

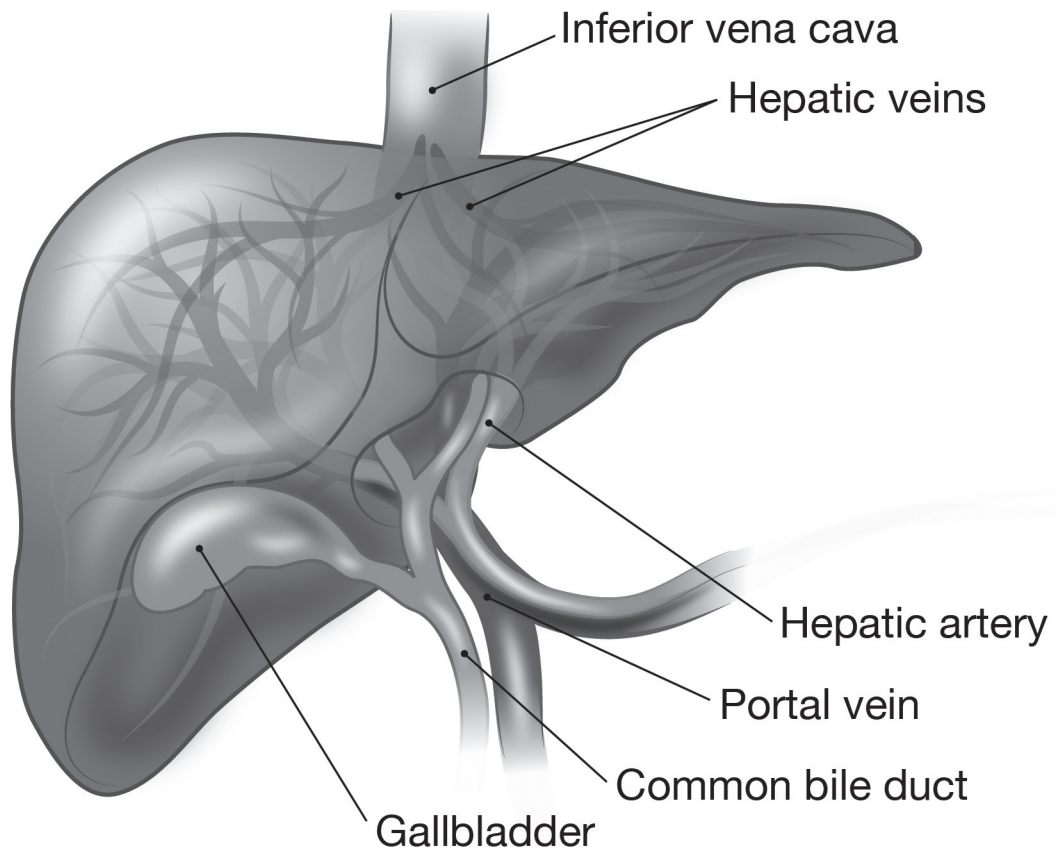
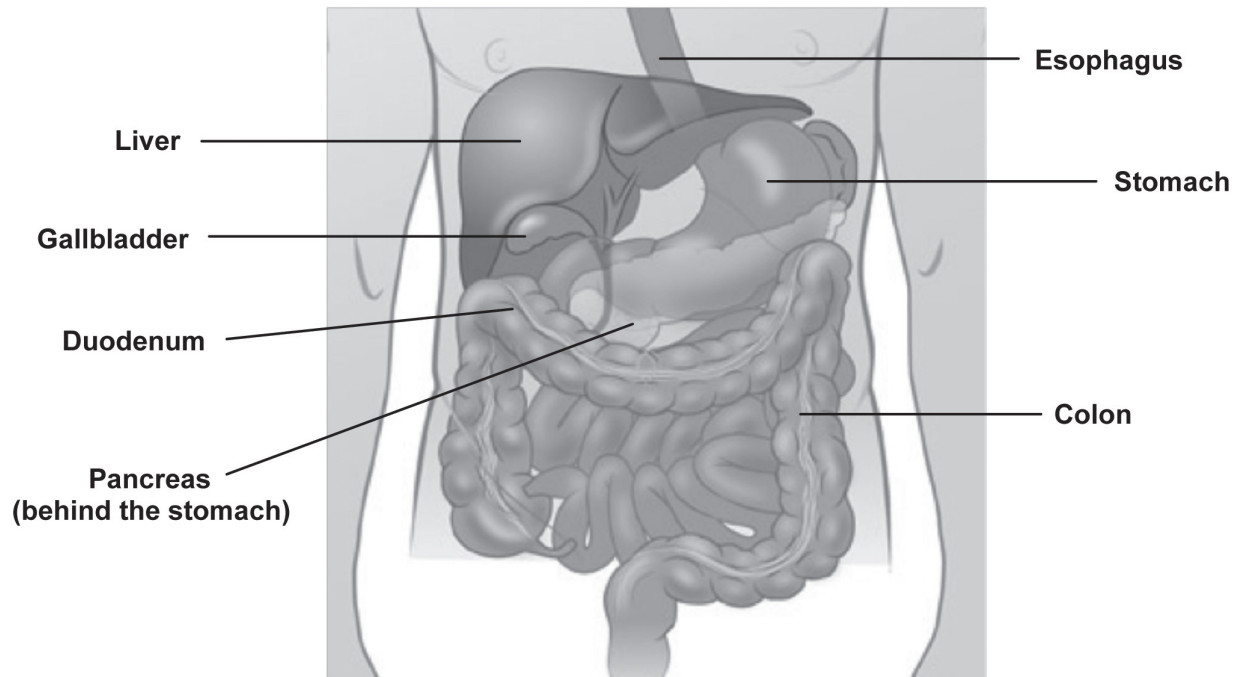
A Patient's Guide to
Liver Cancer



**University of Michigan
Rogel Cancer Center**

**Multidisciplinary
Liver Tumor Clinic**

Anatomy of Digestive System & Liver



Introduction

The doctors and healthcare staff at the University of Michigan Rogel Cancer Center's Multidisciplinary Liver Clinic created this book to explain liver cancer and the treatment options available to you.

This is not a comprehensive guide to treatment options – they are changing every day. Rather, we hope this guide helps you move forward with a firm understanding of liver cancer, how it is treated, and what the experience may include.

With this information in hand, you will be prepared to make thoughtful decisions along with your medical team.

Further Information

You can find more information about liver cancer, and obtain additional copies of this booklet at the Patient Education Resource Center (PERC) located on level B1 of the Cancer Center Building.

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About Liver Cancer

Where is the liver located?

The liver is the largest solid organ in the human body and plays a vital role in regulating many life processes. In an average adult the liver weighs approximately three pounds and is about the size of a football. It is located in the right side of the body, just under the right lung, and is protected by the rib cage. The liver is shaped like a pyramid and is divided into right and left lobes. Unlike most other organs, the liver gets blood from 2 sources. The hepatic artery supplies the liver with blood that is rich in oxygen, and it is about 20% of the blood supply. The portal vein carries nutrient-rich blood from the intestines to the liver, and is about 80% of the blood supply to the liver.

