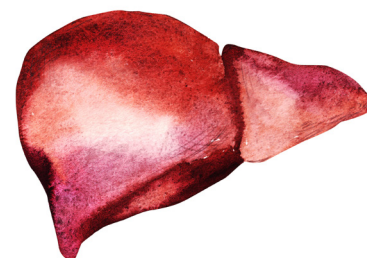


ABOUT LIVER CANCER

Liver cancer is cancer that begins in the cells of the liver. The liver is the largest organ in the human body, after the skin. It is football-sized and sits in the upper right part of the abdomen, beneath the diaphragm and above the stomach. The liver is very busy and has more than 500 jobs such as:

- Processing and storing nutrients
- Removing waste from blood
- Filtering and detoxifying chemicals
- Producing bile to aid with digestion
- Producing albumin, which helps maintain the blood's volume
- Producing coagulation factors that prevent bleeding
- and many other tasks



"The liver is the hidden gem of the body."

Lewis R. Roberts M.B., Ch.B., Ph.D.
Professor of Medicine,
Division of Gastroenterology &
Hepatology at Mayo Clinic

PRIMARY LIVER CANCER

Primary liver cancer is cancer that begins in the cells of the liver. This is different from metastatic, or secondary, cancer that starts in another part of the body and spreads to the liver. The following table provides an overview of the types of primary liver cancer.

Type of Primary Liver Cancer	What to Know	How Common	Most Impacted
Hepatocellular Carcinoma (HCC)	<ul style="list-style-type: none"> • Begins in the hepatocyte cells of the liver 	<ul style="list-style-type: none"> • 75-85% of primary liver cancer cases are HCC 	<ul style="list-style-type: none"> • Men over 60 • People living with a chronic liver disease
Fibrolamellar Hepatocellular Carcinoma (fHCC)	<ul style="list-style-type: none"> • Rare subtype of HCC 	<ul style="list-style-type: none"> • Very rare cancer, representing less than 1% of all HCC cases 	<ul style="list-style-type: none"> • Women under 35
Cholangiocarcinoma (CCA)	<ul style="list-style-type: none"> • Begins in the bile ducts • Intrahepatic CCA begins in the bile ducts inside the liver • Extrahepatic CCA begins in the bile ducts outside the liver 	<ul style="list-style-type: none"> • Represents 10-25% of all primary liver cancer cases 	<ul style="list-style-type: none"> • Men over 60 • People living with a liver fluke infection
Hepatoblastoma	<ul style="list-style-type: none"> • An uncommon childhood cancer 	<ul style="list-style-type: none"> • Very rare 	<ul style="list-style-type: none"> • Children under the age of 4

GLOBAL BURDEN OF LIVER CANCER

Liver cancer is a global problem and in 2020, it was the sixth most common cancer in the world and the third leading cause of cancer death worldwide. According to the World Health Organization, there were more than 900,000 cases of liver cancers and 830,000 deaths from liver cancers in 2020.

LIVER CANCER IN THE UNITED STATES

Liver cancer is a growing problem in the United States, and the percentage of Americans who develop liver cancer has been rising for several decades. The American Cancer Society estimates that more than 42,000 Americans will hear the words “you have liver cancer” in 2021, and more than 30,000 people will die from liver cancer in 2021.

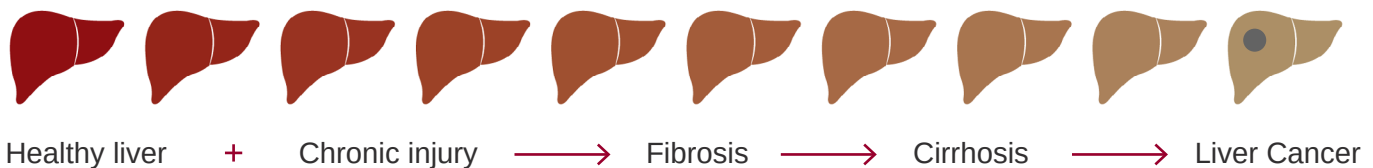
RISK, SCREENING, RISK REDUCTION, AND SYMPTOMS

Certain risk factors increase a person’s chance of developing liver cancer.

