Cryosurgical Ablation of Primary or Metastatic Liver Tumors

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.

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, but much of the treatment-related morbidity and mortality reflect the generally poor health status of patients with advanced hepatic disease.
OBJECTIVE

The objective of this evidence review is to determine whether cryoablation improves the net health outcome in individuals with unresectable primary and metastatic liver tumors.

POLICY STATEMENT

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

POLICY GUIDELINES

None

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA 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.

RATIONALE

Summary of Evidence

For individuals who have unresectable primary hepatocellular carcinoma amenable to locoregional therapy who receive cryosurgical ablation (CSA), the evidence includes a randomized controlled trial (RCT), several nonrandomized comparative studies, and multiple noncomparative studies. The relevant outcomes are overall survival (OS), disease-specific survival, and treatment-related mortality and morbidity. The available RCT comparing cryoablation with RFA 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 (RFA), 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. The relevant outcomes are OS, 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 CRC amenable to locoregional therapy who have CSA, the evidence includes an RCT, several nonrandomized comparative and noncomparative studies, and systematic reviews of these studies. The relevant outcomes are OS, 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...

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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.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

The National Comprehensive Cancer Network (NCCN) indicates that ablative techniques may be used in the treatment of certain hepatic tumors. The NCCN guidelines on hepatobiliary cancer (v.2.2018) include cryoablation in a list of ablative techniques, along with radiofrequency ablation (RFA), percutaneous alcohol ablation, and microwave ablation; however, the literature cited in the guidelines reports on only RFA and ethanol ablation. For hepatocellular carcinoma, the NCCN makes the following category 2A recommendation:

"All patients with HCC [hepatocellular carcinoma] should be evaluated for potential curative therapies (resection, transplantation, and for small lesions, ablative strategies). Locoregional therapy should be considered in patients who are not candidates for surgical curative treatments, or as a part of a strategy to bridge patients for other curative therapies.

Ablation (radiofrequency, cryoablation, percutaneous alcohol injection, microwave):

- All tumors should be amenable to ablation such that the tumor and, in the case of thermal ablation, a margin of normal tissue is treated. A margin is not expected following percutaneous ethanol injection.

- Tumors should be in a location accessible for percutaneous/laparoscopic/open approaches for ablation.

- Caution should be exercised when ablating lesions near major vessels, major bile ducts, diaphragm, and other intra-abdominal organs.

- 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, or with combination of an arterially directed therapy and ablation as long as tumor location is accessible for ablation.

- Unresectable/inoperable lesions >5 cm should be considered for treatment using arterially directed or systemic therapy.

- Sorafenib should not be used as adjuvant therapy post-ablation.”

For intrahepatic cholangiocarcinoma (isolated intrahepatic mass), the guidelines recommend locoregional therapy using arterially directed therapies or external-beam radiotherapy (category 2B recommendations).

The NCCN guidelines on neuroendocrine and adrenal tumors (v.2.2018) address the use of hepatic-directed therapies for patients with unresectable hepatic-predominant progressive metastatic neuroendocrine. These guidelines support consideration of ablative therapies such as RFA or cryoablation if near-complete tumor burden can be achieved (category 2B recommendation).

The NCCN guidelines on the treatment of colon cancer with liver metastases (v.2.2018) consider patients with liver oligometastases as candidates for tumor ablation therapy. Ablative techniques include RFA, microwave ablation, cryoablation, percutaneous ethanol injection, and electro-coagulation. Use of surgery, ablation, or the combination "with the goal of less-than-complete resection/ablation of all known sites of disease, is not recommended" (category 2A recommendations).

U.S. Preventive Services Task Force Recommendations

Not applicable.
Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES


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PMID 21654315.


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### POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

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<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
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<tr>
<td>December 2011</td>
<td>New policy</td>
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<tr>
<td>June 2012</td>
<td>Replace policy</td>
<td>Policy statement changed from investigational to not medically necessary. Related policies added.</td>
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<tr>
<td>March 2013</td>
<td>Replace policy</td>
<td>Policy updated with literature search; references 4, 11, 12, 15 added. Policy statement unchanged.</td>
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<tr>
<td>March 2014</td>
<td>Replace policy</td>
<td>Policy updated with literature review; references added, reordered or removed. Policy statement unchanged.</td>
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<tr>
<td>March 2015</td>
<td>Replace policy</td>
<td>Policy updated with literature review; reference 2 added. Policy statement unchanged.</td>
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<tr>
<td>March 2017</td>
<td>Replace policy</td>
<td>Policy updated with literature review through November 17, 2015; references 3-4 and 8 added. Policy statement unchanged except &quot;not medically necessary&quot; corrected to &quot;investigational&quot; due to FDA 510(k) clearance.</td>
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<tr>
<td>September 2018</td>
<td>Replace policy</td>
<td>Policy updated with literature search through May 7, 2018; no references added. Policy statement unchanged.</td>
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<tr>
<td>December 2019</td>
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<td>Policy updated with literature search through July 7, 2019; no references added. Policy statement unchanged.</td>
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