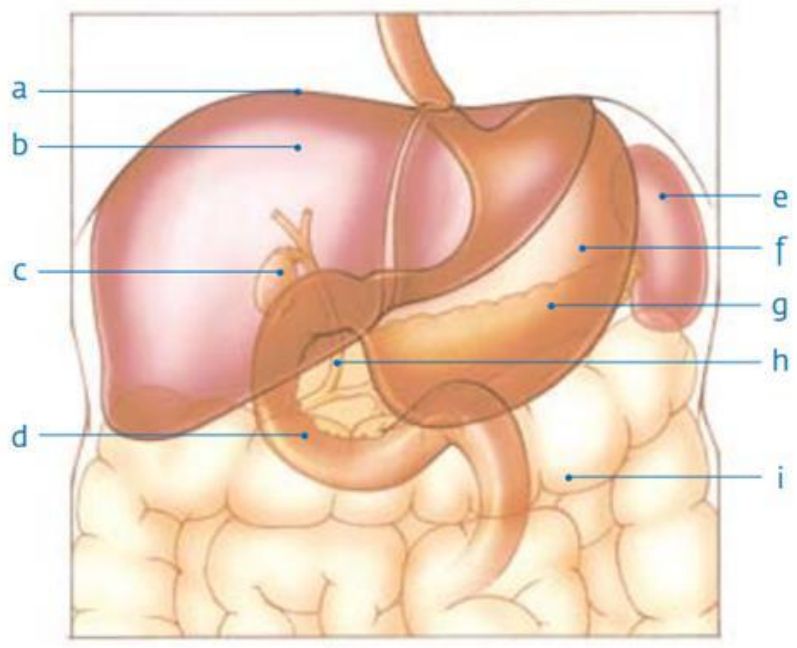
EURACAN Biliary tract domain (G5.2)

Bile duct and gall bladder cancer

Cancer can develop in the bile ducts as well as in the gallbladder. In Europe, bile duct and gall bladder cancer is a rare tumor. Both forms are unfortunately difficult to treat.

1. GALL BLADDER AND BILE DUCTS

Before the functioning of the gallbladder and bile ducts is discussed, it is necessary to understand the function of the liver. The liver ensures that important nutrients from the blood are absorbed and used. In addition, the liver clears toxins and cleans waste materials. One of the substances that the liver produces is bile. Most bile is transported directly to the duodenum via the bile ducts. A small supply of bile is collected in the gallbladder. The liver consists of a left and a right lobe, which in turn are divided into different segments. Each liver segment has its own blood supply and biliary tract. The small bile ducts that provide the segments end up in the large bile ducts. Eventually all bile ducts of the right and the left liver lobe in the right and the left bile duct. Where the left and the right bile duct come together (ductus hepaticus), the large bile duct that carries the bile to the duodenum begins. Via the bile ducts a small part of the bile enters the gall bladder, where the liquid can be stored for extra supply. Most bile goes directly to the intestine. Bile is needed to digest the fat in the food. When eating fat leaves the stomach, bile is delivered to the small intestine via the bile duct. The gallbladder is located in the upper right side of the abdominal cavity, against the bottom of the liver.



(A) diaphragm (B) liver (C) gall bladder (D) duodenum (E) spleen (F) stomach (G) pancreas (H) large bile duct (I) colon © 2013 KWF Kankerbestrijding

2. BILIARY CANCER CAN OCCUR IN FOUR PLACES

• Peripheral (intrahepatic) biliary cancer: the tumor develops in the smaller bile ducts and slowly grows towards the large bile ducts of the liver.

• Klatskin tumor (perihilar): this tumor develops at the location where the left and the right bile duct come together. This is the most common form of biliary tract cancer (60-70%).

• Mid or distal biliary cancer: the tumor is located in the middle or in the last part of the large bile duct. In cancer, malignant cells can grow through other body tissues and the cancer can spread through the body via blood and lymph vessels. Metastasis of biliary tract cancer or gall bladder cancer is usually to the liver or abdominal cavity.

• Gallbladder: the tumor develops in the gallbladder and is often found during a routine operation of the gallbladder due to suspected gallbladder inflammation

3. RISK FACTORS

The causes of bile duct and gall bladder cancer are actually unknown. There are indications, however, that people with gallstones or chronic gallbladder inflammation have a slightly higher risk of developing a gallbladder tumor. An infection or cysts in the bile duct can also play a role. The vast majority of patients with biliary or biliary trauma are older than 60 years. Gallbladder cancer is slightly more common in women than in men. In biliary cancer this distribution is the same.

