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Original Research Article

A Systematic Review of Clinic Pathology and Survival in Gastrointestinal Stromal Tumors

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ABSTRACT

Gastrointestinal stromal tumor is one of the types of cancer in these organs, especially the stomach and small intestine. It causes symptoms such as abdominal pain, nausea and vomiting, and reluctance to eat. Surgery is usually recommended for its treatment. Sometimes targeted drug treatment is used. Gastrointestinal stromal tumor is a type of cancer that occurs mostly in the stomach and small intestine. If you have symptoms related to stromal tumor or a doctor has diagnosed this cancer, stay with us in this article. In the following, we will explain what are the symptoms of this tumor in the digestive system? Why does this type of cancer occur? Which risk factors increase the risk of developing it? How can this disease be diagnosed? Is GIST curable? How dangerous is this tumor? Gastrointestinal stromal tumor is one of the types of gastrointestinal diseases. Sometimes GIST may be benign. But most of the time, GIST is malignant. Benign and malignant GIST are mostly found in the stomach and small intestine; But it can also occur in other parts of the digestive system. This cancer starts from a special type of nerve cells. These cells are called interstitial cells. Sometimes cancer cells may arise from the precursors of these cells. A stromal tumor or several tumors may appear in the digestive tract. Usually, this disease is common in people between 40 and 70 years old. This cancer is less common in children and young people.

Keywords: GIST, Stomach and Intestine, Cancer, Interstitial Cells.

Introduction

Gastrointestinal stromal tumor treatment

This information represents the views of physicians and nurses serving on the editorial board of the American Cancer Society Cancer Database. These views are based on their interpretation of studies published in medical journals, along with their own professional experience [1-3].

The treatment information contained in this document is not official Society policy and is not intended as medical advice to replace the expertise and judgment of your cancer care team. Once a gastrointestinal stromal tumor (GIST) is found and staged (Figure 1), your cancer care team will discuss treatment options with you [4]. Important factors in determining these options include the characteristics of the tumor (including size, location, growth rate, and whether it has spread) and your overall health.

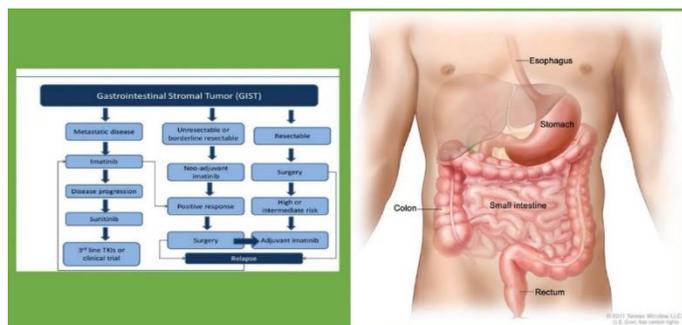


Figure 1. Gastrointestinal stromal tumor treatment

Search strategy and selection of articles

Search in Scopus, Google scholar, PubMed databases and by searching with keywords such as " Clinic Pathology" and " Survival in Gastrointestinal Stromal Tumors" and "Tumors" to obtain articles related to the selected keywords [12]. Case report articles, editorials, and articles that were not published or only an introduction of them were available, as well as summaries of congresses and meetings that were in languages other than English, were ignored. Only the original research articles that evaluated the effectiveness of different drugs in the treatment of COVID-19 using standard methods were studied (figure 2).

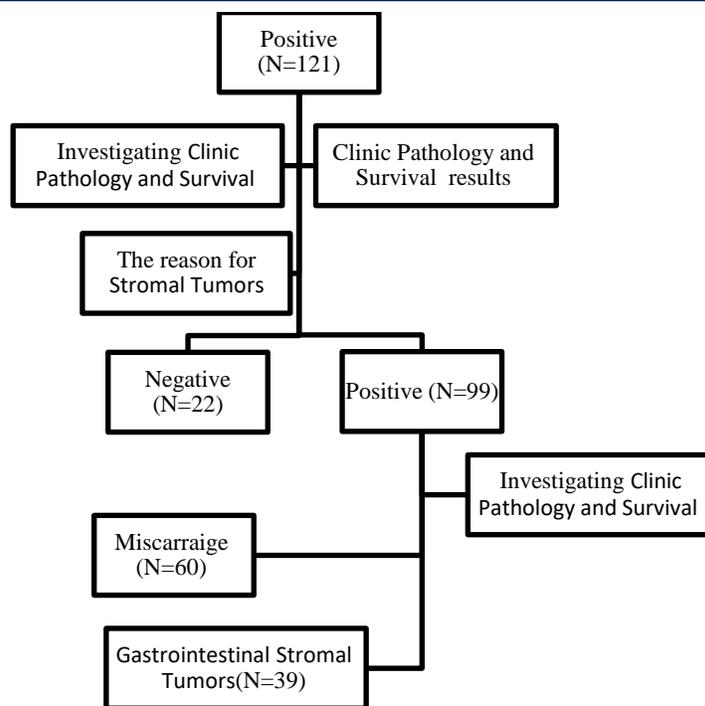


Figure 2. Flow chart of included subjects

The main types of treatment used for GISTs are:

- Surgery;
- Targeted treatment drugs;
- Other treatments, such as chemotherapy and radiation therapy, are used much less frequently.

Depending on your treatment options, you may have different doctors on your treatment team, including:

- **A surgical oncologist:** A doctor who treats cancer with surgery.
- **A clinical oncologist:** A doctor who treats cancer with drugs.
- **A gastroenterologist:** A doctor who specializes in the treatment of diseases of the digestive system.
- **A radiation oncologist:** A doctor who treats cancer with radiation therapy.

Gastrointestinal stromal tissue tumor surgery

The main treatment for a gastrointestinal stromal tumor (GIST) that has not spread is usually surgery. The goal of surgery is to remove all of the cancer. If the tumor is small, it can often be removed along with a small area of surrounding normal tissue [5]. This is done through an incision in the skin, but the

exact type of surgery depends on the location of the tumor. Unlike many other cancers, GIST almost never spreads to lymph nodes, so removal of nearby lymph nodes is usually not needed. For some small cancers, keyhole surgery (laparoscopy) is an option. Instead of making one large incision in the skin to remove the tumor, the surgeon makes several small incisions.

Through an incision, the doctor inserts a thin tube equipped with a light (with a small video camera) called a laparoscope. This allows him to see inside the abdomen. He then uses a long, thin surgical instrument to remove the tumor through other incisions [6-8].

