Carcinoid (Neuroendocrine) Tumors: Staging and Treatment

What is staging for cancer?

Staging is the process of learning how much cancer is in your body and where it is. Tests like blood tests, urine tests, barium studies, biopsies, CTs, and MRIs are done to help stage your cancer. Your providers need to know about your cancer and your health so that they can plan the best treatment for you.

Staging looks at the size of the tumor and where it is, and if it has spread to other organs. In the past, carcinoid (also called neuroendocrine tumors or NET) tumors did not have a formal staging system. They were staged as:

- Localized: The tumor has not spread beyond the wall of the organ or the place it started.
- Regional: The tumor has spread beyond the organ to nearby tissues and lymph nodes.
- Distant Metastatic Spread: The tumor has spread to distant organs and tissues.

The “TNM system,” as described by the American Joint Committee on Cancer is now also used to stage carcinoid tumors of the stomach, duodenum, ampulla, jejunum, ileum, colon/rectum, pancreas, and appendix. It has three parts:

- T-describes the size/location/extent of the “primary” tumor.
- N-describes if the cancer has spread to the lymph nodes.
- M-describes if the cancer has spread to other organs (metastases).

Your healthcare provider will use the results of the tests you had to determine your TNM result and combine these to get a stage from 0 to IV.

How is carcinoid cancer staged?

Staging is based on:

- The size of your tumor.
- Any evidence of spread to other organs (metastasis).
- Surgery to test if your lymph nodes have cancer cells.

Staging is important because it helps guide your treatment options. You may be given both a TNM stage, and may also be told if your cancer is localized, regional, or if you have distant metastatic spread.

The staging system is very complex. Below is a summary of the staging systems. Talk to your provider about the stage of your cancer.

Stomach

- Stage 1 (T1, N0, M0): The tumor is not bigger than 1cm across and has grown into deeper layers like the lamina propria or submucosa. It is not in the lymph nodes or other parts of the body.
- Stage II (T2, N0, M0): The tumor is bigger than 1cm across and has grown into the lamina propria and/or the submucosa or the stomach muscle layer. It is not in the lymph nodes or other parts of the body.
- Stage II (T3, N0, M0): The tumor is in the muscularis propria and the submucosa. It is not in the lymph nodes or other parts of the body.
- Stage III (T4, N0, M0): The tumor has grown into the serosa, the visceral peritoneum, or nearby organs or structures. It is not in the lymph nodes or other parts of the body.
- Stage III (Any T, N1, M0): The tumor is any size and has or has not grown into nearby structures. It has spread to lymph nodes but not distant parts of the body.
- Stage IV (Any T, Any N, M1): The tumor is any size and has or has not grown into nearby structures or lymph nodes, and has spread to other parts of the body.

### Jejunum/Ileum

- Stage I (T1, N0, M0): The tumor is not bigger than 1cm across and has grown into deep layers like the lamina propria or submucosa. It is not in the lymph nodes or other parts of the body.
- Stage II (T2, N0, M0): The tumor has grown into the lamina propria or submucosa and is bigger than 1cm across OR the tumor has grown into the muscularis propria. It is not in the lymph nodes or other distant parts of the body.
- Stage II (T3, N0, M0): The tumor has grown through the muscularis propria and in the subserosa. It is not in the lymph nodes or other parts of the body.
- Stage III (T4, N0, M0): The tumor has grown into the serosa or visceral peritoneum or into nearby organs or structures. It is not in the lymph nodes or other distant parts of the body.
- Stage III (Any T, N1 or N2, M0): The tumor is any size, may or may not have grown into nearby structures, has spread to the lymph nodes, but not to distant parts of the body.
- Stage IV (Any T, Any N, M1): The tumor is any size, may or may not have spread to nearby lymph nodes, and it has spread to distant parts of the body.