4. COMPLAINTS

Complaints of biliary tract or gallbladder cancer often only arise when the tumor has developed into surrounding organs. A bile duct tumor often prevents the discharge of bile. This causes jaundice. Many waste products cannot be transported through the liver and fats are badly digested. Furthermore, gall, which normally turns the stool brown, accumulates in the liver. Eventually the gall is absorbed into the blood and causes a yellowish skin, yellow eye-white and itching all over the body. The gall can also end up in the urine. The complaints that arise:

• Yellow skin and eye white;
• Pain in the upper abdomen;
• Fever and chills;
• Fatigue and lethargy;
• Decreased appetite;
• Weight loss;
• itching all over the body;
• Light colored stools;
• Dark colored urine.

5. DIAGNOSIS IN BILIARY TRACT AND GALLBLADDER CANCER

In order to be able to make the correct diagnosis, investigations must be carried out. The following examinations can take place; blood tests, ultrasound, CT scan, MRI scan, endoscopy (ERCP) and spot surgery (laparoscopy).
In the event of a suspicion of bile duct cancer or gall bladder cancer, your doctor or general practitioner refers you to a specialist. This can be a surgeon, an internist or an gastroenterologist doctor. In order to be able to make the correct diagnosis, investigations must be carried out. The following studies can take place:

- Blood test
- Ultrasound
- CT-scan
- MRI scan
- Endoscopy (ERCP)
- Surgery (laparoscopy)

Not all studies need to apply to you. Your doctor will determine which examinations are needed to diagnose biliary tract cancer or gallbladder cancer and to determine at what stage the disease is. This is necessary to determine which treatment is most suitable for you.

Blood test
In case of a suspicion of gall bladder cancer or biliary cancer, a blood test is often performed. Hepatic function can be determined on the basis of values in your blood. An early stage of jaundice can be detected in the blood. Furthermore, general research is usually done to determine functions of other organs such as the kidneys and blood clotting.

Ultrasound
To be able to diagnose biliary cancer or gall bladder cancer, an ultrasound is often made. To determine the exact expansion of the tumor, ultrasound is usually not sufficient.
An ultrasound is a study in which organs and tissue can be made visible by means of sound waves. The waves are not audible, but the reflection (echo) of them can determine where organs and tissue are located. An echo is not stressful or painful. During the research you will be on a research table. A gel is applied to your skin. Then a device that emits sound waves is moved over your body. This device also measures the echo (return) of these sound waves. The tumor and any metastases can thus be visualized.

CT-scan
The CT scan is one of the most important studies in gallbladder and biliary tract cancer because the expansion to surrounding organs such as the blood vessels of the liver can be visualized. It can also be determined whether the tumor has caused metastases to other organs. Furthermore, a CT scan can determine whether sufficient liver tissue remains in the recovery phase after a possible operation. CT stands for computer tomography. By means of X-rays, organs and tissues are depicted in detail with this device. During the investigation, you are lying on a movable table, which is slowly pushed through the device (in the form of a ring). From a large number of angles around your body, an amount of X-rays is emitted and

then the amount of radiation transmitted is measured in small steps. The CT scanner therefore makes a large number of photographs. Of the many cross-sections, the computer ultimately makes a three-dimensional representation. The tumor and the relationship with organs and blood vessels can be examined. Any metastases can also be detected so that the stage of the disease can be determined. To make blood vessels clearly visible, it is often necessary to use a contrast fluid. This shows whether the tumor has grown into surrounding organs, what the relationship is with surrounding blood vessels and whether there are metastases to other parts of the body. The contrast liquid is offered as a drink or via an infusion. The contrast fluid is sometimes experienced as a warm and wheezy feeling, but is not harmful. Some people are allergic to contrast media, which is important for doctors to know. To prevent nausea, it is often advised to stop eating or drinking a few hours before the examination.