Having a risk factor, or even several risk factors, does not mean that a person will develop the disease, and some people who have no risk factors may develop liver cancer. However, having more than one risk factor does increase the likelihood of a person’s developing liver cancer and most people diagnosed with hepatocellular carcinoma are living with a chronic liver disease.

Fortunately, when diagnosed at an early stage, cancers of the liver can be treated effectively.

The liver has an exceptional capacity to repair itself when injured or damaged. While this regenerative capacity usually lasts a lifetime, where there is ongoing, also called chronic, injury for an extended period of time, the liver exhausts its capacity to repair itself. Once the liver reaches this state of repair exhaustion, further damage results in the replacement of the liver hepatocytes with scar tissue, also called fibrosis, rather than normal functioning liver cells.



Fibrosis makes it harder for the liver to perform its normal functions. When the scar tissue eventually replaces large portions of the liver, it is described as cirrhosis of the liver. Cirrhosis is a potentially life-threatening condition.

Some risk factors, like smoking, can be changed while others, like birth gender and increasing age, cannot. Many risk factors are similar for hepatocellular carcinoma and intrahepatic cholangiocarcinoma, such as:

- Cirrhosis
- Viral hepatitis
- Tobacco
- Alcohol

Extrahepatic cholangiocarcinoma tends to have different risk factors. Visit globalliver.org to learn more about unique risk factors for each type of liver cancer.

If you are at risk for liver cancer, talk with your doctor and make an appropriate plan for screening and reduce your risk whenever possible.



SCREENING

Screening for a condition is done to find the disease early in people at risk. When diagnosed at an early stage, cancers of the liver can be effectively treated. The American Association for the Study of Liver Diseases (AASLD) recommends surveillance for liver cancer in adults with cirrhosis using screening tests every six months with ultrasound with or without the alpha-fetoprotein blood test. Persons with chronic hepatitis B without cirrhosis are also recommended to have liver cancer surveillance, generally above the age of 40 years.

“Liver cancer screening is not recommended for the general population because it has not been proven to reduce the risk of dying of liver cancer. However, people with chronic liver conditions are at increased risk of liver cancer and may consider screening, such as people who have:

- Hepatitis B infection
- Hepatitis C infection
- Nonalcoholic steatohepatitis
- Alcoholic cirrhosis
- Liver cirrhosis from any other cause”

Lewis R. Roberts M.B., Ch.B., Ph.D.
Professor of Medicine,
Division of Gastroenterology & Hepatology at Mayo Clinic

SYMPTOMS

There are few, if any, signs and symptoms of early stage liver cancer. This is partly because there are no pain fibers in the substance of the liver, only in the lining or capsule surrounding the liver. Therefore, a liver cancer can grow to a large size and only cause pain when it begins to stretch the liver capsule.

As liver cancer grows in the body, common symptoms include:

- Pain in the upper part of the belly
- A lump or heaviness in the belly
- Abdominal bloating
- Loss of appetite
- A feeling of fullness after eating a small meal
- Weakness and fatigue
- Nausea and vomiting
- Jaundice (yellowing of the skin) and
- Fever

RISK REDUCTION AND CANCER PREVENTION

The American Cancer Society estimates that up to 70 percent of liver cancer cases, particularly hepatocellular carcinoma, can be prevented with certain lifestyle changes. These can include:

- Hepatitis B vaccine, which is recommended for all infants at birth and adults at increased risk
- Treatment of viral hepatitis – hepatitis C virus can be cured, and hepatitis B virus can be successfully treated and managed
- Avoid excessive alcohol consumption
- Maintain a healthy weight and if you have nonalcoholic fatty liver disease (NAFLD) or nonalcoholic steatohepatitis (NASH), try to implement lifestyle changes
- Don't smoke
- Drink coffee – There is increasing evidence that drinking at least two cups of coffee a day reduces the progression of liver disease and the risk of liver cancer.

When liver cancer is suspected, several different types of tests can be used to gather more information, including blood tests, imaging tests and possibly a liver biopsy. If cancer is diagnosed, additional tests will be done to determine if the cancer has spread from beyond the liver.

This additional information helps the healthcare team make recommendations for appropriate treatment.

