumor diameter, and HBV viral load are clinical parameters that directly influence treatment outcomes and should be incorporated into clinical decision-making for adjuvant TACE. Cbx4, Ki67, MicroRNA-4651, and Crypto-1 show promise in predicting treatment response to adjuvant TACE; however, current evidence primarily stems from small-sample, single-center retrospective studies. Validation in large-scale, multicenter, prospective cohorts is urgently needed before these can be adopted as standard clinical biomarkers.

Based on the above evidence, we have developed a decision pathway to guide clinical decision-making regarding adjuvant TACE following surgery for HCC (Figure 2).

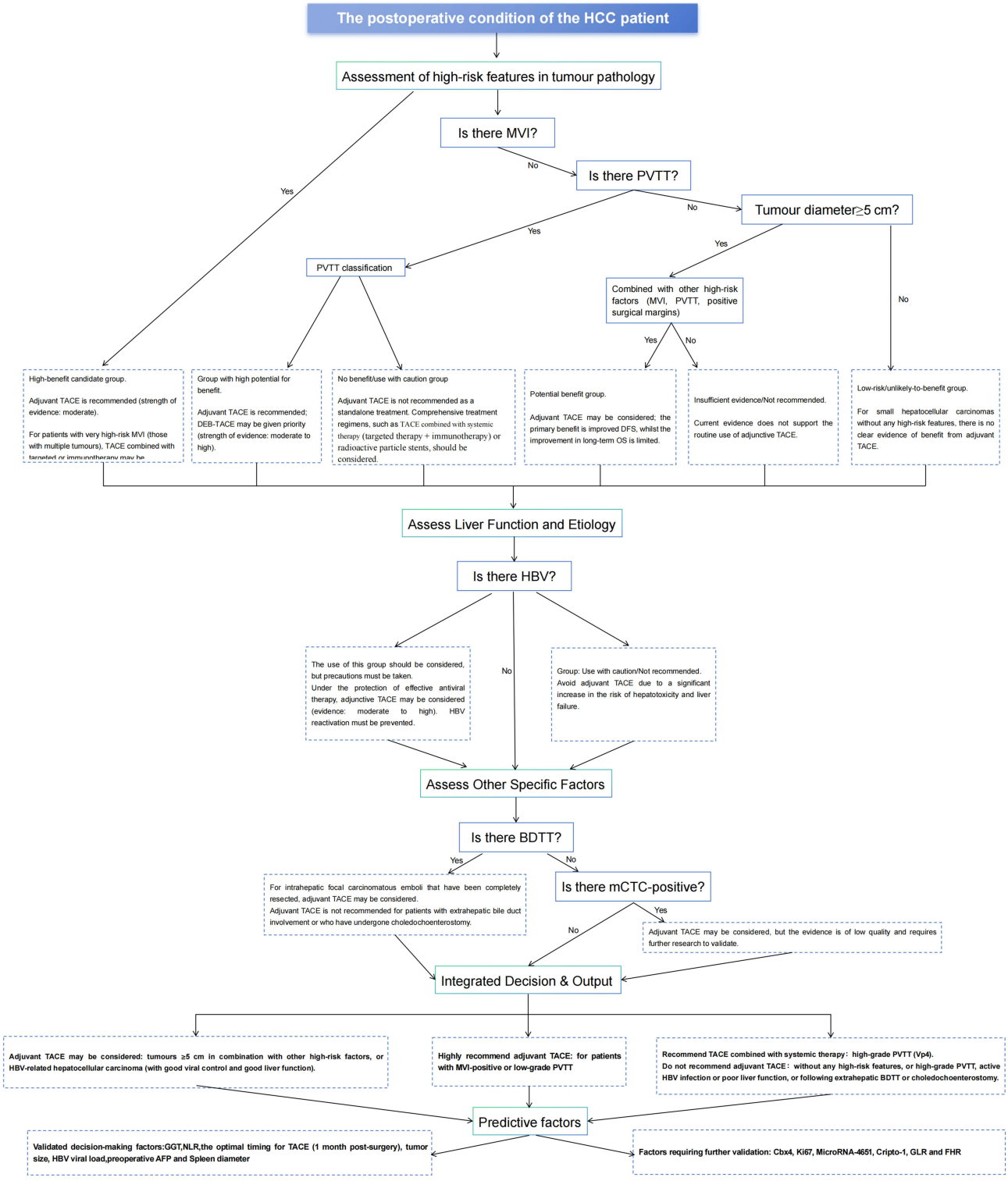

Figure 2 Clinical decision algorithm diagram.

Future Prospects

Although this review has identified patient groups that may benefit from postoperative adjuvant TACE therapy for HCC, due to tumor heterogeneity and the current limitations and controversies, further studies are needed to precisely identify the beneficiary population. To address the limitations of the current evidence and optimize the

use of TACE, future research should focus on the following areas: conducting large-scale randomized controlled trials in key subgroups, such as those involving patients with MVI-positive or low-grade PVTT, to validate the findings of retrospective studies; developing standardized predictive models; constructing nomograms that integrate clinical factors, serum markers, and molecular biomarkers; and conducting external validation to ensure clinical applicability; Optimizing combination therapy strategies by exploring the use of TACE in combination with various emerging therapies, with the primary goal of maximizing therapeutic efficacy and minimizing the incidence of adverse events; and exploring treatment strategies for specific subgroups by conducting large-scale cohort studies in patients with Vp4-PVTT and mCTC-positive PVTT to investigate the efficacy of adjuvant TACE combined with immunotherapy or targeted therapy in these populations. In summary, adjuvant TACE is a treatment strategy that can effectively prevent postoperative recurrence of HCC, but its efficacy depends on patient selection. Future high-level prospective clinical trials and retrospective case-control studies are still needed to identify the patient subgroups that benefit from adjuvant TACE after HCC surgery, to guide the development of clinical treatment protocols, and to improve the survival and quality of life of HCC patients. By identifying and evaluating clinical predictors of adjuvant TACE after HCC surgery and taking into account the specific type of liver cancer, the optimal treatment strategy for HCC patients can be formulated.