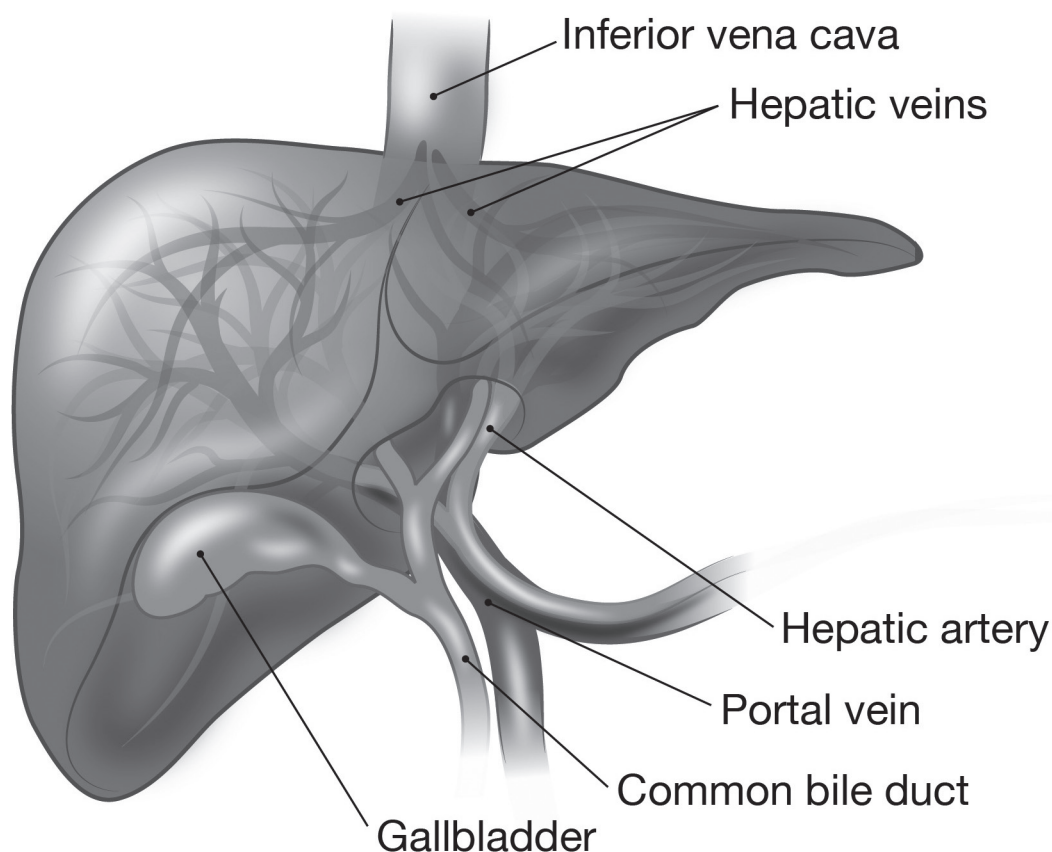


Figure 1. Anatomy of the liver

What does the liver do?

The liver plays a major role in the composition and circulation of blood; therefore, it impacts all body systems. Some of the liver's many jobs include:

- Making proteins to help blood clot to stop bleeding if you are cut or injured
- Clearing some wastes from the body,
- Making bile, a yellowish-green fluid needed for digestion and absorption of food and vitamins
- Breaking down and storing many of the nutrients that are absorbed from food by the intestines
- Storing vitamins, minerals and iron
- Purifying blood by breaking down and removing medications and poisons, such as alcohol and nicotine
- Making hormones, proteins and enzymes

What is cancer and how does it affect the liver?

Normal cells grow, divide, and die in a controlled fashion that is regulated in the body. Cancer is a disease where cells divide and grow in an abnormal, poorly controlled manner. In cancer, the balance of cell growth and death is disturbed.

Cells that continue to grow and divide unchecked become a malignant mass or tumor that can affect how an organ works. The original site of the abnormal cell growth is called the cancer's primary site. In liver cancer, the primary site is the liver. Even when the liver cancer is found in areas outside the liver, such as the lung, the disease is still called liver cancer.

Abnormal or unchecked cells can also grow to invade nearby organs and structures. Cancer cells spread and invade organs by traveling to other structures in the body by way of the lymphatic system and the blood stream. This spreading is called metastasis.

How common is liver cancer and who is at risk?

The American Cancer Society estimates that 24,120 men and women were diagnosed with primary liver cancer in 2010. This cancer is more common in men than women and is usually found in people over the age of 60.

Some factors that increase the risk of liver cancer are:

- Cirrhosis – a disease of the liver that is caused by liver cells being damaged and replaced by scar tissue. It can be caused by alcohol abuse, chronic infection via hepatitis B and C, fatty liver, primary sclerosing cholangitis and other causes of liver disease. This is the most important factor.
- Aflatoxin – is a harmful substance made by certain types of mold. This is not a problem in the United States, but is still found in Asia and Africa.
- Family history
- Environmental - alcohol and tobacco are important toxins that are important for the development of liver cancer.

Besides taking steps to avoid hepatitis and cirrhosis, there is no reliable way to prevent liver cancer. General cancer prevention guidelines, however, include eating a high-fiber, low-fat diet, exercising, and avoiding alcohol and smoking.

Is liver cancer hereditary?

If you have a family member who has had liver cancer you may be at higher risk for liver cancer. Most liver cancers, however, are caused by factors other than heredity.

What are the symptoms of liver cancer?

In its early stage many people with liver cancer will have no symptoms. As the cancer grows it may start to cause symptoms, including:

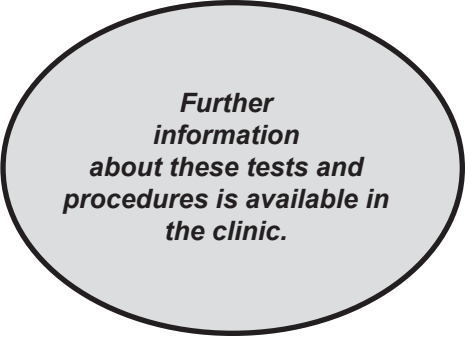
- Pain in the upper right part of the abdomen, which may extend to your back and shoulder
- Swollen or bloated stomach
- Unexplained weight loss
- Loss of appetite or feeling full without eating
- Feeling weak or very tired
- Nausea and vomiting
- Unexplained fever
- Jaundice, yellow discoloration of the eyes and skin

How is liver cancer diagnosed?

Patients with symptoms suspicious for liver cancer will undergo tests to determine the cause of these symptoms.

Blood tests and physical exam:

The doctor will examine your skin for signs of jaundice and will feel the abdomen for lumps or a change in the shape or size of the liver. The doctor will also check for ascites, which is an abnormal buildup of fluid. Blood will be drawn to



***Further
information
about these tests and
procedures is available in
the clinic.***

check for alpha-fetoprotein (AFP) or carcinogenic antigen 19-9 (CA 19-9). These blood tests can be elevated in patients with liver cancer.

Ultrasound of the abdomen:

An ultrasound is usually the first test that is ordered if liver cancer is suspected. A scan can identify a tumor or mass in the liver.

Computed Tomography (CT)

The CT scan can show small tumors as well as important blood vessels that the tumor might be growing into or around. A CT scan can also look at surrounding organs for spread (metastasis) of the cancer into lymph nodes, liver and other areas. You may be given an injection of a special dye for the CT so that the liver shows up clearly in the pictures. The CT will be reviewed by the radiologist and the consulting doctor in 1-2 days.

Magnetic Resonance Imaging (MRI)

In some cases, the MRI allows additional diagnostic information regarding liver tumors. It may also provide imaging of the bile ducts, as well as looking at the surrounding blood vessels, organs, and lymph nodes. A special dye is used for the MRI, to give additional information to the radiologist; therefore a temporary IV (intravenous catheter) will be placed prior to the scan.

ERCP (endoscopic retrograde cholangiopancreatography)

An ERCP is done with a lighted tube called an endoscope and is used to look at the bile ducts. It can also be used to place a stent or tube to open a blocked bile duct for drainage. The patient is not awake during the test (sedation is given through an IV in most cases). The ERCP helps determine what is causing the blockage. Some causes of these blockages include bile duct cancer (cholangiocarcinoma) and gall bladder cancer. Bile duct fluid and tissue samples may be obtained and sent to the pathologist to evaluate for cancer cells.

PTC (Percutaneous transhepatic cholangiography)

A PTC is done by looking at the liver bile ducts with a small catheter. The patient is not awake during the test (sedation is given through an IV in most cases). This procedure helps to identify blockages that are higher up in the bile ducts. Some causes of these blockages include a type of liver cancer that arises from bile duct (cholangiocarcinoma) and gall bladder cancer. Bile duct fluid and tissue samples may be obtained and sent to the pathologist to evaluate for cancer cells.

