Molina Clinical Policy
Radiofrequency Ablation of Primary or Metastatic Liver Tumors
Policy No. 391

Last Approval: 12/14/2022
Next Review Due By: December 2023

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Hepatic tumors can arise either as primary liver cancer (such as hepatocellular carcinoma) or by metastasis to the liver from other primary cancer sites. HCC is the fifth most common malignant tumor in the world, and the third leading cause of cancer-related mortality worldwide. (Ghouri YA, et al. 2017). HCC is a primary liver cancer that most commonly affects patients with chronic liver disease and cirrhosis.

Treatment options are based on staging, resectability, presence of comorbidities, performance status, and the metastatic burden. AASLD guidelines divide therapeutic options into curative and noncurative interventions (AASLD 2018). Curative therapies, which offer the chance of long-term response and improved survival, include the following: surgical resection, liver transplantation and ablative techniques (e.g., thermal ablation). Noncurative therapies, which attempt to prolong survival by slowing tumor progression, include transarterial chemoembolization (TACE), transarterial radioembolization (TARE), stereotactic body radiation therapy (SBRT), and systemic chemotherapy (AASLD 2018). Currently, surgical resection with adequate margins or liver transplantation is considered the treatments of choice and are viewed as potentially curative. However, while surgical resection and liver transplantation provide potentially curative treatment, these procedures have limited applicability and unresectable at diagnosis due to either to anatomic location, size, number of lesions, underlying liver reserve or comorbid conditions.

Radiofrequency Ablation (RFA) includes nonsurgical liver-directed therapies are commonly accepted as the best option for patients with HCCs that are confined to the liver and with no worse than Child-Turcotte-Pugh class A or B cirrhosis, who do not meet resectability or transplantation criteria and yet are candidates for a liver-directed procedure based on tumor factors and underlying liver disease (Curley, SA 2021). In RFA, a needle electrode is used to deliver high-frequency alternating electrical current, which results in cellular necrosis. The technique involves image-guided application of the probe primarily using ultrasound guidance. The cells killed by RFA are not removed but are gradually replaced by fibrosis and scar tissue. RFA is performed by surgical oncologists in an inpatient clinical setting. For patients who are reasonable surgical candidates, surgery is generally preferred over nonsurgical ablation, even for small tumors (Curley, SA 2021).

Regulatory Status

RFA devices are cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. Food and Drug Administration product code GEI.

COVERAGE POLICY

This policy focuses on RFA of primary or metastatic liver tumors and does not address other ablative therapies.

Enrollment in a clinical trial is encouraged for patients with HCC. For a list of trials recruiting patients with advanced disease, refer to clinicaltrials.gov

A. UNRESECTABLE (Inoperable) Primary or Metastatic HCC
RFA may be considered medically necessary for members who are **NOT** currently awaiting liver transplantation when **ALL** of the following criteria are met:

1. Tumor(s) is/are unresectable (e.g., due to comorbidities or an estimate of inadequate liver volume following resection). Prescriber submit rationale for the determination that the member is not a surgical candidate or the tumor is unresectable.

AND

2. Member meets **ONE** of the following (a, b, or c):

   a. Unresectable primary HCC as a primary treatment meeting the Milan criteria:
      - A single tumor(s) 5 cm or less (≤5 cm) in diameter; **AND**
      - No more than 3 hepatic nodules less than 3 cm (< 3 cm)

   OR

   b. Hepatic metastases from neuroendocrine tumors (carcinoid and noncarcinoid) meeting the following criteria:
      - The disease is symptomatic. Documentation of tumor-related symptoms required; **AND**
      - Systemic therapy has failed to control symptoms, or the member is not a candidate for systemic therapy

   OR

   c. Hepatic metastases from colorectal tumors (including but not limited to adenocarcinoma) meeting the following criteria:
      - Metastases are of colorectal origin; **AND**
      - Meets the Milan criteria:
        - A single tumor(s) 5 cm or less (≤5 cm) in diameter; **AND**
        - No more than 3 hepatic nodules less than 3 cm (< 3 cm)
      - No extrahepatic metastatic disease is present

B. Inoperable HCC awaiting Liver Transplant
RFA may be considered medically necessary for members who are currently *awaiting liver transplantation* when **ALL** of the following criteria are met:

1. RFA is intended to prevent tumor progression or decrease tumor size to achieve or maintain a member's candidacy for liver transplant; **AND**
2. Preserved liver function defined as Child-Pugh Class A or B; **AND**
3. THREE or fewer encapsulated nodules and each nodule is less than or equal to 5 centimeters in diameter; **AND**
4. No evidence of the following conditions:
   a. Extra-hepatic metastases
   b. Severe renal function impairment
   c. Portal vein occlusion

LIMITATIONS AND EXCLUSIONS

The following are considered **experimental, investigational and unproven** based on insufficient evidence:

1. Any indications other than those listed above

2. RFA as a treatment for all other benign or malignant liver tumors that do not meet the medical necessity criteria above, including but not limited to the following:
    a. More than 3 HCC tumors or when not all sites of tumor foci can be adequately treated
    b. More than 5 metastatic colorectal tumors in the liver
    c. Metastatic or primary liver tumors larger than 5 cm in diameter
    d. Metastases to the liver from organ tumors other than colorectal, asymptomatic neuroendocrine tumors, or neuroendocrine tumors with symptoms controlled by systemic therapy.

3. RFA ablation of primary HCC when used to downstage (downsize) HCC in members being considered for liver transplant.
Informational Note: Downstaging can facilitate liver transplantation for patients outside of Milan criteria with more advanced HCC so that patients may qualify for the priority listing by the Milan criteria (Tsoulfas G, 2020); however, the optimal protocol and downstaging outcomes are poorly defined. It is noted that there is no universal or consensus of the optimal method for downstaging, selection criteria, and factors predicting effective downstaging from locoregional therapies prior to liver transplantation. To determine success and post-transplant survival in this cohort of patients, large prospective studies utilizing standardized reporting criteria are needed to compare downstaging modalities and protocols. (Parikh ND; 2016)

4. Primary, Operable HCC
For individuals who have primary, operable HCC who receive RFA, the evidence includes RCTs, meta-analyses of these RCTs, and a database analysis. Systematic reviews and meta-analyses have also reported superior survival and lower recurrence rates with hepatic resection compared with RFA, though resection was accompanied by higher rates of complications. [Feng et al. (2014); Wang et al. (2014); Qi et al. (2014); Duan et al (2013); Jia et al. (2017); Xu et al. (2018)] These findings support the use of RFA only for unresectable HCC. **The evidence is insufficient to determine the effects of the technology RFA on health outcomes.**

5. Hepatic Metastases NOT of Colorectal or Neuroendocrine Origin
For individuals who have hepatic metastases not of colorectal or neuroendocrine origin who receive RFA, the evidence includes small nonrandomized comparative studies and small case series which is not sufficient to determine whether RFA improves outcomes [Gastric Cancer: Li et al (2017); Nasopharyngeal Cancer: Li et al (2017); Ovarian Cancer Liu et al (2017); Pancreatic Cancer: Hua et al (2017)]. The evidence is insufficient to determine the effects of the technology RFA on health outcomes.

Sarcoma
- Jones et al. (2010) evaluated RFA in a series of patients with sarcoma. 13 gastrointestinal stromal tumor (GIST) patients and 12 with other histologic subtypes received RFA for metastatic disease in the liver: 12 responded to the first RFA procedure and 1 patient achieved stable disease. 2 GIST patients received RFA on 2 occasions for separate lesions within the liver, and both responded to the second RFA procedure. Of the other subtypes, 7 patients underwent RFA to liver lesions, 5 of whom responded to RFA, 1 patient progressed, and another was not assessable at the time of analysis. It was reported that RFA was well-tolerated in this series of sarcoma patients. While RFA may have a role in patients with GIST who have progression in a single metastasis but stable disease elsewhere, the authors recommended that larger should be conducted to define the role of this RFA in this patient population.
- Pawlik et al. (2006) reported on a case series of 66 patients who underwent hepatic resection (n=35), resection and RFA (n=18), or RFA alone (n=13). After a median follow-up of 35.8 months, 44 patients had recurrence (intrahepatic only, n=16; extrahepatic only, n=11; both, n=17). The 1, 3, and 5-year overall survivall rates were 91.5%, 65.4%, and 27.1%, respectively.