Disclosure

The authors report no other conflicts of interest in this work.

References

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2024;74(3):229–263. doi:10.3322/caac.21834
2. Cao R, Jiang H, Liang G, Zhang W. SEER-based risk stratification system for patients with primary non-cirrhotic liver cancer. *J Cancer Res Clin Oncol*. 2023;149(13):12033–12045. doi:10.1007/s00432-023-05057-7
3. European Association for the Study of the Liver. EASL clinical practice guidelines on the management of hepatocellular carcinoma. *J Hepatol*. 2025;82(2):315–374. doi:10.1016/j.jhep.2024.08.028
4. Benson AB, D'Angelica MI, Abbott DE, et al. Hepatobiliary cancers, version 2.2021, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw*. 2021;19(5):541–565. doi:10.6004/jnccn.2021.0022
5. Lucatelli P, Guiu B. 2022 update of BCLC treatment algorithm of HCC: what's new for interventional radiologists? *Cardiovasc Intervent Radiol*. 2022;45(3):275–276. doi:10.1007/s00270-021-03047-1
6. Hao X, Xu L, Lan X, et al. Impact of hepatic inflammation and fibrosis on the recurrence and long-term survival of hepatitis B virus-related hepatocellular carcinoma patients after hepatectomy. *BMC Cancer*. 2024;24(1):475.
7. Chen JJ, Jin ZC, Zhong BY, et al. Locoregional therapies for hepatocellular carcinoma: the current status and future perspectives. *United European Gastroenterol J*. 2024;12(2):226–239. doi:10.1002/ueg2.12554
8. Bianchi V, Nure E, Nesci C, et al. Bridge Therapy before Liver Transplant for Advanced Hepatocellular Carcinoma. *Medicina*. 2024;60(6):1010. doi:10.3390/medicina60061010
9. Wu Z, Cui L, Qian J, et al. Efficacy of adjuvant TACE on the prognosis of patients with HCC after hepatectomy: a multicenter propensity score matching from China. *BMC Cancer*. 2023;23(1):325. doi:10.1186/s12885-023-10802-9
10. Manjunatha N, Ganduri V, Rajasekaran K, et al. Transarterial chemoembolization and unresectable hepatocellular carcinoma: a narrative review. *Cureus*. 2022;14(8):e28439. doi:10.7759/cureus.28439
11. Bai S, Yang P, Liu J, et al. Surgical margin affects the long-term prognosis of patients with hepatocellular carcinoma undergoing radical hepatectomy followed by adjuvant TACE. *Oncologist*. 2023;28(8):e633–e644. doi:10.1093/oncolo/oyad088
12. Feng AL, Zhu JK, Yang Y, et al. Repeated postoperative adjuvant TACE after curative hepatectomy improves outcomes of patients with HCC. *Minim Invasive Ther Allied Technol*. 2021;30(3):163–168. doi:10.1080/13645706.2019.1707689
13. Lin C, Chen C, Huang G, et al. TACE combined with portal particle implantation in a case of stage IIIa primary hepatocellular carcinoma treated with sequential anlotinib. *J Contemp Brachytherapy*. 2023;15(4):283–289. doi:10.5114/jcb.2023.131239
14. Yang Y, Lin K, Liu L, et al. Impact of preoperative TACE on incidences of microvascular invasion and long-term post-hepatectomy survival in hepatocellular carcinoma patients: a propensity score matching analysis. *Cancer Med*. 2021;10(6):2100–2111. doi:10.1002/cam4.3814
15. Wang J-H, Li X-S, Tang H-S, et al. Vessels that encapsulate tumor clusters (VETC) pattern predicts the efficacy of adjuvant TACE in hepatocellular carcinoma. *J Cancer Res Clin Oncol*. 2023;149(8):4163–4172. doi:10.1007/s00432-022-04323-4
16. Zheng Z, Guan R, Jianxi W, et al. Microvascular invasion in hepatocellular carcinoma: a review of its definition, clinical significance, and comprehensive management. *J Oncol*. 2022;2022:9567041. doi:10.1155/2022/9567041
17. Yang D, Zhu M, Xiong X, et al. Clinical features and prognostic factors in patients with microvascular infiltration of hepatocellular carcinoma: development and validation of a nomogram and risk stratification based on the SEER database. *Front Oncol*. 2022;12:987603. doi:10.3389/fonc.2022.987603
18. Xiang YJ, Wang K, Zheng YT, et al. Prognostic value of microvascular invasion in eight existing staging systems for hepatocellular carcinoma: a bi-centeric retrospective cohort study. *Front Oncol*. 2021;11:726569. doi:10.3389/fonc.2021.726569

19. Tang Y, Xu L, Ren Y, et al. Identification and validation of a prognostic model based on three MVI-Related genes in hepatocellular carcinoma. *Int J Biol Sci*. 2022;18(1):261–275. doi:10.7150/ijbs.66536
20. Yao LQ, Li C, Diao YK, et al. Grading severity of microscopic vascular invasion was independently associated with recurrence and survival following hepatectomy for solitary hepatocellular carcinoma. *Hepatobiliary Surg Nutr*. 2024;13(1):16–28. doi:10.21037/hbsn-22-411
