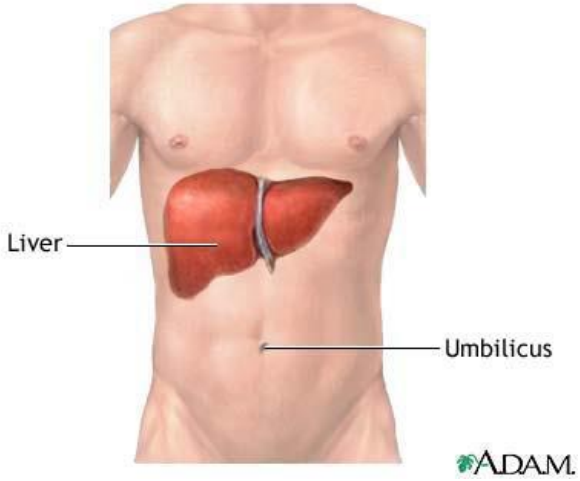
Cancer Association of South Africa (CANSA)

Research • Educate • Support

Fact Sheet on Liver Cancer

Introduction

[Picture Credit: Liver]



The liver, *hepar*, is a vital organ present in vertebrates and some other animals. It has a wide range of functions, including detoxification, protein synthesis, and production of biochemicals necessary for digestion. The liver is necessary for survival; there is currently no way to compensate for the absence of liver function in the long term, although new liver dialysis techniques can be used in the short term.

This organ plays a major role in metabolism and has a number of functions in the body, including glycogen storage, decomposition of red blood cells, plasma protein synthesis, hormone production, and detoxification. It lies below the diaphragm in the abdominal-pelvic region of the abdomen. It produces bile, an alkaline compound which aids in digestion via the emulsification of lipids. The liver's highly specialized tissues regulate a wide variety of high-volume biochemical reactions, including the synthesis and breakdown of small and complex molecules, many of which are necessary for normal vital functions.

Medical terms related to the liver often start in *hepato-* or *hepatic* from the Greek word for liver, *hēpar* (ἡπαρ).

Liver Cancer

Liver cancer (hepatocellular carcinoma) is a cancer arising from the liver. It is also known as primary liver cancer or hepatoma. The liver is made up of different cell types (for example, bile ducts, blood vessels, and fat-storing cells). However, liver cells (hepatocytes) make up 80% of the liver tissue. Thus, the majority of primary liver cancers (over 90%-95%) arises from liver cells and is called hepatocellular cancer or carcinoma (MedicineNet).

Incidence of Liver Cancer in South Africa

According to the National Cancer Registry (2012) the following number of liver and bile duct cancer cases was histologically diagnosed in South Africa during 2012:

Group - Males 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	296	1:561	0,80%
Asian males	11	1:504	1,26%
Black males	185	1:600	1,58%
Coloured males	20	1:729	0,46%
White males	81	1:434	0,40%

Group - Females 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	218	1:997	0,58%
Asian females	7	1:1 882	0,68%
Black females	125	1:1 139	0,76%
Coloured females	23	1:844	0,56%
White females	62	1:716	0,39%

The frequency of histologically diagnosed cases of liver and bile duct cancer in South Africa for 2012 was as follows (National Cancer Registry, 2012):

Group - Males 2012	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	9	11	22	53	50	75	39	25
Asian males	0	0	0	2	0	4	2	1
Black males	9	7	15	34	36	34	18	10
Coloured males	0	2	1	4	3	4	5	0
White males	0	2	3	7	9	30	11	14

Group - Females 2012	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	4	7	21	27	41	51	35	29
Asian females	0	0	1	2	1	3	0	0
Black females	3	4	16	16	23	24	20	10
Coloured females	0	1	0	6	5	5	4	1
White females	0	2	3	3	9	18	8	16

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

Causes of Liver Cancer

Hepatitis B can be caused by contaminated blood products or used needles or sexual contact but is frequent among Asian children from contamination at birth or even biting among children at play. The role of hepatitis B virus (HBV) infection in causing liver cancer is well established. Several lines of evidence point to this strong association. As noted earlier, the frequency of liver cancer relates to (correlates with) the frequency of chronic hepatitis B virus infection. In addition, the patients with hepatitis B virus who are at greatest risk for liver cancer are men with hepatitis B virus cirrhosis (scarring of the liver) and a family history of liver cancer. Perhaps the most convincing evidence, however, comes from a prospective (looking forward in time) study done in the 1970s in Taiwan involving male government employees over the age of 40. In this study, the investigators found that the risk of

developing liver cancer was 200 times higher among employees who had chronic hepatitis B virus infection as compared to employees without this infection.

Hepatocellular carcinoma accounts for most liver cancers. This type of cancer occurs more often in men than women. It is usually seen in people age 50 or older. However, the age varies in different parts of the world.

The disease is more common in parts of Africa and Asia than in North or South America and Europe.