Because the incisions are small, patients usually recover more quickly from this type of surgery than traditional surgery, which requires an incision several inches long. If the tumor is large or is growing to other organs, the surgeon can still try to remove it completely. To do this, the doctor may have to remove parts of the organs. The surgeon may also remove GISTs that have spread to other parts of the abdomen, such as the liver. Another treatment for tumors that are large or have grown into nearby areas is to first give the patient imatinib [9-11]. Regardless of the type of surgery performed, it is very important that it is performed carefully and by a surgeon experienced in treating GISTs (Figure 3). GISTs are often fragile tumors, and surgeons must be careful not to open the lining surrounding them, as this may increase the risk of cancer spreading. Also, GISTs are likely to have a large number of blood vessels, so the surgeon will be careful to control any bleeding from the tumor [12].

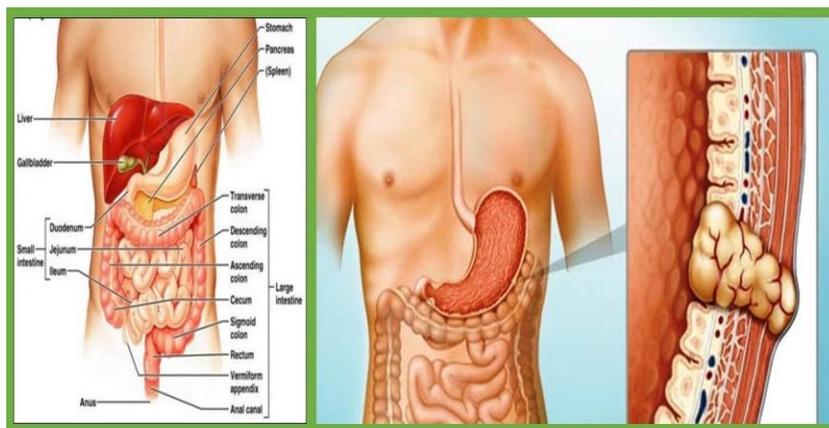


Figure 3. Gastrointestinal stromal tissue tumor surgery

Excision and embolization for the treatment of gastrointestinal stromal tissue tumors

Treatments such as excision and embolization are often used to treat cancers that start in the liver, but they can also be used to treat areas of cancer that have spread to the liver.

Eradication

Eradication can be used to remove tumors within the liver caused by the spread of a gastrointestinal stromal tumor (GIST). This method can be used if there are several small tumors in the liver [13].

Because excision often removes some of the normal tissue surrounding the tumor, it may not be a good option for treating tumors near major blood vessels, the diaphragm (the muscle below the lungs), or major ducts within the liver. You will not usually need to be hospitalized for this type of treatment (Figure 4). Often, eradication can be done without surgery by sending a needle or probe into the tumor through the skin [14]. The needle or probe is guided into the site by ultrasound or CT scan. However, it is sometimes done during surgery to ensure that the treatment is aimed in the right direction.

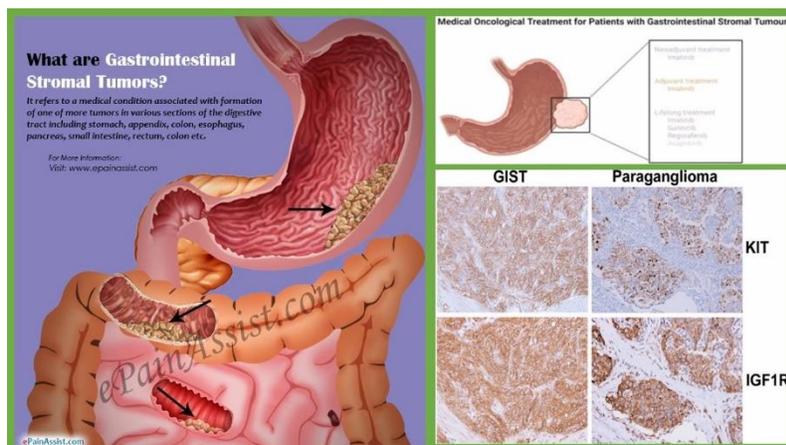


Figure 4. Immunohistochemical Analysis of Tumor Tissues from a Carney Triad Patient

There are different types of rooting:

- **Radiofrequency ablation (RFA)**, which uses high-energy radio waves to heat the tumor and destroy cancer cells.
- **Ethanol eradication**, in which a high concentration of alcohol is injected directly into the tumor to kill cancer cells.
- **Short wave thermotherapy**, in which short waves sent through a probe placed in the tumor are used to heat and destroy cancer cells.
- **Cryosurgery (cryotherapy)**, which uses a thin metal probe to destroy the tumor by freezing it. Sometimes this procedure requires general anesthesia (where you are deeply asleep and unable to feel pain).

Possible side effects after root canal treatment include abdominal pain, infection in the liver, and bleeding into the chest cavity or abdomen. Serious side effects are rare, but can occur.

Embolization

Embolization is a process that injects substances into the cancer cells in the liver in order to try to prevent or reduce the blood flow. The liver is unusual in that it has two sources of blood supply. Most normal liver cells are fed by branches of the portal vein, while cancer cells within the liver are usually fed by branches of the hepatic artery [15]. Blocking the tumor-feeding branch of the hepatic artery is effective in killing cancer cells, but leaves healthiest liver cells unharmed because they are supplied with blood from the portal vein. Embolization reduces part of the blood flow to the normal tissue of the liver, so it may not be a good option for some patients whose liver is damaged by diseases such as hepatitis or cirrhosis [16].

The main type of embolization for the treatment of gastrointestinal stromal tissue tumors that have spread to the liver is arterial embolization (also known as intra-arterial embolization or TAE).

In this method, a probe (narrow flexible tube) is inserted into an artery through a small incision in the inner part of the thigh and is passed up to the hepatic artery inside the liver. At this time, a special type of x-ray, a dye is injected into the bloodstream to help the doctor monitor the path of the vein through angiography. Once the catheter is in place, small particles will be injected into the artery to close it [17-19]. Possible complications after embolization include abdominal pain, fever, nausea, intrahepatic infection, inflammation of the gallbladder, and blood clots in the main blood vessels of the liver. Because healthy liver tissue may be affected, there is a risk of worse liver function after embolization.

Targeted treatment for gastrointestinal stromal tissue tumor

Some drugs are able to target gene changes in GIST cells found in recent years. These drugs work differently than conventional chemotherapy (chemical) drugs [20]. Targeted drugs are very useful in the treatment of GISTs, while conventional chemotherapy drugs are usually not effective. All these drugs are in the form of tablets, which are taken once a day.

Imatinib

Imatinib is used to treat most patients with advanced stage GIST. This drug targets both the KIT and PDGFRA proteins, preventing their ability to cause tumor cells to grow and divide. GIST cells often have too much of these proteins. In general, about 2 out of 3 tumors are reduced by at least half when

treated with imatinib. Some other tumors shrink less or at least stop growing for a while.

This method of treatment will not be useful for a small number of tumors. If a GIST has been completely removed by surgery, many doctors will recommend that you take imatinib for at least a year after the operation to reduce the risk of the cancer coming back [21-23].

