Medical Policy

Transcatheter Arterial Chemoembolization to Treat Primary or Metastatic Liver Malignancies

Table of Contents

Policy Number: 634

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NCD/LCD: N/A

Related Policies

- Cryosurgical Ablation of Primary or Metastatic Liver Tumors, #633
- Radiofrequency Ablation of Primary or Metastatic Liver Tumors, #286
- Radioembolization for Primary and Metastatic Tumors of the Liver, #292

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue℠ and Medicare PPO Blue℠ Members

Transcatheter arterial chemoembolization of the liver, including the use of drug-eluting beads[1], may be considered **MEDICALLY NECESSARY**:

- To treat hepatocellular cancer that is unresectable but confined to the liver and not associated with portal vein thrombosis and liver function not characterized as Child-Pugh class C
- As a bridge to transplant in patients with hepatocellular cancer where the intent is to prevent further tumor growth and to maintain a patient's candidacy for liver transplant.
- To treat liver metastasis in symptomatic patients with metastatic neuroendocrine tumor whose symptoms persist despite systemic therapy and who are not candidates for surgical resection, or
- To treat liver metastasis in patients with liver-dominant metastatic uveal melanoma.

Transcatheter arterial chemoembolization of the liver, including the use of drug-eluting beads[1], is considered **INVESTIGATIONAL**:

- As neoadjuvant or adjuvant therapy in hepatocellular cancer that is considered resectable.
- As part of combination therapy (with radiofrequency ablation) for resectable or unresectable hepatocellular carcinoma.
- To treat unresectable cholangiocarcinoma.

- To treat liver metastases from any other tumors or to treat hepatocellular cancer that does not meet the criteria noted above, including recurrent hepatocellular carcinoma.
- To treat hepatocellular tumors prior to liver transplantation except as noted above.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	This procedure is performed in the inpatient setting.
Commercial PPO and Indemnity	This procedure is performed in the inpatient setting.
Medicare HMO Blue℠	This procedure is performed in the inpatient setting.
Medicare PPO Blue℠	This procedure is performed in the inpatient setting.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue, and Medicare PPO Blue:

CPT Codes

CPT Codes	Code Description
37243	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; for tumors, organ ischemia, or infarction
75894	Transcatheter therapy, embolization, any method, radiological supervision and interpretation

Description

Transcatheter Arterial Chemoembolization

TACE is a minimally invasive procedure performed by interventional radiologists who inject highly concentrated doses of chemotherapeutic agents into the tumor tissues and to restrict tumor blood supply. The embolic agent(s) causes ischemia and necrosis of the tumor and slows anticancer drug washout. The most common anticancer drugs used in published TACE studies for hepatocellular carcinoma include doxorubicin (36%), followed by cisplatin (31%), epirubicin (12%), mitoxantrone (8%), and mitomycin C (8%).[1]

The TACE procedure requires hospitalization for placement of a hepatic artery catheter and workup to establish eligibility for chemoembolization. Before the procedure, the patency of the portal vein must be demonstrated to ensure an adequate posttreatment hepatic blood supply. With the patient under local anesthesia and mild sedation, a super selective catheter is inserted via the femoral artery and threaded

into the hepatic artery. Angiography is then performed to delineate the hepatic vasculature, followed by injection of the embolic chemotherapy mixture. Embolic material varies but may include a viscous collagen agent, polyvinyl alcohol particles, or ethiodized oil. Typically, only 1 lobe of the liver is treated during a single session, with subsequent embolization procedures scheduled 5 days to 6 weeks later. In addition, because the embolized vessel recanalizes, chemoembolization can be repeated as many times as necessary.

Adverse Events
TACE of the liver has been associated with potentially life-threatening toxicities and complications, including severe postembolization syndrome, hepatic insufficiency, abscess, or infarction. TACE has been investigated to treat resectable, unresectable, and recurrent hepatocellular carcinoma, cholangiocarcinoma, liver metastases, and in the liver transplant setting. Treatment alternatives include resection when possible, other locally ablative techniques (eg, radiofrequency ablation, cryoablation), and chemotherapy administered systemically or by hepatic artery infusion. Hepatic artery infusion involves the continuous infusion of chemotherapy with an implanted pump, while TACE is administered episodically. Hepatic artery infusion does not involve the use of embolic material.

Summary

Transcatheter arterial chemoembolization (TACE) of the liver is a proposed alternative to conventional systemic or intra-arterial chemotherapy and to various nonsurgical ablative techniques, to treat resectable and nonresectable tumors. TACE combines the infusion of chemotherapeutic drugs with particle embolization. Tumor ischemia secondary to the embolization raises the drug concentration compared with infusion alone, extending the retention of the chemotherapeutic agent and decreasing systemic toxicity. The liver is especially amenable to such an approach, given its distinct lobular anatomy, the existence of 2 independent blood supplies, and the ability of healthy hepatic tissue to grow and thus compensate for tissue mass lost during chemoembolization.