21. Gu J, Liang BY, Zhang EL, et al. Scientific hepatectomy for hepatocellular carcinoma. *Curr Med Sci*. 2023;43(5):897–907. doi:10.1007/s11596-023-2761-2
22. Li H, Zhang D, Pei J, et al. Dual-energy computed tomography iodine quantification combined with laboratory data for predicting microvascular invasion in hepatocellular carcinoma: a two-centre study. *Br J Radiol*. 2024;97(1160):1467–1475. doi:10.1093/bjr/tqae116
23. Ye JZ, Chen JZ, Li ZH, et al. Efficacy of postoperative adjuvant transcatheter arterial chemoembolization in hepatocellular carcinoma patients with microvascular invasion. *World J Gastroenterol*. 2017;23(41):7415–7424. doi:10.3748/wjg.v23.i41.7415
24. Wang H, Du P-C, Wu M-C, et al. Postoperative adjuvant transarterial chemoembolization for multinodular hepatocellular carcinoma within the Barcelona Clinic Liver Cancer early stage and microvascular invasion. *Hepatobiliary Surg Nutr*. 2018;7(6):418–428. doi:10.21037/hbsn.2018.09.05
25. Qian J, Shen Y, Cui L, et al. Survival effects of postoperative adjuvant TACE in early-HCC patients with microvascular invasion: a multicenter propensity score matching. *J Cancer*. 2024;15(1):68–78. doi:10.7150/jca.87435
26. Luo L, Shan R, Cui L, et al. Postoperative adjuvant transarterial chemoembolisation improves survival of hepatocellular carcinoma patients with microvascular invasion: a multicenter retrospective cohort. *United European Gastroenterol J*. 2023;11(2):228–241. doi:10.1002/ueg2.12365
27. Xiang C, Shen X, Zeng X, et al. Effect of transarterial chemoembolization as postoperative adjuvant therapy for intermediate-stage hepatocellular carcinoma with microvascular invasion: a multicenter cohort study. *Int J Surg*. 2024;110(1):315–323. doi:10.1097/JS9.0000000000000805
28. Mo A, Lin B, Chen D. Efficacy of sequential TACE on primary hepatocellular carcinoma with microvascular invasion after radical resection: a systematic review and meta-analysis. *World J Surg Oncol*. 2023;21(1):277. doi:10.1186/s12957-023-03160-0
29. Chen ZH, Zhang XP, Zhou TF, et al. Adjuvant transarterial chemoembolization improves survival outcomes in hepatocellular carcinoma with microvascular invasion: a systematic review and meta-analysis. *Eur J Surg Oncol*. 2019;45(11):2188–2196. doi:10.1016/j.ejso.2019.06.031
30. Wei W, Jian PE, Li SH, et al. Adjuvant transcatheter arterial chemoembolization after curative resection for hepatocellular carcinoma patients with solitary tumor and microvascular invasion: a randomized clinical trial of efficacy and safety. *Cancer Commun*. 2018;38(1):61. doi:10.1186/s40880-018-0331-y
31. Qi YP, Zhong JH, Liang ZY, et al. Adjuvant transarterial chemoembolization for patients with hepatocellular carcinoma involving microvascular invasion. *Am J Surg*. 2019;217(4):739–744. doi:10.1016/j.amjsurg.2018.07.054
32. Wang L, Wang W, Yao X, et al. Postoperative adjuvant radiotherapy is associated with improved survival in hepatocellular carcinoma with microvascular invasion. *Oncotarget*. 2017;8(45):79971–79981. doi:10.18632/oncotarget.20402
33. Wang YY, Wang LJ, Xu D, et al. Postoperative adjuvant transcatheter arterial chemoembolization should be considered selectively in patients who have hepatocellular carcinoma with microvascular invasion. *HPB*. 2019;21(4):425–433. doi:10.1016/j.hpb.2018.08.001
34. Fan W, Zhu B, Chen S, et al. Survival in patients with recurrent intermediate-stage hepatocellular carcinoma: sorafenib plus TACE vs TACE alone randomized clinical trial. *JAMA Oncol*. 2024;10(8):1047–1054. doi:10.1001/jamaoncol.2024.1831
35. Chen X, Wu X, Peng W, et al. Combined TACE with targeted and immunotherapy versus TACE alone improves DFS in HCC with MVI: a multicenter propensity score matching study. *J Hepatocell Carcinoma*. 2025;12:561–577. doi:10.2147/JHC.S504016
36. Zhang M, Ding Q, Bian C, et al. Progress on the molecular mechanism of portal vein tumor thrombosis formation in hepatocellular carcinoma. *Exp Cell Res*. 2023;426(1):113563. doi:10.1016/j.yexcr.2023.113563
37. Song WJ, Xu J, Nie Y, et al. Conversion therapy of a giant hepatocellular carcinoma with portal vein thrombus and inferior vena cava thrombus: a case report and review of literature. *World J Clin Cases*. 2024;12(16):2847–2855. doi:10.12998/wjcc.v12.i16.2847
38. Elkrief L, Hernandez-Gea V, Senzolo M, et al. Portal vein thrombosis: diagnosis, management, and endpoints for future clinical studies. *Lancet Gastroenterol Hepatol*. 2024;9(9):859–883. doi:10.1016/S2468-1253(24)00155-9
