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Recent Advances in Interventional Therapy for Hepatocellular Carcinoma

Xuan Lan[1]; Xinyue Zhang[1]; Encun Hou[2]*

[1]Graduate School, Guangxi University of Chinese Medicine, Nanning, Guangxi, China.

[2]Ruikang Hospital, Guangxi University of Chinese Medicine, Nanning, Guangxi, China.

Abstract

Hepatocellular Carcinoma (HCC) is one of the most prevalent and lethal cancers globally. Early diagnosis remains challenging due to the disease's subtle symptoms, often leading to detection at advanced stages with limited treatment options and poor outcomes. In recent years, interventional therapies have emerged as promising strategies to enhance tumor response and improve patient prognosis. This review examines the latest advancements in interventional treatments for HCC, including Transarterial Embolization (TAE/TACE), percutaneous liver tumor ablation techniques (RFA, MWA), and Transarterial Radioembolization (TARE). We evaluate the effectiveness and limitations of these therapies in clinical practice, integrating current research findings. Furthermore, we explore the growing trend towards personalized treatment approaches and identify future research directions, aiming to guide clinical practice and inform further studies.

Keywords: Hepatocellular carcinoma; Interventional therapy; Hepatic artery chemoembolization; Radiofrequency ablation; Recent advances in nanotechnology into therapy.

Introduction

Hepatocellular Carcinoma (HCC) is among the most prevalent and deadly cancers globally. Recent cancer statistics reveal that the incidence and mortality rates of HCC rank among the highest in many countries. This cancer predominantly affects individuals with risk factors such as hepatitis B and C infections, cirrhosis, and metabolic conditions like nonalcoholic fatty liver disease. The difficulty in early diagnosis, due to the absence of clear symptoms, often results in detection at advanced stages, where treatment options are limited and the prognosis is poor. As a result, the pursuit of more effective treatments and technologies is crucial to improving patient survival rates. Although progress has been made in diagnosis and therapies-including surgical resection, liver transplantation, and local ablation-treatment options for unresectable HCC (uHCC) remain limited. Nonetheless, recent advancements in interventional therapies have shown considerable potential in enhancing tumor response rates and improving patient outcomes.

Interventional therapy is a vital component in the localized treatment of liver cancer. Unlike traditional surgery and systemic therapies, interventional approaches offer the benefits of less trauma and faster recovery. Key treatments in this category include hepatic artery embolization, percutaneous tumor ablation techniques such as radiofrequency and microwave ablation, transarterial chemoembolization, transarterial radioembolization, and venous embolization. These methods allow for direct targeting of the tumor, effectively controlling its growth and spread while enhancing the patient's quality of life, as outlined in Table 1.

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Correspondance: *Encun Hou, Ruikang Hospital, Guangxi University of Chinese Medicine, Nanning, Guangxi, China.*

Email: houec2008@sina.com

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Table 1: Comparison of various interventional therapies for hepatocellular carcinoma.