Hepatocellular carcinoma is not the same as metastatic liver cancer, which starts in another organ (such as the breast or colon) and spreads to the liver. In most cases, the cause of liver cancer is usually scarring of the liver (cirrhosis). Cirrhosis may be caused by:

- Alcohol
- Autoimmune diseases of the liver
- Hepatitis B or C viral infections
- Inflammation of the liver that is long-term (chronic)
- Iron overload in the body (haemochromatosis)

(MedicineNet; PubMed Health).

Risk Factors for Liver Cancer

Factors that increase the risk of primary liver cancer include:

- Gender – research shows that men are more likely to develop liver cancer than are women
- Age - in North America, Europe and Australia, liver cancer most commonly affects older adults. In developing countries of Asia and Africa, liver cancer diagnosis tends to occur at a younger age — between 20 and 50
- Chronic infection with hepatitis B virus (HBV) or hepatitis C virus (HCV) - chronic infection with HBV or HCV increases the risk for liver cancer even if there is no development of cirrhosis
- Cirrhosis - this progressive and irreversible condition causes scar tissue to form in the liver and increases the chances of developing liver cancer
- Certain inherited liver diseases - liver diseases that can increase the risk for liver cancer include haemochromatosis (a disease that causes the body to store too much iron in the liver and other organs, also sometimes referred to as ‘iron storage disease’) and Wilson's disease
- Diabetes - people with this blood sugar disorder have a greater risk of liver cancer than do people who don't have diabetes
- Non-alcoholic fatty liver disease - an accumulation of fat in the liver increases the risk of liver cancer
- Exposure to aflatoxins - consuming foods contaminated with fungi that produce aflatoxins greatly increases the risk of liver cancer. Crops such as corn and peanuts can become contaminated with aflatoxins and is more common in parts of Africa and Asia
- Obesity - having an unhealthy body mass index increases the risk of liver cancer.
- Alcohol consumption – alcohol has been declared a Group 1 carcinogen, which means that there is sufficient evidence that it causes cancer in humans

(Mayo Clinic; ScienceDaily; National Cancer Institute; Life is Beautiful)

Signs and Symptoms of Liver Cancer
Most people don't have signs and symptoms in the early stages of primary liver cancer. When signs and symptoms do appear, it may include:

- losing weight not associated with changes in diet
- loss of appetite
- upper abdominal pain
- nausea and vomiting
- general weakness and fatigue
- an enlarged liver
- enlarged spleen which is felt as a mass under the ribs on the left side of the abdomen
- abdominal swelling
- yellow discoloration of your skin and the whites of the eyes (jaundice)
- dark urine
- white, chalky stools
- easy bruising or bleeding
- enlarged abdomen
- fever

(Mayo Clinic; Cancer Treatment Centers of America; Canadian Cancer society; WebMD; National Cancer Institute).

Diagnosis of Liver Cancer
The following procedures contribute towards the diagnosis of liver cancer:

Ultrasound - This test uses sound waves to look for masses in the liver

Computed tomography (CT) - The CT scan is an x-ray test that produces detailed cross-sectional images of your body. A CT scan of the abdomen is very useful in identifying many types of liver tumours. It can provide precise information about the size, shape, and position of any tumours in the liver or elsewhere in the abdomen, as well as nearby blood vessels. CT scans can also be used to guide a biopsy needle precisely into a suspected tumour (called a *CT-guided needle biopsy*). If someone is found to have liver cancer, a CT of the chest may also be done to look for possible spread of the cancer to the lungs

Instead of taking one picture like a standard x-ray, a CT scanner takes many pictures as it rotates around the patient. A computer then combines these into detailed images of slices of the part of the body that is being studied.

For this test, the patient may be asked to drink 450ml to 1 000ml of a liquid called *oral contrast*. This helps outline the intestine so that certain areas are not mistaken for tumours. The patient may also receive an IV (intravenous) line through which a different kind of contrast (IV contrast) is injected. This helps better outline structures in the body. The injection can cause some flushing (redness and warm feeling). Some people are allergic and get hives or, rarely, more serious reactions like trouble breathing and low blood pressure. The presiding doctor will usually enquire about any possible allergies or a previous reaction to any contrast material used for x-rays.

If a doctor suspects that a patient may have liver cancer, one set of CT scans may be requested of the patient's abdomen before taking a second set with IV contrast. Other sets of scans may then be taken over the next several minutes as the contrast passes through the liver and other parts of the body. These sets of scans (together known as a *4-phase* or *multiphase CT scan*) can help spot different types of liver tumours.

CT scans take longer than regular x-rays. The patient needs to lie still on a table while the scans are being done. During the test, the table slides in and out of the scanner, a ring-shaped machine that completely surrounds the table. Some patients might feel a bit confined by the ring they have to lie in while the pictures are being taken. *Spiral CT* (also known as helical CT), which uses a faster machine and yields more detailed pictures, is now used in many medical centres.