Biopsy

In some cases, the doctor may remove a sample of tissue. A pathologist uses a microscope to look for cancer cells in the tissue. The doctor may obtain tissue in several ways. One way is by inserting a thin needle into the liver to remove a small amount of tissue. This is called fine-needle aspiration. A doctor in the Interventional Radiology department may use CT or ultrasound to guide the needle. Sometimes the doctor obtains a sample of tissue with a thick needle (core biopsy) or by inserting a thin, lighted tube (laparoscope) into a small incision in the abdomen. Another way is to remove tissue during an operation.

Are there different kinds of liver cancer?

Yes, there are several types of liver cancer, or cancers that start in the liver. In this book we will talk about cancer of the liver that is a “primary” cancer. That means that the cancer started in the liver, rather than beginning in another part of the body and spreading to the liver.

Hepatocellular Carcinoma (HCC)

The most common type of primary liver cancer is called Hepatocellular Carcinoma (HCC), or malignant hepatoma. This type of cancer starts in cells called hepatocytes, the main type of liver cells.

Cholangiocarcinoma

Cholangiocarcinoma is bile duct cancer. The cancers start in the bile ducts, which are small tubes that carry bile to the gallbladder.

Angiosarcoma

Cancers that start in the blood vessels of the liver are called angiosarcomas and hemangiosarcomas. These cancers are very rare, but grow very quickly. They have often spread so far by the time they are found that surgery is not an option.

Hepatoblastoma

The last type of liver cancer is usually found in children younger than 4 years old and is called hepatoblastoma.

Cancers that arises from other organs and travel (metastasize) to the liver are also seen in our clinic.

This book will focus on hepatoma and cholangiocarcinoma.

What is tumor staging?

The stage of a cancer is a description (usually numbers I to IV with IV having more progression) of the extent the cancer has spread. The stage often takes into account the size of a tumor, how deeply it has penetrated, whether it has invaded nearby organs, how many lymph nodes it has spread to (if any), and whether it has spread to distant organs. Staging of cancer is the most important predictor of survival, and cancer treatment is primarily determined by staging.

For liver cancers, besides the tumor size liver function and involvement of the portal vein (main blood vessel in the liver) are important for determining staging.

What will be done in the initial evaluation?

Prior to the visit, we will request the records from your doctors. This is important in order to know the type of cancer involved, the laboratory and radiological tests and any biopsy results that have been obtained. This information is important and we utilize it to assure that the appropriate specialist sees you at the visit. In most situations, our liver pathologists will review the biopsy to determine the type of liver cancer involved. In some situations, we may require you to have a CT or MRI scan prior to your visit at the University of Michigan to get the necessary tumor information that will determine the best treatment options for you.

During the initial visit, you will see one of our liver cancer specialists (liver disease specialists, surgeon, radiation oncologist, medical oncologist, or interventional radiologist). Depending on the tumor stage, you will likely see more than one of the specialists in the same day to discuss the treatment options and to start planning. The goal is that in one visit we can provide you the best information about your cancer and develop a comprehensive treatment plan.

Most of the patients are discussed in the liver tumor board conference. This is a weekly meeting of more than 20 liver cancer specialists at the University of Michigan. This meeting provides an important opportunity to discuss the best treatment options available for each individual patient case. It is particularly helpful to have these specialists available to review complex patient situations. This tumor board conference is also used to evaluate individual patients' response to treatment.

To summarize, on the initial evaluation you can expect:

1. a thorough review of all testing that has been performed to date
2. to see the appropriate liver cancer specialists for your diagnosis
3. to obtain up-to-date laboratory data that includes liver function tests and tumor markers such as AFP and CA 19-9
4. to have your case reviewed at the liver tumor board (for most cases)
5. to leave the visit with a treatment plan of action

Treatment of Liver Cancer

What are the treatment options?

After liver cancer is diagnosed, it must be staged in order to decide on the best plan of treatment. Liver cancer can be classified (or staged) into three main groups;

- Localized resectable (operable) cancer,
- Localized unresectable cancer, and
- Advanced cancer

These classification groups help to determine the most effective way to treat the cancer. If it's determined that the cancer can be successfully removed, then surgery is considered. For patients with localized, but not operable, cancer, the general strategies include intra-arterial, local ablation, systemic chemotherapy, and radiation therapies, alone or in combination.

Chemotherapy is a treatment for patients with cancer that has spread.

Doctors and nurses discussing treatment options stress the importance of treating the disease while at the same time making those treatments as tolerable as possible. The goal of treatment is to stop the growth of the cancer, to shrink it, if possible, and to help the patient live a quality life for as long as possible.

Operable cancer means a tumor is able to be surgically removed. (also called resectable)

• • • • •

Localized unresectable cancer means the tumor is found only in the liver with no evidence of spread to other organs. Tumors at this stage are not able to be removed by surgery because of the condition of the liver, the location of the tumor, or other health problems.

• • • • •

Metastatic or Advanced cancer means that the cancer has spread to both lobes of the liver or to other parts of the body.

How does a patient decide on treatment?

The Multidisciplinary Liver Tumor Clinic has liver disease specialists; surgeons, radiologists, medical oncologists and radiation oncologists who will review and discuss your individual case. Based on this evaluation, your doctor will inform you whether or not your tumor can be removed. Surgical removal of the tumor, along with part of the liver, generally offers the best chance of a cure. Whichever treatment you choose, it will generally start in a week or two from your initial evaluation. There is time to discuss options and to learn more about liver cancer, treatment approaches, and the clinical trials that are available at the University of Michigan Rogel Cancer Center.

What factors affect prognosis or chance of recovery and treatment options?

The prognosis (chance of recovery) and treatment options for liver cancer depend on many factors. Some of these are:

- The stage of the cancer (the size of the tumor and whether the cancer has spread outside the liver to nearby tissues or lymph nodes or to other places in the body).
- Whether or not the tumor can be removed by surgery; is operable or resectable.
- Whether the cancer is newly diagnosed or has come back (recurred).
- The overall function of the liver
- Your general health

Liver cancer can be controlled for a lifetime, or cured, only if it is found before it is spread and it can be removed in its entirety by surgery. If the cancer has spread, or is inoperable, your doctors will discuss treatments that can improve your quality of life by controlling the symptoms and complications of the disease.

When is surgery a treatment for liver cancer?

When patients are diagnosed with liver cancer, about 20% of the tumors are able to be removed by surgery. There are two options for surgery: either resection or liver transplant.

If the liver is otherwise healthy, up to 75% of it can be safely removed in order to treat the cancer. The liver has the ability to grow back after part of it has been removed.

Surgical resection

There are four types of resection:

- **Wedge resection**
removal of a small tumor along with some surrounding liver tissue
- **Hepatic lobectomy**
removal of one half or one side of the liver for larger tumors or those involving the major blood supply to one side of the liver
- **Segmentectomy**
removal of one or more segments of the liver (there are 8 segments to the liver)
- **Bile duct resection**
removal of the gallbladder and the main bile duct draining the liver; reconstruction of bile drainage is performed using a portion of the small intestine

If there is not enough healthy liver to allow a resection, it may be possible to have a procedure called a Portal Vein Embolization (PVE). This is an outpatient procedure done about 6 weeks before surgery to allow healthy liver tissue to begin to grow.

The surgical resection can be performed in an “open” procedure that causes a large abdominal scar to allow removal of the tumor. A picture of a scar from an open liver resection is illustrated in Figure 2.