Breast Cancer
- Veltri et al. (2014) analyzed 45 women treated with RFA for 87 breast cancer liver metastases (mean size, 23 mm). Complete ablation was reported on initial follow-up in 90% of tumors, but tumors recurred in 19.7%

within 8 months. RFA did not impact overall survival rates, which at 1 year was 90% and at 3 years was 44%.

- Meloni et al. (2009), in a retrospective review, assessed local control and intermediate- and long-term survival in 52 patients. Local tumor progression occurred in 25% of patients, and new intrahepatic metastases developed in 53%. Median OS, from the time of first liver metastasis diagnosis, was 42 months, and 5-year survival was 32%. Patients with tumors 2.5 cm in diameter or larger had a worse prognosis than those with smaller tumors. The authors concluded that the survival rates comparable to those reported in the literature for surgery or laser ablation.
- Jakobs et al. (2009) in a case series (2009) of 43 breast cancer patients with 111 liver metastases, tumor ablation was achieved in 107 (96%) metastases. During follow-up, local tumor progression was observed in 15 metastases. Estimated median OS was 58.6 months. Survival was significantly lower among patients with extrahepatic disease, except skeletal metastases.
- Lawes et al. (2006) reported a series of 19 patients (8 patients had disease confined to the liver, with 11 also having stable extrahepatic disease). At the time of reporting, 7 patients, with disease confined to the liver at presentation, were alive, as were 6 patients with extrahepatic disease (median follow-up after RFA, 15 months; range, 0-77 months). Survival at 30 months was 41.6%. It was noted that RFA failed to control hepatic disease in 3 patients.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

RFA as a Treatment of Primary, Operable HCC

RFA provides a treatment option that is an alternative to, or an improvement on existing therapies, such as surgical resection, in patients with primary HCC.

Systematic Review and Meta-Analysis

Yu et al. (2020) performed a meta-analysis focused on comparative OS and disease-free survival between percutaneous RFA and partial hepatectomy in patients with primary HCC meeting Milan criteria. The analysis included only RCTs, accounting for 5 trials (N=761). The authors evaluated the quality of the included studies and judged 4 of 5 to be high quality based on the Jadad score. Overall survival and disease-free survival were similar between groups, but RFA was associated with a higher long-term recurrence rate (2-year overall recurrence: relative risk [RR]=1.56, 95% confidence interval [CI]: 1.12 to 2.16; 5-year overall recurrence: RR=1.48, 95% CI: 1.19 to 1.84). Treatment-related complications with RFA were significantly lower compared to partial hepatectomy, but the analysis had a high degree of heterogeneity (I^2=79%).

Li et al. (2020) conducted a meta-analysis (1 RCT and 15 retrospective observational studies) of the efficacy of RFA compared with surgical resection for HCC with particular emphasis on overall survival and disease-free survival rates. The studies included patients with HCC meeting the Milan criteria with liver function Child-Pugh scores of grade A or B. Surgical resection was demonstrated to show superior 1-, 3- and 5-year overall survival and disease-free survival rates than RFA for patients with small HCC that were eligible for surgical treatment. However, RFA can be an alternative therapeutic option for patients with small single HCC tumors that are not suitable for surgical resection. The results indicate that surgical resection is superior to RFA for promoting the survival of selected patients with resectable HCC. However, it was noted that future randomized controlled trials are required to investigate the specific relevance of these modalities in the treatment of HCC

Weis et al. (2013) evaluated studies on RFA for HCC versus other interventions in a Cochrane systematic review. Moderate-quality evidence demonstrated that hepatic resection had superior survival outcomes compared with RFA; however, resection might have greater rates of complications and longer hospital stays. It was noted that other systematic reviews and meta-analyses have also found superior survival with hepatic resection but higher rates of

complications than RFA [Feng et al. (2015); Wang et al. (2014); Qi et al. (2014); Duan et al. (2013)]. This finding reinforces the use of RFA only for unresectable HCC. The Cochrane review also reported on the moderate quality evidence demonstrating superior survival with RFA over percutaneous ethanol injection (PEI). Evidence on RFA versus acetic acid injection, microwave ablation, or laser ablation was insufficient to draw conclusions.