Many doctors now recommend imatinib for at least 3 years after surgery for patients who are at higher risk of their tumors coming back (based on tumor size, location, and growth rate). For larger tumors that may be difficult to remove with surgery, imatinib may be used initially to try to shrink the tumor and make the surgery more successful. Often, the drug is given again after surgery. Also, in the case of advanced GISTs that have spread to very distant areas, imatinib is usually the treatment option for surgical removal. The drug probably won't cure such patients, but it can often shrink tumors or slow their growth for several years, helping them live longer and feel better [24]. If the drug stops working and the tumor starts growing again, increasing the dose of imatinib may help prevent growth for a while, but higher doses have more side effects. These side effects may include mild stomach upset, diarrhea, muscle pain, and itchy skin. Stomach upset is reduced if the medicine is taken with food. Imatinib can also cause people to lose fluid [25]. This will often cause slight swelling in the face or ankles. This medicine rarely causes more severe problems if fluid builds up in the lungs or abdomen. It can also affect heart function in some people [26]. Another concern of using this drug to treat large GISTs is that most of these types of tumors have a large number of fragile blood vessels. If imatinib causes rapid tumor size reduction, it may lead to internal bleeding (Figure 5). For this reason, doctors carefully monitor patients when they first start taking this drug.

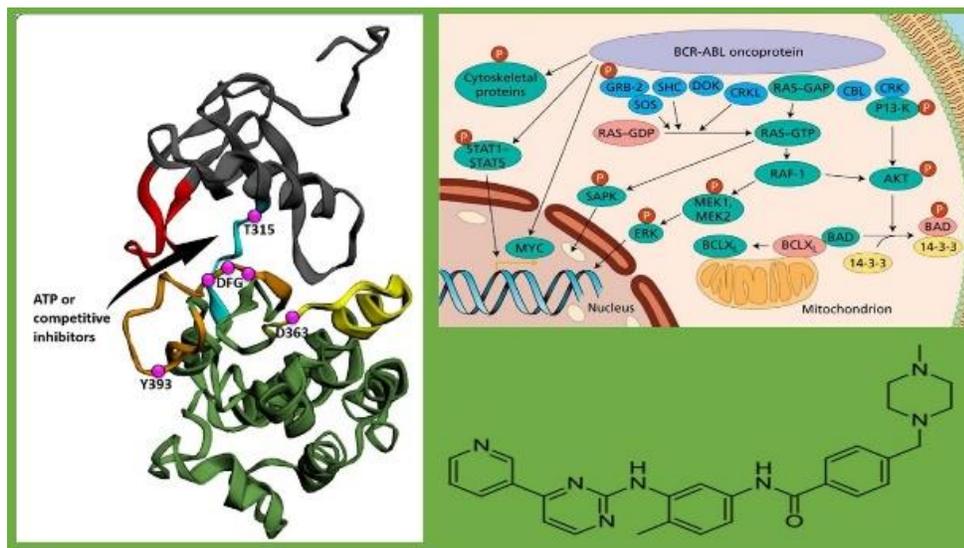


Figure 5. Imatinib

Sunitinib

When imatinib does not work, or patients cannot take imatinib due to its side effects, this drug can be useful in the treatment of GIST. Sunitinib targets KIT and PDGFRA proteins. Sunitinib usually helps some patients by slowing tumor growth. It can also shrink tumors in a small number of patients. More importantly, patients taking this drug may live longer. The most common side effects of sunitinib are lethargy, diarrhea, stomatitis, and skin and hair color changes. More severe side effects can include high blood pressure, increased risk of bleeding, swelling, heart problems, and serious liver problems.

Regorafenib

After imatinib and sunitinib no longer work for patients, they are given regorafenib to treat GIST. This drug targets many proteins, including KIT and PDGFRA. In studies, regorafenib has slowed tumor growth and even made some tumors smaller [27]. However, it has not yet been determined whether it helps patients live longer. Common side effects include diarrhea, lethargy, high blood pressure, stomatitis, hair loss, loss of appetite, and other problems. with redness, pain or even blisters on the palms of the hands and feet (called hand-foot syndrome). More information about the types of drugs considered under targeted therapy can be found in our targeted therapy document.

Chemotherapy for gastrointestinal stromal tissue tumor

Chemotherapy is the use of drugs to treat cancer. In most cases, these drugs are injected into a vein (IV) or given orally. They enter the bloodstream and travel throughout the body, making this treatment potentially useful for cancers that have spread beyond the organ where they started.

Any drug used in the treatment of cancer can be considered chemotherapeutic, even the targeted therapy drugs discussed earlier. But the chemical term is often used to describe certain drugs that attack rapidly growing cells anywhere in the body, including cancer cells. Before the discovery of the use of targeted therapy drugs such as imatinib (Glyoc) in the treatment of gastrointestinal stromal tissue tumors (GISTs), traditional chemical drugs were used. GISTs rarely shrink in response to such drugs, so this type of treatment is rarely used now that targeted drugs are available [28]. Because traditional chemotherapy has not worked well against GISTs, no established chemotherapy regimen is recommended.

It is recommended that patients considering chemotherapy also consider participating in a clinical trial. Chemical drugs attack rapidly dividing cells, which is why they work against cancer cells. But other

cells in the body, such as those in the bone marrow (where new blood cells are made), the lining of the mouth and intestines, and hair buds, also divide rapidly. These cells may also be affected by the chemical drug, which can lead to side effects. Side effects depend on the specific drugs used, their amount and duration of treatment.

The common side effects of the chemical method are:

- Nausea and vomiting;
- Loss of appetite;
- Oral ulcers;
- Diarrhea;
- Hair loss;
- Increased chance of infection (caused by lack of white blood cells);
- Problems with bleeding or bruising (caused by lack of blood platelets);
- Weakness or shortness of breath (caused by low red blood cells).

In addition to the above risks, some chemical drugs can cause other side effects. Most side effects improve as soon as treatment is stopped, but some can persist for a long time. If you have side effects, tell your health care team so they can be treated. There are ways to prevent or treat many of the side effects of chemotherapy. For example, many medications can help prevent or treat nausea and vomiting.

Radiation therapy for gastrointestinal stromal tissue tumor

Radiation therapy is the use of x-rays (or particles) with high energy to kill cancer cells. The radiation method is not very effective in the treatment of gastrointestinal stromal tissue tumors (GISTs), so it is not often used. But it can be used to relieve symptoms such as bone pain. Before your treatment begins, the radiation team will take detailed measurements to determine the correct angles to aim the radiation beams and the appropriate amount of radiation [29]. Radiation therapy is very similar to getting an x-ray, but the radiation is much stronger. This process is painless. The treatment process will only take a few minutes, although the setup time – getting you into position for the treatment – usually takes longer. You may receive radiation treatment for several days in a row. Depending on where the radiation therapy is targeted, side effects may include:

- Skin changes – from redness to blistering and peeling;
- Nausea and vomiting;
- Diarrhea;

- Laxity;
- Low blood cell count.