Unresectable and Resectable Hepatocellular Carcinoma
For individuals who have unresectable HCC confined to the liver and not associated with portal vein thrombosis who receive TACE, the evidence includes several randomized controlled trials (RCTs), large observational studies, and systematic reviews. Relevant outcomes are overall survival (OS), disease-specific survival, quality of life (QOL), and treatment-related mortality and morbidity. Evidence from 1 RCT has suggested that survival with TACE is at least as good as with systemic chemotherapy. One systematic review has highlighted possible biases associated with RCTs that compared TACE with no therapy. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have resectable HCC who receive neoadjuvant or adjuvant TACE, the evidence includes several RCTs and systematic reviews. Relevant outcomes are OS, disease-specific survival, QOL, and treatment-related mortality and morbidity. Studies have shown little to no difference in OS rates with neoadjuvant TACE compared with surgery alone. A meta-analysis found no significant improvements in survival or recurrence with preoperative TACE for resectable HCC. While both RCTs and the meta-analysis that evaluated TACE as adjuvant therapy to hepatic resection in HCC reported positive results, the quality of individual studies and the methodologic issues related to the meta-analysis preclude certainty when interpreting the results. Well-conducted multicentric trials from the U. S. or Europe representing relevant populations with adequate randomization procedures, blinded assessments, centralized oversight and publication in peer-reviewed journals are required. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have resectable HCC who receive TACE plus RFA, the evidence includes a single RCT and a systematic review.

Relevant outcomes are OS, disease-specific survival, QOL, and treatment-related mortality and morbidity. The RCT failed to show the superiority in survival benefit with combination TACE plus RFA treatment compared with surgery for HCC lesions 3 cm or smaller.

Further, an ad hoc subgroup analysis showed a significant benefit for surgery in recurrence and OS in patients with lesions larger than 3 cm. It cannot be determined from this trial whether TACE plus RFA is as effective as a surgical resection for these small tumors. The systematic review, which included mostly retrospective observational studies, did not find a survival benefit with TACE plus RFA over surgery alone. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have unresectable HCC who receive TACE plus RFA, the evidence includes multiple systematic reviews and RCTs. Relevant outcomes are OS, disease-specific survival, QOL, and treatment-related mortality and morbidity. Multiple meta-analyses and RCTs have shown a consistent benefit in survival and recurrence-free survival favoring combination TACE plus RFA over RFA alone.

However, results of these meta-analyses are difficult to interpret because the pooled data included heterogeneous patient populations and, in a few cases, data from a study retracted due to questions about data veracity. A larger well-conducted RCT has reported a relative reduction in the hazard of death by 44% and a 14% difference in 4-year survival favoring combination therapy. The major limitations of this trial were its lack of a TACE-alone arm and the generalizability of its findings to patient populations that have unmet needs such as those with multiple lesions larger than 3 cm and Child-Pugh class B or C. Further, this single-center trial was conducted in China, and until these results have been reproduced in patient populations representative of pathophysiology and clinical stage more commonly found in the U. S. or Europe, the results may not be generalizable. The evidence is insufficient to determine the effects of the technology on health outcomes.

Bridge to Liver Transplant
For individuals who have a single hepatocellular tumor less than 5 cm or no more than 3 tumors each less than 3 cm in size, absence of extrahepatic disease or vascular invasion, and Child-Pugh class A or B seeking to prevent further tumor growth and to maintain patient candidacy for liver transplant who receive pretransplant TACE, the evidence includes multiple small prospective studies. Relevant outcomes are OS, disease-specific survival, QOL, and treatment-related mortality and morbidity. There is a lack of comparative trials on various locoregional treatments as a bridge therapy for liver transplantation. Multiple small prospective studies have demonstrated that TACE can prevent dropouts from the transplant list. TACE has become an accepted method to prevent tumor growth and progression while patients are on the liver transplant waiting list. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Unresectable Cholangiocarcinoma
For individuals who have unresectable cholangiocarcinoma who receive TACE, the evidence includes several retrospective observational studies and systematic reviews. Relevant outcomes are OS, disease-specific survival, QOL, and treatment-related mortality and morbidity. RCTs evaluating the benefit of adding TACE to the standard of care for patients with unresectable cholangiocarcinoma are lacking. Results of retrospective studies have shown a survival benefit with TACE over the standard of care. These studies lacked matched patient controls. Although the observational data are consistent, the lack of randomization limits definitive conclusions. The evidence is insufficient to determine the effects of the technology on health outcomes.

TACE for Symptomatic Unresectable Neuroendocrine Tumors
For individuals who have symptomatic metastatic neuroendocrine tumors despite systemic therapy and are not candidates for surgical resection who receive TACE, the evidence includes retrospective single-cohort studies. Relevant outcomes are OS, disease-specific survival, QOL, and treatment-related mortality and morbidity. There is a lack of evidence from RCTs supporting the use of TACE.

Uncontrolled trials have suggested that TACE reduces symptoms and tumor burden and improves hormone profiles. Generally, the response rates are over 50% and include patients with massive hepatic tumor burden. While many studies have demonstrated symptom control, survival benefits are less clear. Despite the uncertain benefit on survival, the use of TACE to palliate the symptoms associated with

