Complications of Hepatitis C

Liver Cancer

People with hepatitis C-related cirrhosis have an increased risk of liver cancer. The prevalence of liver cancer is increasing in the U.S. Liver cancer is the fifth leading cause of cancer death in men, and eighth leading cause in women. There are two categories of liver cancer—primary and secondary. Primary refers to cancer that starts in the liver. The most common primary liver cancer in adults is hepatocellular carcinoma (HCC), sometimes called hepatoma. There are other types of benign and malignant tumors of the liver.

Secondary or metastatic cancer, occurs when cancer starts in another part of the body and spreads to the liver. Colorectal cancer is known for this, with roughly half of all cases metastasizing to the liver.

Risk Factors

The majority of HCC occurs in people with risk factors. The more risk factors, the greater the chances are for developing liver cancer. Anything that leads to cirrhosis, including hepatitis C, is a liver cancer risk. Cirrhosis is linked to more than 80 percent of all HCC. Although the majority of primary liver cancers begin with cirrhosis, the majority of those with cirrhosis will never get liver cancer. Other risk factors for HCC are:

- Viral hepatitis
- Age (greater than 60 years old)
- Long-term, heavy alcohol consumption
- Race/ethnicity—In the U.S., Asian Americans and Pacific Islanders have the highest rates of liver cancer, followed by American Indians/Alaska Natives and Hispanics/Latinos, African Americans, and whites.
- Heavy alcohol use
- Family history of liver cancer
- Tobacco use
- Obesity or poor diet
• Diabetes
• Use of anabolic steroids or male hormones
• Certain inherited diseases, such as hemochromatosis (excess iron storage)
• Ingestion of arsenic, such as in drinking water
• Exposure to certain industrial chemicals
• Aflatoxins, a poison produced by a fungus sometimes found on peanuts, corn, grains and nuts.

   In the U.S., most commercially available grains and nuts are safe.

Signs and Symptoms

One of the reasons that liver cancer is particularly life-threatening is because signs and symptoms often do not appear until it is in its later stages. Symptoms of liver cancer include:

• Pain or discomfort in the upper right side of the abdomen
• Lump on right side or heavy feeling in abdomen
• Pain in the back or right shoulder
• Appetite loss or feeling extremely full after a small meal
• Unexplained weight loss
• Bloated or swollen belly
• Unexplained fatigue or weakness
• Itching
• Fever
• Bruising, bleeding
• Nausea or vomiting
• Jaundice (yellow skin and eyes)
• Dark tea-colored urine
• Pale, clay-colored stools
• Tremors, confusion, disorientation
• Enlarged veins on the belly that can be seen through the skin
• Abnormal bruising or bleeding.
• Breast enlargement (gynecomastia) and/or shrinkage of the testicles in men
• Low blood sugar levels (hypoglycemia), which can cause fatigue or fainting

Screening

Liver cancer screening with ultrasound exams every six months is recommended for hepatitis C-positive people who have advanced liver damage (stage III fibrosis or stage IV cirrhosis). Ultrasound is a painless procedure that uses sound waves to take pictures of the liver.

Prevention

Everything that prevents hepatitis or cirrhosis reduces liver cancer risk. Drinking caffeinated coffee reduces risk of developing cirrhosis, and thus HCC. Hepatitis A and B immunization is advised for those with hepatitis B or C. Treating hepatitis C may reduce HCC risk, particularly if treated prior to the development of cirrhosis. Other ways to reduce HCC risk:

• Abstain from alcohol
• Maintain a normal weight
• Quit smoking
• Avoid anabolic steroid use

Assessing Liver Cancer

Once diagnosed, HCC is evaluated to determine how advanced it is. This is called staging. Treatment is based on staging information.

First, the tumor is measured. Is there more than one tumor, and if so, how many? Is the tumor contained or has it spread? Has it invaded nearby blood vessels, lymph nodes or other parts of the body?

Liver cancer that has spread to other body parts is said to have metastasized. For instance, if liver cancer cells are found in the lungs, this is due to metastasis. Tests are done to determine if HCC has spread. These may include chest X-ray, CT scan, PET scan, MRI, ultrasound, and a bone scan.

For adults, the stages of primary liver cancer are:

• Stage I There is only one tumor, and it has not spread to any nearby blood vessels or sites.
• Stage II There is only one tumor that has invaded nearby blood vessels or there is more than one tumor, each less than 2 inches (5 centimeters) in size.
• Stage III There are several tumors and at least one of them is larger than 2 inches (5 cm) in size, or the tumor has invaded certain surrounding areas or nearby lymph nodes.

• Stage IV The cancer has metastasized to other parts of the body.

Treating Liver Cancer

There are a number of treatment options, including ablation, chemotherapy, embolization, immunotherapy, liver transplantation, radiation, surgery, and targeted therapy.

Ablation is a general term meaning to remove or destroy tissue. There are various types of ablations. The most common ablation for HCC is radiofrequency ablation (RFA). This is done for small tumors when surgery or transplantation is not feasible. A probe is inserted into the tumor and cancer cells are heated and destroyed using radio waves. Another type of ablation is percutaneous ethanol injection. Alcohol is injected directly into the liver cancer cells, usually in an outpatient setting.

Chemotherapy is not usually effective against HCC, although this may be used in conjunction with other forms of treatment. A variety of drugs may be used and the side effects depend on which drugs are given.

Embolization is a procedure that injects substances to try to block or reduce the blood flow to cancer cells in the liver. Various substances are used to deliberately block the flow of blood to the tumor, causing it to die. Chemoembolization is the most commonly used embolization technique for HCC. Chemotherapy is injected directly into the tumor. Radioembolization involves the insertion of high-dose radiation through the artery. Immunotherapy uses the body's immune system to fight cancer. Opdivo (nivolumab) is an immunotherapy that was FDA-approved on September 22, 2017 for the treatment of HCC for people who were previously treated with Nexavar (sorafenib). In November 2018, the FDA approved a second drug for people with HCC who were previously treated with Nexavar, the checkpoint inhibitor Keytruda (pembrolizumab).

Liver transplantation potentially cures HCC, as the entire organ is removed rather than just the tumor. This is a better option for patients with cirrhosis, as transplantation gives them an organ that is both tumor- and cirrhosis-free.

Radiation is sometimes used to shrink the tumor and help relieve cancer pain. It may also be
used in conjunction with another form of treatment.

Surgical resection (removal of the tumor) is performed if the tumor is small and hasn’t spread into the blood vessels.

Targeted therapy specifically targets cancer cells, and interferes with cell growth. The oral drug **Nexavar** (sorafenib) was the first targeted therapy approved for HCC. In April 2017, the FDA approved **Stivarga** (regorafenib) for people previously treated with Nexavar. On August 16, 2018, the FDA approved the multikinase inhibitor **Lenvima (lenvatinib)** as a first-line treatment for people with HCC that cannot be surgically removed. On January 14, 2019, the FDA approved the multikinase inhibitor **Cabometyx (cabozantinib)** for people with previously treated HCC. On May 10, 2019, the Food and Drug Administration (FDA) approved the VEGFR2 inhibitor **Cyramza (ramucirumab)** for people with HCC who have a high alpha-fetoprotein level and who were previously treated with Nexavar.

In November 2018, the FDA approved **Vitrakvi** (larotrectinib), the first drug developed to treat cancer with a specific genetic feature rather than the tumor’s location in the body. Vitrakvi is a different type of site-agnostic therapy that works against rare mutations anywhere in the body. Although not likely to be used specifically for HCC, the approval of Vitraki opens the door wider to medicine’s approach to treating cancer.


Last Reviewed: May 22, 2019