Most side effects go away shortly after the treatment ends, although it may take longer for the looseness and skin changes to resolve.

Treatment options for gastrointestinal stromal tumor based on tumor spread

Treatment for gastrointestinal stromal tumors (GISTs) depends on the size of the tumor, where it is located, how far it has spread, and how fast it is growing. The main treatment is surgery to remove the tumor whenever possible, but targeted therapies and other treatments may also be helpful in some situations.

Smaller local tumors (Removable)

The main treatment for smallest tumors is surgery. For tumors that are small and not growing fast, this method is often the only treatment needed. A GIST is more likely to come back after surgery if the tumor is larger or did not start in the stomach, or if the cancer cells are dividing rapidly (have a high mitotic rate) [30]. If, based on these factors, the doctor believes that the risk of cancer regrowth is moderate or high, adjuvant treatment with the targeted drug imatinib (Glyoc) is usually recommended for at least one year after surgery. In the case of tumors that are very likely to return, many doctors currently recommend patients to use imatinib for at least 3 years. For some very small tumors that are found incidentally and do not cause any symptoms, another option may be to just keep a close eye on them with an endoscope once or twice a year. If the tumor is not growing, you may not need further treatment.

Larger local tumors (Marginally Removable)

Tumors that are larger or located in certain locations may be more difficult to remove completely, and may require more extensive surgery, which can lead to health problems later on. For this reason, when biopsy is done to confirm a tumor is GIST, treatment with imatinib is usually started.

This will continue at least until the tumor stops shrinking. If the tumor is small enough, surgery may be performed if the doctor believes that the remaining tumor can be safely removed. The patient may continue to take imatinib after surgery to reduce the chance of the cancer coming back. If the tumor does not shrink enough to allow surgery, imatinib is often continued until it seems to be working (Figure 6). If the drug no longer works or if the side effects are too severe, sunitinib may be tried instead. If sunitinib no longer works, the targeted drug regorafenib may help some patients.

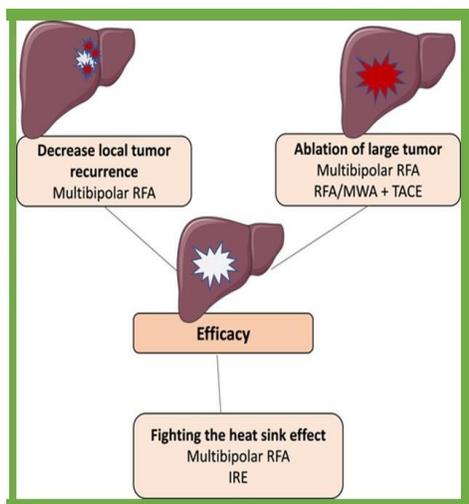


Figure 6. Larger local tumors (Marginally Removable)

Tumors that cannot be removed or have spread to distant areas (Unrespectable Tumors)

Treatment options for GISTs that cannot be surgically removed (unrespectable) or have spread (metastatic) depend on the location and extent of the spread. For many of these tumors, imatinib is the preferred first-line treatment [31]. As long as the tumor does not grow (and the patient can tolerate the side effects of this drug), the drug is continued. If the tumor begins to grow again, it may respond to an increase in the amount of imatinib. If the tumor continues to grow or the side effects from imatinib are too severe, switching to sunitinib may be helpful. If sunitinib no longer works, regorafenib may help some patients. If the tumor shrinks enough with targeted therapy, then surgery may be an option for some patients.

If targeted therapy is still effective, this may be followed by more treatment. If the cancer has spread to only 1 or 2 areas in the abdomen (such as the liver), the surgeon's advice may be to remove the original tumor. If so, be sure to talk to your doctor about the goals of the treatment (trying to cure the cancer, help you live longer, or prevent or reduce symptoms), along with the possible benefits and risks. Usually, this should only be considered for tumors that are slow growing or those that cause local complications such as uncontrollable bleeding. Other options for treating cancers that have spread to the liver include excision and embolization. These treatments may include radiofrequency ablation (RFA; using electric currents to heat the tumor) or ethanol ablation (injecting high-concentration alcohol into the tumor). For eradication, a probe or needle is sent through the skin and guided to the tumor by CT scan (computed tomography) or ultrasound images, then the tumor is destroyed by heat, cold, or alcohol injection. In embolization, substances are injected into the large blood vessels feeding the tumor to block blood flow

and kill cancer cells. These treatments can shrink tumors inside the liver, but are not expected to cure the cancer [32].

Cancers that no longer respond to the targeted drugs discussed above can be difficult to treat. Some doctors may recommend trying other targeted drugs, including sorafenib or nilotinib, although it's not yet clear how beneficial these drugs are. Conventional chemotherapy drugs are usually not that effective. Participating in a clinical trial for a newer treatment may be an option for some people.

Recurrent Tumors

If the cancer returns after treatment, it is called recurrent. If the cancer returns (comes back) in or near the place where it started, it is called a local recurrence. If it recurs in other areas (such as the lung or liver), it is called a distant relapse [33]. Treatment options for GISTs that recur after treatment depend on the location and extent of the recurrence. In many cases of recurrence, as long as the drug is still effective and the patient can tolerate it, treatment with imatinib is probably the best option for small It is a tumor. If the initial dose of imatinib does not work, the dose can be increased.

What is a gastrointestinal stromal tumor (GIST)?

Gastrointestinal stromal tumor is a cancerous soft tissue that may develop in any part of the digestive tract. Gastrointestinal stromal tumor refers to cancerous soft tissue that may develop in any part of the digestive tract; But it mostly occurs in the stomach and small intestine. A GIST tumor begins to form in certain nerve cells in the wall of the digestive tract. These nerve cells are part of the autonomic nervous system and control digestive processes including the movement of food along the intestines. A specific change in the DNA of these nerve cells causes a GIST tumor. A small GIST tumor may not have symptoms and grow so slowly that it does not leave any special effects. People with large GIST tumors usually experience vomiting and bloody stools and should seek medical attention. Other possible symptoms of gastrointestinal stromal tumor include:

Undefined

- Anemia (anemia); Because of tumor bleeding;
- Abdominal pain;
- Sensation of a mass in the abdomen;
- Nausea;
- Vomit;

- Anorexia;
- Weight Loss;
- Difficulty in swallowing.

GIST tumor may develop at any age; But their prevalence is higher between the ages of 50 and 70 and almost never occurs before the age of 40. In rare cases, an inherited genetic mutation causes a gastrointestinal stromal tumor.