39. Abdelhamed W, Shousha H, El-Kassas M. Portal vein tumor thrombosis in hepatocellular carcinoma patients: is it the end. *Liver Res*. 2024;8(3):141–151. doi:10.1016/j.livres.2024.09.002
40. Kim TS, Yang K, Choi GH, et al. Surgical outcome and risk scoring to predict survival after hepatic resection for hepatocellular carcinoma with portal vein tumor thrombosis. *Ann Hepatobiliary Pancreat Surg*. 2024;28(2):134–143. doi:10.14701/ahbps.24-048
41. Glantzounis GK, Paliouras A, Stylianidi MC, et al. The role of liver resection in the management of intermediate and advanced stage hepatocellular carcinoma. A systematic review. *Eur J Surg Oncol*. 2018;44(2):195–208. doi:10.1016/j.ejso.2017.11.022
42. Chen ZH, Zhang XP, Lu YG, et al. Actual long-term survival in HCC patients with portal vein tumor thrombus after liver resection: a nationwide study. *Hepatol Int*. 2020;14(5):754–764. doi:10.1007/s12072-020-10032-2
43. Zhang Y, Wu JL, Li LQ. Efficacy comparison of optimal treatments for hepatocellular carcinoma patients with portal vein tumor thrombus. *Ann Hepatol*. 2022;27(1):100552. doi:10.1016/j.aohep.2021.100552
44. Yang J, Kim JM, Rhu J, et al. Surgical resection is preferred in selected solitary hepatocellular carcinoma with portal vein tumor thrombosis. *Dig Surg*. 2022;39(1):42–50. doi:10.1159/000521827
45. Zhao HT, Cai JQ. Chinese expert consensus on neoadjuvant and conversion therapies for hepatocellular carcinoma. *World J Gastroenterol*. 2021;27(47):8069–8080. doi:10.3748/wjg.v27.i47.8069
46. Xu JX, Qin SL, Wei HW, et al. Prognostic factors and an innovative nomogram model for patients with hepatocellular carcinoma treated with postoperative adjuvant transarterial chemoembolization. *Ann Med*. 2023;55(1):2199219. doi:10.1080/07853890.2023.2199219
47. Liu F, Guo X, Dong W, et al. Postoperative adjuvant TACE-associated nomogram for predicting the prognosis of resectable hepatocellular carcinoma with portal vein tumor thrombus after liver resection. *Int J Biol Sci*. 2020;16(16):3210–3220. doi:10.7150/ijbs.46896
48. Liu S, Guo L, Li H, et al. Postoperative adjuvant trans-arterial chemoembolization for patients with hepatocellular carcinoma and portal vein tumor thrombus. *Ann Surg Oncol*. 2018;25(7):2098–2104. doi:10.1245/s10434-018-6438-1
49. Zhou TY, Tao GF, Zhou GH, et al. Comparison of drug-eluting bead with conventional transcatheter arterial chemoembolization for hepatocellular carcinoma with portal vein tumor thrombus: a randomized clinical trial. *Int J Surg*. 2024;110(9):5527–5537. doi:10.1097/JS9.0000000000001691

50. Tan ZB, Zhang J. Recent advances in treatment strategies for hepatocellular carcinoma with portal vein cancer thrombus. *Eur Rev Med Pharmacol Sci*. 2023;27(17):8119–8134. doi:10.26355/eurrev_202309_33572
51. Qiu G, Xie K, Jin Z, et al. The multidisciplinary management of hepatocellular carcinoma with portal vein tumor thrombus. *Biosci Trends*. 2021;15(3):148–154. doi:10.5582/bst.2021.01173
52. Yuan Y, He W, Yang Z, et al. TACE-HAIC combined with targeted therapy and immunotherapy versus TACE alone for hepatocellular carcinoma with portal vein tumour thrombus: a propensity score matching study. *Int J Surg*. 2023;109(5):1222–1230. doi:10.1097/JS9.0000000000000256
53. You R, Cheng Y, Diao L, et al. Immune-targeted therapy with or without Transarterial Chemoembolization (TACE) for advanced hepatocellular carcinoma with Portal Vein Tumor Thrombosis (PVTT): a multicenter retrospective study. *Biomedicines*. 2024;12(9):2124. doi:10.3390/biomedicines12092124
54. Lu J, Guo JH, Ji JS, et al. Irradiation stent with 125 I plus TACE versus sorafenib plus TACE for hepatocellular carcinoma with major portal vein tumor thrombosis: a multicenter randomized trial. *Int J Surg*. 2023;109(5):1188–1198. doi:10.1097/JS9.0000000000000295
55. Yoon JH, Lee WJ, Kim SM, et al. Simple parameters predicting extrahepatic recurrence after curative hepatectomy for hepatocellular carcinoma. *Sci Rep*. 2021;11(1):12984. doi:10.1038/s41598-021-92503-6
56. Yoon JH, Choi SK, Cho SB, et al. Early extrahepatic recurrence as a pivotal factor for survival after hepatocellular carcinoma resection: a 15-year observational study. *World J Gastroenterol*. 2022;28(36):5351–5363. doi:10.3748/wjg.v28.i36.5351