RFA For Hepatic Metastases of Neuroendocrine Origin

The available evidence indicates that durable tumor and symptom control of neuroendocrine liver metastases can be achieved by RFA in individuals whose symptoms are not controlled by systemic therapy. The evidence on RFA for patients with liver metastases of neuroendocrine origin consists of case series (Berber and Siperstein, 2008) and a systematic review of case series (Mohan H, et al. 2015). Reports of RFA treatment for neuroendocrine liver metastases includes small numbers of patients or subsets of patients in reports of multiple ablative methods (Elias et al. 2009), or very small subsets of larger case series of patients with various diagnoses (Mazzaglia et al. 2007).

Mohan et al. (2015) conducted a systematic review of RFA as a treatment for unresectable metastases from neuroendocrine tumors was published in 2015. The review included 7 unique studies (total N=301 patients), all retrospective case series from a single institution. The most common tumor type was carcinoid (59%), followed by nonfunctional pancreatic tumors (21%) and functional pancreatic tumors (13%). A high degree of variability in the length of follow-up and surveillance, and a wide range of local recurrence rates, from less than 5% to 50%, The reported 5-year survival rates ranged from 57% to 80%. There were 2 periprocedural deaths (rate, 0.7%), and the overall rate of complications was 10%, including hemorrhage, abscess, viscus perforation, bile leak, biliopleural fistula, transient liver insufficiency, pneumothorax, grounding pad burn, urinary retention, pneumonia, pleural effusion. Improvement in symptoms was reported in 92% (117/127) of symptomatic patients, with a median duration of relief ranging from 14 to 27 months.

National and Specialty Organizations

American Association for the Study of Liver Diseases (AASLD)
The 2018 AASLD Practice Guidelines on the diagnosis, staging and management of HCC notes that surgical resection remains the treatment of choice for resectable HCC. The location of tumors can also impact the effectiveness of available therapies. Surgical resection of isolated primary, multifocal and metastatic tumors continue to be the established gold standard for curative intent of colorectal and neuroendocrine carcinomas as well as HCC. The AASLD does not recommend one form of locoregional treatments (consisting of either local ablation or transarterial treatment) over another noting that it is not possible to identify a preferred type of locoregional treatments based on the available evidence.

The guidelines further concur that liver transplantation is the best available curative option for patients with early-stage non-resectable HCC who meet the Milan criteria (single tumors ≤ 5 cm in diameter or no more than three nodules ≤ 3 cm in diameter in patients with multiple tumors). Ablation should be considered as definitive treatment for patients with stage 0-A tumors who are not candidates for resection or transplantation. NCCN and AASLD guidelines also recommend ablation as a possible bridge therapy for patients awaiting transplantation (AASLD 2018; NCCN 2021).

Current guidelines recommend a bridging therapy with locoregional treatments for patients within Milan criteria who are expected to remain on the transplant waitlist for more than 6 months, according to the AASLD (Heimbach et al., 2018), or for more than 3 months, according to the European guideline by ESMO (Vogel et al., 2018). However, due to unpredictable waiting times and risk of tumor progression, most patients receive some form locoregional treatments while awaiting transplant (Kulik et al., 2018).

National Comprehensive Cancer Network (NCCN)
The NCCN (v.4.2022) guidelines on hepatobiliary cancers state that "ablation alone may be curative in treating tumors ≤ 3 cm. In well-selected patients with small, properly located tumors, ablation should be considered as definitive treatment in the context of a multidisciplinary review. Lesions 3 to 5 cm may be treated to prolong survival using arterially directed therapies, alone or with combination of an arterially directed therapy and ablation as long as the tumor is accessible for ablation" (category 2A).

The NCCN (v.2.2022) guidelines on colon cancer metastatic to the liver state that "Ablative techniques may be considered alone or in conjunction with resection. All original sites of disease need to be amenable to ablation or resection" (category 2A). The guidelines note that there is substantial evidence that RFA is a viable treatment option for non-surgical candidates and for recurrent disease after hepatectomy with small liver metastases that can be treated with clear margins.