Magnetic Resonance Imaging (MRI) - Like CT scans, MRI scans provide detailed images of soft tissues in the body, but use radio waves and strong magnets instead of X-rays. The energy from the radio waves is absorbed and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into a very detailed image of parts of the body.

When MRI is used to look at liver tumours, several sets of images may be taken. After the first set is done, a contrast material called *gadolinium* is injected into a vein to help see details more clearly. Then other sets of images are taken over the next several minutes as the contrast moves through the liver and other parts of the body. This is known as *dynamic contrast-enhanced MRI*.

MRI scans can be very helpful in looking at liver tumours. Sometimes it can tell a benign tumour from a malignant one. It can also be used to look at blood vessels in and around the liver and can help show if liver cancer has spread to other parts of the body.

MRI scans may be a little more uncomfortable than CT scans and it often takes longer. The patient may be placed inside a narrow tube, which is confining and can upset people with a fear of enclosed spaces. Newer, more open MRI machines are now available. The MRI machine also makes buzzing and clicking noises that some patients may find disturbing. Some places will provide earplugs to help block these noises out.

Angiography - An angiogram is an x-ray test for looking at blood vessels. Contrast medium, or dye, is injected into an artery to outline blood vessels while x-ray images are taken. Angiography can be used to show the arteries that supply blood to a liver cancer, which can help doctors decide if a cancer can be removed and to help plan the operation. It can also be used to help guide some types of non-surgical treatment, such as embolisation.

Angiography can be uncomfortable because the doctor doing the test has to put a small catheter (a flexible hollow tube) into the artery leading to the liver to inject the dye. Usually the catheter is put into an artery in the inner thigh and threaded up into the liver artery. A local anaesthetic is often used to numb the area before inserting the catheter. Then the dye is injected quickly to outline all the vessels while the x-rays are being taken.

Angiography may also be done with a CT scanner (CT angiography) or an MRI scanner (MR angiography). These techniques are often used instead of x-ray angiography because it can give information about the blood vessels in the liver without the need for a catheter in the

artery. The patient may still need an IV line so that a contrast dye can be injected into the bloodstream during the imaging.

Bone scan - A bone scan can help look for cancer that has spread to bones. Doctors don't usually order this test for people with liver cancer unless they have symptoms such as bone pain, or if there's a chance that they may be eligible for a liver transplant to treat the cancer.

For this test, a small amount of low-level radioactive material is injected into a vein (IV). The substance settles in areas of damaged bone throughout the entire skeleton over the course of a couple of hours. The patient then lies on a table for about 30 minutes while a special camera detects the radioactivity and creates a picture of the skeleton.

Areas of active bone changes appear as 'hot spots' on the skeleton – that is, it attracts the radioactive substance. These areas may suggest the presence of cancer, but other bone diseases can also cause the same pattern. To distinguish between these conditions, other imaging tests such as plain x-rays or MRI scans, or even a bone biopsy might be needed.

Other Procedures

Other types of tests may be done if the doctor thinks the patient might have liver cancer but the imaging test results aren't conclusive.

Laparoscopy - in this procedure, a doctor inserts a thin, lighted tube with a small video camera on the end through a small incision (cut) in the front of the abdomen to look at the liver and other internal organs. (Sometimes more than one cut is made.) This procedure is done in the operating room. The patient is usually under general anaesthesia (in a deep sleep), although in some cases the patient may only be sedated (made sleepy) and the area of the incision will be numbed.

Laparoscopy can help plan surgery or other treatments and can help doctors confirm the stage (extent) of the cancer. If needed, doctors can also insert instruments through the incisions to remove biopsy samples, which are then looked at under a microscope to make or confirm the diagnosis of cancer.

Laparoscopy is usually done at an outpatient surgery centre. Because the surgeon only makes a small incision to insert the tubes, the patient should not have much pain after surgery. Such patients should be able to go home after they recover from the anaesthesia.

Biopsy - a biopsy is the removal of a sample of tissue to see if there is cancer present. Sometimes, the only way to be certain that liver cancer is present is to take a biopsy and look at it under a microscope.

But in some cases, doctors can be fairly certain that a person has liver cancer based on the results of imaging tests such as CT and MRI scans. In these cases, a biopsy may not be needed. Doctors are often concerned that sticking a needle into the tumour or otherwise disturbing it without completely removing it might help cancer cells spread to other areas. This is a major concern if a liver transplant might be an option to try to cure the cancer, as any spread of the cancer might make the person ineligible for a transplant.