57. Mo A, Zhang Q, Xia F, et al. Preoperative transcatheter arterial chemoembolization and prognosis of patients with solitary large hepatocellular carcinomas (≥5 cm): multicenter retrospective study. *Cancer Med*. 2023;12(7):7734–7747. doi:10.1002/cam4.5529
58. Haak F, Karli T, Takes M, et al. A retrospective cohort analysis of transarterial chemoembolization for hepatocellular cancer at a tertiary center in Switzerland. *J Clin Med*. 2024;13(11):3279. doi:10.3390/jcm13113279
59. Feng LH, Zhu YY, Zhou JM, et al. Adjuvant TACE may not improve recurrence-free or overall survival in HCC patients with low risk of recurrence after hepatectomy. *Front Oncol*. 2023;13:1104492. doi:10.3389/fonc.2023.1104492
60. Gao ZY, Jin LM, Fang ZK, et al. Survival benefit of adjuvant TACE for patients with hepatocellular carcinoma and child-pugh B7 or B8 after hepatectomy. *BMC Cancer*. 2024;24(1):1241. doi:10.1186/s12885-024-13028-5
61. Wang H, Yu H, Qian YW, et al. Postoperative adjuvant transcatheter arterial chemoembolization improves the prognosis of patients with huge hepatocellular carcinoma. *Hepatobiliary Pancreat Dis Int*. 2021;20(3):232–239. doi:10.1016/j.hbpd.2020.12.018
62. Liang L, Li C, Diao YK, et al. Survival benefits from adjuvant transcatheter arterial chemoembolization in patients undergoing liver resection for hepatocellular carcinoma: a systematic review and meta-analysis. *Therap Adv Gastroenterol*. 2020;13:1756284820977693. doi:10.1177/1756284820977693
63. Peng Y, Shen S, Feng Y, et al. Prognostic analysis and limited efficacy of adjuvant TACE in hepatocellular carcinoma following hepatectomy: a propensity score-matched study. *Langenbecks Arch Surg*. 2025;410(1):92. doi:10.1007/s00423-025-03663-2
64. Chan KS, Tay WX, Cheo FY, et al. Preoperative transarterial chemoembolization (TACE) + liver resection versus upfront liver resection for large hepatocellular carcinoma (≥5 cm): a systematic review and meta-analysis. *Acta Chir Belg*. 2023;123(6):601–617. doi:10.1080/00015458.2023.2256539
65. Xiang Z, Li G, Mu L, et al. TACE combined with lenvatinib and camrelizumab for unresectable multiple nodular and large hepatocellular carcinoma (>5 cm). *Technol Cancer Res Treat*. 2023;22:15330338231200320. doi:10.1177/15330338231200320
66. Burki T. WHO's 2024 global hepatitis report. *Lancet Infect Dis*. 2024;24(6):e362–e363. doi:10.1016/S1473-3099(24)00307-4
67. Li Y, Ou Z, Yu D, et al. The trends in death of primary liver cancer caused by specific etiologies worldwide: results from the Global Burden of Disease Study 2019 and implications for liver cancer management. *BMC Cancer*. 2023;23(1):598. doi:10.1186/s12885-023-11038-3
68. Sun F, Liu Z, Wang B. Correlation between low-level viremia and hepatitis B-related hepatocellular carcinoma and recurrence: a retrospective study. *BMC Cancer*. 2021;21(1):1103. doi:10.1186/s12885-021-08483-3
69. Huang Y, Chen H, Zeng Y, et al. Development and validation of a machine learning prognostic model for hepatocellular carcinoma recurrence after surgical resection. *Front Oncol*. 2021;10:593741. doi:10.3389/fonc.2020.593741
70. He Z, Tang D. Perioperative predictors of outcome of hepatectomy for HBV-related hepatocellular carcinoma. *Front Oncol*. 2023;13:1230164. doi:10.3389/fonc.2023.1230164
71. Heo S, Yang J, Park J, et al. Association between viral replication activity and postoperative recurrence of HBV-Related hepatocellular carcinoma. *Aliment Pharmacol Ther*. 2025;61(10):1680–1691. doi:10.1111/apt.70085
72. Xiang YJ, Wang K, Qin YY, et al. Trajectories of postoperative hepatitis B virus (HBV) DNA and HBV-related hepatocellular carcinoma outcomes. *Eur J Surg Oncol*. 2025;51(2):109492. doi:10.1016/j.ejso.2024.109492
73. Choi WM, Kim GA, Choi J, et al. Non-linear association of baseline viral load with on-treatment hepatocellular carcinoma risk in chronic hepatitis B. *Gut*. 2024;73(4):649–658. doi:10.1136/gutjnl-2023-330225
74. Yan Q, Ni J, Zhang GL, et al. Efficacy of postoperative antiviral combined transcatheter arterial chemoembolization therapy in prevention of hepatitis B-related hepatocellular carcinoma recurrence. *Chin Med J*. 2013;126(5):855–859. doi:10.3760/cma.j.issn.0366-6999.20121871
75. Tu X, Zhang J, Li M, et al. Development and validation of a prediction model for hepatitis b virus-related hepatocellular carcinoma patients receiving postoperative adjuvant transarterial chemoembolization. *J Hepatocell Carcinoma*. 2023;10:1881–1895. doi:10.2147/JHC.S422565