	Characteristics	Indications	Advantages	Disadvantages	Main complications
Transarterial Embolization/ Chemoembolization (TAE/TACE)	Injection of embolic agents or chemotherapy drugs into the hepatic artery to block tumor blood supply.	Intermediate or advanced hepatocellular carcinoma (HCC), patients ineligible for surgical resection.	Improves local tumor control, effective for larger tumors, good local ablation effect.	Potential for TACE resistance; lower response rate in some patients.	Liver dysfunction, abdominal pain, fever, nausea, vomiting, liver abscess. Reference studies .
Radiofrequency Ablation (RFA)	Uses high-frequency electrical currents to generate heat and destroy tumor tissue.	Early-stage HCC, tumor diameter ≤3 cm, patients ineligible for surgery.	Minimally invasive, quick recovery, comparable therapeutic effect to surgery.	Limited to smaller tumor sizes, possible recurrence.	Bleeding, infection, bile duct injury, liver abscess. Studies show recurrence rates vary .
Microwave Ablation (MWA)	Tumor cells are ablated through microwave heating.	Early and locally advanced HCC, tumor diameter ≤5 cm, patients ineligible for surgery.	Wide ablation range, fast ablation speed, suitable for larger tumors.	Higher equipment cost, requires precise control during treatment.	Bleeding, infection, bile duct injury, liver abscess. Device precision and operator experience impact outcomes .
Transarterial Radioembolization (TARE/Selective Internal Radiation Therapy - SIRT)	Injection of radioactive microspheres into the hepatic artery, releasing radiation to kill tumor cells.	Advanced HCC, especially for patients with portal vein invasion.	Minimal damage to surrounding normal tissue, effective for portal vein invasion cases.	Requires individualized dose and treatment plan, radiation-related side effects.	Radiation hepatitis, gastrointestinal ulcers, liver dysfunction, radiation pneumonitis. Long-term survival varies .
Portal Vein Embolization (PVE)	Blocking portal vein branches to induce liver regeneration in the non-tumor portion.	Patients preparing for liver resection with insufficient liver reserve function.	Promotes liver regeneration, increases success rate of liver resection.	Risk of portal vein thrombosis.	Portal vein thrombosis, liver dysfunction, abdominal pain. Typically used in pre-surgical strategies .
Percutaneous Ethanol Injection	Injection of absolute ethanol into the tumor to cause dehydration and necrosis of tumor tissue.	HCC <3 cm, patients ineligible for surgery or other interventional therapies.	Simple, cost-effective, effective for small HCCs.	Poor efficacy for larger tumors, may require multiple treatments.	Localized pain, tissue damage from ethanol leakage. Recommended for early-stage cases .
Combination Therapy	Use of multiple interventional treatments to enhance therapeutic efficacy.	Complex cases where a single treatment is ineffective for HCC.	Improves overall survival and disease-free survival rates, adaptable for tumors of varying sizes.	Complex treatment process, multiple considerations required.	Varies based on specific combination therapy used. Combining TACE with thermal ablation shows improved outcomes .
Interferon Therapy	Reduces recurrence rates by inducing interferon-related genes or combining with other drugs.	Post-surgery or post-treatment to prevent recurrence.	Improves post-surgery survival rates, reduces recurrence risks.	Uncertain mechanisms, potential side effects.	Flu-like symptoms, leukopenia, depression. Commonly combined with antiviral therapy.
Nanotechnology Applications	Uses nanomaterials to enhance drug delivery and reduce side effects.	All stages of HCC, especially difficult-to-treat cases.	Enhances drug release at target sites, improves therapeutic outcomes.	Still in research stage, limited clinical application.	Toxicity and side effects depend on the specific nanomaterials used. Potential future breakthrough for difficult cases.

As technology advances, interventional therapy techniques are continuously improving in effectiveness. Staying informed on the latest research and clinical data is crucial to providing the most effective treatment options.

This review aims to provide an overview of the latest advancements in interventional therapy for hepatocellular carcinoma, focusing on the most widely used methods and exploring emerging technologies and strategies. By analyzing techniques such as radiofrequency ablation, microwave ablation, TACE, and TARE, and incorporating the latest clinical research, we will assess the effectiveness and challenges of these approaches in clinical practice. Additionally, we will discuss the shift toward individualized treatment and outline future research directions to guide clinical practice and inform further studies.

Hepatic Artery Embolization (TAE/TACE)

Hepatic Artery Embolization (TAE) and Hepatic Artery Chemoembolization (TACE) are among the most common interventional treatments for liver cancer. These procedures involve injecting embolic agents or chemotherapeutic drugs into the hepatic artery to block the blood supply to the tumor, leading to tumor hypoxia and necrosis. In TAE, only embolic agents are used to obstruct blood flow, while in TACE, chemotherapeutic drugs are administered first, followed by embolization to enhance the therapeutic effect. TACE is the standard treatment for mid-stage hepatocellular carcinoma, particularly for patients who are not candidates for surgical resection. Recent advancements in TACE technology, including the development of new drugs and embolization materials, have improved treatment efficacy, safety, patient survival

rates, and quality of life. However, the response rate remains suboptimal. Research into the molecular mechanisms underlying TACE resistance is crucial for identifying new therapeutic targets and refining TACE treatment strategies [1-9]. Additionally, combining hepatic resection with TACE has been shown to significantly improve survival rates in patients with giant hepatocellular carcinoma [2].

