CONDITION

Cholangiocarcinoma

Learn about cholangiocarcinoma, a cancer of the bile ducts, including symptoms, risk factors, diagnosis, treatment options, complications, and follow-up care.

WHAT IT IS
Cancer beginning in the bile ducts

BODY SYSTEM
Digestive

MAIN SYMPTOMS
Jaundice, itching, upper right abdominal pain, unintended weight loss

WHAT CAUSES IT
Usually unknown DNA changes

HOW IT IS DIAGNOSED
Biopsy with microscopic examination

MAIN TREATMENT
Surgery or systemic therapy

CAN IT BE CURED?
Sometimes - surgery may cure localized disease

IS IT AN EMERGENCY?
Sometimes - fever or chills with jaundice

LONG-TERM OUTLOOK
Variable from surgical cure to growth or spread

Overview

Cholangiocarcinoma is cancer that begins in the bile ducts. These thin tubes carry bile, a digestive fluid made by the liver, to the small intestine. Cholangiocarcinoma is also called bile duct cancer.

Doctors group cholangiocarcinoma by where it starts:

The location matters because it affects symptoms, surgery, and other treatment options. Intrahepatic tumors may behave more like other liver tumors, while perihilar and distal tumors often block bile flow.

Cholangiocarcinoma can grow into nearby liver tissue, blood vessels, lymph nodes, or other organs. It can also spread to distant areas. Some tumors are found while they can still be

removed with surgery, but others are discovered after they have grown around important structures or spread.

Treatment has changed in recent years. Surgery remains the main treatment that may cure localized disease. Drug treatment, radiation, procedures to improve bile flow, and tumor testing can also play important roles. Care is often coordinated by a team experienced in liver and bile duct cancers.

- Intrahepatic cholangiocarcinoma begins in bile ducts inside the liver.
- Perihilar cholangiocarcinoma begins where the right and left bile ducts join as they leave the liver. It is sometimes called a Klatskin tumor.
- Distal cholangiocarcinoma begins farther down the main bile duct, near the pancreas and small intestine.

Symptoms

Early cholangiocarcinoma may not cause noticeable symptoms. Intrahepatic tumors can sometimes become fairly large before causing problems. Tumors in the larger bile ducts are more likely to cause symptoms when they block bile flow.

Possible symptoms include:

These symptoms are not specific to cancer. Gallstones, hepatitis, infections, and other liver or bile duct conditions can cause similar problems. A medical evaluation is needed to determine the cause.

Blocked bile ducts can become infected. Fever or chills together with jaundice or worsening upper abdominal pain require urgent, same-day medical attention. Confusion, fainting, severe weakness, trouble breathing, or signs of shock are reasons to seek emergency care.

- Yellow skin or eyes, called jaundice
- Dark urine and pale, gray, or clay-colored stools
- Itching, sometimes severe
- Pain or pressure in the upper right abdomen
- Loss of appetite or feeling full quickly
- Unintended weight loss
- Nausea, tiredness, or weakness
- Fever or chills

- A swollen abdomen

Causes and risk factors

Cholangiocarcinoma develops when bile duct cells acquire changes in their DNA. These changes allow cells to grow when they should not and may eventually form a tumor. In most people, it is not possible to identify one specific cause.

Certain conditions that produce long-term inflammation or abnormal bile flow can raise the risk. Important risk factors include:

Inflammatory bowel disease is associated with cholangiocarcinoma mainly because some people with inflammatory bowel disease also have primary sclerosing cholangitis.

A small number of cases may be connected to an inherited cancer syndrome or inherited gene change. Most cholangiocarcinomas, however, are not directly inherited. Genetic counseling may be considered when personal or family history suggests an inherited risk.

Having a risk factor does not mean that a person will develop this cancer. Many people diagnosed with cholangiocarcinoma have no recognized risk factor. There is no routine screening test recommended for people at average risk. People with primary sclerosing cholangitis or another high-risk condition should discuss individualized monitoring with their specialist.

- Primary sclerosing cholangitis , a disease that causes inflammation and scarring of the bile ducts
- Bile duct cysts, including choledochal cysts
- Stones within the liver's bile ducts, called hepatolithiasis
- Chronic infection with certain liver flukes, especially in parts of Southeast Asia
- Cirrhosis, which is severe scarring of the liver
- Chronic hepatitis B or hepatitis C infection
- Some developmental abnormalities where the bile ducts join the pancreatic duct
- Older age

Diagnosis

The evaluation usually begins with a medical history, physical examination, and blood tests. Blood tests may look for abnormal bilirubin and liver enzyme levels. These results can show

that bile flow is blocked, but they cannot confirm cancer.

CA 19-9 and CEA are substances that may be measured in the blood as tumor markers. A high level can support the evaluation, but it does not prove that cancer is present. Bile duct infections and blockages can also raise CA 19-9, and some people do not produce this marker.

Imaging helps identify the tumor and determine whether it has spread. Testing may include ultrasound, a computed tomography scan, or CT, and magnetic resonance imaging with magnetic resonance cholangiopancreatography, known as MRI/MRCP. These tests show the liver, bile ducts, blood vessels, lymph nodes, and nearby organs. Chest imaging may also be performed.

An endoscopic procedure may be needed for tumors outside the liver. During endoscopic retrograde cholangiopancreatography, or ERCP , a flexible tube is passed through the mouth into the small intestine. Dye is placed into the bile ducts so they can be viewed. The doctor may collect cells, take small tissue samples, or place a stent to keep a blocked duct open.