76. Zhu SL, Zhong JH, Ke Y, et al. Comparative efficacy of postoperative transarterial chemoembolization with or without antiviral therapy for hepatitis B virus-related hepatocellular carcinoma. *Tumour Biol*. 2015;36(8):6277–6284. doi:10.1007/s13277-015-3313-6
77. Li X, Liang X, Li Z, et al. A novel stratification scheme combined with internal arteries in CT imaging for guiding postoperative adjuvant transarterial chemoembolization in hepatocellular carcinoma: a retrospective cohort study. *Int J Surg*. 2024;110(5):2556–2567. doi:10.1097/JS9.0000000000001191
78. Wang Z, Ren Z, Chen Y, et al. Adjuvant transarterial chemoembolization for HBV-Related hepatocellular carcinoma after resection: a randomized controlled study. *Clin Cancer Res*. 2018;24(9):2074–2081. doi:10.1158/1078-0432.CCR-17-2899
79. Li F, Guo Z, Zhang Y, et al. Postoperative adjuvant arterial chemoembolization improves the survival of hepatitis B virus-related hepatocellular carcinoma: a retrospective control study. *Ir J Med Sci*. 2015;184(4):753–759. doi:10.1007/s11845-014-1164-6
80. Hu H, Han XK, Long XR, et al. Prognostic nomogram for post-surgical treatment with adjuvant TACE in hepatitis B virus-related hepatocellular carcinoma. *Oncotarget*. 2016;7(36):58302–58314. doi:10.18632/oncotarget.11078

81. Shen J, Wang X, Wang N, et al. HBV reactivation and its effect on survival in HBV-related hepatocarcinoma patients undergoing transarterial chemoembolization combined with tyrosine kinase inhibitors plus immune checkpoint inhibitors. *Front Cell Infect Microbiol*. 2023;13:1179689. doi:10.3389/fcimb.2023.1179689
82. Wang L, Cao J, Liu Z, et al. Enhanced interactions within microenvironment accelerates dismal prognosis in HBV-related HCC after TACE. *Hepatol Commun*. 2024;8(10):e0548. doi:10.1097/HC9.0000000000000548
83. Li TE, Zhang Z, Wang Y, et al. A novel immunotype-based risk stratification model predicts postoperative prognosis and adjuvant TACE benefit in Chinese patients with hepatocellular carcinoma. *J Cancer*. 2021;12(10):2866–2876. doi:10.7150/jca.54408
84. Tadokoro T, Tani J, Morishita A, et al. The treatment of hepatocellular carcinoma with major vascular invasion. *Cancers*. 2024;16(14):2534. doi:10.3390/cancers16142534
85. Pham AT, Duc Vu T, Nguyen TD, et al. Surgical management for hepatocellular carcinoma with concurrent portal vein tumour thrombus and bile duct tumour thrombus: a case report. *Ann Med Surg*. 2024;86(6):3667–3673. doi:10.1097/MS9.0000000000002035
86. Conticchio M, Maggialetti N, Rescigno M, et al. Hepatocellular carcinoma with bile duct tumor thrombus: a case report and literature review of 890 patients affected by uncommon primary liver tumor presentation. *J Clin Med*. 2023;12(2):423. doi:10.3390/jcm12020423
87. Sun J, Wu J, Shi J, et al. Thrombus-First surgery for hepatocellular carcinoma with bile duct tumor thrombus. *J Gastrointest Surg*. 2021;25(8):1973–1979. doi:10.1007/s11605-020-04813-1
88. Huang LM, Zeng ZX, Wu JY, et al. Surgical outcomes of hepatocellular carcinoma with extrahepatic bile duct tumor thrombus: a multicenter study. *Front Oncol*. 2023;13:1291479. doi:10.3389/fonc.2023.1291479
89. Iizumi T, Okumura T, Hasegawa N, et al. Proton beam therapy for hepatocellular carcinoma with bile duct invasion. *BMC Gastroenterol*. 2023;23(1):267. doi:10.1186/s12876-023-02897-y
90. Xiangji L, Weifeng T, Bin Y, et al. Surgery of hepatocellular carcinoma complicated with cancer thrombi in bile duct: efficacy for criteria for different therapy modalities. *Langenbecks Arch Surg*. 2009;394(6):1033–1039. doi:10.1007/s00423-009-0496-6
91. Chen ZH, Feng JK, Sun JX, et al. Postoperative adjuvant transarterial chemoembolization improves outcomes of hepatocellular carcinoma associated with bile duct tumor thrombus: a propensity score matching analysis. *HPB*. 2022;24(4):547–557. doi:10.1016/j.hpb.2021.09.005
92. Huang Q, Lin K, Wang L, et al. Postoperative adjuvant transarterial chemoembolization improves short-term prognosis of hepatocellular carcinoma with bile duct tumor thrombus: a propensity-score matching study. *Cancer Manag Res*. 2020;Volume 12:9183–9195. doi:10.2147/CMAR.S270467
93. Feng JK, Chen ZH, Sun JX, et al. Concurrent bile duct resection versus concomitant thrombectomy for hepatocellular carcinoma associated with bile duct tumor thrombus: a propensity score matching analysis. *Ann Transl Med*. 2021;9(6):457. doi:10.21037/atm-20-6449