### Colon or Rectum

- Stage I (T1, N0, M0): The tumor is not more than 2cm across and has grown into deeper layers like the lamina propria and the submucosa. It is not in the lymph nodes or distant parts of the body.
- Stage IIA (T2, N0, M0): The tumor is 2cm across or bigger and has grown into the lamina propria and/or submucosa; OR the tumor has grown into the muscularis propria. It is not in the lymph nodes or distant parts of the body.
- Stage IIB (T3, N0, M0): The tumor has grown through the muscularis propria into the subserosa but not into the lymph nodes or distant parts of the body.
- Stage IIIB (Any T, N1, M0): The tumor is any size, may or may not have grown into nearby structures, has spread to the lymph nodes, but not to distant parts of the body.
- Stage IV (Any T, Any N, M1): The tumor is any size and may or may not have grown into nearby structures, it may or may not have spread to nearby lymph nodes, and it has spread to distant parts of the body.

### Pancreatic

- Stage I (T1, N0, M0): The tumor is less than 2cm and only in the pancreas. It is not in the lymph nodes or in distant parts of the body.
- Stage II (T2, N0, M0): Tumor is between 2 and 4cm across and only in the pancreas. It is not in the lymph nodes or in distant parts of the body.
- Stage II (T3, N0, M0): The tumor is more than 4cm across and is still in the pancreas, or has grown into the duodenum, or the common bile duct. It is not in the lymph nodes or in distant parts of the body.
- Stage III (T4, N0, M0): The tumor has grown into nearby organs or blood vessels. It is not in the lymph nodes or in distant parts of the body.
- Stage III (Any T, N1, M0): The tumor is any size and has or has not grown outside of the pancreas. It has spread to nearby lymph nodes but not distant parts of the body.
- Stage IV (Any T, Any N, M1): The tumor is any size, may or may not have grown outside of the pancreas, may or may not be in the lymph nodes, and has spread to distant parts of the body.

### Appendix

- Stage I (T1, N0, M0): The tumor is no bigger than 2cm across and it has not spread to the lymph nodes or distant parts of the body.
- Stage II (T2, N0, M0): The tumor is between 2 and 4 cm across and has not spread to the lymph nodes or distant parts of the body.
- Stage II (T3, N0, M0): The tumor is bigger than 4 cm across or has grown into the subserosa or mesoappendix. It has not spread to the lymph nodes or distant parts of the body.
- Stage III (T4, N0, M0): The tumor has grown into the peritoneum that covers the appendix or into nearby organs or structures. It has not spread to the lymph nodes or distant parts of the body.
- Stage III (Any T, N1, M0): The tumor is any size, has or has not grown into nearby structures, and has spread to the lymph nodes but not distant parts of the body.
- Stage IV (Any T, Any N, M1): The tumor is any size, has or has not grown into nearby structures, has or has not spread to the lymph nodes, and has spread to distant parts of the body.