Combined treatment of TACE and surgical resection

Surgical Resection (SR) is a curative treatment for HCC, but postoperative recurrence remains a challenge for long-term outcomes. Some studies suggest that preoperative TACE can increase the resection rate, reduce tumor recurrence, and improve prognosis. However, other research indicates that preoperative TACE does not enhance long-term survival and may even negatively impact the resection rate [10-22]. Further studies are necessary to identify the factors that influence the effectiveness of combining preoperative TACE with surgical resection. A meta-analysis comparing the survival benefits of Partial Hepatectomy (PH) and Transcatheter Arterial Chemoembolization (TACE) in patients with BCLC-B stage multiple HCC found that those who underwent PH had significantly higher Overall Survival (OS) rates than those treated with TACE, with clear advantages at 1, 3, and 5 years. These findings suggest that partial hepatectomy may offer greater survival benefits for eligible patients with BCLC-B stage multiple HCC [21].

Combined treatment of TACE and portal vein embolization

HCC is often complicated by dual blood supply and portal vein tumor thrombus, which can reduce the effectiveness of TACE. Theoretically, combining TACE with Portal Vein Embolization (PVE) could enhance therapeutic outcomes for HCC. Studies investigating the feasibility, efficacy, long-term survival benefits, and side effects of this combination therapy have shown that it significantly improves treatment response and survival rates [19]. A meta-analysis assessed the efficacy and safety of combining Stereotactic Body Radiotherapy (SBRT) with Transcatheter Arterial Chemoembolization (TACE) versus using either SBRT or TACE alone in patients with inoperable Hepatocellular Carcinoma (HCC) and Portal Vein Tumor Thrombosis (PVTT). The study, which included data from nine studies involving 938 patients, found that the combination of SBRT and TACE significantly outperformed monotherapy in terms of 1- and 2-year Overall Survival (OS) and Objective Response Rate (ORR), while also reducing the rate of disease Progression (PD). Subgroup analysis revealed that the combination therapy was more effective when the treatment interval was less than 28 days, with no significant difference observed when the interval was 28 days or longer. The conclusion is that SBRT combined with TACE is superior to monotherapy and is recommended for patients with inoperable HCC with PVTT [23-28].

TACE combined with radioablation therapy

The combination of TACE with radio ablative therapy has proven effective in enhancing tumor response and survival rates in HCC patients. Compared to TACE alone, this approach offers superior tumor control and improved survival outcomes [27].

Comparison of conventional TACE and drug-eluting microsphere TACE

A meta-analysis compared the clinical safety and efficacy of Conventional TACE (C-TACE) with Drug-Eluting microsphere TACE (DEB-TACE). The findings indicated that DEB-TACE achieved significantly higher complete response rates, disease control rates, and 3-year survival rates compared to C-TACE. However, there were no significant differences between the two in terms of 1- and 2-year survival rates, 30-day mortality rates, or complete necrosis rates [4].

The role of TACE in the management of Intrahepatic Cholangiocarcinoma (ICC)

A systematic review and meta-analysis evaluated the effectiveness of TACE in patients with Intrahepatic Cholangiocarcinoma (ICC). The results demonstrated that TACE significantly improved Overall Survival (OS), with Postoperative Prophylactic TACE (PPTACE) showing particularly favorable survival outcomes. However, TACE had no significant impact on Disease-Free Survival (DFS) and was less effective than surgical resection. Another meta-analysis focused on postoperative adjuvant TACE for ICC found that while TACE significantly improved 1-year OS, it had no notable effect on 3- and 5-year OS. Additionally, TACE significantly reduced the Hazard Ratio (HR) for ICC patients, indicating its effectiveness in treating ICC [11].

Management of TACE complications

TACE is a widely used nonsurgical treatment for advanced HCC, but it carries risks of complications, such as acute necrotizing pancreatitis caused by fatty acid contrast agents, though these are extremely rare. To prevent such complications, prophylactic measures include injecting embolic material into the distal branches of the hepatic artery to prevent drug backflow [20].