Endoscopic ultrasound uses an ultrasound probe on the tip of an endoscope. It can help examine nearby lymph nodes and guide a biopsy. In some cases, bile duct drainage or tissue sampling is performed through the skin.

A biopsy removes cells or tissue for examination under a microscope. Biopsy is often needed before drug treatment. However, the biopsy approach must be planned carefully for a potentially removable perihilar tumor. Passing a needle through the tumor can affect eligibility for certain liver transplant protocols. Evaluation at an experienced center before biopsy may therefore be important.

If cancer is confirmed, doctors determine its stage , meaning how far it has grown or spread. They also assess whether it is resectable , or removable with surgery. Staging may involve additional scans, laparoscopy, or evaluation during surgery.

For advanced disease, tumor tissue or blood may be tested for molecular changes. Findings involving genes or proteins such as FGFR2, IDH1, HER2, BRAF, NTRK, or mismatch repair may help identify targeted treatment or immunotherapy options.

Treatment and management

Treatment depends on the tumor's location, stage, molecular features, and whether it can be removed safely. Liver function, other health conditions, and the person's goals also matter. Because treatment can be complex, review by a multidisciplinary team is valuable.

Surgery offers the main chance for cure when the cancer is localized and removable. The operation varies by location. Intrahepatic disease may require removal of part of the liver.

Perihilar disease may require removal of the affected bile ducts, nearby lymph nodes, and part of the liver. Distal disease may be treated with a pancreaticoduodenectomy, also called a Whipple procedure, which removes parts of the pancreas, bile duct, and small intestine.

Surgery is major treatment and requires careful assessment of liver health and blood vessel involvement. The surgeon aims to remove the cancer with a border of normal tissue, called a negative margin. Chemotherapy may be recommended after recovery from surgery to lower the risk of recurrence. Capecitabine is one option commonly considered after complete removal.

For a small, carefully selected group with early perihilar cholangiocarcinoma that cannot be removed in the usual way, treatment with chemotherapy and radiation followed by liver transplantation may be possible under a specialized protocol. Transplantation is not appropriate for most cases and requires evaluation at an experienced transplant center.

When surgery is not possible, systemic therapy treats cancer throughout the body. Initial treatment commonly combines gemcitabine and cisplatin with an immune checkpoint inhibitor such as durvalumab or pembrolizumab. The best approach depends on health, organ function, previous treatment, and local approvals.

If the cancer grows after initial treatment, other chemotherapy may be considered. Molecular testing can be especially important at this stage. Targeted medicines may be available for tumors with certain FGFR2 fusions, IDH1 mutations, HER2 changes, BRAF V600E mutations, NTRK fusions, or other actionable findings. Immunotherapy may also be considered for tumors with particular features, such as mismatch repair deficiency or high microsatellite instability.

Radiation therapy may be used to control a tumor in a specific area, ease symptoms, or support a treatment plan before transplantation. Some liver-focused treatments, such as ablation or radiation delivered through the liver's blood vessels, may be considered for selected intrahepatic tumors.

Supportive care is part of treatment at every stage. A blocked bile duct may be opened with a stent or drainage catheter. Itching, pain, nausea, poor appetite, and nutrition problems can also be treated. Palliative care specialists can help manage symptoms and support decision-making while a person continues cancer treatment.

Clinical trials may provide access to new drug combinations, targeted therapies, or local treatments. Trial suitability depends on the cancer's location, stage, previous treatment, and molecular results.

Complications

Cholangiocarcinoma can block bile drainage and cause jaundice, itching, and difficulty absorbing fats and fat-soluble vitamins. A blockage may also lead to cholangitis , an infection within the bile ducts. This can become serious if it is not treated promptly.

Other possible complications include:

Treatment teams monitor for these problems and may adjust therapy, replace a stent, treat an infection, or provide rehabilitation and nutrition support.

- Reduced liver function or liver failure
- Repeated infections or blocked stents
- Bleeding or blood clots
- Fluid buildup in the abdomen
- Weight loss, muscle loss, and poor nutrition
- Pain from local growth or spread
- Spread to lymph nodes, lungs, bones, the abdominal lining, or other organs
- Side effects from surgery, chemotherapy, immunotherapy, targeted therapy, or radiation

Follow up

After surgery, regular follow-up looks for recurrence and addresses the effects of treatment. Visits may include a symptom review, physical examination, blood tests, and imaging. The timing depends on the original tumor, treatment received, and the care center's plan.

People receiving active therapy usually need more frequent visits. Blood counts and kidney and liver function may be checked before treatment. Scans are used at intervals to see whether the cancer is shrinking, stable, or growing. New symptoms should be reported rather than saved for the next scheduled scan.

Routine follow-up is appropriate for questions about ongoing fatigue, appetite, mild digestive changes, medication side effects, or emotional concerns. Contact the cancer team promptly for new jaundice, worsening itching, persistent vomiting, increasing abdominal swelling, uncontrolled pain, or inability to eat or drink.

Fever or chills with jaundice or upper abdominal pain may indicate an infected bile duct and needs urgent assessment. Emergency care is appropriate for confusion, fainting, severe breathing difficulty, uncontrolled bleeding, or sudden severe illness.

Sources