hepatic neuroendocrine metastases can provide a clinically meaningful improvement in net health outcome. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Liver-Dominant Metastatic Uveal Melanoma
For individuals who have liver-dominant metastatic uveal melanoma who receive TACE, the evidence includes observational studies and reviews. Relevant outcomes are OS, disease-specific survival, QOL, and treatment-related mortality and morbidity. There is a lack of evidence from RCTs assessing the use of TACE. Noncomparative prospective and retrospective studies have reported improvements in tumor response and survival compared with historical controls. Given the very limited treatment response from systemic therapy and the rarity of this condition, the existing evidence may support conclusions that TACE meaningfully improves outcomes for patients with hepatic metastases from uveal melanoma. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Other Unresectable Hepatic Metastases
For individuals who have unresectable hepatic metastases from any other types of primary tumors (eg, colorectal or breast cancer) who receive TACE, the evidence includes multiple RCTs, observational studies, and systematic reviews. Relevant outcomes are OS, disease specific survival, QOL, and treatment-related mortality and morbidity. Multiple RCTs and numerous nonrandomized studies have compared TACE with alternatives in patients who have colorectal cancer and metastases to the liver. Nonrandomized studies have reported that TACE can stabilize disease in 40% to 60% of treated patients but whether this translates into a prolonged survival benefit relative to systemic chemotherapy alone is uncertain. Two small RCTs have reported that TACE with drug-eluting beads has resulted in statistically significant improvements in response rate and progression-free survival. Whether this translates into a prolonged survival benefit relative to systemic chemotherapy alone is uncertain. For cancers other than colorectal, the evidence is extremely limited, and no conclusions can be made. Studies have assessed small numbers of patients and the results have varied due to differences in patient selection criteria and treatment regimens used. The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy History

Date	Action
12/2020	New investigational indications described for TACE as part of combination therapy (with radiofrequency ablation) for resectable or unresectable hepatocellular carcinoma. Effective 12/1/2020.
9/2019	BCBSA National medical policy review. Description, summary and references updated. Policy statements unchanged.
9/2018	BCBSA National medical policy review. No changes to policy statements. New references added. Background and summary clarified.
12/2017	BCBSA National medical policy review. Medically necessary criteria revised. Effective 12/1/2017.
10/2016	New references added from BCBSA National medical policy.
11/2015	New references added from BCBSA National medical policy.
12/2014	New references added from BCBSA National medical policy.
8/2014	Clarified coding information.
1/2014	New references added from BCBSA National medical policy.
1/2014	Updated to remove deleted code 37204.
2/2013	BCBSA National medical policy review. Changes to policy statement. Effective 2/4/2013.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
12/2011	BCBSA National medical policy review. No changes to policy statements.

10/2011	Reviewed - Medical Policy Group - Gastroenterology, Nutrition and Organ Transplantation. No changes to policy statements.
7/2011	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
11/2010	Reviewed - Medical Policy Group - Gastroenterology, Nutrition and Organ Transplantation. No changes to policy statements.
9/2010	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
6/2010	BCBSA National medical policy review. No changes to policy statements.
9/2009	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
9/2009	BCBSA National medical policy review. No changes to policy statements.
11/2008	Reviewed - Medical Policy Group - Gastroenterology, Nutrition and Organ Transplantation. No changes to policy statements.
10/2008	BCBSA National medical policy review. No changes to policy statements.
9/2008	BCBSA National medical policy review. Changes to policy statements.
1/2008	BCBSA National medical policy review. Changes to policy statements.
9/2007	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

References

1. Marelli L, Stigliano R, Triantos C, et al. Transarterial therapy for hepatocellular carcinoma: which technique is more effective? A systematic review of cohort and randomized studies. Cardiovasc Intervent Radiol. Jan-Feb 2007; 30(1): 6-25. PMID 17103105
2. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Transcatheter arterial chemoembolization of hepatic tumors. TEC Assessments. 2000;Volume 15;Tab 22.
3. National Cancer Institute, Surveillance Epidemiology and End Results Program. Cancer Stat Facts: Liver and Intrahepatic Bile Duct Cancer. n.d.; https://seer.cancer.gov/statfacts/html/livibd.html. Accessed June 1, 2020.
4. Qi X, Wang D, Su C, et al. Hepatic resection versus transarterial chemoembolization for the initial treatment of hepatocellular carcinoma: A systematic review and meta-analysis. Oncotarget. Jul 30 2015; 6(21): 18715-33. PMID 26243835
5. Tian X, Dai Y, Wang DQ, et al. Transarterial chemoembolization versus hepatic resection in hepatocellular carcinoma treatment: a meta-analysis. Drug Des Devel Ther. 2015; 9: 4431-40. PMID 26309396
6. Oliveri RS, Wetterslev J, Gluud C. Transarterial (chemo)embolisation for unresectable hepatocellular carcinoma. Cochrane Database Syst Rev. Mar 16 2011; (3): CD004787. PMID 21412886
7. Xie F, Zang J, Guo X, et al. Comparison of transcatheter arterial chemoembolization and microsphere embolization for treatment of unresectable hepatocellular carcinoma: a meta-analysis. J Cancer Res Clin Oncol. Mar 2012; 138(3): 455-62. PMID 22179199
8. Ahmad J, Rhee J, Carr BI. The effects of hepatic artery chemotherapy on viral hepatitis in patients with hepatocellular carcinoma. Dig Dis Sci. Feb 2005; 50(2): 331-5. PMID 15745096
9. Akamatsu M, Yoshida H, Obi S, et al. Evaluation of transcatheter arterial embolization prior to percutaneous tumor ablation in patients with hepatocellular carcinoma: a randomized controlled trial. Liver Int. Dec 2004; 24(6): 625-9. PMID 15566514