Transarterial Radioactive Microsphere Therapy (TARE)

Transarterial Radioactive Microsphere Therapy (TARE), also known as Selective Internal Radiation Therapy (SIRT), involves injecting radioisotope microspheres into the hepatic artery to target the blood vessels supplying the tumor. These microspheres are absorbed by the tumor tissue, releasing radioactive particles that directly destroy tumor cells while minimizing damage to surrounding healthy liver tissue. TARE is especially suitable for patients with advanced, unresectable liver cancer and has shown good therapeutic effects in cases involving portal vein invasion. To optimize therapeutic efficacy and minimize side effects, TARE requires individualized dosage and treatment planning. In patients with HCC and concomitant portal vein tumor thrombus, combining TACE with portal vein Radioactive Seed Implantation (RSI) significantly improves Overall Survival (OS) and reduces the progression of tumor thrombus. This combined treatment enhances efficacy while maintaining a safety profile and side effects comparable to conventional TACE [26]. A meta-analysis revealed that combining transarterial chemoembolization (TACE) with I-125 seed implantation significantly enhances the clinical response rate and extends overall survival in patients with advanced Hepatocellular Carcinoma (HCC). This combination therapy has demonstrated promising clinical outcomes, making it a potential treatment strategy for improving patient prognosis [6].

Percutaneous hepatic puncture for liver tumor ablation

Percutaneous Hepatopuncture Liver Tumor Ablation is an imaging-guided technique used to locally treat liver cancer by inserting a fine needle through the skin. The two common methods of ablation are Radiofrequency Ablation (RFA) and Microwave Ablation (MWA). RFA destroys tumor tissue by generating heat through high-frequency electrical currents, while MWA heats tumor cells using microwaves. Both methods have proven effective in reducing tumor size and have demonstrated good therapeutic outcomes in early-stage and locally advanced liver cancer. When selecting between these ablation techniques, factors such as tumor size, location, and the patient's overall health must be carefully considered. Image-guided Local Thermal Ablation (LTA) is particularly valuable for treating Hepatocellular Carcinoma (HCC) in patients who are not candidates for surgical resection. RFA and MWA are two of the most widely used LTA techniques in clinical practice. For tumors ≤3 cm in diameter, RFA can achieve therapeutic outcomes comparable to surgical resection, while MWA is effective for tumors up to 5 cm. Additionally, for patients with borderline liver function, LTA may offer significant benefits as a first-line treatment option [3]. The combination of Transarterial Chemoembolization (TACE) and Radiofrequency Ablation (RFA) has demonstrated significant improvements in tumor response rates and survival outcomes for patients with Hepatocellular Carcinoma (HCC). Compared to TACE or RFA alone, this combination therapy provides superior overall survival and recurrence-free survival, particularly in patients with tumors larger than 3 cm in diameter [15]. Studies suggest that combining Transarterial Chemoembolization (TACE) with thermal ablation may lead to improved prognosis. However, clear evidence regarding the efficacy and safety of this combination therapy remains limited [10].

Percutaneous hepatic puncture drug injection

Percutaneous hepatic puncture drug injection involves delivering drugs directly into the tumor via a needle. Commonly administered drugs include local chemotherapeutic agents and targeted therapies. This method allows for higher drug concentrations within the tumor while minimizing the impact on surrounding healthy liver tissue. Local chemotherapy injections are typically used for smaller tumors, while targeted therapies are designed to act on specific molecular targets. Although less frequently employed in clinical practice, this approach offers a viable treatment option for patients who cannot undergo other therapies. Arsenic Trioxide (ATO), a treatment used in China for centuries, has recently been applied in the management of liver cancer. Studies indicate that combining ATO with Transarterial Chemoembolization (TACE) enhances the objective response rate, disease control rate, and overall survival in patients with hepatocellular carcinoma, while maintaining a favorable safety profile [1].