Gastrointestinal stromal tumor diagnosis

After asking questions and answers about the symptoms and history of other diseases, the doctor will carefully examine you for the presence of a tumor in the abdomen. If the symptoms indicate that you may have a GIST tumor, tests will be performed to check the location of the tumor and the rate and pattern of its spread to other organs (metastasis).

These tests include:

- **CT scan:** In this test, you will have to swallow a liquid that makes the stomach and small intestine clearer when X-rayed. A contrast agent may also be injected. The scanner then emits multiple X-rays and moves around the abdomen. The computer provides detailed, cross-sectional images of the abdominal organs that show the location and size of the GIST tumor.
- **Endoscopy of the upper part of the digestive tract:** In this test, the doctor examines the inner layer of the esophagus, stomach and the beginning of the small intestine with a flexible tube equipped with light (endoscope) that is inserted through the patient's mouth. It is possible to remove small samples of abnormal tissue during endoscopy. In this test, the patient receives mild sedatives intravenously [34].
- **Endoscopic ultrasound (EUS):** An endoscope is also used in this test; But at the tip of this endoscope, there is an ultrasound probe. The sound waves from the probe produce echoes that return to the probe; Meanwhile, a computer converts these echoes into an image of the structures inside the abdomen that shows the exact location of the tumor. If the tumor has metastasized to the liver or abdominal lining, it can be detected with this test. EUS also helps to identify the depth of the tumor in the stomach wall and other parts of the digestive system.
- **Fine needle aspiration biopsy:** A small sample of tumor tissue is required for a definitive diagnosis of GIST. The preferred method for obtaining a biopsy specimen is EUS with fine-needle aspiration. This process is the same as EUS; with the difference that a thin and

perforated needle is located at the tip of the endoscope. This needle is used to remove small amounts of tissue for laboratory analysis. Sometimes these tests are not possible or even the results are inconclusive. Therefore, in this case, only surgery can help determine the location of the GIST tumor. After removing the tumor, tissue analysis is done.

- **Laboratory tests on the biopsy:** These tests provide the doctor with information about the proteins that the tumor cells produce. One such test, called immunohistochemistry, detects specific proteins controlled by genes in GIST cells. Identifying these proteins helps to decide on treatment.

Sometimes genetic testing of the biopsy sample is needed to determine the location of the GIST genes in the tumor's DNA. GIST tumor cells are also viewed under a microscope to determine the number of cells that are actively dividing. This number is known as "mitotic rate". The higher the mitosis rate of a tumor, the more aggressive the tumor is and the more likely it is to spread to other organs [35].

Gastrointestinal stromal tumor treatment

Small and asymptomatic GIST tumors, in certain cases, may be removed with care.

But in general, treatment approaches for gastrointestinal stromal tumors include two things:

- Surgery;
- Targeted drug therapy.

Surgery

Usually, large and symptomatic GIST tumors are surgically removed; Unless they are too big or involve too many organs and tissues for surgery. Surgery is usually not performed in people whose general health status is high-risk for surgery, such as people who have metastasized GIST. It is usually possible to remove the GIST tumor with small and non-invasive surgeries. In this type of surgery, a tube called a laparoscope and other surgical instruments are inserted into the body through small abdominal incisions [36].

Targeted drug therapy

Targeted drug therapy focuses on specific abnormalities in cancer cells. Targeted drug therapy by eliminating these abnormalities can cause the death of cancer cells. In the case of GIST tumors, these drugs target an enzyme called tyrosine kinase that helps cancer cells grow. The first line of treatment to

prevent the recurrence of stromal tumors of the gastrointestinal tract after surgery is "Imatinib".

Also, this drug is used in the following cases:

- Shrinking tumors before surgery;
- In situations where surgery is not possible;
- Control of recurrent GIST tumors.

Drug therapy is usually continued as long as the drug is effective. If tumors do not respond to imatinib or become resistant to it over time, there are other drugs that target tyrosine kinase. Targeted drug therapy is an active area of cancer research, and new drugs are likely to become available in the future. Gastrointestinal stromal tumors (GISTs) are tumors or clusters of overgrown cells in the gastrointestinal tract. The gastrointestinal tract is the system responsible for digestion and absorption of food and nutrients in the body.

This system consists of the following components:

- Mouth;
- Stomach;
- Small intestine;
- Large intestine (colon).

Gastrointestinal stromal tumors start in special cells that are part of the autonomic nervous system. These cells are embedded in the wall of the gastrointestinal tract and regulate the movement of muscles to absorb food. The majority of gastrointestinal stromal tumors are formed in the stomach.

Sometimes this formation takes place in the small intestine. They are much less common in the colon, esophagus, and rectum. Gastrointestinal stromal tumors may be malignant (cancerous) or benign (noncancerous).

Symptoms of gastrointestinal stromal tumors

Symptoms depend on the size of the tumor and its location. Because of this, they often vary in severity from person to person.

Symptoms of these tumors can include the following:

- Bloody stools;
- Pain or discomfort in the abdomen;
- Nausea and vomiting;
- Ileus;
- A palpable mass in the abdomen;
- Extreme fatigue or feeling very tired;
- A feeling of fullness in the stomach after eating a small amount of food;
- Pain or difficulty swallowing.

Survival Rate

The survival rate shows the percentage of people with the same type and stage of tumors that survive in a period of time after diagnosis. For example, a local survival rate of 93% means that people with this stage of tumor growth are on average 93% more likely to survive for 5 years than people without it [37]. Survival rates are based on statistics from the National Cancer Institute's "Survey, Epidemiology, and End Results Data." It should be remembered that survival rates are only estimates. The body of each patient responds differently to gastrointestinal stromal tumors and their treatment. It should also be noted that survival rates to some extent do not take into account recent treatment advances.

They are determined based on the diagnosis and treatment carried out at least 5 years ago. Based on people diagnosed with gastrointestinal stromal tumors between 2010 and 2016, the 5-year survival rates for each stage are as follows:

- Local: 93 percent;
- Regional: 80 percent;
- With distance: 83% (data metastases);
- Integration of all steps: 83 percent.

Diagnosis of gastrointestinal stromal tumors

To diagnose gastrointestinal stromal tumors, the doctor will first ask about the person's medical history and then perform a clinical examination (Figure 7). If your doctor suspects GISTs, any of the tests listed below can help make the diagnosis:

- **CT scan.** This procedure uses specialized X-rays and provides a detailed image of the gastrointestinal tract.
- **MRI scan.** This scan provides detailed images of the gastrointestinal tract.
- **Upper endoscopy.** An endoscope, a narrow instrument equipped with a light and a lens, enters the gastrointestinal tract through the mouth and allows a visual examination of the organs.
- **Endoscopic ultrasound.** This test uses an endoscope with a probe capable of sending and receiving sound waves. This allows the reflections produced by the sonogram to provide an image of the body's tissues.
- **Fine needle endoscopic ultrasound aspiration biopsy.** Using an endoscope equipped with a fine needle attached to it, the doctor can remove a small sample of the tumor for a biopsy. The biopsy sample is examined under a microscope by a pathologist who can determine the type of tumor. In case of diagnosis of gastrointestinal stromal tumors, other tests may be performed to determine the spread of cancer cells in the body.