Needle biopsy - for a needle biopsy, a hollow needle is placed through the skin in the abdomen and into the liver. The skin is first numbed with local anaesthesia before the needle is placed. Different sized needles may be used, namely:

- for a fine needle aspiration (FNA) biopsy, tumour cells are sucked into a very thin needle with a syringe
- a core needle biopsy uses a slightly larger needle to get a bigger sample

There are pros and cons to both types of needle biopsies. Fine needle aspirations can usually confirm a cancer, but sometimes it doesn't provide enough information to be sure about the type of cancer. Some doctors prefer a core needle biopsy over an fine needle aspiration, as it provides a larger sample and therefore, more information about the tumour. The risk of complications is lower with a fine needle aspiration, especially when tumours are near large blood vessels.

The doctor may use ultrasound or CT scanning to guide the needle into the tumour. With this approach, the doctor slowly advances the needle while its position is checked by one of these imaging tests. When the images show that the needle is in the tumour, a sample is removed and sent to the lab to be looked at under a microscope.

Laparoscopic biopsy - biopsy specimens can also be taken during laparoscopy. This lets the doctor see the surface of the liver and take samples of abnormal-appearing areas.

Surgical biopsy - in some cases, a biopsy sample may not be obtained until surgery that is meant to treat the tumour. An incisional biopsy (removing a piece of the tumour) or an excisional biopsy (removing the entire tumour and some surrounding normal liver tissue) can be done during an operation since doctors often prefer to know the exact type of tumour before surgery, other types of biopsy methods may also be used.

Laboratory Tests

The treating doctor may order lab tests for a number of reasons:

- to help diagnose liver cancer
- to help determine what might have caused your liver cancer
- to learn how well the liver is working, which may affect what types of treatments the patient can have
- to get an idea of the patient's general health and how well the other organs are working, which also may affect what types of treatments the patient can have
- to see how well treatment is working
- to look for signs that the cancer has come back after treatment

Alpha-fetoprotein blood (AFP) test – this is a blood test to look for alpha-fetoprotein (AFP) in the blood. AFP is normally made by a foetus's liver. It is the main protein during the first three months of development. AFP greatly decreases by age 1 and should only be found in adults in very low levels. It is one of several tumour markers. Tumour markers are molecules in the blood that are higher when a person has certain cancers. AFP is found mainly in liver cancer and non-seminomatous germ cell tumours, which are rare. These are found in the

pineal gland (a small endocrine gland) in the brain. Some people with cirrhosis or chronic active hepatitis also have higher blood levels of AFP.

It can be helpful in determining if a liver mass might be cancer. A low or normal value on this test means it is less likely that the patient has liver cancer, while a high value makes it more likely. This test is not always accurate, so other test and examination results also have to be taken into account.

This test can also be useful in people already diagnosed with liver cancer. The AFP level can help determine what treatment options might be appropriate. During treatment, the test can be used to help give an idea of how well it is working, as the AFP level should go down if treatment is effective. The test can be used after treatment as well, to look for possible signs that the cancer has come back (recurred).

Other Blood Tests

Liver function tests (LFTs) - liver cancer often develops in livers already damaged by hepatitis and/or cirrhosis, therefore, doctors need to know the condition of the patient's liver before starting with treatment. A series of blood tests can help assess the condition of the part of the liver not affected by the cancer. They measure levels of certain substances in the blood that show how well the liver is working.

If the liver is not healthy, the patient might not be able to have surgery to try to cure the cancer, as the surgery might require removal of a large part of the liver. This is a common problem in people with liver cancer.

Blood clotting tests - the liver also makes proteins that help blood clot when one is bleeding. A damaged liver may not make enough of these clotting factors, which could increase the risk of bleeding. The treating doctor may order blood tests such as a prothrombin time (PT) to help assess this risk.

Tests for viral hepatitis - if liver cancer has not yet been diagnosed, the doctor may order blood tests to check for hepatitis B and C. Results showing that a patient has been infected with either of these viruses may make it more likely that the patient has liver cancer.

These tests are also done in people newly diagnosed with liver cancer, if not done previously.

Kidney function tests - tests of blood urea nitrogen (BUN) and creatinine levels are often done to assess how well the patient's kidneys are functioning.

Complete blood count (CBC) - this test measures levels of red blood cells, white blood cells (which fight infections) and platelets (which help with blood clot). It gives an idea of how well the bone marrow, where new blood cells are made, is functioning.

Blood chemistry tests and other tests - blood chemistry tests check the levels of a number of minerals and other substances in the blood, some of which might be affected by liver cancer.

For example, liver cancer can cause blood levels of calcium to rise, while blood glucose levels may fall. Liver cancer may also cause cholesterol levels to go up, so it needs to be checked as well.
(American Cancer Society)

Staging of Liver Cancer
Staging is a way of describing where the cancer is located, if or where it has spread, and whether it is affecting the functions of other organs in the body. Doctors use diagnostic tests to determine the cancer's stage, so staging may not be complete until all of the tests are finished. Knowing the stage helps the doctor decide what kind of treatment is best and can help predict a patient's prognosis (chance of recovery).