10. Bruix J, Llovet JM, Castells A, et al. Transarterial embolization versus symptomatic treatment in patients with advanced hepatocellular carcinoma: results of a randomized, controlled trial in a single institution. Hepatology. Jun 1998; 27(6): 1578-83. PMID 9620330
11. Cao GW, Hu S, Li G, et al. The clinical and experimental research of transhepatic arterial injection of 32P-glass microsphere therapy for hepatic carcinoma. J Med Imaging. 2005;15(8):678681.
12. Cao XC, Wang X, Tan J, et al. Clinical research of intra-arterial radioembolization with 32P-gass microspheres combined with chemoembolization for treatment of liver cancer. Chin J Radiol. 2005;39(10):10681072.
13. Carr BI, Kondragunta V, Buch SC, et al. Therapeutic equivalence in survival for hepatic arterial chemoembolization and yttrium 90 microsphere treatments in unresectable hepatocellular carcinoma: a two-cohort study. Cancer. Mar 01 2010; 116(5): 1305-14. PMID 20066715
14. Cheng SQ, Wu MC, Chen H, et al. [Transcatheter hepatic arterial chemoembolization and thymosin alpha1 in postoperative treatment of hepatocellular carcinoma]. Zhonghua Zhong Liu Za Zhi. May 2004; 26(5): 305-7. PMID 15312371
15. Doffoel M, Bonnetain F, Bouche O, et al. Multicentre randomised phase III trial comparing Tamoxifen alone or with Transarterial Lipiodol Chemoembolisation for unresectable hepatocellular carcinoma in cirrhotic patients (Federation Francophone de Cancerologie Digestive 9402). Eur J Cancer. Mar 2008; 44(4): 528-38. PMID 18242076
16. Du W, Lin S, Luo K, et al. Clinical analysis of TACE plus 32P-GMS in advanced hepatic carcinoma. J Hepatobilia Surg. 2002;10(5):351352.
17. Groupe d'Etude et de Traitement du Carcinome Hepatocellulaire. A comparison of lipiodol chemoembolization and conservative treatment for unresectable hepatocellular carcinoma. N Engl J Med. May 11 1995; 332(19): 1256-61. PMID 7708069
18. Hao N, Xiao X, Han X, et al. Efficacy of intra-arterial chemoembolization using drug microspheres in compare with chemoembolization in the treatment of primary hepatic carcinoma. Tumor (Shanghai). 2000;20(5):375378.
19. Hou P, Guan G, Zhang X, Lu H, Wang S. Effects of intra-advanced 32P glass microspheres for advanced hepatic carcinoma. Academic Journal of Fujian Medical University. 2006;40(1):4850.
20. Kirchhoff TD, Rudolph KL, Layer G, et al. Chemoocclusion vs chemoperfusion for treatment of advanced hepatocellular carcinoma: a randomised trial. Eur J Surg Oncol. Mar 2006; 32(2): 201-7. PMID 16373084
21. Kooby DA, Egnatashvili V, Srinivasan S, et al. Comparison of yttrium-90 radioembolization and transcatheter arterial chemoembolization for the treatment of unresectable hepatocellular carcinoma. J Vasc Interv Radiol. Feb 2010; 21(2): 224-30. PMID 20022765
22. Lee W, Luo J, Yan Z, et al. Hepatic radioembolization with epirubicin mixed microsphere for the treatment of hepatocellular carcinoma. J Nantong Univ (Medical Sciences). 2008;28(4):268270.
23. Lewandowski RJ, Kulik LM, Riaz A, et al. A comparative analysis of transarterial downstaging for hepatocellular carcinoma: chemoembolization versus radioembolization. Am J Transplant. Aug 2009; 9(8): 1920-8. PMID 19552767
24. Li JQ, Zhang YQ, Zhang WZ, et al. Randomized study of chemoembolization as an adjuvant therapy for primary liver carcinoma after hepatectomy. J Cancer Res Clin Oncol. 1995; 121(6): 364-6. PMID 7541051
25. Li Q, Wang J, Sun Y, et al. Postoperative transhepatic arterial chemoembolization and portal vein chemotherapy for patients with hepatocellular carcinoma: a randomized study with 131 cases. Dig Surg. 2006; 23(4): 235-40. PMID 16943671
26. Liu T, Zu M. Treatment of primary hepatic carcinoma by hepatic arterial chemoembolization with KMG microspheres and chemotherapeutic agents. Acad Med Xuzhou. 2005;25(2):126129.
27. Llovet JM, Real MI, Montana X, et al. Arterial embolisation or chemoembolisation versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: a randomised controlled trial. Lancet. May 18 2002; 359(9319): 1734-9. PMID 12049862
28. Lo CM, Ngan H, Tso WK, et al. Randomized controlled trial of transarterial lipiodol chemoembolization for unresectable hepatocellular carcinoma. Hepatology. May 2002; 35(5): 1164-71. PMID 11981766
29. Pelletier G, Roche A, Ink O, et al. A randomized trial of hepatic arterial chemoembolization in patients with unresectable hepatocellular carcinoma. J Hepatol. Sep 1990; 11(2): 181-4. PMID 2174933