MRI scan

For bile duct and gall bladder cancer, an MRI scan has a comparable value to a CT scan. These scans are sometimes both performed to complement each other. An MRI scan is similar in many ways to a CT scan. The big difference, however, is that instead of X-rays, magnetic radiation is used in an MRI. As a result, an MRI is less harmful than a CT scan. The disadvantage of an MRI scan is that the MRI scanner is much larger and makes a lot of noise. An MRI scan is not suitable for people who have metals in their body, this one are attracted by the magnetic radiation. In addition, the MRI is not suitable for people with claustrophobia.

Endoscopy (ERCP)

During an ERCP, an endoscope is examined in the body. The endoscope is a thin, flexible controllable hose with a light and a camera at the end. The endoscope is inserted through the esophagus and the stomach to the beginning of the small intestine. There is the joint exit of the bile ducts and the pancreas. Various operations can be performed via the endoscope. First, the inside of the intestine can be viewed with an endoscope. A contrast fluid can also be injected into the pancreatic drain tube through the endoscope to obtain a clearer image. Furthermore, cells can also be removed by the endoscope, this is done by means of a small brush. The cells can then be examined under the microscope. Finally, it is also possible to place a tube (stent) in the bile ducts with the endoscope, for example if the tumor compresses the bile duct. This way the bile can flow back to the small intestine and the jaundice disappears.

Surgery (laparoscopy)

During a viewing operation, the abdomen is examined to assess whether there are no metastases of the tumor in the abdominal cavity or the liver. The surgery is also called laparoscopy: looking into the abdomen. This research is only carried out when there are doubts about whether the tumor can be operated. During the operation, the surgeon assesses the surface of the liver, the inside of the peritoneum and the vascular structures to the liver. Based on these data, the surgeon determines whether surgery to remove the tumor is possible. If previous studies have shown that the tumor can be operated, this examination will not be carried out and an operation will be planned immediately.
To perform the surgery, a small wound is made under the navel. Via this wound, carbon dioxide is introduced into the abdominal cavity with a thin needle, which causes the abdominal wall to separate from the organs. Then the viewing tube is inserted and

connected to a video camera. This makes the operating area visible on a monitor. To also place surgical instruments in the abdomen, access is also made at other locations. With these instruments, for example, biopsies or punctures can be taken as tissue or cells need to be further examined under the microscope.

6. STAGING

In order to then draw up a treatment plan for biliary cancer or gall bladder cancer, your specialist must first determine the stage of the tumor. This is done on the basis of the location and size of the tumor, the extent of growth in the surrounding tissue and the presence of metastases to lymph nodes and / or organs elsewhere in the body. These factors are important for drawing up a good treatment plan.

7. TREATMENT BILIARY AND GALL BLADDER CANCER

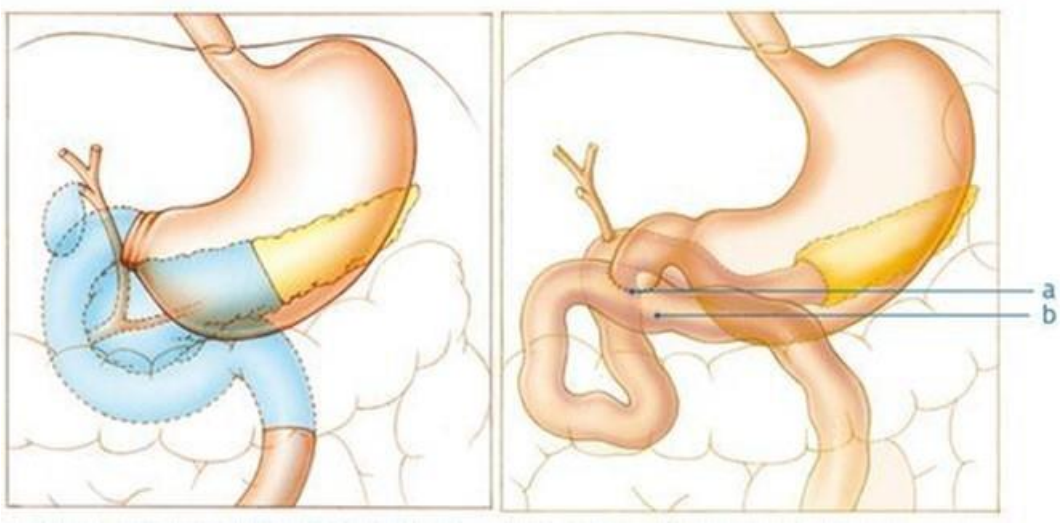
The treatment of gall bladder cancer or biliary cancer can have several goals: first of all, it will be tried to cure the disease, but if that is not feasible, the treatment will focus on reducing symptoms.

