

Protocol

Cryosurgical Ablation of Primary or Metastatic Liver Tumors

(70175)

Medical Benefit		Effective Date: 07/01/10	Next Review Date: 01/20
Preauthorization	No	Review Dates: 02/07, 02/08, 01/09, 01/10, 01/11, 01/12, 01/13, 01/14, 01/15, 01/16, 01/17, 01/18, 01/19	

This protocol considers this test or procedure investigational. If the physician feels this service is medically necessary, preauthorization is recommended.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • With unresectable primary hepatocellular carcinoma amenable to locoregional therapy	Interventions of interest are: • Cryosurgical ablation	Comparators of interest are: • Radiofrequency ablation • Microwave tumor ablation • Locoregional ablation other than radiofrequency ablation	Relevant outcomes include: • Overall survival • Disease-specific survival • Treatment-related mortality • Treatment-related morbidity
Individuals: • With unresectable liver metastases from neuroendocrine tumors amenable to locoregional therapy	Interventions of interest are: • Cryosurgical ablation	Comparators of interest are: • Radiofrequency ablation • Microwave tumor ablation • Locoregional ablation other than radiofrequency ablation	Relevant outcomes include: • Overall survival • Disease-specific survival • Symptoms • Treatment-related mortality • Treatment-related morbidity
Individuals: • With unresectable liver metastases from colorectal cancer amenable to locoregional therapy	Interventions of interest are: • Cryosurgical ablation	Comparators of interest are: • Radiofrequency ablation • Microwave tumor ablation • Locoregional ablation other than radiofrequency ablation	Relevant outcomes include: • Overall survival • Disease-specific survival • Treatment-related mortality • Treatment-related morbidity

DESCRIPTION

Cryosurgical ablation (CSA) involves the freezing of target tissues, often by inserting a probe through which coolant is circulated into the tumor. CSA can be performed as an open surgical technique or percutaneously or laparoscopically, typically with ultrasound guidance.

SUMMARY OF EVIDENCE

For individuals who have unresectable primary hepatocellular carcinoma amenable to locoregional therapy who receive CSA, the evidence includes a randomized controlled trial (RCT), several nonrandomized comparative studies, and multiple noncomparative studies. Relevant outcomes are overall survival, disease-specific survival,

and treatment-related mortality and morbidity. The available RCT comparing cryoablation with radiofrequency ablation demonstrated lower rates of local tumor progression with cryoablation, but no differences in survival outcomes between groups. Although this trial provided suggestive evidence that cryoablation is comparable with radiofrequency ablation, trial limitations would suggest findings need to be replicated. Additional comparative evidence is needed to permit conclusions about the effectiveness of cryoablation compared with other locoregional therapies. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have unresectable liver metastases from neuroendocrine tumors amenable to locoregional therapy who receive CSA, the evidence includes a Cochrane review and case series. Relevant outcomes are overall survival, disease-specific survival, symptoms, and treatment-related mortality and morbidity. The available evidence base is very limited. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have unresectable liver metastases from colorectal cancer amenable to locoregional therapy who have CSA, the evidence includes an RCT, several nonrandomized comparative and noncomparative studies, and systematic reviews of these studies. Relevant outcomes are overall survival, disease-specific survival, and treatment-related mortality and morbidity. The available RCT comparing surgical resection with cryoablation was judged at high risk of bias. Some nonrandomized comparative studies have reported improved survival outcomes for patients managed with cryotherapy compared with those managed with resection alone; however, these studies were subject to bias in the selection of patients for treatments. Additional controlled studies are needed to permit conclusions about the effectiveness of cryoablation compared with other locoregional therapies. The evidence is insufficient to determine the effects of the technology on health outcomes.

POLICY

Cryosurgical ablation of either primary or metastatic tumors in the liver is **investigational**.