94. Prasoppokakorn T, Buntho A, Ingrungruanglert P, et al. Circulating tumor cells as a prognostic biomarker in patients with hepatocellular carcinoma. *Sci Rep*. 2022;12(1):18686. doi:10.1038/s41598-022-21888-9
95. Lei Y, Wang X, Tian Y, et al. Effect of various hepatectomy procedures on circulating tumor cells in postoperative patients: a case-matched comparative study. *Front Med*. 2023;10:1209403. doi:10.3389/fmed.2023.1209403
96. Zhang J, Peng H, Wang B, et al. Efficacy of postoperative adjuvant transcatheter arterial chemoembolization in hepatocellular carcinoma patients with mesenchymal circulating tumor cell. *J Gastrointest Surg*. 2021;25(7):1770–1778. doi:10.1007/s11605-020-04755-8
97. Zhao YF, Xiong X, Chen K, et al. Evaluation of the therapeutic effect of adjuvant transcatheter arterial chemoembolization based on Ki67 after hepatocellular carcinoma surgery. *Front Oncol*. 2021;11:605234. doi:10.3389/fonc.2021.605234
98. Zhang TQ, Su QQ, Huang XY, et al. Micro RNA-4651 serves as a potential biomarker for prognosis when selecting hepatocellular carcinoma patients for postoperative adjuvant transarterial chemoembolization therapy. *Hepatol Commun*. 2018;2(10):1259–1273. doi:10.1002/hep4.1245
99. Li XS, Wang JH, Yang XZ, et al. Beneficial effects of Cripto-1 for transarterial chemoembolization in hepatocellular carcinoma. *Aging*. 2019;11(10):2998–3011. doi:10.18632/aging.101951
100. Feng GY, Shi ZR, Zhao YF, et al. Therapeutic effect of postoperative adjuvant transcatheter arterial chemoembolization based on the neutrophil-to-lymphocyte ratio. *Front Surg*. 2022;9:1072451. doi:10.3389/fsurg.2022.1072451
101. Gu J, Zhang X, Cui R, et al. Prognostic predictors for patients with hepatocellular carcinoma receiving adjuvant transcatheter arterial chemoembolization. *Eur J Gastroenterol Hepatol*. 2019;31(7):836–844. doi:10.1097/MEG.0000000000001346
102. Wang M, Qian G, Xiao H, et al. Prognostic significance of postoperative serological incomplete conversion of AFP and PIVKA-II after hepatic resection for hepatocellular carcinoma: a multicenter analysis of 1,755 patients. *Oncologist*. 2024;29(12):e1723–e1733. doi:10.1093/oncolo/oyae139
103. Zhao H, Liu X, Xu R, et al. Predictive value of and relationship between the gamma-glutamyl transpeptidase to lymphocyte ratio and CT features in hepatocellular carcinoma patients with postoperative adjuvant TACE. *J Buon*. 2021;26(4):1346–1354.
104. Chen MY, Juengpanich S, Hu JH, et al. Prognostic factors and predictors of postoperative adjuvant transcatheter arterial chemoembolization benefit in patients with resected hepatocellular carcinoma. *World J Gastroenterol*. 2020;26(10):1042–1055. doi:10.3748/wjg.v26.i10.1042
105. Xia Z, Zhao Y, Zhao H, et al. Serum alanine aminotransferase to hemoglobin ratio and radiological features predict the prognosis of postoperative adjuvant TACE in patients with hepatocellular carcinoma. *Front Oncol*. 2022;12:989316. doi:10.3389/fonc.2022.989316
106. Liang Y, Yang R, Shang J, et al. Lung immune prognostic index-based nomogram for recurrence of hepatocellular carcinoma after postoperative adjuvant TACE. *J Cancer Res Clin Oncol*. 2023;149(18):16461–16471. doi:10.1007/s00432-023-05413-7
107. Sun H, Wang H, Wang Y, et al. Adjuvant transarterial chemoembolization timing after radical resection is an independent prognostic factor for patients with hepatocellular carcinoma. *Front Oncol*. 2023;13:1129065. doi:10.3389/fonc.2023.1129065
108. Niekamp S, Marr SK, Oei TA, et al. Modularity of PRC1 composition and chromatin interaction define condensate properties. *Mol Cell*. 2024;84(9):1651–1666.e12. doi:10.1016/j.molcel.2024.03.001
109. Badr EAE, Elmongy EI, Mostafa RG, et al. The role of LINC01564, RAMS11, CBX4 and TOP2A in hepatocellular carcinoma. *Biomedicines*. 2022;11(1):56. doi:10.3390/biomedicines11010056
110. Wang B, Tang J, Liao D, et al. Correction to: chromobox homolog 4 is correlated with prognosis and tumor cell growth in hepatocellular carcinoma. *Ann Surg Oncol*. 2021;28(Suppl 3):885–886. doi:10.1245/s10434-021-10400-8
111. Jiao HK, Xu Y, Li J, et al. Prognostic significance of Cbx4 expression and its beneficial effect for transarterial chemoembolization in hepatocellular carcinoma. *Cell Death Dis*. 2015;6(3):e1689. doi:10.1038/cddis.2015.57

112. Li W, Chen H, Wang Z, et al. Chromobox 4 (CBX4) promotes tumor progression and stemness via activating CDC20 in gastric cancer. *J Gastrointest Oncol*. 2022;13(3):1058–1072. doi:10.21037/jgo-22-549