The NCCN (v.1.2022) guidelines for neuroendocrine tumors state that "…ablative therapies such as RFA or cryoablation may be considered if near-complete treatment of tumor burden can be achieved (category 2B). For unresectable liver metastases...(arterial embolization, chemoembolization, or radioembolization [category 2B]) is recommended."

SUPPLEMENTAL INFORMATION

Child-Pugh score: Used to assess prognosis of chronic liver disease and cirrhosisIt consists of five clinical features with values worth 1, 2, or 3 points. The number of points accumulated (5-15) indicate estimated chance of 1-year survival. Class A (5-6 points total) indicates an estimated 100% chance of 1-year survival.

Milan criteria: Defined as a single HCC less than 5 cm in the maximum diameter, having up to three nodules with each no larger than 3 cm, with no angio invasion and no extrahepatic involvement (AASLD 2018; ESMO 2018; NCCN 2020: Hepatobiliary cancers)

Neuroendocrine tumors: A heterogeneous group of neoplasms that are thought to arise from neuroendocrine cells and their precursors located throughout the body; classically characterized by the ability to secrete peptides resulting in distinctive hormonal syndromes. Ablation can be used as a primary treatment modality for neuroendocrine liver metastases or as an adjunct to surgical resection. Neuroendocrine tumors include the following: Carcinoid Tumors; Islet Cell Tumors (also known as Pancreatic Endocrine Tumors); Neuroendocrine Unknown Primary; Adrenal Gland Tumors; Pheochromocytoma/paraganglioma; Poorly Differentiated (High Grade or Anaplastic)/Small Cell; Multiple Endocrine Neoplasia, Type 1 (also known as MEN-1 syndrome or Wermer's syndrome); Multiple Endocrine Neoplasia, Type 2 a or b (also known as pheochromocytoma and amyloid producing medullary thyroid carcinoma, PTC syndrome, or Sipple syndrome).

CODING & BILLING INFORMATION

CPT Codes

CPT	Description
47370	Laparoscopy, surgical, ablation of 1 or more liver tumor(s); radiofrequency
47380	Ablation, open, of 1 or more liver tumor(s); radiofrequency
47382	Ablation, 1 or more liver tumor(s), percutaneous, radiofrequency
76940	Ultrasound guidance for, and monitoring of, parenchymal tissue ablation

HCPCS Codes – N/A

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

12/14/2022	Policy reviewed and updated. No changes in coverage criteria, updated references.
12/8/2021	Policy reviewed and updated. No changes in coverage criteria, updated references. Converted to new format.
12/9/2020	New policy. IRO Peer Review: 11/16/2020. Practicing physician board-certified in Radiation Oncology.

REFERENCES

Government Agency

1. Centers for Medicare and Medicaid Services (CMS). Medicare coverage database (search: Radiofrequency Ablation; RFA). Available from CMS. Accessed November 2022.
   - *No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were located at the time of the last policy review date.*

Peer Reviewed Publications

Hepatocellular Carcinoma

1. Ghouri YA, Mian I, Rowe JH. Review of hepatocellular carcinoma: Epidemiology, etiology, and carcinogenesis. *J Carcinog*. 2017;16:1. Published 2017 May 29. doi:10.4103/jcar.JCar_9_16.
2. Kulik L, Heimbach JK, Zaiem F, et al. Therapies for patients with hepatocellular carcinoma awaiting liver transplantation: A systematic review and meta-analysis. Hepatology. 2018; 67(1):381-400.
3. Li JK, Liu XH, Cui H, Xie XH. Radiofrequency ablation vs. surgical resection for resectable hepatocellular carcinoma: A systematic review and meta-analysis. Mol Clin Oncol. 2020;12(1):15-22. doi:10.3892/mco.2019.1941.
4. Parikh ND, Waljee AK, Singal AG. Downstaging hepatocellular carcinoma: A systematic review and pooled analysis. Liver Transpl. 2015 Sep;21(9):1142-52. doi: 10.1002/lt.24169. Erratum in: Liver Transpl. 2016 Jan;22(1):138. PMID: 25981135.
5. Weis, S, Franke, A, Mossner, J, Jakobsen, JC, Schoppmeyer, K. Radiofrequency (thermal) ablation versus no intervention or other interventions for hepatocellular carcinoma. The Cochrane database of systematic reviews. 2013;12:CD003046. PMID: 24357457.
6. Yu C, Wu S, Zhao J, et al. Evaluation of efficacy, safety and treatment-related outcomes of percutaneous radiofrequency ablation versus partial hepatectomy for small primary liver cancer meeting the Milan criteria: A systematic review and meta-analysis of randomized controlled trials. Clin Res Hepatol Gastroenterol. Jan 17 2020. PMID 31959566.