For liver cancer, the staging information below is specifically for hepatocellular carcinoma (HCC), based on whether a tumour can be surgically removed, called resectable. When resection is not an option, the doctor will use additional factors, such as overall liver function, to determine the treatment plan and predict prognosis.

Localised resectable**:** cancer is in one place in the liver and the other part of the liver is healthy. The cancer is resectable, meaning it can be removed through surgery.

Localised unresectable**:** cancer is found in one part of the liver, but it cannot be removed by surgery (unresectable). A smaller tumour may not always be removable by surgery because the liver itself is seriously damaged (usually with cirrhosis) and there would not be enough of the liver left after the operation to keep a person healthy.

Advanced**:** cancer has spread throughout the liver and/or to other parts of the body, such as the lungs and bones.

Recurrence**:** recurrent cancer is cancer that comes back after treatment. If there is a recurrence, the cancer may need to be staged again (called re-staging).

To describe the stage in more detail, doctors sometimes use the TNM system, outlined below. This staging system is most useful for patients whose tumour can be surgically removed. This system judges three factors: the tumour itself, the lymph nodes around the tumour, as well as if the tumour has spread to the rest of the body. The results are combined to determine the stage of cancer for each person. There are four stages: stages I through IV (one through four). The stage provides a common way of describing the cancer, so doctors can work together to plan the best treatments.

TNM is an abbreviation for tumour (**T**), node (**N**) and metastasis (**M**). Doctors look at these three factors to determine the stage of cancer:

- How large is the primary tumour and where is it located? **(Tumour, T)**
- Has the tumour spread to the lymph nodes? **(Node, N)**
- Has the cancer metastasised to other parts of the body? **(Metastasis, M)**

Tumour. Using the TNM system, the ‘T’ plus a letter or number (0 to 4) is used to describe the size and location of the tumour. Some stages are also divided into smaller groups that

help describe the tumour in even more detail. If there is more than one tumour, the lowercase letter ‘m’ (multiple) is added to the ‘T’ category. Specific tumour stage information for HCC is listed below.

TX: The primary tumour cannot be evaluated
T0: There is no evidence of a primary tumour
T1: The tumour is 2 centimeters (cm) or smaller. It does not involve nearby blood vessels
T2: Either of these:
- Any tumour that involves nearby blood vessels
- More than one tumour, but none larger than 5 cm

T3a: There is more than one tumour and at least one is larger than 5 cm
T3b: The tumour (of any size) involves the major veins around the liver
T4: Either of these:
- The tumour has spread to the organs near the liver (except the gallbladder)
- The tumour has broken through the visceral peritoneum (layer of tissue that lines the abdomen)

Node. The "N" in the TNM staging system stands for lymph nodes, the tiny, bean-shaped organs that help fight infection. Lymph nodes near the liver are called regional lymph nodes. Lymph nodes in other parts of the body are called distant lymph nodes

NX: The regional lymph nodes cannot be evaluated
N0: Cancer has not spread to the regional lymph nodes
N1: The cancer has spread to the regional lymph nodes

Distant Metastasis. The ‘M’ in the TNM system indicates whether the cancer has spread to other parts of the body.

MX: The tumour cannot be evaluated
M0: The cancer has not spread to other parts of the body
M1: The tumour has spread to another part of the body

Cancer Stage Grouping
Doctors assign the stage of the HCC by combining the T, N, and M classifications

Stage I: This is the earliest stage of HCC. The tumour has not spread to the blood vessels, lymph nodes, or other parts of the body (T1, N0, M0
Stage II: The tumour involves nearby blood vessels, but it has not spread to the regional lymph nodes or other parts of the body (T2, N0, M0)
Stage IIIA: The cancer has not spread beyond the liver, but the area of the cancer is larger than stage I or II (T3a, N0, M0)
Stage IIIB: The cancer involves a major vein around the liver, but it has not spread to nearby lymph nodes or other parts of the body (T3b, N0, M0)
Stage IIIC: Any tumour that has spread to the organs near the liver (except the gallbladder), or if the tumour has broken through the visceral peritoneum. There is no spread to nearby lymph nodes or other parts of the body (T4, N0, M0)

Stage IVA: Any tumour that has spread to the regional lymph nodes but not to other parts of the body (any T, N1, M0)
Stage IVB: Any tumour that has spread to other parts of the body (any T, any N, M1) (Cancer.Net).

Treatment of Liver Cancer
The treatment will depend on the size, location and stage of the tumour and whether it has spread.

Surgery - surgery often offers the best chance for a cure. Surgery may involve removing (resecting) the diseased part of the liver to eliminate the cancer or transplant surgery to remove the liver and replace it with a donor's healthy liver.

Aggressive surgery or a liver transplant can successfully treat small or slow-growing tumours if they are diagnosed early. However, few patients are diagnosed early.