30. Pelletier G, Ducreux M, Gay F, et al. Treatment of unresectable hepatocellular carcinoma with lipiodol chemoembolization: a multicenter randomized trial. Groupe CHC. J Hepatol. Jul 1998; 29(1): 129-34. PMID 9696501
31. Salem R, Lewandowski RJ, Kulik L, et al. Radioembolization results in longer time-to-progression and reduced toxicity compared with chemoembolization in patients with hepatocellular carcinoma. Gastroenterology. Feb 2011; 140(2): 497-507.e2. PMID 21044630
32. Xiao E, Li D, Shen S, et al. Effect of preoperative transcatheter arterial chemoembolization on apoptosis of hepatocellular carcinoma cells. Chin Med J. Feb 2003; 116(2): 203-7. PMID 12775230
33. Bush DA, Smith JC, Slater JD, et al. Randomized Clinical Trial Comparing Proton Beam Radiation Therapy with Transarterial Chemoembolization for Hepatocellular Carcinoma: Results of an Interim Analysis. Int J Radiat Oncol Biol Phys. May 01 2016; 95(1): 477-482. PMID 27084661
34. Mabed M, Esmaeel M, El-Khodary T, et al. A randomized controlled trial of transcatheter arterial chemoembolization with lipiodol, doxorubicin and cisplatin versus intravenous doxorubicin for patients with unresectable hepatocellular carcinoma. Eur J Cancer Care (Engl). Sep 2009; 18(5): 492-9. PMID 19453695
35. Shen PC, Chang WC, Lo CH, et al. Comparison of Stereotactic Body Radiation Therapy and Transarterial Chemoembolization for Unresectable Medium-Sized Hepatocellular Carcinoma. Int J Radiat Oncol Biol Phys. Oct 01 2019; 105(2): 307-318. PMID 31175903
36. Biederman DM, Titano JJ, Korff RA, et al. Radiation Segmentectomy versus Selective Chemoembolization in the Treatment of Early-Stage Hepatocellular Carcinoma. J Vasc Interv Radiol. Jan 2018; 29(1): 30-37.e2. PMID 29169782
37. Molinari M, Kachura JR, Dixon E, et al. Transarterial chemoembolisation for advanced hepatocellular carcinoma: results from a North American cancer centre. Clin Oncol (R Coll Radiol). Nov 2006; 18(9): 684-92. PMID 17100154
38. Takayasu K, Arii S, Ikai I, et al. Prospective cohort study of transarterial chemoembolization for unresectable hepatocellular carcinoma in 8510 patients. Gastroenterology. Aug 2006; 131(2): 461-9. PMID 16890600
39. Biselli M, Andreone P, Gramenzi A, et al. Transcatheter arterial chemoembolization therapy for patients with hepatocellular carcinoma: a case-controlled study. Clin Gastroenterol Hepatol. Sep 2005; 3(9): 918-25. PMID 16234031
40. Si T, Chen Y, Ma D, et al. Preoperative transarterial chemoembolization for resectable hepatocellular carcinoma in Asia area: a meta-analysis of random controlled trials. Scand J Gastroenterol. Dec 2016; 51(12): 1512-1519. PMID 27598831
41. Zhou Y, Zhang X, Wu L, et al. Meta-analysis: preoperative transcatheter arterial chemoembolization does not improve prognosis of patients with resectable hepatocellular carcinoma. BMC Gastroenterol. Mar 19 2013; 13: 51. PMID 23509884
42. Chua TC, Liauw W, Saxena A, et al. Systematic review of neoadjuvant transarterial chemoembolization for resectable hepatocellular carcinoma. Liver Int. Feb 2010; 30(2): 166-74. PMID 19912531
43. Kaibori M, Tanigawa N, Kariya S, et al. A prospective randomized controlled trial of preoperative whole-liver chemolipiodolization for hepatocellular carcinoma. Dig Dis Sci. May 2012; 57(5): 1404-12. PMID 22271410
44. Zhou WP, Lai EC, Li AJ, et al. A prospective, randomized, controlled trial of preoperative transarterial chemoembolization for resectable large hepatocellular carcinoma. Ann Surg. Feb 2009; 249(2): 195-202. PMID 19212170
45. Cui H, Gao QQ, Li YY, et al. Influence of preventive effects of transcatheter arterial chemoembolization on primary hepatocellular carcinoma. J Med Forum. 2003;24:13.
46. Yamasaki S, Hasegawa H, Kinoshita H, et al. A prospective randomized trial of the preventive effect of pre-operative transcatheter arterial embolization against recurrence of hepatocellular carcinoma. Jpn J Cancer Res. Feb 1996; 87(2): 206-11. PMID 8609071
47. Wu CC, Ho YZ, Ho WL, et al. Preoperative transcatheter arterial chemoembolization for resectable large hepatocellular carcinoma: a reappraisal. Br J Surg. Jan 1995; 82(1): 122-6. PMID 7881929
48. Yeh ML, Huang CI, Huang CF, et al. Neoadjuvant transcatheter arterial chemoembolization does not provide survival benefit compared to curative therapy alone in single hepatocellular carcinoma. Kaohsiung J Med Sci. Feb 2015; 31(2): 77-82. PMID 25645985