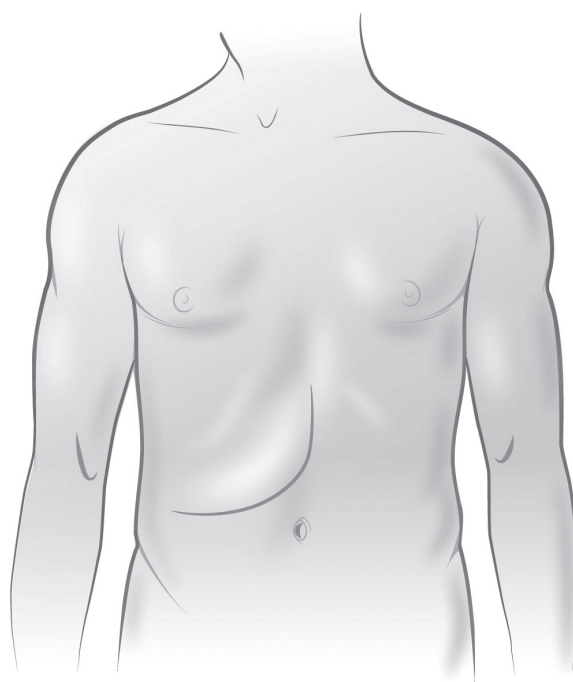


Figure 2: Scar from an open liver resection

Another type of surgical resection is the laparoscopic approach. In this approach, a small incision (about ½” long) is used to insert a small camera and light (called a laparoscope) into the abdomen. Several other small incisions are made that allow long, thin instruments to be used to separate the part of the liver containing the tumor away from the healthy liver. A hand port may be used through a 3” incision near the belly button. Benefits of the laparoscopic approach may include smaller scars, quicker recovery / return to normal life, shorter hospital stay, less pain, and less blood loss during surgery. The liver cancer surgeons at the University of Michigan perform more than 50 laparoscopic resections per year and are able to offer this approach to approximately 2 out of 3 people requiring liver surgery.

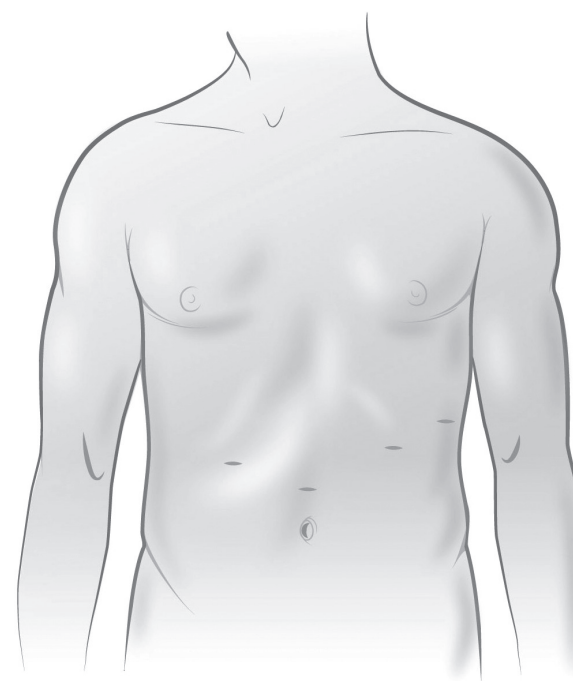


Figure 3: Incision areas of a laparoscopic liver resection.

Figure 3 demonstrates the small incisions used for a laparoscopic liver resection along with a small plastic tube (drain) that is left in place after surgery.

On laparoscopy, the mass could be seen growing out of the left lobe of the liver. Laparoscopic instruments were used to separate the liver attached to the tumor from the healthy liver. The 15cm mass was then removed from a 7cm incision near the belly button.

The recovery time for the laparoscopic and open surgeries may vary from person to person. In general, someone undergoing an open liver resection can expect to be in the hospital for 5-10 days and may not return to full activity for 6-8 weeks after surgery. Someone undergoing a laparoscopic liver resection can expect to be in the hospital for 3-5 days and can usually return to full activity between 3-6 weeks after surgery.

Liver transplant

The other surgical option is liver transplantation. This means the entire liver is removed and replaced with a new one (or a portion of one) from a donor. This is only an option if the cancer has not spread outside the liver, and if a donated liver can be found. The liver cancer surgeons in the liver cancer clinic are also liver transplant surgeons, which have the appropriate training for complex resection of liver tumors, bile duct reconstruction and reconstruction of the blood vessels in the liver.

Our liver cancer clinic is one of fewer than 5 centers in the United States with approved protocols for the treatment of 3 types of primary liver cancer: Hepatocellular carcinoma, Cholangiocarcinoma and Hepatoblastoma. We work closely with the University of Michigan Transplant Center and can facilitate transplant evaluations.

When surgery is not an option

Radiofrequency ablation (RFA)

This is usually done as an outpatient procedure, most commonly by Interventional Radiologists. A special probe that contains tiny electrodes is placed into the tumor using ultrasound guidance. Sometimes the probe is placed directly through the skin, and only local anesthesia is needed. In other cases the doctor will insert the probe through a small cut in the abdomen. In these cases the procedure is done under general anesthesia.

Once the probe is in the tumor, it is “heated” which results in tumor destruction. This is done under general anesthesia.

After RFA you will return to the clinic in six weeks (or sooner if needed). After the first follow-up appointment you will be seen every 3 months for 1 year unless your medical condition requires more frequent monitoring. Thereafter, patients will return to the clinic every 6 months. During these visits you will have the following blood tests: CBC, liver function tests, prothrombin time, alpha-fetoprotein.

At 6 weeks, 3 months, 6 months, and every 6 months thereafter you will have an MRI (CT if not able to have MRI). If you have residual tumor or recurrence by

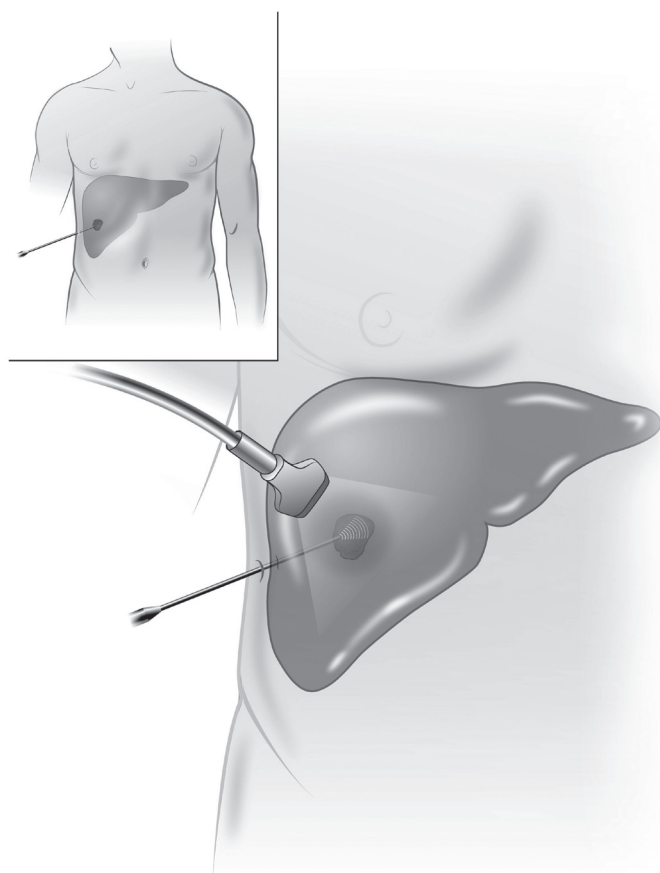


Figure 4: Radiofrequency ablation

imaging at 6 weeks, you will be re-treated with RFA. However, if imaging tests show that the tumor did not respond to the RFA after two treatment sessions, no further RFA treatment will be done.

Some patients experience pain at the sight of ablation. In rare cases, fluid in the lungs can happen too.