Hepatic Metastases Of Neuroendocrine Origin

7. Berber E, Siperstein A. Local recurrence after laparoscopic radiofrequency ablation of liver tumors: an analysis of 1032 tumors. Ann Surg Oncol. Oct 2008;15(10):2757-2764. PMID 18618182.;
8. Elias D, Goere D, Leroux G, et al. Combined liver surgery and RFA for patients with gastroenteropancreatic endocrine tumors presenting with more than 15 metastases to the liver. Eur J Surg Oncol. Oct 2009;35(10):1092-1097. PMID 19464140.
9. Mazzaglia PJ, Berber E, Siperstein AE. Radiofrequency thermal ablation of metastatic neuroendocrine tumors in the liver. Curr Treat Options Oncol 2007; 8:322.
10. Mohan H, Nicholson P, Winter DC, et al. Radiofrequency ablation for neuroendocrine liver metastases: a systematic review. J Vasc Interv Radiol. Jul 2015; 26(7):935-942 e931. PMID 25840836.

Primary, Operable Hepatocellular Carcinoma

11. Feng Q, Chi Y, Liu Y, et al. Efficacy and safety of percutaneous radiofrequency ablation versus surgical resection for small hepatocellular carcinoma: a meta-analysis of 23 studies. J Cancer Res Clin Oncol. Jun 3 2014. PMID 24889505.
12. Wang Y, Luo Q, Li Y, et al. Radiofrequency ablation versus hepatic resection for small hepatocellular carcinomas: a meta-analysis of randomized and nonrandomized controlled trials. PLoS One. 2014;9(1):e84484. PMID 24404166.
13. Qi X, Tang Y, An D, et al. Radiofrequency ablation versus hepatic resection for small hepatocellular carcinoma: a meta-analysis of randomized controlled trials. J Clin Gastroenterol. May-Jun 2014;48(5):450-457. PMID 24172183.
14. Duan C, Liu M, Zhang Z, et al. Radiofrequency ablation versus hepatic resection for the treatment of early-stage hepatocellular carcinoma meeting Milan criteria: a systematic review and meta-analysis. World J Surg Oncol. 2013;11(1):190. PMID 23941614.
15. Jia JB, Zhang D, Ludwig JM, et al. Radiofrequency ablation versus resection for hepatocellular carcinoma in patients with Child-Pugh A liver cirrhosis: a meta-analysis. Clin Radiol. Dec 2017;72(12):1066-1075. PMID 28851491.
16. Xu XL, Liu XD, Liang M, et al. Radiofrequency ablation versus hepatic resection for small hepatocellular carcinoma: systematic review of randomized controlled trials with metaanalysis and trial sequential analysis. Radiology. May 2018;287(2):461-472. PMID 29135366.

Hepatic Metastases NOT of Colorectal Or Neuroendocrine Origin (Breast Cancer, Sarcoma)