49. Choi GH, Kim DH, Kang CM, et al. Is preoperative transarterial chemoembolization needed for a resectable hepatocellular carcinoma?. World J Surg. Dec 2007; 31(12): 2370-7. PMID 17912587
50. Liao M, Zhu Z, Wang H, et al. Adjuvant transarterial chemoembolization for patients after curative resection of hepatocellular carcinoma: a meta-analysis. Scand J Gastroenterol. Jun 2017; 52(6-7): 624-634. PMID 28276833
51. Li Q, Wang J, Sun Y, et al. Efficacy of postoperative transarterial chemoembolization and portal vein chemotherapy for patients with hepatocellular carcinoma complicated by portal vein tumor thrombosis--a randomized study. World J Surg. Nov 2006; 30(11): 2004-11; discussion 2012-3. PMID 17058027
52. Zhong C, Guo RP, Li JQ, et al. A randomized controlled trial of hepatectomy with adjuvant transcatheter arterial chemoembolization versus hepatectomy alone for Stage III A hepatocellular carcinoma. J Cancer Res Clin Oncol. Oct 2009; 135(10): 1437-45. PMID 19408012
53. Peng BG, He Q, Li JP, et al. Adjuvant transcatheter arterial chemoembolization improves efficacy of hepatectomy for patients with hepatocellular carcinoma and portal vein tumor thrombus. Am J Surg. Sep 2009; 198(3): 313-8. PMID 19285298
54. Gui CH, Baey S, D'cruz RT, et al. Trans-arterial chemoembolization + radiofrequency ablation versus surgical resection in hepatocellular carcinoma - A meta-analysis. Eur J Surg Oncol. May 2020; 46(5): 763-771. PMID 31937433
55. Liu H, Wang ZG, Fu SY, et al. Randomized clinical trial of chemoembolization plus radiofrequency ablation versus partial hepatectomy for hepatocellular carcinoma within the Milan criteria. Br J Surg. Mar 2016; 103(4): 348-56. PMID 26780107
56. Ako S, Nakamura S, Nouso K, et al. Transcatheter Arterial Chemoembolization to Reduce Size of Hepatocellular Carcinoma before Radiofrequency Ablation. Acta Med Okayama. Feb 2018; 72(1): 47-52. PMID 29463938
57. Haochen W, Jian W, Li S, et al. Transarterial chemoembolization plus multi-imaging-guided radiofrequency ablation for elimination of hepatocellular carcinoma nodules measuring 3.1 to 5.0 cm: a single-center study. J Int Med Res. Jul 2018; 46(7): 2650-2657. PMID 29683022
58. Bholee AK, Peng K, Zhou Z, et al. Radiofrequency ablation combined with transarterial chemoembolization versus hepatectomy for patients with hepatocellular carcinoma within Milan criteria: a retrospective case-control study. Clin Transl Oncol. Jul 2017; 19(7): 844-852. PMID 28070766
59. Lan T, Chang L, Rahmathullah MN, et al. Comparative Efficacy of Interventional Therapies for Early-stage Hepatocellular Carcinoma: A PRISMA-compliant Systematic Review and Network Meta-analysis. Medicine (Baltimore). Apr 2016; 95(15): e3185. PMID 27082558
60. Li L, Tian J, Liu P, et al. Transarterial chemoembolization combination therapy vs monotherapy in unresectable hepatocellular carcinoma: a meta-analysis. Tumori. Jun 02 2016; 2016(3): 301-10. PMID 27002950
61. Lu Z, Wen F, Guo Q, et al. Radiofrequency ablation plus chemoembolization versus radiofrequency ablation alone for hepatocellular carcinoma: a meta-analysis of randomized-controlled trials. Eur J Gastroenterol Hepatol. Feb 2013; 25(2): 187-94. PMID 23134976
62. Wang X, Hu Y, Ren M, et al. Efficacy and Safety of Radiofrequency Ablation Combined with Transcatheter Arterial Chemoembolization for Hepatocellular Carcinomas Compared with Radiofrequency Ablation Alone: A Time-to-Event Meta-Analysis. Korean J Radiol. Jan-Feb 2016; 17(1): 93-102. PMID 26798221
63. Peng ZW, Zhang YJ, Liang HH, et al. Recurrent hepatocellular carcinoma treated with sequential transcatheter arterial chemoembolization and RF ablation versus RF ablation alone: a prospective randomized trial. Radiology. Feb 2012; 262(2): 689-700. PMID 22157201
64. Morimoto M, Numata K, Kondou M, et al. Midterm outcomes in patients with intermediate-sized hepatocellular carcinoma: a randomized controlled trial for determining the efficacy of radiofrequency ablation combined with transcatheter arterial chemoembolization. Cancer. Dec 01 2010; 116(23): 5452-60. PMID 20672352
65. Shibata T, Isoda H, Hirokawa Y, et al. Small hepatocellular carcinoma: is radiofrequency ablation combined with transcatheter arterial chemoembolization more effective than radiofrequency ablation alone for treatment?. Radiology. Sep 2009; 252(3): 905-13. PMID 19567647