Chemoembolization

A procedure called transarterial chemoembolization (TACE) is primarily used for hepatocellular carcinoma (HCC). TACE is performed by Interventional Radiologists, usually as an outpatient procedure to interrupt the blood supply of the tumor itself. The doctor in interventional radiology will insert a tiny catheter into an artery in your leg. Using x-rays as a guide, the doctor will then move the catheter into the hepatic artery and inject an anticancer drug into that artery. The artery is then blocked with tiny particles so that the drug is forced to stay in the liver longer. This blockage may be temporary or permanent. While the hepatic artery is blocked the healthy liver tissues continue to receive blood from the hepatic portal vein, which carries blood from the stomach and intestine. Therefore, this treatment involves the introduction of anticancer drug (chemo) and blockage of hepatic artery (embolization). This procedure requires a hospital stay for 24 hours for pain control and monitoring.

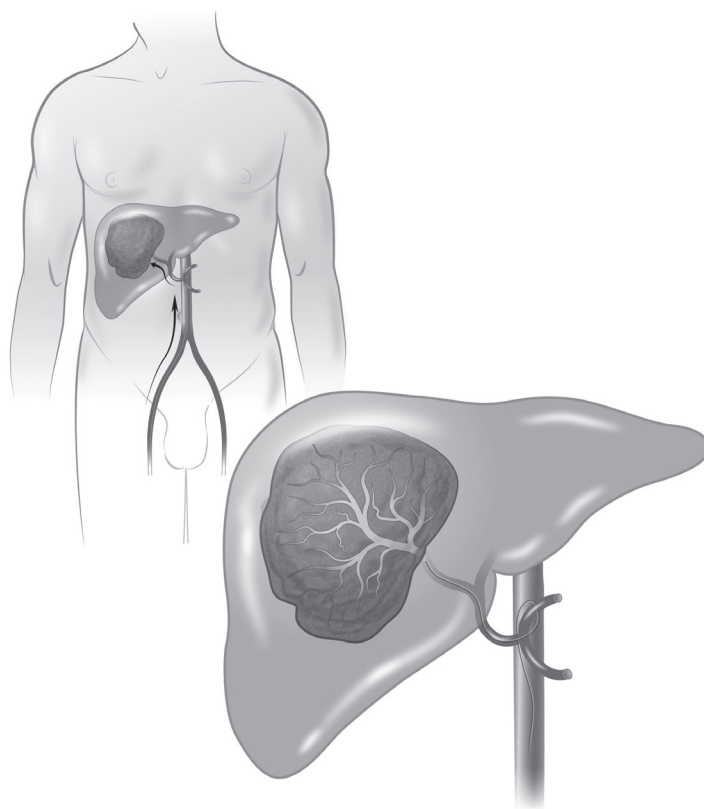


Figure 5: Chemoembolization Procedure

You will return to the clinic 6 weeks after treatment or sooner. After that you return every 3 months for 1 year, then every 6 months. During these visits you will have the following blood tests: CBC, liver function tests, prothrombin time, and alpha-fetoprotein. Some patients have medical needs or conditions that require more frequent monitoring.

You will also have an MRI (CT if not able to have MRI) at 6 weeks, 3 months, 6 months, and every 6 months thereafter. The initial follow up MRI should be scheduled to be done before the clinic visit.

If, at six weeks post TACE, you have tumor remaining (residual) or tumor that returned (recurrence) you will be retreated after discussion with your treating doctor and interventional radiology team.

Side effects can include abdominal pain, which occurs mostly the first week following treatment. This is due to tumor cells dying, necrosis. It causes low grade fever, fatigue and occasionally nausea. Since the anticancer drugs are given directly into the liver, and not to the rest of the body, it rarely causes the side effects seen with infusion of these agents.

Radioembolization

This is a type of internal radiation therapy used for unresectable liver cancer. Internal radiation therapy, called brachytherapy, is a way of giving a higher dose of radiation to the tumor area, while sparing or reducing radiation exposure to other organs such as the liver. This requires an evaluation by radiation oncologists and interventional radiologists.

A type of radioembolization is TheraSphere®, in which beads are loaded with radioactive material (Yttrium 90) and injected directly into the liver. A doctor in Interventional Radiology first makes a small incision in the patient's leg and places a long, flexible plastic tube called a catheter, into the major blood vessel in the leg. Guided by X-ray images, the doctor then moves the catheter up through the blood vessels to the hepatic artery, which is one of two blood vessels that feeds the liver. The doctor will guide the catheter into the branch of the hepatic artery that feeds the tumor in the liver. The TheraSphere® beads are infused through the catheter into the blood that supplies the tumor. This allows radiation to be delivered directly to your tumor. You will be conscious throughout the procedure.

You will have a return visit 8 weeks after treatment in the multidisciplinary liver tumor clinic, and then every 3 months for 1 year. After this, patients will be seen every 6 months. Some medical conditions may require more frequent monitoring; your doctor will discuss this with you if necessary.

During the follow-up visits the following blood tests will be evaluated: CBC, liver function tests, prothrombin time, and alpha-fetoprotein.

MRI (CT if not able to have MRI) at 8 weeks, 3 months, 6 months, and every 6 months thereafter. If the patient is determined to have residual tumor or recurrence by imaging at 8 weeks, they will be re-treated after discussion with treating physician and IR team.

What is chemotherapy?

Chemotherapy is the treatment of cancer with drugs that can destroy cancer cells. These drugs often are called “anticancer” drugs.

How Does Chemotherapy Work?

Normal cells grow and die in a controlled way. When cancer occurs, the abnormal tumor cells keep dividing and forming more cells without control. Anticancer drugs destroy cancer cells by stopping them from growing or multiplying. Healthy cells can also be harmed, especially those that divide quickly. Harm to healthy cells is what causes side effects. These cells usually repair themselves after chemotherapy.

Because some drugs work better together than alone, two or more drugs are often given at the same time. This is called combination chemotherapy.

Other types of drugs may be used to treat your cancer. These may include certain drugs that can block or increase the effect of your body’s response to the cancer.

When is chemotherapy a treatment for liver cancer?

Chemotherapy is the treatment of choice for cancer that is locally advanced or metastatic (spread to other organs). These drugs can have an effect on the cancer by stopping the growth of cancer cells or their ability to multiply.

The goals of chemotherapy treatment are to control the cancer, keep it from spreading by slowing the cancer's growth and improve or reduce the symptoms of the disease.

If the cancer has spread outside the liver and the patient has hepatocellular carcinoma, a standard therapy plan is to use sorafenib (Nexavar®) alone or in combination with other drugs. Sorafenib has been proven to extend life in advanced Hepatocellular carcinoma. For advanced Cholangiocarcinoma, the standard therapy is to use gemcitabine (Gemox®) alone or in combinations.

Chemotherapy treatment is planned by an oncologist. The oncologist considers the patient's medical condition and other factors when deciding on the type of chemotherapy. Therefore, other chemotherapy agents and combinations may be recommended.

Side effects of sorafenib and gemcitabine chemotherapy are located in Tables 1 and 2 on the following pages. General information about chemotherapy, the infusion areas at the University of Michigan Rogel Cancer Center and specific information about each chemotherapy agent can be found at <http://medlineplus.gov>.

Table 1: Overview of sorafenib (Nexavar®) Therapy

This table contains condensed information only. For comprehensive drug information, visit <http://medlineplus.gov> (select “drug information”).

What is sorafenib?	A chemotherapy taken by mouth used to treat liver cancer.
How does it work?	Sorafenib works by blocking hormone production by the cancer, and by killing the adrenal cancer cells.
How is it taken?	Sorafenib is taken by mouth, usually several times a day. Take sorafenib without food, 1 hour before or 2 hours after a meal. Take sorafenib at around the same times every day. Swallow the tablets whole with water. Do not split, chew, or crush them.
What side effects may occur?	<p>Very common Side Effects (Occur in ≥ 10% of patients)</p> <ul style="list-style-type: none"> (1) Nausea or vomiting (2) Feeling tired [fatigue] (3) Skin rashes including hand-and-foot reaction (4) Diarrhea (5) High blood pressure [hypertension] (6) Bleeding [hemorrhage] <p>Common (Occurring in ≥1% to < 10% of patients)</p> <ul style="list-style-type: none"> (1) Indigestion or "upset stomach" (2) Difficulty swallowing (3) Sores on the lining of the mouth including dry mouth and pain of the tongue (4) Decreased appetite [anorexia] (5) Influenza-like illness (such as, headaches, muscle aches, fever, weakness, and cough) (6) Fever (7) Acne (8) Pain in joints or muscles (9) Depression (10) Erectile dysfunction (11) Ringing in the ears or head noises
What should I do if I miss a dose?	Sorafenib must be taken on a regular schedule. Call your doctor if you miss a dose or if you vomit after taking your medicine.