Purpose of treatment of gall bladder cancer and biliary cancer
If a treatment has the purpose to heal, it is called a curative treatment. However, treatment for curation does not guarantee cure. Therefore additional treatments are given in addition to the primary treatment, an operation. These are called adjuvant treatments. If, for example, a tumor is removed by surgery, it may be that you will receive chemotherapy afterwards. This additional treatment has the aim to combat any non-observable metastases. Sometimes it can also be useful to give adjuvant treatments just before the operation. This is then called a neo-adjuvant treatment.
If biliary tract cancer or gall bladder cancer cannot be cured anymore, palliative treatment can be started. This type of treatment focuses on inhibiting the growth of the tumor by means of chemotherapy but can also only be intended to reduce or prevent certain complaints.

Treatment options for biliary cancer and gallbladder cancer
When drawing up a treatment plan for biliary tract cancer or gall bladder cancer, several factors are important: the stage of the disorder, the location, size and shape of the tumor and your physical condition. Depending on these factors, there are different treatment options:
•operation
• placing a stent
• chemotherapy
• radiotherapy

<u>Operation</u>
The aim of surgery for biliary cancer or gallbladder cancer is to remove the tumor with adjacent tissue as well as possible. This is only possible if the local tumor is not too extensive and if there are no metastases to other organs.
If the tumor is in the lower part (distal) of the bile duct, during the operation the head of the pancreas, the gall bladder, the duodenum and part of the bile duct will be removed. This

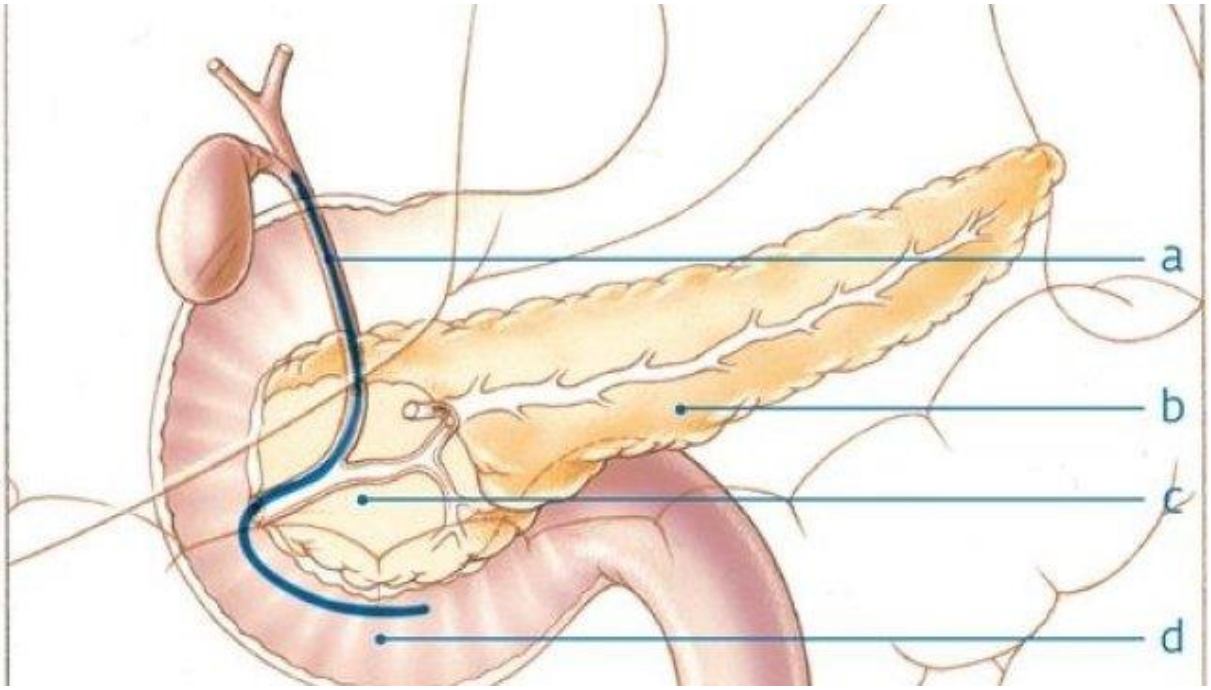
operation is called a Whipple operation, or also called Pylorus Preserving Pancreatico Duodenectomy (PPPD). Lymph nodes are also removed around the bile ducts. Subsequently, all organs are again connected to the intestine so that the digestion juices can get back to the food. This operation is drastic and takes an average of 4 hours. It is therefore important that your condition is good. After the surgery you will stay in hospital for 10 days on average. The duration of this depends mainly on whether you experience complications from the operation.
If the tumor is more towards the liver, the bile duct will be removed together with one of the liver halves. This operation is drastic and takes an average of 8 hours. It is therefore important that your condition is good and the jaundice has disappeared. After the surgery you will stay in the hospital for an average of 14 days. The duration of this depends mainly on whether you are experiencing complications from the operation. The surgeon will inform you about the type of operation and the chance of complications.