BACKGROUND

LIVER METASTASES

Hepatic tumors can be due to primary liver cancer or metastases to the liver from nonhepatic primary tumors. Primary liver cancer can arise from hepatocellular tissue (hepatocellular carcinoma) or intrahepatic biliary ducts (cholangiocarcinoma). Multiple tumors metastasize to the liver, but there is particular interest in the treatment of hepatic metastases from colorectal cancer (CRC) given the propensity of CRC to metastasize to the liver and its high prevalence. Liver metastases from neuroendocrine tumors present a unique clinical situation. Neuroendocrine cells produce and secrete a variety of regulatory hormones (or neuropeptides), which include neurotransmitters and growth factors. Overproduction of the specific neuropeptides by cancerous cells causes various symptoms, depending on the hormone produced.

Treatment

Treatment of liver metastases is undertaken to reduce endocrine-related symptoms, in addition to prolonging survival and reducing symptoms related to the hepatic mass.

Surgical resection with tumor-free margins and liver transplantation are the primary treatments available that have curative potential. Many hepatic tumors are unresectable at diagnosis, due either to their anatomic location, size, the number of lesions, or underlying liver reserve. Local therapy for hepatic metastasis is indicated only when there is no extrahepatic disease, which rarely occurs for patients with primary cancers other than CRC or certain neuroendocrine malignancies. For liver metastases from CRC, postsurgical adjuvant chemotherapy has

been reported to decrease recurrence rates and prolong time to recurrence. Combined systemic and hepatic arterial chemotherapy may increase disease-free intervals for patients with hepatic metastases from CRC but apparently is not beneficial for those with unresectable hepatocellular carcinoma.

Various locoregional therapies for unresectable liver tumors have been evaluated: cryosurgical ablation (cryosurgery); radiofrequency ablation; laser ablation; transhepatic arterial embolization, chemoembolization, or radioembolization with yttrium-90 microspheres; microwave coagulation; and percutaneous ethanol injection. Cryosurgical ablation occurs in tissue that has been frozen by at least three mechanisms: (1) formation of ice crystals within cells, thereby disrupting membranes and interrupting cellular metabolism among other processes; (2) coagulation of blood, thereby interrupting blood flow to the tissue, in turn causing ischemia and apoptosis; and (3) induction of apoptosis.

Recent studies, including a small randomized controlled trial and case series, have reported on experience with cryosurgical and other ablative methods used in combination with subtotal resection and/or procedures such as transarterial chemoembolization.^{1,2}

Procedure-Related Complications

Cryosurgery is not a benign procedure. Treatment-related deaths occur in approximately 2% of study populations and are most often caused by cryoshock, liver failure, hemorrhage, pneumonia/sepsis, and acute myocardial infarction. Clinically significant nonfatal complication rates in the reviewed studies ranged from 0% to 83% and were generally due to the same causes as treatment-related deaths. The likelihood of complications arising from cryosurgery might be predicted, in part, by the extent of the procedure,³ but much of the treatment-related morbidity and mortality reflect the generally poor health status of patients with advanced hepatic disease.

REGULATORY STATUS

Several cryosurgical devices have been cleared by the U.S. Food and Drug Administration. For example, in 1996, the Endocare™ Cryocare System (Endocare) was cleared for marketing through the 510(k) process for “use in general surgery, dermatology, neurology, thoracic surgery, ENT [ears, nose, throat], gynecology, oncology, proctology and urology for the ablation of tissue, including liver metastases, skin lesions, warts, and removal of prostate tissue.” U.S. Food and Drug Administration product code: GEH.

RELATED PROTOCOLS

Cryosurgical Ablation of Miscellaneous Solid Tumors Other Than Liver, Prostate, or Dermatologic Tumors

Microwave Tumor Ablation

Radioembolization for Primary and Metastatic Tumors of the Liver

Radiofrequency Ablation of Miscellaneous Solid Tumors Excluding Liver Tumors

Radiofrequency Ablation of Primary or Metastatic Liver Tumors

Transcatheter Arterial Chemoembolization to Treat Primary or Metastatic Liver Malignancies

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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