66. Cheng BQ, Jia CQ, Liu CT, et al. Chemoembolization combined with radiofrequency ablation for patients with hepatocellular carcinoma larger than 3 cm: a randomized controlled trial. JAMA. Apr 09 2008; 299(14): 1669-77. PMID 18398079
67. DeAngelis CD, Fontanarosa PB. Retraction: Cheng B-Q, et al. Chemoembolization combined with radiofrequency ablation for patients with hepatocellular carcinoma larger than 3 cm: a randomized controlled trial. JAMA. 2008;299(14):1669-1677. JAMA. May 13 2009; 301(18): 1931. PMID 19380477
68. Yi Y, Zhang Y, Wei Q, et al. Radiofrequency ablation or microwave ablation combined with transcatheter arterial chemoembolization in treatment of hepatocellular carcinoma by comparing with radiofrequency ablation alone. Chin J Cancer Res. Feb 2014; 26(1): 112-8. PMID 24653633
69. Peng ZW, Zhang YJ, Chen MS, et al. Radiofrequency ablation with or without transcatheter arterial chemoembolization in the treatment of hepatocellular carcinoma: a prospective randomized trial. J Clin Oncol. Feb 01 2013; 31(4): 426-32. PMID 23269991
70. Martin AP, Bartels M, Hauss J, et al. Overview of the MELD score and the UNOS adult liver allocation system. Transplant Proc. Dec 2007; 39(10): 3169-74. PMID 18089345
71. Organ Procurement and Transplantation Network (OPTN). OPTN Policies. 2020; https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf. Accessed June 2, 2020.
72. Mazzaferro V, Regalia E, Doci R, et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. N Engl J Med. Mar 14 1996; 334(11): 693-9. PMID 8594428
73. Pomfret EA, Washburn K, Wald C, et al. Report of a national conference on liver allocation in patients with hepatocellular carcinoma in the United States. Liver Transpl. Mar 2010; 16(3): 262-78. PMID 20209641
74. Si T, Chen Y, Ma D, et al. Transarterial chemoembolization prior to liver transplantation for patients with hepatocellular carcinoma: A meta-analysis. J Gastroenterol Hepatol. Jul 2017; 32(7): 1286-1294. PMID 28085213
75. Graziadei IW, Sandmueller H, Waldenberger P, et al. Chemoembolization followed by liver transplantation for hepatocellular carcinoma impedes tumor progression while on the waiting list and leads to excellent outcome. Liver Transpl. Jun 2003; 9(6): 557-63. PMID 12783395
76. Maddala YK, Stadheim L, Andrews JC, et al. Drop-out rates of patients with hepatocellular cancer listed for liver transplantation: outcome with chemoembolization. Liver Transpl. Mar 2004; 10(3): 449-55. PMID 15004776
77. Obed A, Beham A, Pullmann K, et al. Patients without hepatocellular carcinoma progression after transarterial chemoembolization benefit from liver transplantation. World J Gastroenterol. Feb 07 2007; 13(5): 761-7. PMID 17278200
78. Yao FY. Liver transplantation for hepatocellular carcinoma: beyond the Milan criteria. Am J Transplant. Oct 2008; 8(10): 1982-9. PMID 18727702
79. Gabr A, Abouchaleh N, Ali R, et al. Comparative study of post-transplant outcomes in hepatocellular carcinoma patients treated with chemoembolization or radioembolization. Eur J Radiol. Aug 2017; 93: 100-106. PMID 28668402
80. Park SY, Kim JH, Yoon HJ, et al. Transarterial chemoembolization versus supportive therapy in the palliative treatment of unresectable intrahepatic cholangiocarcinoma. Clin Radiol. Apr 2011; 66(4): 322-8. PMID 21356394
81. Seidensticker R, Seidensticker M, Doegen K, et al. Extensive Use of Interventional Therapies Improves Survival in Unresectable or Recurrent Intrahepatic Cholangiocarcinoma. Gastroenterol Res Pract. 2016; 2016: 8732521. PMID 26966431
82. Boehm LM, Jayakrishnan TT, Miura JT, et al. Comparative effectiveness of hepatic artery based therapies for unresectable intrahepatic cholangiocarcinoma. J Surg Oncol. Feb 2015; 111(2): 213-20. PMID 25176325
83. Knuppel M, Kubicka S, Vogel A, et al. Combination of conservative and interventional therapy strategies for intra- and extrahepatic cholangiocellular carcinoma: a retrospective survival analysis. Gastroenterol Res Pract. 2012; 2012: 190708. PMID 21776251
84. Nazario J, Gupta S. Transarterial liver-directed therapies of neuroendocrine hepatic metastases. Semin Oncol. Apr 2010; 37(2): 118-26. PMID 20494704