113. Yang X, Ni H, Lu Z, et al. Mesenchymal circulating tumor cells and Ki67: their mutual correlation and prognostic implications in hepatocellular carcinoma. *BMC Cancer*. 2023;23(1):10. doi:10.1186/s12885-023-10503-3
114. Xu JX, Xing WT, Peng YC, et al. Outcomes of postoperative adjuvant transarterial chemoembolization for hepatocellular carcinoma according to the Ki67 index. *Future Oncol*. 2022;18(17):2113–2125. doi:10.2217/fon-2021-1443
115. Su Y, Xie R, Xu Q. Upregulation of miR-1266-5p serves as a prognostic biomarker of hepatocellular carcinoma and facilitates tumor cell proliferation, migration and invasion. *Acta Biochim Pol*. 2021;68(2):293–300. doi:10.18388/abp.2020_5569
116. Hamdy H, Yang Y, Cheng C, et al. Identification of potential hub genes related to aflatoxin B1, liver fibrosis and hepatocellular carcinoma via integrated bioinformatics analysis. *Biology*. 2023;12(2):205. doi:10.3390/biology12020205
117. Arnouk H, Yum G, Shah D. Cripto-1 as a key factor in tumor progression, epithelial to mesenchymal transition and cancer stem cells. *Int J Mol Sci*. 2021;22(17):9280. doi:10.3390/ijms22179280
118. Ke Q, Xiang F, Xiao C, et al. Exploring the clinical value of preoperative serum gamma-glutamyl transferase levels in the management of patients with hepatocellular carcinoma receiving postoperative adjuvant transarterial chemoembolization. *BMC Cancer*. 2021;21(1):1117. doi:10.1186/s12885-021-08843-z
119. Liu H, Zhang A, Qian N, et al. Postoperative transarterial chemoembolization benefits patients with high γ-glutamyl transferase levels after curative hepatectomy for hepatocellular carcinoma: a survival stratification analysis. *Tohoku J Exp Med*. 2012;227(4):269–280. doi:10.1620/tjem.227.269
120. Shesh BP, Connor JR. A novel view of ferritin in cancer. *Biochim Biophys Acta Rev Cancer*. 2023;1878(4):188917. doi:10.1016/j.bbcan.2023.188917
121. Fan M, Niu T, Lin B, et al. Prognostic value of preoperative serum ferritin in hepatocellular carcinoma patients undergoing transarterial chemoembolization. *Mol Clin Oncol*. 2024;20(3):22. doi:10.3892/mco.2024.2720
122. Society of Chemotherapy, Chinese Anti-Cancer Association; Committee of Neoplastic Supportive-Care, China Anti-Cancer Association. Consensus on the clinical diagnosis, treatment, and prevention of cancer related anemia in China (2023 edition). *Zhonghua Zhong Liu Za Zhi*. 2023;45(12):1032–1040. doi:10.3760/cma.j.cn112152-20230711-00289
123. Baj J, Kołodziej M, Kobak J, et al. Significance of immune and non-immune cell stroma as a microenvironment of hepatocellular carcinoma-from inflammation to hepatocellular carcinoma progression. *Int J Mol Sci*. 2024;25(19):10233. doi:10.3390/ijms251910233
124. Xu C, Wu F, Du L, et al. Significant association between high neutrophil-lymphocyte ratio and poor prognosis in patients with hepatocellular carcinoma: a systematic review and meta-analysis. *Front Immunol*. 2023;12:18686.
125. Qin R, Jin T, Xu F. Biomarkers predicting the efficacy of immune checkpoint inhibitors in hepatocellular carcinoma. *Front Immunol*. 2023;14:1326097. doi:10.3389/fimmu.2023.1326097
126. Li S, Feng X, Cao G, et al. Prognostic significance of inflammatory indices in hepatocellular carcinoma treated with transarterial chemoembolization: a systematic review and meta-analysis. *PLoS One*. 2020;15(3):e0230879. doi:10.1371/journal.pone.0230879
127. Nelli F, Fabbri A, Virtuoso A, et al. Early changes in LIPI score predict immune-related adverse events: a propensity score matched analysis in advanced non-small cell lung cancer patients on immune checkpoint blockade. *Cancers*. 2024;16(2):453. doi:10.3390/cancers16020453
128. Li B, Qin Y, Qiu Z, et al. A cohort study of hepatectomy-related complications and prediction model for postoperative liver failure after major liver resection in 1,441 patients without obstructive jaundice. *Ann Transl Med*. 2021;9(4):305. doi:10.21037/atm-20-5472
129. Wei T, Zhang XF, Bagante F, et al. Postoperative infectious complications worsen long-term survival after curative-intent resection for hepatocellular carcinoma. *Ann Surg Oncol*. 2022;29(1):315–324. doi:10.1245/s10434-021-10565-2
130. Wang L, Lin N, Lin K, et al. The clinical value of postoperative transarterial chemoembolization for resectable patients with intermediate hepatocellular carcinoma after radical hepatectomy: a propensity score-matching study. *J Gastrointest Surg*. 2021;25(5):1172–1183. doi:10.1007/s11605-020-04588-5