Recent technologies and advances

Application of triple therapy

In recent years, Chinese researchers have developed and implemented a triple therapy approach involving Transcatheter Arterial Chemoembolization (TACE), levatinib, and anti-PD-1 antibodies. This treatment strategy has demonstrated significant tumor response rates and has improved patient outcomes by converting some previously unresectable tumors into resectable ones [24].

Mechanisms and applications of interferon therapy

The role of interferon in treating hepatocellular carcinoma has been extensively researched. Interferon, either through the induction of interferon-related genes or in combination with other drugs, has been shown to reduce postoperative recurrence rates and improve survival outcomes [16]. However, the specific mechanism of interferon's action in liver cancer treatment remains to be fully understood, necessitating further research to optimize its therapeutic application.

Effectiveness of multidrug combination therapy

The use of multidrug combination therapy in advanced hepatocellular carcinoma has gained considerable attention. A case report demonstrated that combining TACE, FOLFOX-based Hepatic Artery Infusion Chemotherapy (HAIC), and treatment with karelizumab and lysovirus led to significant tumor shrinkage, ultimately allowing for successful surgical resection [13]. This suggests that multidrug combination therapy may provide new therapeutic options for patients with advanced hepatocellular carcinoma that is initially unresectable.

Nanotechnology in liver cancer

Nanotechnology holds significant promise for liver cancer treatment. By designing and utilizing nanomedicine carriers, such as SPIONs and PLGA microspheres, nanoparticles can selectively target tumor cells, minimizing the impact on healthy tissues and increasing drug concentration at the tumor site. These nanoparticles enhance therapeutic efficacy by improving drug delivery and release directly at the target, while nanomaterials enable targeted drug release by responding to the tumor microenvironment, such as changes in pH, temperature, or redox conditions. This approach reduces systemic side effects and improves the overall safety of the treatment [25]. Nanotechnology has garnered significant attention in the monitoring, imaging, pathological diagnosis, and treatment of Hepatocellular Carcinoma (HCC). Clinically, it plays a crucial role in diagnosing early-stage HCC and delivering precise treatment for advanced stages, ultimately enhancing therapeutic efficacy and improving patient outcomes. Nanotechnology shows great potential in various treatment modalities, including thermal ablation, systemic therapy, Transarterial Chemoembolization (TACE), molecular targeted therapy, and immunomodulatory therapy [23].

Impact of combination therapy on specific cases

In complex cases, such as liver cancer with cancerous thrombus in the inferior vena cava and right atrium, a multidisciplinary approach combined with cardiac-priority surgery can significantly extend survival [15]. Treating Hepatocellular Carcinoma (HCC) in patients with Chronic Kidney Disease (CKD) presents significant challenges. These patients often have a high incidence of viral hepatitis, which increases their risk of developing HCC. Renal insufficiency can adversely affect both immediate and long-term outcomes of cancer treatment. While treatments such as thermal ablation, TACE, hepatic resection, and liver transplantation are available for patients with CKD, there is a lack of validated treatment algorithms specifically tailored to this population [18]. This highlights the importance of individualized multimodal treatment strategies for complex cases. For patients with Hepatocellular Carcinoma (HCC) who are initially ineligible for transplantation,

downstaging offers a promising approach to reduce tumor burden to within transplantation criteria, leading to favorable postoperative survival outcomes. Various therapies, including TACE, Transarterial Radiation Therapy (TARE), Percutaneous Ethanol Injection (PEI), and Radiofrequency Ablation (RFA), have been employed for downstaging. However, further discussion is needed to standardize and optimize these downstaging treatments [7]. Gastrointestinal Stromal Tumors (GIST) are the most common mesenchymal tumors of the digestive tract, accounting for 1%-3% of gastrointestinal tumors. Primary hepatic GIST is a rare form of this tumor, potentially linked to cells resembling Cajal mesenchymal cells. Although imaging can characterize primary hepatic GIST, it often presents without specific signs or symptoms, making definitive diagnosis dependent on pathological and genetic analysis. Local resection is the primary treatment approach, while imatinib is the preferred chemotherapeutic agent for unresectable advanced cases. Additionally, treatments such as TACE, Radiofrequency Ablation (RFA), and Microwave Ablation (MWA) have been shown to improve overall survival in these patients [17]. Primary hepatic neuroendocrine carcinoma is a rare tumor often associated with elevated Procalcitonin (PCT) levels. A case report demonstrated that while the patient's PCT levels remained high despite antibiotic treatment, they significantly decreased following effective TACE therapy. This suggests that PCT levels could serve as a useful biomarker for monitoring treatment response [5]. Primary hepatobiliary spindle cell sarcoma is a rare tumor, with surgical resection being the primary treatment option. For patients who decline adjuvant chemotherapy and radiotherapy, TACE can serve as an effective palliative treatment [12].

