

# Intra-Arterial Therapies for Liver Masses

## Data Distilled



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### KEYWORDS

- Hepatocellular carcinoma • Colorectal cancer • Liver metastasis • Radioembolization • Chemoembolization

### KEY POINTS

- Staging of hepatocellular carcinoma (HCC) is complex due to cirrhosis, and the Barcelona Clinic Liver Cancer system is commonly utilized.
- Conventional trans arterial chemoembolization (cTACE) has demonstrated a survival benefit for appropriately selected patients with HCC in randomized controlled trials (RCTs).
- Drug-eluting bead trans arterial chemoembolization (DEB TACE) is an evolution of cTACE with an improved pharmacokinetic profile for treatment of HCC and metastatic colorectal cancer (mCRC). However, in an RCT, drug-eluting bead TACE failed to show a response improvement over cTACE for HCC.
- Radioembolization provides selective internal radiation to primary and liver mCRC due to their preferential arterial blood supply. Lack of macroscopic vessel occlusion allows safe treatment of lesions with vascular invasion and limits postembolization syndrome.
- Embolization is a safe and effective alternative treatment for focal nodular hyperplasia and hepatic adenoma.

### INTRODUCTION

The liver is a frequent site of metastatic disease, most commonly from a colorectal origin, and also a site of lethal primary malignancy.<sup>1</sup> Hepatocellular carcinoma (HCC) is the most common primary liver tumor and the third most common cause of cancer mortality.<sup>2,3</sup> Colorectal metastatic disease carries utmost prognostic implications, with a median survival of about 2 years in patients with advanced disease treated with chemotherapy.<sup>4</sup> Given the import of liver containing tumor, its treatment draws from multiple cancer specialties, yielding a wide range of treatment options. These include systemic chemotherapy and biologic agents, surgical resection, ablation,

and stereotactic body radiation therapy (SBRT); regional therapies include chemoembolization, radioembolization, and chemo infusion. The liver is also affected by benign masses, some of which carry the potential for malignant degeneration. This article presents the current level of evidence on intra-arterial therapies for liver masses, both malignant and benign, including discussions of patient selection, outcomes, and complications.

### HEPATOCELLULAR CARCINOMA

#### Background

HCC develops almost exclusively in a background of cirrhosis, producing 2 disease states in 1 organ. It is the sixth most common cancer, and unlike

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other solid malignancies, the incidence in the United States is on the rise, mostly because of the dissemination of hepatitis C virus.<sup>5</sup> Surveillance programs can achieve an early diagnosis of HCC; however, only about half of the population at risk receives appropriate screening, resulting in frequent disease presentation without curative options.<sup>6</sup>

Noninvasive imaging is the preferred method of HCC diagnosis, where pathognomonic features yield a specificity of greater than 95%.<sup>7,8</sup> Biopsy should be reserved for atypical imaging features, as can be seen with infiltrative disease.<sup>9</sup>

Staging in HCC must account for variables beyond tumor burden, as underlying liver function also affects prognosis.<sup>9</sup> Various staging systems exist, reflecting worldwide patient population differences. The most commonly used system for Western disease is the Barcelona Clinic Liver Cancer (BCLC) classification, and it carries the endorsement of both the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL).<sup>9,10</sup> This system links the stage of disease with treatment modalities, and subsequently an estimation of life expectancy. The BCLC system separates those patients with early disease, who are eligible for curative therapies, from those with intermediate and advanced disease, who benefit from palliative treatments.<sup>11</sup>

A newly developed prognostic staging system with treatment guidelines, the Hong Kong Liver Cancer Staging (HKLC) classification, produces better survival outcomes when compared with the BCLC system. The HKLC system was developed using data from 3927 patients at a single center in Asia, where about 80% of patients were hepatitis B carriers. Notably, BCLC intermediate and advanced stage patients were further stratified in the HKLC system to receive more aggressive treatment, yielding improved survival. Application of this aggressive treatment schedule outside of Asia requires performance validation in a Western HCC patient population.<sup>12</sup> Nonetheless, the HKLC system reflects an evolution of curative and palliative treatment options for patients with HCC.

Treatment of HCC is complex given the frequent background of cirrhosis, which affects survival and the ability to treat. A multispecialty approach is required, with participation from hepatologists, oncologists, surgeons, radiologists, and pathologists.<sup>9</sup> In deciding on treatment, it is important to recognize that the level of evidence for most therapeutic options is restricted to cohort studies, with a few randomized controlled trials (RCTs), mostly in the setting of advanced disease.<sup>13,14</sup> As such,

patient care is individualized and often reflects opinion, local expertise, and resources.

Potentially curative therapies for HCC are surgical resection, transplantation, and ablation.<sup>13</sup> Palliative therapies include transarterial treatment with chemoembolization, radioembolization, and bland embolization, along with sorafenib, a systemic agent.<sup>9,15</sup> Transarterial therapy for HCC will be explored, with specific attention to evidence and outcomes.

### **Chemoembolization for Hepatocellular Carcinoma**

HCC demonstrates intense neo-angiogenic activity during its progression.<sup>16,17</sup> Chemoembolization produces localized chemotherapy delivery to the tumor, along with tumor ischemia.<sup>16</sup> Chemoembolization is performed by conventional technique (cTACE) utilizing ethiodized oil (lipiodol) or by drug-eluting bead technique (DEB-TACE).

#### **Conventional chemoembolization for hepatocellular carcinoma**

Various chemotherapeutic agents have been used in cTACE, including doxorubicin, epirubicin, cisplatin, and mitomycin C. All of these drugs exhibit preferential extraction when delivered intrahepatically and can achieve favorable intratumoral concentrations with lower systemic concentrations.<sup>18</sup> No clear evidence exists to support one or a combination of these agents.<sup>18</sup> Today, the most commonly used agent in the United States is doxorubicin.<sup>18</sup>

Intra-arterial delivery of the aqueous chemotherapy and lipiodol emulsion is followed by, or concurrent with, delivery of embolic material in cTACE. Embolization material serves 2 purposes: preventing cytotoxic chemotherapy washout and inducing intratumoral ischemic necrosis<sup>18</sup> (**Fig. 1**).

**Patient selection** cTACE is used as palliative care, in combination with ablation, or as a bridge to liver transplant. Preserved liver function is essential, as the antitumor effect of chemoembolization can be offset by treatment-induced liver failure.<sup>18</sup> According to the BCLC staging system, cTACE is recommended for those with intermediate stage disease.

#### **Evidence and outcome**

The survival benefits of chemoembolization were reported in 2 landmark RCTs in 2002. Llovet and colleagues<sup>19</sup> randomized patients to one of three treatment arms, namely, fixed interval cTACE (doxorubicin), gel foam embolization, or conservative treatment. The trial was stopped when a survival benefit of patients treated with cTACE was identified as compared to conservative treatment.

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