Special considerations of sorafenib therapy	<ul style="list-style-type: none">• Store this medicine in a closed container at room temperature. Avoid heat, moisture and direct light. Do not store this medication in a bathroom due to the humid environment.• Keep this medicine away from children.• Notify your doctor if you are taking blood thinners such as warfarin (Coumadin®), seizure medication, or St. John's wort.• This medication may make you dizzy or drowsy. Avoid driving, using heavy machines or doing anything that could be dangerous if you are not alert.• Patients taking sorafenib require frequent monitoring by their physician including routine blood work.• Continue to take sorafenib even if you feel well. Do not stop taking sorafenib without talking to your doctor.
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Table 2: Overview of gemcitabine (Gemzar®) Therapy

This table contains condensed information only. For comprehensive drug information, visit <http://medlineplus.gov> (select “drug information”).

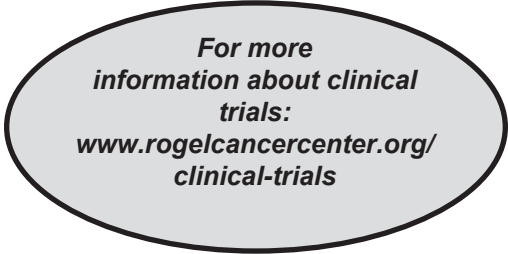
What is gemcitabine?	A chemotherapy administered intravenously for the treatment of cancer.
How does it work?	Gemcitabine works by slowing or stopping the growth of cancer cells. The length of treatment depends on the types of drugs you are taking, how well your body responds to them, and the type of cancer you have.
How is it taken?	You will receive gemcitabine in a cancer therapy infusion center. The medication is given through a needle in your arm, or through an infusion catheter or port.
What side effects may occur?	Nausea, vomiting, blood work abnormalities, hair thinning or becoming brittle, diarrhea or constipation, skin rash or itching.
What are the more serious side effects?	Allergic reaction (hives, itching), chest pain, sudden or severe headache, swelling of your hands or feet.
Special considerations of gemcitabine therapy	<ul style="list-style-type: none">• Patients will be seen monthly in clinic to evaluate for side effects of gemcitabine therapy• This medicine lowers the number of some types of blood cells in your body. Because of this, you may bleed or get infections more easily.• Talk to your doctor before getting flu shots or other vaccines• Gemcitabine may interfere with the normal menstrual cycle (period) in women and may stop sperm production in men. However, you should not assume that you cannot get pregnant or that you cannot get someone else pregnant. Women who are pregnant or breast-feeding should tell their doctors before they begin taking this drug. You should not plan to have children while receiving chemotherapy or for a while after treatments. (Talk to your doctor for further details.) Use a reliable method of birth control to prevent pregnancy. Gemcitabine may harm the fetus.

Clinical Trials

Your doctor may suggest that you consider participating in a clinical trial (a research study or protocol) for the treatment of liver cancer. Clinical trials are one very important reason that the University of Michigan Rogel Cancer Center is able to offer our patients access to the latest cancer treatments.

Clinical trials are used to test and develop new treatments. The goal of these trials is to find ways to improve therapy and / or decrease side effects. While a trial or study is active or in-progress we will not know whether any potential improvement has been achieved. The trial must be closed and the data analyzed before the treatment is made widely available to patients.

There may be some additional risks associated with research. Your doctor will discuss in detail with you both the potential risks and benefits and obtain your written permission before you can be started on a research protocol.



*For more
information about clinical
trials:
[www.rogelcancercenter.org/
clinical-trials](http://www.rogelcancercenter.org/clinical-trials)*

Oversight committees at Michigan Medicine conduct an extensive review of all clinical trials. These committees include an “institutional review board” or IRB composed of other cancer doctors, doctors in other specialties and lay people. The IRB reviews all protocols before they are available to patients and again at different times during the research to ensure that the protocol remains appropriate and safe for patients.

All patients who are on a protocol receive the best supportive care possible, and their reactions to the treatment are watched very closely. If the treatment does not seem to be helping, a doctor can stop the treatment and take a patient out of a study. Also, the patient may choose to leave the study at any time.

If a patient leaves a study for any reason, standard care and treatment will be initiated.

Clinical trials are voluntary. Your liver cancer will be treated whether you decide to join a protocol or not.

Meeting Obstacles

If you have cancer, you may notice every ache, pain, or sign of illness. Even little aches may make you worry. We hope you find the information in this section will lessen your fear and allow you to participate in your own care. This information is designed to help you be an informed partner in your care. Remember though, that this information is only a guide. Self-help can never take the place of professional health care. Ask your medical team any questions you may have. Also don't hesitate to tell them about any side effects you may have. They want and need to know about how you are physically and emotionally doing.

Not all patients will experience the symptoms or side effects listed in this section. We include them to help you understand what may be happening to you. We know these are obstacles to your health and quality of life. Our multidisciplinary team is here to work with you in reducing or eliminating these problems.

When to call the doctor?

There are times when symptoms can be managed by you at home, and other times when you should notify your medical team. Never hesitate to call the clinic if you are unsure or have new symptoms.

The following are reasons to notify your doctor:

- Shaking chills or fever (a temperature of 100.5° F or 38.3° C). Notify your doctor immediately if you develop a temperature, do not delay.
- Unusual cough, sore throat, lung congestion or shortness of breath
- Burning discomfort when you urinate
- Redness, pain or sores in your mouth

- Nausea, vomiting or inability to eat or drink for more than 24 hours.
- Diarrhea (loose, watery stools) for more than 24 hours.
- Constipation (no bowel movement in 2-3 days)
- Bleeding or unusual bruising
- Gain or lose more than 5 pounds in a week
- Pain not controlled by your current medications
- Feeling confused or forgetful
- Any new or unusual symptom that concerns you

Recognizing Ascites

Ascites is an accumulation of fluid in the abdominal cavity. When this occurs the following steps are recommended:

- Weigh yourself each morning and keep a record of your weight history.
- Restrict sodium intake to less than 2,000 mg per day. More tips on how to do this can be found in the Resources section of this handbook.
- Your doctor may want you to take a diuretic (water pill) to help remove some of the retained fluid. The most commonly used water pills are Lasix® (furosemide) and Aldactone® (spironolactone).
- If diuretics do not help you may need to go to the hospital to have the fluid drained. This procedure is called paracentesis or abdominal tap.
- If an infection is found in the fluid you will be given antibiotics to prevent future infections

Encephalopathy

Encephalopathy is a condition of the brain and central nervous system caused by toxins not filtered out of the blood by the liver. It causes personality changes, intellectual impairment and a depressed level of consciousness. Patients with mild and moderate encephalopathy demonstrate decreased short-term memory and concentration. Patients may also show signs of a flapping tremor of the hands, called asterixis.

If you have symptoms of encephalopathy you will most likely be given a medicine called Lactulose. This drug will change the bacteria in your abdomen and will very likely increase the number of bowel movements you have each day. The dose may be adjusted until you have three to four bowel movements daily, or if you still feel confused after taking it.

Esophageal Varices

Esophageal varices are dilated veins in the walls of the esophagus (food pipe) or sometimes in the upper part of the stomach. These are varicose veins in the food pipe that develop from an increased blood pressure in the portal vein. This is called portal hypertension. It develops when there is resistance to blood flowing normally through the liver. The increased pressure in the veins causes them to distend and may break, which would cause you to vomit blood, have bloody stools, or black tarry stools.