Doege-Potter syndrome is a hypoglycemic condition caused by a non-pancreatic islet cell tumor, with complete tumor resection being the primary treatment. In cases where the tumor is unresectable, TACE can be used as a palliative measure to potentially make the patient eligible for future surgery [8]. For advanced Hepatocellular Carcinoma (HCC), treatment options include surgery, radiotherapy, and TACE. In recent years, significant progress in molecularly targeted therapies and immunotherapies has also provided new hope for patients [29]. Combining these treatments with individualized care and proactive management by a multidisciplinary team can help optimize treatment strategies [14].

Conclusion

In summary, interventional therapy for hepatocellular carcinoma has made significant strides in areas such as nanotechnology, multimodal combination treatments, and tailored approaches for specific patient populations. Comparisons between partial hepatectomy and TACE in patients with BCLC-B stage multiple HCC suggest that surgical resection may offer a greater survival benefit. Additionally, the use of TACE in Intrahepatic Cholangiocarcinoma (ICC) and its combination with thermal ablation or I-125 seed implantation have shown considerable therapeutic potential. Future research should focus on optimizing current treatment options and evaluating emerging technologies to improve liver cancer outcomes. This will enable the development of more effective treatment strategies, ultimately enhancing patient prognosis and quality of life.

Declarations

Conflict of interest: The authors declare no conflicts of interest.

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References

1. Chen J, et al. The application of arsenic trioxide in cancer: An umbrella review of meta-analyses based on randomized controlled trials. J Ethnopharmacol. 2023; 316: 116734.
2. Chierici A, et al. Multimodal treatment confers best overall survival results in patients with huge hepatocellular carcinoma: A systematic review and network meta-analysis. HPB (Oxford). 2014; 26(7): 895-902.
3. Deng M, et al. Recent Advances in Local Thermal Ablation Therapy for Hepatocellular Carcinoma. Am Surg. 2023; 89(5): 1966-1973.
4. Han T, et al. The clinical safety and efficacy of conventional transcatheter arterial chemoembolization and drug-eluting beads-transcatheter arterial chemoembolization for unresectable hepatocellular carcinoma: A meta-analysis. Biosci Trends. 2019; 13(5): 374-381.
5. Han X, et al. Elevated procalcitonin levels in primary hepatic neuroendocrine carcinoma: Case report and literature review. Medicine (Baltimore). 2020; 99(31): e21210.
6. Hou JP, et al. I-125 seeds insertion with TACE for advanced HCC: a meta-analysis of randomized controlled trials. Minim Invasive Ther Allied Technol. 2023; 31(6): 848-855.
7. Jiang G, et al. Downstaging treatment for patients with hepatocelluar carcinoma before transplantation. Transplant Rev (Orlando). 2021; 35(2): 100606.
8. Jin K, et al. Targeting-intratumoral-lactic-acidosis transcatheter-arterial-chemoembolization for non-islet cell tumor hypoglycemia secondary to a liver metastatic solitary fibrous tumor: A case report and literature review. Front Endocrinol (Lausanne). 2022; 13: 955687.
9. Li J, et al. Molecular mechanisms of TACE refractoriness: Directions for improvement of the TACE procedure. Life Sci. 2024; 342: 122540.
10. Liu B, et al. The combination of transcatheter arterial chemoembolisation (TACE) and thermal ablation versus TACE alone for hepatocellular carcinoma. Cochrane Database Syst Rev 1. 2022; 1: Cd013345.
11. Liu JB, et al. Prognosis for intrahepatic cholangiocarcinoma patients treated with postoperative adjuvant transcatheter hepatic artery chemoembolization. Curr Probl Cancer. 2020; 44(6): 100612.
12. Long X, et al. Primary spindle cell sarcoma of gallbladder: An unusual case report and a literature review. Medicine (Baltimore). 2022; 101(2): e28549.
13. Lu G, et al. Case Report and Literature Review of Multi-drugs Synergy and Targeted Comprehensive Treatment in Advanced Hepatocellular Carcinoma. Curr Cancer Drug Targets. 2024; 24(3): 368-374.