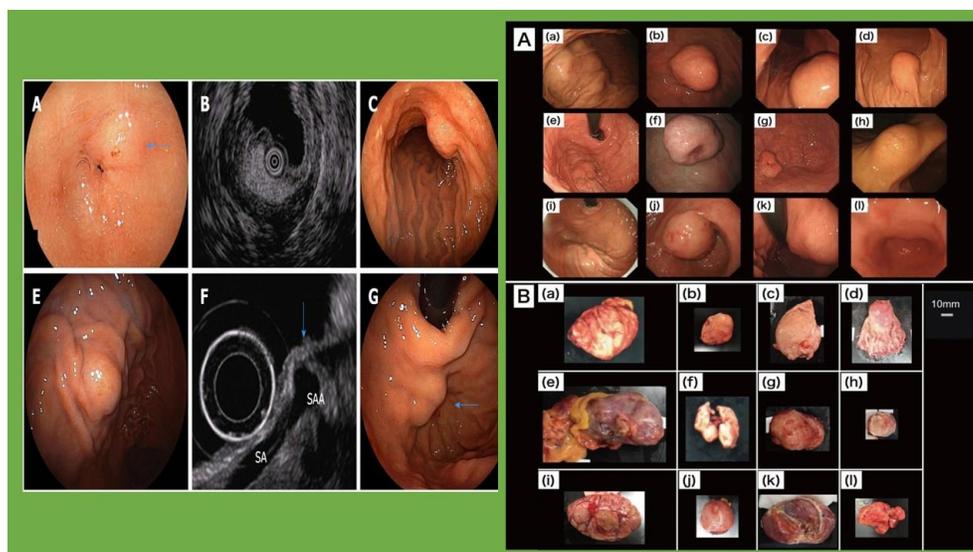


Figure 7. Diagnosis of gastrointestinal stromal tumors

These tests include the following:

- CAT scan;
- MRI;
- X-rays for the chest;
- Positron emission tomography (PET) scan.

PET scan helps the doctor to determine the extent of malignant tumors in the body.

Treatment of gastrointestinal stromal tumors

Treatment options depend on whether the tumor can be surgically removed or whether the cancer has metastasized and spread to other parts of the body.

There are four standard treatments for these tumors:

- **Surgery.** If gastrointestinal stromal tumors have not spread in the body and surgical treatment is safe, the doctor may surgically remove the tumor and surrounding tissue. For this operation, the laparoscopic method may be used, in which a tube called a laparoscope makes incisions in the cancerous position and removes the tissues from there.
- **Targeted treatment.** Your doctor may prescribe drugs such as tyrosine kinase inhibitors (TKIs), which block messages related to the growth of tumors. These drugs are less harmful to healthy cells than chemotherapy or radiation therapy.
- **Vigilant care.** The doctor will monitor the patient's condition but will not prescribe treatment until there is a change in the symptoms or signs [38].
- **Supportive care.** To improve the patient's quality of life, if the gastrointestinal stromal tumor worsens or the treatment causes side effects, this type of care will be provided to the patient. While targeted therapy such as imatinib, sunitinib, and regorafenib may be effective, secondary kit or PDGFRA mutations develop that are resistant to these drugs in 90% of gastrointestinal stromal tumors. The majority of these tumors develop with KIT or PDGFRA mutations.

Gastrointestinal stromal tumor

Gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor of the digestive tract and is mostly seen in the stomach or small intestine. These tumors arise from interstitial cells of Cajal (ICCs) or precursors of these cells. These types of tumors are most often seen in people between 40 and 70 years old, and children and younger people rarely show this disease. Tumors can be cancerous (malignant) or non-cancerous (benign). Early tissue lesions seen in gastrointestinal stromal tumor disease were classified as leiomyoma because they had smooth muscle characteristics under light microscopy.

In the 1970s, evidence from electron microscopy studies identified smooth muscle as the origin of these tumors. In the 1980s, the advent of immunohistochemically techniques showed that these tumors lacked the immunophenotypic characteristics of smooth muscle cells and instead expressed antigens associated with horn cells. Mazur and Clark in 1983 and Schaldenbrand and Appleman in 1984 were the first to use the diagnostic title "stromal tumors" as a separate term.

According to the work of Kindblom and colleagues reported in 1998, the true cell that is the origin of gastrointestinal stromal tumors is a pluripotent mesenchymal stem cell that is programmed to become interstitial cells of Cajal (ICCs). Until the late 1990s, most non-epithelial tumors of the gastrointestinal tract were called gastrointestinal stromal tumors (GIST). At that time, histopathologists were unable to distinguish between the types known today. Later, CD34 and CD117 were identified, which are used as DNA markers to diagnose different types of tumors.

Gastrointestinal stromal tumors (GIST) belong to a group of cancers called soft tissue sarcomas. These cancers spread in the supporting or connective tissues of the body and unlike most tumors of the digestive system, they are non-epithelial. The wall of the digestive system is made up of muscle layers. The origin of this type of tumor is the cells that are between the muscle layers. These specialized cells found in the digestive tract are called interstitial cells. The progenitor cells of these interstitial cells can also be the origin of the tumor. The interstitial cells of Kajal are among the cells of the autonomic nervous system. These cells are sometimes called the "pace maker" cells of the digestive system because they signal the muscles of the digestive system to contract to move food and liquids along the digestive tract.

Clinical symptoms of gastrointestinal stromal tumor

People without family history of this type of tumor (single gastrointestinal stromal tumor); They usually have a tumor. People with a family history of this disease (gastrointestinal stromal tumor) often show multiple tumors and more symptoms, such as excessive and non-cancerous growth (hyperplasia) of other cells in the digestive tract and patches of dark skin in multiple areas of the body [38]. Some people with this cancer also suffer from a skin disease called urticarial pigmentosa or cutaneous mastocytosis, which is characterized by prominent brown patches of skin that burn when touched or itch. Small tumors usually do not cause any signs or symptoms, although some people with a gastrointestinal stromal tumor (GIST) may experience the following symptoms:

- Abdominal pain or swelling;
- Nausea;
- Vomit;
- Loss of appetite;
- Weight Loss;
- Bleeding, which ultimately leads to a decrease in the number of red blood cells (anemia), weakness and fatigue.
- Intestinal bleeding causes black stools and bleeding in the throat or stomach causes blood to rise.
- Sometimes tumors grow so large that they block the passage of food through the stomach or intestines. This blockage causes severe abdominal pain and vomiting and may even cause a hole (perforation). Emergency surgeries are required to remove the blockage.