If you develop an esophageal varice you may be placed on a medicine called a beta-blocker to help prevent bleeding. This medication will lower your heart rate and blood pressure by decreasing the blood pressure in the portal vein. Other medical or surgical treatment may be needed to help prevent future problems. These treatments include:

- Endoscopic therapy – a device with a light, called an endoscope, allows your doctor to look into your esophagus. The veins can either be injected with a blood clotting medicine or the bleeding can be stopped with a type of rubber band that is put around the bleed.
- Transjugular Intrahepatic Portosystemic Shunt (TIPS) is a procedure to correct the blood flow problem in your liver. It is performed in the Radiology department. The doctor will make a small tunnel through the liver to connect the portal vein to one of the hepatic veins. This will allow blood to flow out of the liver. After the tunnel is made, the doctor will insert a small metal tube, called a shunt or stent, to keep the tunnel open. This procedure is only used after other efforts have been tried because it can result in worsening or new encephalopathy.

Nutrition

What should my nutrition goals be?

Liver cancer patients should try to achieve the following:

- Consume enough calories to correct or prevent weight loss and improve nutrition
- Restrict the sodium in your diet to 2,000 mg (one teaspoon) per day if you have swelling in your legs or feet or if you have a buildup of fluid in your abdomen
- Consume small frequent meals and bedtime snacks to prevent long periods of going without food.
- Consuming adequate calories and protein will help with liver cell regeneration and improve liver function

Cancer nutrition specialists are available for consultation during your clinic visits. Also, nutrition specialists are available at the cancer center for individual appointments where they can offer suggestions and guidance, and will prepare a dietary plan during your treatment. The nutrition clinic is open Monday through Friday from 8am to 3pm.

Appointments can be made in advance at your clinic checkout area or you can call 1-877-907-0859

Tips for Reducing Sodium in Your Diet

Sodium, also known as sodium chloride, is a mineral found in the body and in the food we eat. Salt is the main source of sodium in our diet. For a low sodium diet you should consume no more than one teaspoon (2,000 mg) of sodium in any 24-hour period. The average person's diet contains 4,000 to 6,000 mg each day.

Although salt is the common source of sodium, you should also be aware of foods that have sodium and you may not realize it. Softened or bottled water, and some medications contain sodium. Make sure you check the labels of everything you eat or drink.

In general avoid any food that has more than 400 mg of sodium per serving. The best choices are those foods that contain 200 mg or less of sodium.

Other tips:

- Cook low sodium meals at home and freeze them
- Look for convenience or processed foods containing less than 200mg of sodium
- If it is necessary to eat a frozen meal, look for one containing no more than 500-600 mg of sodium.
- Look for sodium free brands of canned foods, or rinse the food with water to reduce some of the sodium.
- Experiment with new spices and herbs to flavor food without adding sodium.

When dining out:

- Avoid fast food restaurants
- Order broiled meat or fish
- Order sauces on the side and use very small amounts
- Use a limited amount of condiments such as mustard, ketchup, and salad dressing
- Avoid bacon, cheese and croutons in salad

What can be done for itching and yellowing of the skin (jaundice)?

Why does this happen?

Jaundice (yellowing of the skin) occurs when bilirubin builds up in the bloodstream. Bilirubin is made in the liver and moves from the liver through the gallbladder and bile duct to be dumped into the small intestine. Jaundice is a sign that the bile duct is partially or completely blocked, possibly by a liver mass. When a liver mass causes a blockage, bilirubin can't get through and has nowhere to go, so it backs up in the bloodstream. This causes a yellowing of the skin, the whites of the eyes and a darkening of the urine.

What can be done?

Jaundice can be treated by relieving the blockage with a bile duct stent. There are ways to make you more comfortable if jaundice continues.

Some suggestions include:

- Good skin care using mild soaps to bathe,
- Avoid using very hot water or anything that might dry your skin,
- Apply lotions or creams to prevent skin dryness,
- Keep room temperatures cooler and hydrated. This may help to decrease itching.

Lastly, there are medications that can be suggested for itching. Talk to your doctor about these if you have tried other treatments.

What can be done to treat pain?

Why does this happen?

Patients who are diagnosed with liver cancer commonly have pain. Pain is described differently by each patient, but many describe it as a cramping, aching, and radiating (spreading) to back or shoulders. The most common areas of pain experienced by patients with liver cancer are the upper abdominal and back areas. There are many causes of pain including the cancer itself, which may cause pressure on other organs, nerves and vessels.

What can be done?

Pain can be treated, but oftentimes there are barriers that prevent proper treatment. Some of these barriers are a lack of understanding in how to take the pain medications, fear of addiction and a concern that pain may be uncontrollable later if medicines are used at the time of initial pain. These are all issues that should be addressed with your medical team. Do not let these barriers prevent you from keeping any pain you may have under control.

Good pain control can lead to increased physical activity and well-being in patients with liver cancer. Patients who have chronic pain may need to take medications regularly to obtain the best control of pain. An understanding of how to take these medications will help you get better control of your pain.

There are many different medications used to treat pain. Narcotics are the most common. Other types of medications used to treat pain include antidepressants, anticonvulsants (anti-seizure medications), anti-inflammatory and steroid medications.

Narcotic medications come in several forms: tablets, liquids, skin patches and intravenously via a pump. These medicines are available as a sustained release or long acting preparation, and as an immediate release pain medication. The long acting and immediate release pain medications are often used together.

Sustained release or long acting pain medications

These should be taken on a regular, scheduled time, usually morning and evening, whether you have pain or not. They are taken on a schedule and work best when that schedule is not changed.

Examples of these types of medications include;

- Fentanyl (Duragesic® patch)
- Morphine (Oramorph®, MSContin®)
- Oxycodone (Oxycontin®)

Long Acting Pain Medications (sustained release) work best when taken on a regular schedule that does not change.

Immediate release medications “Breakthrough pain medications”

The immediate release medications should be taken when you are having pain while taking a long acting pain medication. This is called “breakthrough pain” as it occurs while you are taking regularly scheduled medication, but may need some extra medication for control and to prevent it from becoming severe.

These medications work within 15-20 minutes and are usually taken on an ‘as needed’ basis because pain can vary from day to day. These medications can be taken at any time, even if it is the same time as the sustained release or long-acting pain medications.

Examples of breakthrough pain medications;

- Oxycodone
- Morphine immediate release(MSIR)
- Hydrocodone (Vicodin®)
- Morphine oral solution (Roxanol®)
- Hydromorphone (Dilaudid®)
- Fentanyl lozenge (Actiq®)

Suggestions for patients on sustained release/long-acting pain medications:

- Continue the sustained release medication on a regular basis whether you are having pain or not at that time.

Do not change this schedule without talking to your doctor.

- Use your 'breakthrough' pain medication as needed.

Do not wait until pain becomes severe or it will become difficult to get good control.

- Keep a record of the breakthrough medications taken over a 24 hour period. This information is helpful when you call your doctor about poor pain control.

Rule of thumb:

If breakthrough pain medication is needed 4-6 times a day regularly

OR

if pain keeps you up consistently at night

OR

Notify your doctor who may consider increasing your sustained release pain medication.

Celiac Plexus Nerve Block

If medications taken by mouth or patch are not adequate to control pain then a nerve block may be considered.

Pain sensations from your abdomen pass through the bundle of nerves called a plexus. A celiac plexus block is the injection of a local anesthetic into your back in the area of a nerve bundle (called a plexus) that goes to the organs in your abdomen (see Illustrations on inside front cover). Doctors who specialize in pain anesthesia can inject a drug that will damage the nerve plexus. The drug

stops the pain sensation from reaching the nerves for a longer period of time. This is called a 'block'. Blocking the nerve should help decrease the feeling of pain. This procedure is available to patients who are seen in the interventional pain clinic and can be further discussed, if needed.