17. Hua YQ, Wang P, Zhu XY, et al. Radiofrequency ablation for hepatic oligometastatic pancreatic cancer: An analysis of safety and efficacy. Pancreatology. Nov - Dec 2017;17(6):967-973. PMID 29129384.
18. Jakobs TF, Hoffmann RT, Schrader A, et al. CT-guided radiofrequency ablation in patients with hepatic metastases from breast cancer. Cardiovasc Intervent Radiol. Jan 2009; 32(1):38-46. PMID 18575933.
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20. Lawes D, Chopada A, Gillams A et al. Radiofrequency ablation (RFA) as a cytoreductive strategy for hepatic metastasis from breast cancer. Ann R Coll Surg Engl 2006; 88(7):639- 42. PMID 17132311.
21. Li J, Zhang K, Gao Y, et al. Evaluation of hepatectomy and palliative local treatments for gastric cancer patients with liver metastases: a propensity score matching analysis. Oncotarget. Sep 22 2017;8(37):61861-61875. PMID 28977910.
22. Li W, Bai Y, Wu M, et al. Combined CT-guided radiofrequency ablation with systemic chemotherapy improves the survival for nasopharyngeal carcinoma with oligometastasis in liver: Propensity score matching analysis. Oncotarget. Aug 8 2017;8(32):52132-52141. PMID 28881719.
23. Liu B, Huang G, Jiang C, et al. Ultrasound-Guided Percutaneous Radiofrequency Ablation of Liver Metastasis from Ovarian Cancer: A Single-Center Initial Experience. Int J Gynecol Cancer. Jul 2017;27(6):1261-1267. PMID 28640176.
24. Pawlik TM, Vauthey JN, Abdalla EK, et al. Results of a single-center experience with resection and ablation for sarcoma metastatic to the liver. Arch Surg. Jun 2006; 141(6):537-543; discussion 543-534. PMID 16785353.
25. Meloni MF, Andreano A, Laeseke PF, et al. Breast cancer liver metastases: US-guided percutaneous radiofrequency ablation--intermediate and long-term survival rates. Radiology. Dec 2009; 253(3):861-869. PMID 19709994.

26. Veltri A, Gazzera C, Barrera M, et al. Radiofrequency thermal ablation (RFA) of hepatic metastases (METS) from breast cancer (BC): an adjunctive tool in the multimodal treatment of advanced disease. Radiol Med. May 2014; 119(5):327-333. PMID 24297589.

National and Specialty Organizations

1. American Association for the Study of Liver Diseases (AASLD)
    a. 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.
    b. Marrero JA, Kulik LM, Sirlin CB, et al. Diagnosis, Staging, and Management of Hepatocellular Carcinoma: 2018 practice guidance by the American Association for the Study of Liver Diseases. Hepatology. 2018 Aug;68(2):723-750. doi: 10.1002/hep.29913. PMID: 29624699.
2. National Comprehensive Cancer Network (NCCN). Available from NCCN. Registration and login required.
    a. Hepatobiliary cancers (version 4.2022). Published December 9, 2022. Accessed November 2022.
    b. Colon cancer (version 2.2022). Published October 27, 2022. Accessed November 2022.
    c. Neuroendocrine and adrenal tumors (ver. 1.2022). Published May 23, 2022. Accessed November 2022.
3. Vogel A, Cervantes A, Chau I, Daniele B, et al; ESMO Guidelines Committee. Hepatocellular carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2018 Oct 1;29(Supplement_4):iv238-iv255. Available here. Accessed November 2022.

Other Peer Reviewed Publications

1. UpToDate. Available from UpToDate.
    a. Curley SA, Stuart KE, et al. Localized hepatocellular carcinoma: Liver-directed therapies for nonsurgical candidates not eligible for local thermal ablation. Updated Dec 06, 2022. Topic 15589 Version 68.0
    b. Localized hepatocellular carcinoma: Liver-directed therapies for nonsurgical candidates who are eligible for local ablation. Updated Sep 16, 2022. Topic 2487 Version 54.0
    c. Abdalle EK, Stuart KE, Singal AG. Overview of treatment approaches for hepatocellular carcinoma. Updated Oct 31, 2022. Topic 2489 Version 44.0
    d. Tsoulfas G, et al. Liver transplantation for hepatocellular carcinoma. Available from UpToDate. Updated February 22, 2021.

Other Peer Reviewed and National Organization Publications (used in the development of this policy)

1. DynaMed. Management of Hepatocellular Carcinoma in Adults. EBSCO Information Services. Available from Dynamed Accessed December 13, 2022
2. Tian G, Yang S, Yuan J, et al. Comparative efficacy of treatment strategies for hepatocellular carcinoma: systematic review and network meta-analysis. BMJ Open 2018;8:e021269. doi: 10.1136/bmjopen-2017-021269.
3. Zhang, W., Luo, E., Gan, J. et al. Long-term survival of hepatocellular carcinoma after percutaneous radiofrequency ablation guided by ultrasound. World J Surg Onc 15, 122 (2017). https://doi.org/10.1186/s12957-017-1189-1.

APPENDIX

Reserved for State specific information *(to be provided by the individual States, not Corporate). Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*