The colored parts are removed in a gastric sparing operation. (a) gastric sphincter (b) small intestine. *© 2013 KWF Kankerbestrijding*

Stent placement

Usually it will occur that the tumor compresses the bile ducts. A blockage of the bile discharge can be removed by placing a metal or plastic tube (stent) in the bile duct. This happens during an endoscopy, an ERCP. In the case of gall bladder cancer or biliary cancer, the stent is placed in the bile ducts. As a result, the tube keeps the bile ducts open and the bile can flow back to the small intestine. You do not have to be admitted to hospital for the placement of a stent. The stent may become blocked causing the jaundice to return and / or a high fever. In that case, the stent must be replaced by endoscopy. It is also possible that it is no longer possible to place a stent. In this case, a Percutaneous Transhepatic Cholangiography Drainage (PTCD) will be applied. This is also called a gallow drainage. During this procedure, a tube is laid in the bile ducts through the skin and with the aid of an ultrasound. Gal can still be discharged by means of this tube. The bile is then collected in a bag that is attached to your body. For this treatment you will receive an anesthetic and a scow. The PTCD treatment then takes 30-60 minutes.



(A) stent in the large bile duct (B) pancreas (C) tumor (D) duodenum © 2013 KWF Kankerbestrijding

Chemotherapy

If surgery for biliary tract or gall bladder cancer is not possible, chemotherapy can be considered. Chemotherapy is a treatment that aims to kill cancer cells. In biliary or gall bladder cancer, treatment with chemotherapy is often palliative. This means that the treatment mainly focuses on inhibiting the growth of the tumor, which reduces the symptoms. There are different types of chemotherapy. Chemotherapy can be given as a single agent, but also in combination. Most chemotherapy is administered via an infusion. The frequency of administration depends on the type of chemotherapy. Chemotherapy can also affect healthy cells in addition to cancer cells. This may cause side effects. Common side effects include hair loss, nausea, bowel dysfunction, fatigue and an increased risk of infections. The side effects are different for each chemotherapy and will also differ per person. Your doctor will discuss with you the consequences of chemotherapy.

Radiotherapy

Radiotherapy has a limited role in the treatment of gallbladder and biliary tract cancer. To prevent the spread of cancer cells, three irradiations are given prior to surgery for biliary

cancer. The radiotherapist will inform you extensively about this procedure. During radiotherapy, the tumor is irradiated radioactively from outside. Cancer cells can worse against radiation than healthy cells. Because of the radioactive radiation, the tumor cells become damaged and they break down. Radiotherapy reduces tumor growth and there is a possibility that the tumor becomes smaller. The radiation is focused as much as possible on the tumor. However, it is not possible to prevent healthy cells from being irradiated. This causes you to deal with side effects. In general, radiotherapy often causes fatigue. In addition, the irradiated skin can turn red. This is accompanied by itching and a burning sensation. With radiation in the area of the stomach, patients often have nausea symptoms. Your radiotherapist can prescribe medication for this. You can also suffer from your bowels.

Radiotherapy usually takes place several times a week. There is no need for hospitalization.

Psychosocial help

From the moment you are told that you may have biliary tract or gallbladder cancer, you are faced with great uncertainties. Dealing with this is not self-evident. The period of examinations and treatments are very heavy, but after the treatment you have to learn to live with your new situation. This applies not only to you as a patient, but also to your family, friends and any partner and children. There are organizations that can support you and your environment in learning to live with cancer, both inside and outside the hospital.