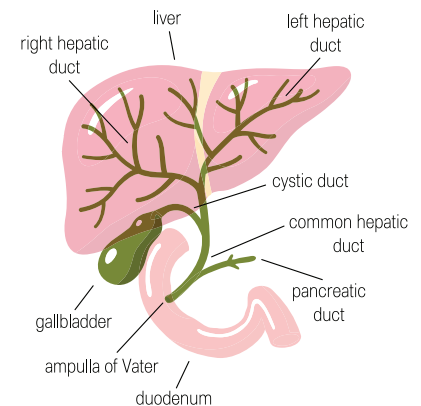
CHOLANGIOCARCINOMA

This more rare type of liver cancer develops in the bile ducts. There are bile ducts inside the liver and when cancer develops in these, it is called intrahepatic cholangiocarcinoma. When bile ducts outside of the liver develop cancer, this is called extrahepatic cholangiocarcinoma.

Extrahepatic cholangiocarcinomas are sometimes divided into peri-hilar or hilar cholangiocarcinomas, which are in the bile ducts close to the liver, and distal cholangiocarcinomas, which are in the section of the bile ducts closer to where the bile ducts drain into the small intestine.

Once a diagnosis of cholangiocarcinoma has been made, additional tests will be done to determine if the cancer has spread and if so, how far. This process, called staging, helps the treatment team understand how much cancer is in the body and helps to inform discussions about treatment options.

The most commonly used system is the TNM system from the American Joint Committee on Cancer (AJCC). TNM stands for Tumor Node Metastasis, and the system classifies cancer stage and defines the extent of the cancer including size, location and number of tumors. TNM Stages are I, II, III, IV.



BILE DUCT ANATOMY

CHOLANGIOCARCINOMA TREATMENT

Treatment for cholangiocarcinoma will depend upon several factors, including the stage of disease. Treatment may include:

- Surgery
- Radiation
- Chemotherapy
- Targeted therapy
- Immunotherapy
- Supportive (palliative) care

For more information about treatment options for cholangiocarcinoma, visit globalliver.org/livercancer

HEPATOCELLULAR CARCINOMA

This more common type of liver cancer begins in the hepatocytes. Most HCC, more than 90 percent, occurs in people with a chronic liver disease such as cirrhosis, viral hepatitis, alcohol-related liver disease, or nonalcoholic steatohepatitis.

When liver cancer is suspected, several different types of tests can be used to gather more information, including blood tests, imaging tests and a liver biopsy. If cancer is diagnosed, additional tests will be done to determine if the cancer has spread from beyond the liver.

This additional information that describes a stage helps the healthcare team make recommendations for appropriate treatment based on where the disease is located and if it has spread. This process is called staging. There are two commonly used staging systems for HCC in the U.S.: the TNM system from the American Joint Committee on Cancer (AJCC) and the Barcelona Clinic Liver Cancer (BCLC) system.

- TNM Stages are I, II, III, IV
- BCLC Stages are O, A, B, C, D

Both systems are evidence-based and may be used to guide HCC management and care. Treatment is recommended based on the location of the cancer in the liver. Each liver cancer is different, and it is important to work with a multidisciplinary team to create a treatment plan that is unique to each individual's needs.

HEPATOCELLULAR CARCINOMA TREATMENT

Treatment for hepatocellular carcinoma will depend upon several factors, including the stage of disease and the health of the liver. There are multiple treatment options available including:

- Surgery, including liver transplantation
- Ablation
- Embolization
- Radiation
- Targeted drug therapy including:
 - Kinase inhibitors
 - Monoclonal antibodies
 - Immunotherapy
- Supportive (palliative) care

For more information about treatment options for HCC, visit globalliver.org/livercancer

CLINICAL TRIALS

Clinical trials are research studies that involve people. Through clinical trials, new treatments and ways to improve liver cancer care are moved forward. Clinical trials also determine if treatments are safe and effective in the treatment of liver cancer.