Chemotherapy – chemotherapy which is delivered straight into the liver with a catheter can help, but it will not cure the disease. Sorafenib tosylate (Nexavar), an oral medicine that blocks tumour growth, is now approved for patients with advanced hepatocellular carcinoma.

Radiation therapy – radiation treatments in the area of the cancer may also be helpful. However, many patients have liver cirrhosis or other liver diseases that make these treatments more difficult.
(PubMed Health; MedicineNet; Mayo Clinic).

Prognosis for Liver Cancer Patients
The outcome of liver cancer is extremely variable and depends as much upon the state of the liver and the person's health as on any characteristic of the cancer itself. Patients with more than a solitary tumour in the setting of cirrhosis might not live for six months, while those able to undergo surgery of transplant might be fully cured. Therapies such as radiofrequency ablation, chemo-embolisation, cryo-ablation, radiosurgery, radio-embolisation, and systemic therapy are frequently performed sequentially over a patient's lifetime, depending upon the changes as the disease progresses. Average survival for patients who are able to be treated with these methods is between one and two years.

Despite these grim statistics, there is still room for optimism in this disease. Creative use of multiple techniques can lead to significant prolongation of a patient's life, while keeping them feeling as well as possible. Experimental drugs are becoming increasingly common as researchers have recognised the molecular defects causing this cancer and using this knowledge to develop new targets. The evolution and improvement in radiologic and interventional technology for treating localised tumours has meant that millions of people who would previously never have been treated have experienced meaningful prolongation of their lives. In fact, the chance of living for more than two years with liver cancer has more than doubled since the early 1990s.
(eMedicineHealth).

The course and outcome of liver cancer is dependent on several factors:

Type and location of tumour – hepatic tumours are easily seen and sometimes cured compared to malignancies that originates from the bile ducts and blood vessels

Stage – the extent to which the cancer has spread and the degree of damage it has done to the body

Grade – the severity of the malignancy based on the degree of cell abnormality and how fast the cancer is spreading

Age – on average older individuals show increased mortality rates compared to young adults

Alpha-fetoprotein (AFP) levels – AFP is a plasma protein produced by the foetus, particularly in the liver. Levels are high during the foetal stage. AFP greatly decreases by age 1 and should only be found in adults in very low levels. In adults, AFP is produced by primary liver tumours and germ cell tumours
(Liver Cancer Prognosis Center).

Complications of Liver Cancer
The complications of liver cancer include:

- Budd-Chiari syndrome - hepatic vein obstruction prevents blood from flowing out of the liver and back to the heart. This blockage can cause liver damage. Obstruction of this vein can be caused by a tumour or growth pressing on the vessel, or by a clot in the vessel (hepatic vein thrombosis). Hepatic vein obstruction is the most common cause of Budd-Chiari syndrome
- cancer spread to other organs
- internal bleeding - gastrointestinal bleeding
- liver failure
- tumour rupture.

About Clinical Trials
Clinical trials are research studies that involve people. These studies test new ways to prevent, detect, diagnose, or treat diseases. People who take part in cancer clinical trials have an opportunity to contribute to scientists' knowledge about cancer and to help in the development of improved cancer treatments. They also receive state-of-the-art care from cancer experts.

Types of Clinical Trials
Cancer clinical trials differ according to their primary purpose. They include the following types:

Treatment - these trials test the effectiveness of new treatments or new ways of using current treatments in people who have cancer. The treatments tested may include new drugs or new combinations of currently used drugs, new surgery or radiation therapy techniques, and vaccines or other treatments that stimulate a person's immune system to fight cancer. Combinations of different treatment types may also be tested in these trials.

Prevention - these trials test new interventions that may lower the risk of developing certain types of cancer. Most cancer prevention trials involve healthy people who have not had cancer; however, they often only include people who have a higher than average risk of developing a specific type of cancer. Some cancer prevention trials involve people who have had cancer in the past; these trials test interventions that may help prevent the return (recurrence) of the original cancer or reduce the chance of developing a new type of cancer

Screening - these trials test new ways of finding cancer early. When cancer is found early, it may be easier to treat and there may be a better chance of long-term survival. Cancer screening trials usually involve people who do not have any signs or symptoms of cancer. However, participation in these trials is often limited to people who have a higher than average risk of developing a certain type of cancer because they have a family history of that type of cancer or they have a history of exposure to cancer-causing substances (e.g., cigarette smoke).

Diagnostic - these trials study new tests or procedures that may help identify, or diagnose, cancer more accurately. Diagnostic trials usually involve people who have some signs or symptoms of cancer.

Quality of life or supportive care - these trials focus on the comfort and quality of life of cancer patients and cancer survivors. New ways to decrease the number or severity of side effects of cancer or its treatment are often studied in these trials. How a specific type of cancer or its treatment affects a person's everyday life may also be studied.