Other Ways to Reduce Pain

In addition to medications, a number of other treatment strategies can be employed to relieve pain. Although on their own, these tools might not be enough to eliminate moderate to severe pain, they are often helpful when used in combination with medication. Some of these strategies, commonly referred to as complementary therapies include:

- Relaxation, guided imagery,
- Hypnosis,
- Biofeedback,
- Creative therapies such as music and art,
- Prayer, meditation,
- Massage,
- Acupressure and acupuncture,
- Application of heat or cold, and
- Therapeutic exercise.

Many pain medications cause constipation.

If you are taking pain medications on a regular basis, you will need to review the next section on preventing constipation.

What can be done to prevent and treat constipation?

Why does this happen?

Constipation is common during cancer treatment. Constipation is a decrease in the number of bowel movements combined with hard stool, excessive straining, bloating, increased gas, and/or abdominal cramping.

Liver cancer patients are at risk for constipation because they are often treated with pain medications, receive chemotherapy and anti-nausea medications, have decreased their physical activity and have had a change in their eating and drinking habits. All of these can cause constipation. Other causes of constipation include dehydration and a lack of fiber in your diet.

What can be done?

There are a number of preventative things to do. These include:

- Increasing the fiber in your diet with foods high in fiber such as fresh or raw fruits and vegetables, whole grains, prunes, nuts and dates.
- Increase fluids in your diet (drink at least 2 quarts of fluid daily).
- Avoid cheese products
- Get regular exercise every day if possible...keep up your activity as much as you are able.
- Go to the bathroom whenever you have an urge to go.

For patients taking pain medications that are narcotics or opioids, we recommend a combination of stool softener and laxative on a regular basis.

Here are some suggestions:

- Take Senokot-S®, two to six tablets daily in divided doses to keep regular bowel movements every day. This can be decreased or increased according to results and tolerance. Generic versions of Senokot-S® can be substituted. Ask your pharmacist for information about generic versions. They are often cheaper.
- If no bowel movement in any 24 hour period (1 day), take two tablespoons of Milk of Magnesia® (MOM) at bedtime with a full glass of water.
- If no bowel movement in any 48 hour period (2 days), take three Senokot-S® tablets twice a day (total of 6 tablets per day) plus two tablespoons of MOM at night before bedtime.
- If no bowel movement in any 72 hour period (3 days), add one of the following:
 1. Magnesium Citrate 8 ounces (1/2 bottle) now then repeat in 6 hours, OR
 2. If no bowel movement, then Dulcolax® tablets, two or three tablets.

How do I cope with my feelings?

If you have been diagnosed with liver cancer, it is normal for you and your family to experience a wide range of emotions. Important issues in the life of any person with cancer may include the following:

- Fear of death.
- Interruption of life plans.
- Changes in body image and self-esteem.
- Changes in social role and lifestyle.
- Money and legal concerns.

Everyone who is diagnosed with cancer will react to these issues in different ways. Many patients experience feelings of anxiety, depression, sadness, stress, and have difficulty sleeping or eating. It is important to know when and where to seek help for these feelings. These symptoms and fears usually lessen as a person adjusts to the diagnosis.

There are many misconceptions about cancer and how people cope with it, such as the following:

- All people with cancer are depressed.
- Depression in a person with cancer is normal.
- Treatment does not help the depression.
- Everyone with cancer faces suffering and a painful death.

A person who cannot adjust to the diagnosis after a long period of time, and who loses interest in usual activities, may be depressed. Mild symptoms of depression can be distressing and may be helped with counseling. Even patients without obvious symptoms of depression may benefit from counseling; however, when symptoms are intense and long lasting, or when they keep coming back, more intensive treatment is important. These are often signs of what is called “major depression”.

Major depression is not simply sadness or a blue mood. Major depression affects about 25% of patients and has common symptoms that can be diagnosed and treated. Symptoms of depression that are noticed when a patient is diagnosed with cancer may be a sign that the patient had a depression problem before the diagnosis of cancer. Anyone experiencing these symptoms, or who has a history of depression should talk to their healthcare team.

It is important to remember that this can be treated. The symptoms of major depression include the following:

- Having a depressed mood for most of the day and on most days.
- Loss of pleasure and interest in most activities.
- Changes in eating and sleeping habits.
- Nervousness or sluggishness.
- Tiredness.
- Feelings of worthlessness or inappropriate guilt.
- Poor concentration.
- Constant thoughts of death or suicide.

Depression can affect caregivers too

Just as patients need to be evaluated for depression throughout their treatment, so do family caregivers. Caregivers experience a good deal more anxiety and depression than people who are not caring for cancer patients.

If the family of a patient diagnosed with cancer is able to express feelings openly and solve problems effectively, both the patient and family members have less depression. Good communication within the family reduces anxiety.

Seeking help

The Multidisciplinary Liver Tumor Team believes that helping patients cope with their cancer diagnosis is an essential part of providing care. Our social worker is an essential member of the team who provides evaluation, counseling, and referral to additional resources such as support groups, the PsychOncology clinic and group therapy. The social worker for the liver tumor clinic can be reached through our call center at 877-907-0859.

Remember, our team is here to help address any emotional needs you or your family may have. Do not hesitate to contact us.

Resources

It is important to us that every patient receives the right support at the right time. However, resources specific to liver cancer are uncommon in the general community. You will find liver cancer resources most commonly on the internet and in large academic healthcare centers that have specialized liver cancer clinics.

We believe support and resources are an essential component of caring for the patient in treatment for liver cancer and their family. Therefore, we offer many support and information resources to patients and families at the University of Michigan Rogel Cancer Center. These programs are available to any patient receiving care at the University of Michigan.

You can find information about the programs available on our cancer center website: www.rogelcancercenter.org/patients-and-families. All of the programs available to you are described in the Patient & Family Support Services Handbook.

- Assistance with Practical Matters:

The Practical Assistance Center (PAC)

Discounted lodging, parking, assistance with transportation and other expenses, prescription assistance programs

Financial counseling

- Resources to Help You Cope:

Social Work

Support groups

PsychOncology Clinic

Complementary Therapies (art, music, guided imagery)

Spiritual Care

- Resources that Address Treatment Side Effects and Symptoms:

Cancer Symptom Management Clinic

Nutrition Services Clinic

Wig Bank Program

RESOURCES

[illegible]

[illegible]

Important Phone Numbers

(all numbers are 734 area code)

Doctors

Dr. Mary Feng	936-4300
Dr. Shawn Pelletier	647-8902
Dr. Kevin Nguyen	647-8902
Dr. Paula Novelli	936-4588
Dr. Chris Sonnenday	647-8902
Dr. Michael Volk	647-8902
Dr. Mark Zalupski	647-8902

Nurses

Kim Vanderwall and Marie Richards	647-8902
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Physician Assistants

Tracy Licari and Marc Moote	647-8902
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Appointments

Multidisciplinary Liver Tumor Clinic (Donna Thayer)	647-8902
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To Reach a Doctor For Medical Problems

Monday-Friday after 5pm, or on weekends and holidays:

Call the UM Page Operator @ 936-6267 and ask them to page:

- the surgical resident if you are a patient of Dr. Pelletier, Dr. Sonnenday or Dr. Nguyen;
- the gastroenterology fellow if you are a patient of Dr. Volk
- the oncology resident if you are patient of or Dr. Zalupski

Resources

Rogel Cancer Center Nutrition	877-907-0859
Patient & Family Support Services	
Practical Assistance Center	877-907-0859
Patient Support Services	877-907-0859
Social Work	877-907-0859
PsychOncology Clinic Appointments	877-907-0859

Operating Rooms

Main OR Family Waiting Room	936-4388
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This document is not intended to take the place of the care and attention of your personal physician or other professional medical services. Our aim is to promote active participation in your care and treatment by providing information and education.

Questions about individual health concerns or specific treatment options should be discussed with your physician.

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