Clinical trials evaluate:

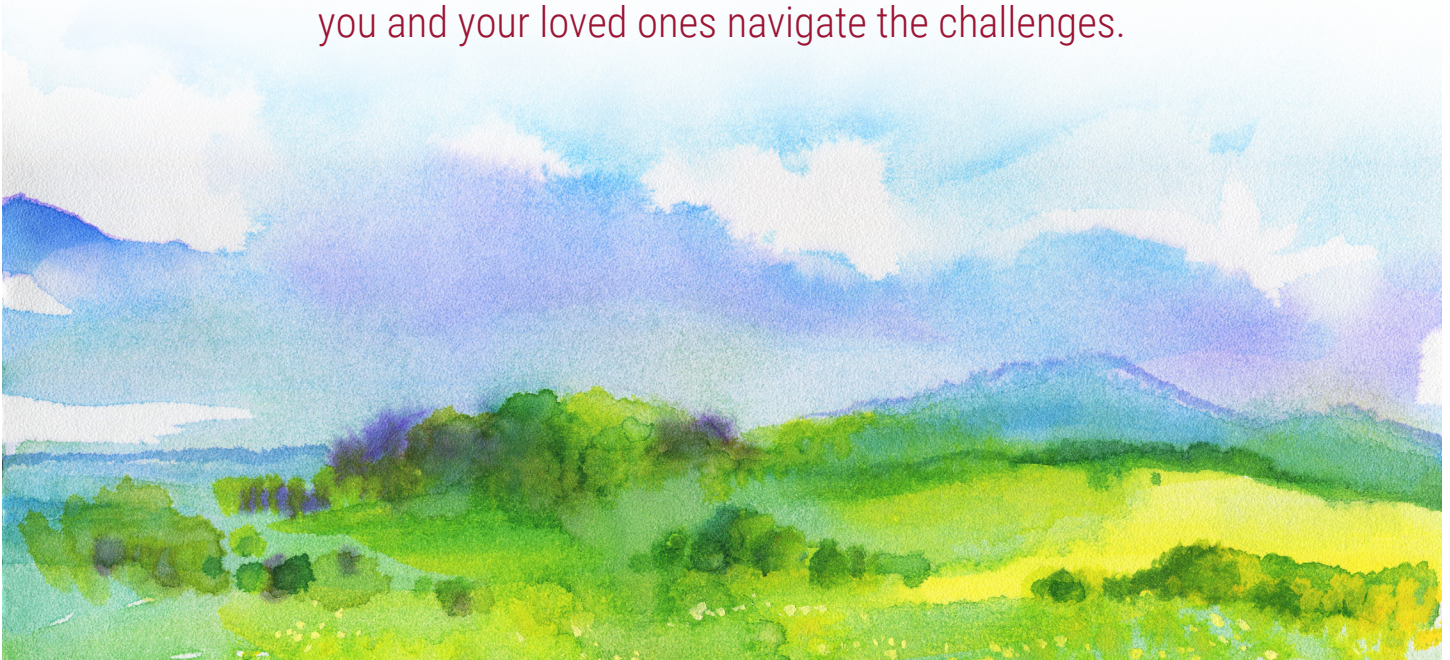
- New diagnostic methods
- New drugs and medicines
- New combinations of treatments
- New approaches to surgery or radiation

Clinical trials are highly controlled and regulated. They can be sponsored by the federal government, medical institutions, pharmaceutical companies, and private foundations. Talk to your provider to learn more about trials that could be right for you and visit ClinicalTrials.gov, a database of privately and publicly funded clinical studies conducted around the world.

SURVIVORSHIP IN LIVER CANCER

Once treatment is completed, ask about a treatment summary as a way to record the exact diagnosis, anti-cancer treatments and other procedures and tests that were a part of the liver cancer journey. This can become a helpful tool for any doctors who provide care in the future.

Your journey is uniquely yours, and liver cancer can be a difficult disease to treat. Consider seeking support to help you and your loved ones navigate the challenges.



RESOURCES

Global Liver Institute www.globalliver.org

National Cancer Institute www.cancer.gov

American Cancer Society www.cancer.org

Cholangiocarcinoma Foundation www.cholangiocarcinoma.org

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Global Liver Institute provides this information as a service. It is not intended to take the place of medical professionals or the recommendations of your healthcare team. We strongly suggest consulting your healthcare team if you have questions about your specific care.