Where Clinical Trials are Conducted

Cancer clinical trials take place in cities and towns in doctors' offices, cancer centres and other medical centres, community hospitals and clinics. A single trial may take place at one or two specialised medical centres only or at hundreds of offices, hospitals, and centres.

Each clinical trial is managed by a research team that can include doctors, nurses, research assistants, data analysts, and other specialists. The research team works closely with other health professionals, including other doctors and nurses, laboratory technicians, pharmacists, dieticians, and social workers, to provide medical and supportive care to people who take part in a clinical trial.

Research Team

The research team closely monitors the health of people taking part in the clinical trial and gives them specific instructions when necessary. To ensure the reliability of the trial's results, it is important for the participants to follow the research team's instructions. The instructions may include keeping logs or answering questionnaires. The research team may also seek to contact the participants regularly after the trial ends to get updates on their health.

Clinical Trial Protocol

Every clinical trial has a protocol, or action plan, that describes what will be done in the trial, how the trial will be conducted, and why each part of the trial is necessary. The protocol also includes guidelines for who can and cannot participate in the trial. These guidelines, called eligibility criteria, describe the characteristics that all interested people must have before they can take part in the trial. Eligibility criteria can include age, sex, medical history, and

current health status. Eligibility criteria for cancer treatment trials often include the type and stage of cancer, as well as the type(s) of cancer treatment already received.

Enrolling people who have similar characteristics helps ensure that the outcome of a trial is due to the intervention being tested and not to other factors. In this way, eligibility criteria help researchers obtain the most accurate and meaningful results possible.

National and International Regulations

National and international regulations and policies have been developed to help ensure that research involving people is conducted according to strict scientific and ethical principles. In these regulations and policies, people who participate in research are usually referred to as "human subjects."

Informed Consent

Informed consent is a process through which people learn the important facts about a clinical trial to help them decide whether or not to take part in it, and continue to learn new information about the trial that helps them decide whether or not to continue participating in it.

During the first part of the informed consent process, people are given detailed information about a trial, including information about the purpose of the trial, the tests and other procedures that will be required, and the possible benefits and harms of taking part in the trial. Besides talking with a doctor or nurse, potential trial participants are given a form, called an informed consent form, that provides information about the trial in writing. People who agree to take part in the trial are asked to sign the form. However, signing this form does not mean that a person must remain in the trial. Anyone can choose to leave a trial at any time—either before it starts or at any time during the trial or during the follow-up period. It is important for people who decide to leave a trial to get information from the research team about how to leave the trial safely.

The informed consent process continues throughout a trial. If new benefits, risks, or side effects are discovered during the course of a trial, the researchers must inform the participants so they can decide whether or not they want to continue to take part in the trial. In some cases, participants who want to continue to take part in a trial may be asked to sign a new informed consent form.

New interventions are often studied in a stepwise fashion, with each step representing a different "phase" in the clinical research process. The following phases are used for cancer treatment trials:

Phases of a Clinical Trial

Phase 0. These trials represent the earliest step in testing new treatments in humans. In a phase 0 trial, a very small dose of a chemical or biologic agent is given to a small number of people (approximately 10-15) to gather preliminary information about how the agent is processed by the body (pharmacokinetics) and how the agent affects the body (pharmacodynamics). Because the agents are given in such small amounts, no information is obtained about their safety or effectiveness in treating cancer. Phase 0 trials are also called micro-dosing studies, exploratory Investigational New Drug (IND) trials, or early phase I trials. The people who take part in these trials usually have advanced disease, and no known, effective treatment options are available to them.

Phase I (also called phase 1). These trials are conducted mainly to evaluate the safety of chemical or biologic agents or other types of interventions (e.g., a new radiation therapy technique). They help determine the maximum dose that can be given safely (also known as the maximum tolerated dose) and whether an intervention causes harmful side effects. Phase I trials enrol small numbers of people (20 or more) who have advanced cancer that cannot be treated effectively with standard (usual) treatments or for which no standard treatment exists. Although evaluating the effectiveness of interventions is not a primary goal of these trials, doctors do look for evidence that the interventions might be useful as treatments.

Phase II (also called phase 2). These trials test the effectiveness of interventions in people who have a specific type of cancer or related cancers. They also continue to look at the safety of interventions. Phase II trials usually enrol fewer than 100 people but may include as many as 300. The people who participate in phase II trials may or may not have been treated previously with standard therapy for their type of cancer. If a person has been treated previously, their eligibility to participate in a specific trial may depend on the type and amount of prior treatment they received. Although phase II trials can give some indication of whether or not an intervention works, they are almost never designed to show whether an intervention is better than standard therapy.

Phase III (also called phase 3). These trials compare the effectiveness of a new intervention, or new use of an existing intervention, with the current standard of care (usual treatment) for a particular type of cancer. Phase III trials also examine how the side effects of the new intervention compare with those of the usual treatment. If the new intervention is more effective than the usual treatment and/or is easier to tolerate, it may become the new standard of care.