Risk factors in gastrointestinal stromal tumor

Any factor that increases the probability of a person contracting a disease is called a risk factor. Having these risk factors does not necessarily mean that you will get cancer; In the same way, not having any of these harmful factors will not mean that you will not get sick.

Some factors that increase the risk of gastrointestinal stromal tumor (GIST) include:

- **Age.** This type of tumor often occurs in people older than 50 years.
- **Gender.** These types of tumors are more common in men.
- **Genetics.** Gastrointestinal stromal tumors rarely run in families, and having an affected family member does not greatly increase your risk of developing the disease. Hereditary syndromes that increase the risk of these tumors include familial gastrointestinal stromal tumor syndrome, neurofibromatosis type 1 (NF1) and Carney-Stratakis syndrome.

Gastrointestinal stromal tumor prevalence

Approximately 5,000 new cases of gastrointestinal stromal tumor (GIST) are diagnosed in the United States each year. Of course, this disease must be more common than this estimate because small tumors often remain undiagnosed.

Overview

Gastrointestinal stromal tumors (GIST) are soft tissue sarcomas that can be located in any part of the digestive system. Their most common place is the stomach and small intestine. GISTs originate from specialized nerve cells located in the walls of the digestive system. 4 These cells are part of the autonomic nervous system. A specific change in the DNA of one of these cells, which controls digestive processes such as the movement of food through the intestines, causes a GIST.

Signs

Small GISTs may have no symptoms and grow so slowly that they have no serious effects. People with larger GISTs usually need medical attention when they vomit blood or pass bloody stools because the tumor is bleeding rapidly (heavily).

Other possible symptoms of GIST include:

- Anemia, caused by gradual tumor bleeding;
- Abdominal pain;
- Changes that a person may feel in the abdominal area;
- Nausea;
- Vomit;

- Loss of appetite;
- Weight Loss;
- Problem (disorder) in swallowing.

GISTs can develop at any age, but are most common between the ages of 50 and 70 and almost never occur before the age of 40. In rare cases, an inherited genetic change (mutation) causes GIST formation [39].

Diagnosis

After asking about symptoms and medical history, the doctor carefully examines the patient's abdomen to check for tumor growth. If the signs and symptoms indicate the presence of GIST, tests are performed to determine its location, to check the possibility of its spread (metastasis) to other organs.

Treatment

Small, asymptomatic GISTs can be found during testing for other diseases in carefully selected cases.

Surgery

Large or symptomatic GISTs are usually surgically removed unless they are too large or involve too many organs and tissues for surgery. Also, surgery is delayed or avoided in people whose general health makes any surgery too risky, and also in people with metastatic GIST. GIST can be repaired using minimally invasive surgery, which can insert a viewing tube (laparoscope) and surgical instruments through small incisions in the abdomen.

Targeted drug therapy

Targeted drugs attack specific weaknesses in cancer cells by blocking these abnormalities, killing cancer cells. In GISTs, these drugs target an enzyme called tyrosine kinase that causes cancer cells to grow. Imatinib (Glyoc) is the first line of treatment used to prevent recurrence of GIST after surgery.

This drug is also used to shrink the tumor before surgery, in situations where surgery is not possible, and also to control recurrent GIST. Treatment generally continues as long as the drug is effective. If the GIST does not respond to imatinib or is resistant to it, other drugs that target tyrosine kinase are recommended. Targeted drug therapy research is very active in cancer research, and new drugs are likely to become available in the future. Gastrointestinal stromal tumors are the most common mesenchymal tumors of the digestive tract. These tumors have a low prevalence compared to the tumors originating

from the mucosa, so there are fewer studies and documents available in this regard. In this article, a summary of the available studies has been discussed. These tumors originate from the mesenteric ganglion cells of the digestive tract wall. Most of these tumors express CD34 and C-Kit antigens, which makes it possible to differentiate these tumors from other mesenchymal tumors. The clinical manifestations of these tumors are not specific and their most common clinical symptom is prolonged gastrointestinal bleeding. Endoscopy and endo-sonography are helpful in diagnosing these lesions. Imatinib, by inhibiting intracellular tyrosine kinase, is an effective drug treatment in the treatment of these patients with advanced and metastatic tumors, which is used both as a pre-surgical treatment and as an adjunct to surgery.

Discuss

Gastrointestinal stromal tumors, the most common of them, are members of a digestive tract mesenchyme. They are a large family that can include the esophagus, stomach, small intestine, large intestine, omentum, and mesentery. The real prevalence of these tumors can hardly be determined. In general, these tumors of the digestive system are more common in patients, and in men they are more than 50 years old, their incidence is rare before 40 years. The GI tract breaks down food for energy and clears the body of solid waste. After chewing and swallowing food, it passes through the esophagus, the tube that carries food from the throat and chest to the stomach.

The esophagus joins the stomach just below the diaphragm (the thin band of muscle below the lungs). The stomach is a bag-like organ that helps the digestion process by mixing food with gastric juice. Food and gastric juices are then emptied into the small intestine. The small intestine, which is about 20 feet long, continues to break down food and absorb most of the nutrients into the bloodstream. The small intestine joins the large intestine; the first part of the large intestine is a muscular tube about 1.5 meters long [31].