85. Ruutiainen AT, Soulen MC, Tuite CM, et al. Chemoembolization and bland embolization of neuroendocrine tumor metastases to the liver. J Vasc Interv Radiol. Jul 2007; 18(7): 847-55. PMID 17609443
86. Gupta S, Yao JC, Ahrar K, et al. Hepatic artery embolization and chemoembolization for treatment of patients with metastatic carcinoid tumors: the M.D. Anderson experience. Cancer J. Jul-Aug 2003; 9(4): 261-7. PMID 12967136
87. Osborne DA, Zervos EE, Strosberg J, et al. Improved outcome with cytoreduction versus embolization for symptomatic hepatic metastases of carcinoid and neuroendocrine tumors. Ann Surg Oncol. Apr 2006; 13(4): 572-81. PMID 16511671
88. Rowcroft A, Loveday BPT, Thomson BNJ, et al. Systematic review of liver directed therapy for uveal melanoma hepatic metastases. HPB (Oxford). Apr 2020; 22(4): 497-505. PMID 31791894
89. Huppert PE, Fierlbeck G, Pereira P, et al. Transarterial chemoembolization of liver metastases in patients with uveal melanoma. Eur J Radiol. Jun 2010; 74(3): e38-44. PMID 19467811
90. Sharma KV, Gould JE, Harbour JW, et al. Hepatic arterial chemoembolization for management of metastatic melanoma. AJR Am J Roentgenol. Jan 2008; 190(1): 99-104. PMID 18094299
91. Bedikian AY, Legha SS, Mavligit G, et al. Treatment of uveal melanoma metastatic to the liver: a review of the M. D. Anderson Cancer Center experience and prognostic factors. Cancer. Nov 01 1995; 76(9): 1665-70. PMID 8635073
92. Patel K, Sullivan K, Berd D, et al. Chemoembolization of the hepatic artery with BCNU for metastatic uveal melanoma: results of a phase II study. Melanoma Res. Aug 2005; 15(4): 297-304. PMID 16034309
93. Zacharias AJ, Jayakrishnan TT, Rajeev R, et al. Comparative Effectiveness of Hepatic Artery Based Therapies for Unresectable Colorectal Liver Metastases: A Meta-Analysis. PLoS ONE. 2015; 10(10): e0139940. PMID 26448327
94. Richardson AJ, Laurence JM, Lam VW. Transarterial chemoembolization with irinotecan beads in the treatment of colorectal liver metastases: systematic review. J Vasc Interv Radiol. Aug 2013; 24(8): 1209-17. PMID 23885916
95. Swierz MJ, Storman D, Riemsma RP, et al. Transarterial (chemo)embolisation versus no intervention or placebo for liver metastases. Cochrane Database Syst Rev. Mar 12 2020; 3: CD009498. PMID 32163181
96. Hunt TM, Flowerdew AD, Birch SJ, et al. Prospective randomized controlled trial of hepatic arterial embolization or infusion chemotherapy with 5-fluorouracil and degradable starch microspheres for colorectal liver metastases. Br J Surg. Jul 1990; 77(7): 779-82. PMID 2200559
97. Eichler K, Zangos S, Mack MG, et al. First human study in treatment of unresectable liver metastases from colorectal cancer with irinotecan-loaded beads (DEBIRI). Int J Oncol. Oct 2012; 41(4): 1213-20. PMID 22842404
98. Martin RC, Scoggins CR, Tomalty D, et al. Irinotecan drug-eluting beads in the treatment of chemo-naive unresectable colorectal liver metastasis with concomitant systemic fluorouracil and oxaliplatin: results of pharmacokinetics and phase I trial. J Gastrointest Surg. Aug 2012; 16(8): 1531-8. PMID 22528576
99. Vogl TJ, Jost A, Nour-Eldin NA, et al. Repeated transarterial chemoembolisation using different chemotherapeutic drug combinations followed by MR-guided laser-induced thermotherapy in patients with liver metastases of colorectal carcinoma. Br J Cancer. Mar 27 2012; 106(7): 1274-9. PMID 22382689
100. Martin RC, Joshi J, Robbins K, et al. Hepatic intra-arterial injection of drug-eluting bead, irinotecan (DEBIRI) in unresectable colorectal liver metastases refractory to systemic chemotherapy: results of multi-institutional study. Ann Surg Oncol. Jan 2011; 18(1): 192-8. PMID 20740319
101. Aliberti C, Fiorentini G, Muzzio PC, et al. Trans-arterial chemoembolization of metastatic colorectal carcinoma to the liver adopting DC Bead(R), drug-eluting bead loaded with irinotecan: results of a phase II clinical study. Anticancer Res. Dec 2011; 31(12): 4581-7. PMID 22199334
102. Fiorentini G, Aliberti C, Tilli M, et al. Intra-arterial infusion of irinotecan-loaded drug-eluting beads (DEBIRI) versus intravenous therapy (FOLFIRI) for hepatic metastases from colorectal cancer: final results of a phase III study. Anticancer Res. Apr 2012; 32(4): 1387-95. PMID 22493375

103. Martin RC, Scoggins CR, Schreeder M, et al. Randomized controlled trial of irinotecan drug-eluting beads with simultaneous FOLFOX and bevacizumab for patients with unresectable colorectal liver-limited metastasis. Cancer. Oct 15 2015; 121(20): 3649-58. PMID 26149602
104. Vogl TJ, Gruber T, Balzer JO, et al. Repeated transarterial chemoembolization in the treatment of liver metastases of colorectal cancer: prospective study. Radiology. Jan 2009; 250(1): 281-9. PMID 19092099
105. Vogl TJ, Mack MG, Balzer JO, et al. Liver metastases: neoadjuvant downsizing with transarterial chemoembolization before laser induced thermotherapy. Radiology. Nov 2003; 229(2): 457-64. PMID 14500854
106. Hong K, McBride JD, Georgiades CS, et al. Salvage therapy for liver-dominant colorectal metastatic adenocarcinoma: comparison between transcatheter arterial chemoembolization versus yttrium-90 radioembolization. J Vasc Interv Radiol. Mar 2009; 20(3): 360-7. PMID 19167245
107. Vogl TJ, Naguib NN, Nour-Eldin NE, et al. Transarterial chemoembolization (TACE) with mitomycin C and gemcitabine for liver metastases in breast cancer. Eur Radiol. Jan 2010; 20(1): 173-80. PMID 19657653
108. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Hepatobiliary Cancers, Version 3.2020. Updated June 1, 2020. https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. Accessed June 1, 2020.
109. Heimbach JK, Kulik LM, Finn RS, et al. AASLD guidelines for the treatment of hepatocellular carcinoma. Hepatology. Jan 2018; 67(1): 358-380. PMID 28130846
110. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Neuroendocrine and Adrenal Tumors, Version 1.2019. Updated March 5, 2019. https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed June 3, 2020.
111. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Uveal Melanoma, Version 1.2020. Updated May 21, 2020. https://www.nccn.org/professionals/physician_gls/pdf/uveal.pdf. Accessed June 1, 2020.
112. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Colon Cancer, Version 3.2020. Updated May 6, 2020. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed June 1, 2020.
113. Chiorean EG, Nandakumar G, Fadelu T, et al. Treatment of Patients with Late-Stage Colorectal Cancer: ASCO Resource-Stratified Guideline. JCO Glob Oncol. Mar 2020; 6: 414-438. PMID 32150483
114. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Breast Cancer, Version 4.2020. Updated May 8, 2020. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed June 1, 2020.

Endnotes

[1] Based on local expert opinion