14. Lu J, et al. Management of patients with hepatocellular carcinoma and portal vein tumour thrombosis: comparing east and west. Lancet Gastroenterol Hepatol. 2019; 4(9): 721-730.

15. Nishiwaki Y, et al. Fifteen-year survival of a hepatocellular carcinoma extending into the right atrium treated by surgical resection with the heart-first approach under cardiopulmonary bypass: a case report and review of the literature. Clin J Gastroenterol. 2024; 17(1): 118-129.

16. Peng C, et al. Mechanism of action and treatment of type I interferon in hepatocellular carcinoma. Clin Transl Oncol. 2024; 26(2): 326-337.

17. Qian XH, et al. A 76-year-old man was diagnosed with multiple hepatocellular carcinomas (HCCs). World J Gastroenterol. 2020; 26(40): 6195-6206.

18. Sarno G, et al. Hepatocellular carcinoma in patients with chronic renal disease: Challenges of interventional treatment. Surg Oncol. 2020; 36: 42-50.

19. Shao Z, et al. Combination of transcatheter arterial chemoembolization and portal vein embolization for patients with hepatocellular carcinoma: A review. World J Surg Oncol. 2021; 19(1): 293.

20. Tan Y, et al. Pancreas lipiodol embolism induced acute necrotizing pancreatitis following transcatheter arterial chemoembolization for hepatocellular carcinoma: A case report and literature review. Medicine (Baltimore). 2019; 98(48): e18095.

21. Wang P, et al. Partial hepatectomy vs. transcatheter arterial chemoembolization for multiple hepatocellular carcinomas of BCLC-B stage: A meta-analysis of high-quality studies. Eur J Surg Oncol. 2022; 48(8): 1685-1691.

22. Wei ZQ, YW Zhang. Transcatheter arterial chemoembolization followed by surgical resection for hepatocellular carcinoma: A focus on its controversies and screening of patients most likely to benefit. Chin Med J (Engl). 2021; 134(19): 2275-2286.

23. Wu H, et al. Nanotechnology for Hepatocellular Carcinoma: From Surveillance, Diagnosis to Management. Small. 2021; 17(6): e2005236.

24. Wu J, et al. Effect of transcatheter arterial chemoembolization combined with lenvatinib plus anti-PD-1 antibodies in patients with unresectable hepatocellular carcinoma: A treatment with Chinese characteristics. Biosci Trends. 2024; 18(1): 42-48.

25. Wu S, et al. Smart nanoparticles and microbeads for interventional embolization therapy of liver cancer: state of the art. J Nanobiotechnology. 2023; 21(1): 42.

26. Yang SB, et al. TACE with portal vein radioactive seeds for HCC with portal vein tumor thrombus: a meta-analysis. Minim Invasive Ther Allied Technol. 2022; 31(6): 856-864.

27. Yuan P, et al. The clinical efficiency of TACE combined with simultaneous computed tomography-guided radiofrequency ablation for advanced hepatocellular carcinoma. Invest New Drugs. 2021; 39(5): 1383-1388.

28. Zhang XF, et al. Stereotactic body radiotherapy plus transcatheter arterial chemoembolization for inoperable hepatocellular carcinoma patients with portal vein tumour thrombus: A meta-analysis. PLoS One. 2022; 17(5): e0268779.

29. Zhu J, et al. Therapeutics for advanced hepatocellular carcinoma: Recent advances, current dilemma, and future directions. J Cell Physiol. 2019; 234(8): 12122-12132.