Phase III trials usually involve large groups of people (100 to several thousand), who are randomly assigned to one of two treatment groups, or “trial arms”: (1) a control group, in which everyone in the group receives usual treatment for their type of cancer, or 2) an investigational or experimental group, in which everyone in the group receives the new intervention or new use of an existing intervention. The trial participants are assigned to their individual groups by random assignment, or randomisation. Randomisation helps ensure that the groups have similar characteristics. This balance is necessary so the researchers can have confidence that any differences they observe in how the two groups respond to the treatments they receive are due to the treatments and not to other differences between the groups.

Randomisation is usually done by a computer program to ensure that human choices do not influence the assignment to groups. The trial participants cannot request to be in a particular group, and the researchers cannot influence how people are assigned to the groups. Usually, neither the participants nor their doctors know what treatment the participants are receiving.

People who participate in phase III trials may or may not have been treated previously. If they have been treated previously, their eligibility to participate in a specific trial may depend on the type and the amount of prior treatment they received.
In most cases, an intervention will move into phase III testing only after it has shown promise in phase I and phase II trials.

Phase IV (also called phase 4). These trials further evaluate the effectiveness and long-term safety of drugs or other interventions. They usually take place after a drug or intervention has been approved by the medicine regulatory office for standard use. Several hundred to several thousand people may take part in a phase IV trial. These trials are also known as post-marketing surveillance trials. They are generally sponsored by drug companies.

Sometimes clinical trial phases may be combined (e.g., phase I/II or phase II/III trials) to minimize the risks to participants and/or to allow faster development of a new intervention.

Although treatment trials are always assigned a phase, other clinical trials (e.g., screening, prevention, diagnostic, and quality-of-life trials) may not be labelled this way.

Use of Placebos

The use of placebos as comparison or "control" interventions in cancer treatment trials is rare. If a placebo is used by itself, it is because no standard treatment exists. In this case, a trial would compare the effects of a new treatment with the effects of a placebo. More often, however, placebos are given along with a standard treatment. For example, a trial might compare the effects of a standard treatment plus a new treatment with the effects of the same standard treatment plus a placebo.

Possible benefits of taking part in a clinical trial

The benefits of participating in a clinical trial include the following:

- Trial participants have access to promising new interventions that are generally not available outside of a clinical trial.
- The intervention being studied may be more effective than standard therapy. If it is more effective, trial participants may be the first to benefit from it.
- Trial participants receive regular and careful medical attention from a research team that includes doctors, nurses, and other health professionals.
- The results of the trial may help other people who need cancer treatment in the future.
- Trial participants are helping scientists learn more about cancer (e.g., how it grows, how it acts, and what influences its growth and spread).

Potential harms associated with taking part in a clinical trial

The potential harms of participating in a clinical trial include the following:

- The new intervention being studied may not be better than standard therapy, or it may have harmful side effects that doctors do not expect or that are worse than those associated with standard therapy.
- Trial participants may be required to make more visits to the doctor than they would if they were not in a clinical trial and/or may need to travel farther for those visits.

Correlative research studies, and how they are related to clinical trials

In addition to answering questions about the effectiveness of new interventions, clinical trials provide the opportunity for additional research. These additional research studies, called correlative or ancillary studies, may use blood, tumour, or other tissue specimens (also known as 'biospecimens') obtained from trial participants before, during, or after treatment.

For example, the molecular characteristics of tumour specimens collected during a trial might be analysed to see if there is a relationship between the presence of a certain gene mutation or the amount of a specific protein and how trial participants responded to the treatment they received. Information obtained from these types of studies could lead to more accurate predictions about how individual patients will respond to certain cancer treatments, improved ways of finding cancer earlier, new methods of identifying people who have an increased risk of cancer, and new approaches to try to prevent cancer.

Clinical trial participants must give their permission before biospecimens obtained from them can be used for research purposes.

When a clinical trial is over

After a clinical trial is completed, the researchers look carefully at the data collected during the trial to understand the meaning of the findings and to plan further research. After a phase I or phase II trial, the researchers decide whether or not to move on to the next phase or stop testing the intervention because it was not safe or effective. When a phase III trial is completed, the researchers analyse the data to determine whether the results have medical importance and, if so, whether the tested intervention could become the new standard of care.

The results of clinical trials are often published in peer-reviewed scientific journals. Peer review is a process by which cancer research experts not associated with a trial review the study report before it is published to make sure that the data are sound, the data analysis was performed correctly, and the conclusions are appropriate. If the results are particularly important, they may be reported by the media and discussed at a scientific meeting and by patient advocacy groups before they are published in a journal. Once a new intervention has proven safe and effective in a clinical trial, it may become a new standard of care.
(National Cancer Institute).

Medical Disclaimer

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