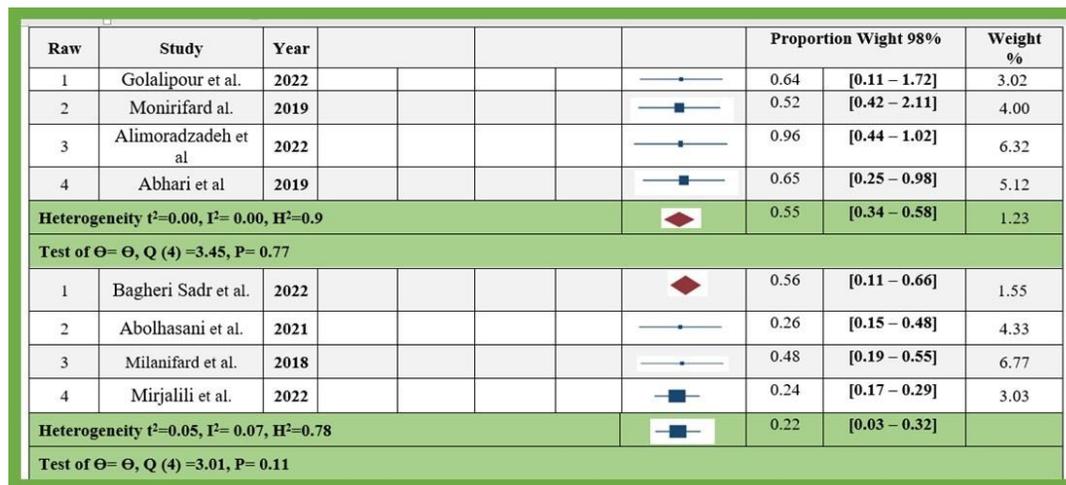


Figure 8. Forest plot showed Gastrointestinal Stromal Tumors

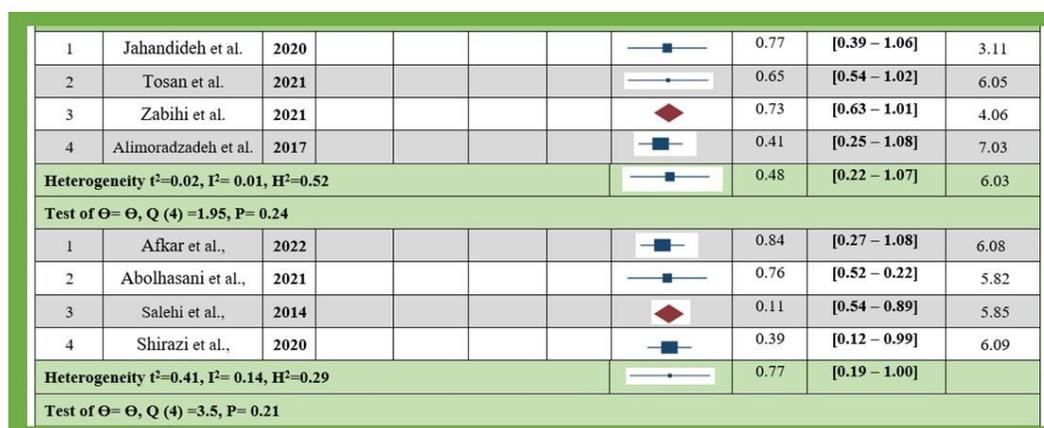


Figure 9. Forest plot showed Clinicopathology

The large intestine absorbs water and mineral nutrients from the remaining food. The waste left after this process (feces) goes into the rectum and is stored there until it leaves the body through the anus. A color image of the digestive system showing the location of the esophagus, stomach, pancreas, rectum, large intestine, small intestine, gallbladder, and liver. Gastrointestinal stromal tumors (GIST) are soft tissue sarcomas that can be located in any part of the digestive system. Their most common place is the stomach and small intestine. GISTs originate from specialized nerve cells located in the walls of the digestive system. These cells are part of the autonomic nervous system. A specific change in the DNA of one of these cells, which controls digestive processes such as the movement of food through the intestines, causes a GIST.

Symptoms of stromal tumors of the digestive tract

Small GISTs may have no symptoms and grow so slowly that they have no serious effects. People with larger GISTs usually need medical attention when they vomit blood or pass bloody stools because the tumor is bleeding rapidly (heavily).

Other possible symptoms of GIST include:

- Anemia, caused by gradual tumor bleeding;
- Abdominal pain;
- Changes that a person may feel in the abdominal area;
- Nausea;
- Vomit;
- Loss of appetite;
- Weight Loss;
- Problem (disorder) in swallowing.

GISTs can develop at any age, but are most common between the ages of 50 and 70 and almost never occur before the age of 40. In rare cases, an inherited genetic change (mutation) causes GIST to form.

Diagnosis of stromal tumors of the digestive tract

After asking about symptoms and medical history, the doctor carefully examines the patient's abdomen to check for tumor growth. If the signs and symptoms indicate the presence of GIST, tests are performed to determine its location, to check the possibility of its spread (metastasis) to other organs. These tests may include the following:

- Computed tomography (CT) scan with contrast. For this test, the patient swallows a liquid that makes the person's stomach and small intestine visible more clearly on X-rays. The patient may also be injected with a similar substance.
- Then, moving on the abdomen, the scanner takes many X-ray images, and the computer provides X-rays in the form of detailed cross-sectional images of the abdominal organs that show the size and location of the tumor.
- Upper endoscopy. The doctor examines the lining of the esophagus, stomach, and the first part of the small intestine with a flexible, clear tube (endoscope) that passes through the mouth.
- Small samples of abnormal tissue may be removed during an upper endoscopy. During the test,

the patient will receive a sedative (analgesic) through an intravenous injection.

- Endoscopic ultrasound (EUS). In this test, an endoscope is used, which has an ultrasound probe at its tip. At the same time as sound waves are generated from the probe, echoes return to the probe, the computer converts the echoes into the shape of the internal structures of the abdomen and shows the exact location of the tumor.
- If the tumor has metastasized to the liver or the lining of the patient's abdomen, these areas may also be visible. EUS is also helpful in detecting the depth of a tumor in the stomach wall or other places in the digestive tract.
- Fine needle aspiration sampling. A small sample of tumor tissue is required for a definitive diagnosis of GIST. The preferred method for obtaining a biopsy sample is endoscopic ultrasound with fine needle aspiration.
- Laboratory tests based on sampling. These tests provide information about the proteins that cancer cells make. One of these tests is called immunohistochemistry, which detects specific proteins that are controlled by genes in GIST cells.
- Identification of these proteins helps in therapeutic diagnosis. Sometimes, genetic testing of the biopsy is necessary to detect the position of the GIST genes in the tumor DNA. GIST cells are examined under a microscope to see how many cells are actively dividing from each of 50 different microscopic fields. This number is considered as the rate of mitosis. The higher the rate of mitosis, the more aggressive the tumor is and the more likely it is to spread to other organs.

Surgery for stromal tumors of the digestive tract

Large or symptomatic GISTs are usually surgically removed unless they are too large or involve too many organs and tissues for surgery. Also, surgery is delayed or avoided in people whose general health makes any surgery too risky, and also in people with metastatic GIST. GIST can be repaired using minimally invasive surgery that can insert a viewing tube (laparoscope) and surgical instruments through small incisions in the abdomen.

Conclusion

Targeted drugs attack specific weaknesses in cancer cells by blocking these abnormalities, killing cancer cells. In GISTs, these drugs target an enzyme called tyrosine kinase that causes cancer cells to grow. Imatinib (Glyoc) is the first-line treatment used to prevent recurrence of GIST after surgery. This

drug is also used to shrink the tumor before surgery, in situations where surgery is not possible, and also to control recurrent GIST. Treatment generally continues as long as the medication is effective. If GIST does not respond to or is resistant to imatinib, other drugs that target tyrosine kinase are recommended. Targeted drug therapy research is very active in cancer research, and new drugs are likely to become available in the future. Gastrointestinal stromal tumors are mesenteric tumors that are specific to the digestive system and are the result of gene mutations. The most common location of these tumors is in the stomach and then the small intestine. 40-60% occur in the stomach, 30-40% in the small intestine, and 3-5% in the duodenum. The most common symptom of stromal tumors of the gastrointestinal tract is chronic and mild gastrointestinal bleeding, which then manifests suddenly and severely. Diagnosis is by endoscopy and biopsy.

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