**Lung**

- Occult (hidden) cancer (TX, N0, M0): The main tumor cannot be assessed, and its location can’t be determined. The cancer has not spread to nearby lymph nodes or distant parts of the body.
- Stage 0 (Tis, N0, M0): The tumor is only in the top layers of cells lining the air passages, it is not in the nearby lymph nodes or distant parts of the body.
- Stage IA1 (T1a, N0, M0): The tumor is not bigger than 1 cm across, is not in the membranes that surround the lungs, and is not affecting the main branches of the bronchi. It is not in the lymph nodes or distant parts of the body.
- Stage IA2 (T1b, N0, M0): Tumor is between 1 and 2 cm across, is not in the membranes that surround the lungs, and is not affecting the main branches of the bronchi. It is not in the lymph nodes or distant parts of the body.
- Stage IA3 (T1c, N0, M0): Tumor is between 2 and 3 cm across but has not affected the membrane around the lungs or the main branches of the bronchi. It has not spread to lymph nodes or distant parts of the body.
- Stage IB (T2a, N0, M0): The cancer has not spread to the lymph nodes or distant parts of the body and meets one or more of the following criteria:
  - The tumor is between 3 and 4 cm across.
  - It has grown into the main bronchi but not within 2 cm of the carina and is not more than 4 cm across.
  - It has grown into the visceral pleura.
  - It is clogging some of the airways.
- Stage IIA (T2b, N0, M0): It has not spread to the lymph nodes or distant parts of the body and meets one or more of the following criteria:
  - Is between 4 and 5 cm across.
  - Has grown into the main bronchus but not within 2 cm of the carina.
  - It has grown into the visceral pleura.
  - It is clogging some of the airways.
- Stage IIB (T1a/T1b/T1c, N1, M0): The tumor is smaller than 3 cm across and has not grown into the membranes around the lungs or affected the main branches of the bronchi. It has spread to lymph nodes within and around the lungs and are on the same side as the cancer, but has not spread to distant parts of the body.
- Stage IIB (T2a/T2b, N1, M0): The tumor has spread to the lymph nodes within the lung and/or the area where the bronchus enters the lung. These nodes are on the same side as the cancer but has not spread to other parts of the body. The tumor also meets one or more of the following criteria:
  - It is between 3 and 5 cm across.
  - It has grown into the main bronchus but not within 2 cm of the carina.
  - It has grown into the visceral pleura.
  - It is partially blocking the airways.
- Stage IIB (T3, N0, M0): The cancer has not spread to lymph nodes or distant parts of the body and meets one or more of these criteria:
  - Is 5 to 7 cm across.
  - Has grown into the chest wall, parietal pleura, the phrenic nerve, or the parietal pericardium.
  - There are 1 or more nodules in the same lung lobe.
- Stage IIIA (T1a/T1b/T1c, N2, M0): The cancer is no bigger than 3cm across and has not grown into the membrane around the lungs and does not affect the bronchi main branches. It has spread to the lymph nodes around the carina or the mediastinum. The nodes are on the same side as the primary tumor. It has not spread to distant parts of the body.

- Stage IIIA (T2a/T2b, N2, M0): It has spread to the lymph nodes around the carina or in the mediastinum. The nodes are on the same side as the primary tumor. It has not spread to distant parts of the body. It also meets one or more of the following criteria:
  - Is between 3 and 5cm across.
  - Has grown into the main bronchus but not within 2cm of the carina.
  - It has grown into the visceral pleura.
  - It is partially blocking the airways.

- Stage IIIA (T3, N1, M0): The cancer has spread to the lymph nodes in the lung and/or where the bronchus enters the lung. The nodes are on the same side as the cancer but has not spread to distant parts of the body. It also must meet one or more of the following criteria:
  - It is between 5 and 7cm across.
  - It has grown into the chest wall, the parietal pleura, the phrenic nerve, or the sac surrounding the heart.
  - There are 2 or more nodules in the same lobe of the lung.

- Stage IIIA (T4, N0 or N1, M0): The cancer may or may not have spread to nodes in the lung and/or around the area where the bronchus enters the lung. Affected lymph nodes are on the same side as the cancer but it has not spread to distant parts of the body. It also must meet one or more of the following criteria:
  - Larger than 7cm across.
  - Grown into the mediastinum, the heart, the large blood vessels near the heart, the windpipe, the diaphragm, the backbone, or the carina.
  - There are 2 or more separate tumor nodules in different lobes of the same lung.

- Stage IIIB (T1a/T1b/T1c, N3, M0): The cancer is no bigger than 3cm across, has not grown into the membrane around the lungs or the main branches of the bronchi. It has spread to lymph nodes near the collarbone on either side of the body, and/or to the hilar or mediastinal lymph nodes on the other side from the primary tumor. It has not spread to distant parts of the body.

- Stage IIIB (T2/T2b, N3, M0): The cancer has spread to the lymph nodes near the collar bone on either side of the body, and/or has spread to hilar or mediastinal lymph nodes on either side of the body from the primary tumor. It has not spread to distant parts of the body and meets one or more of the following criteria:
  - It is 3 to 5cm across.
  - It has grown into the main bronchus but not within 2cm of the carina.
  - It has grown into the visceral pleura.
  - It is partially blocking the airways.

- Stage IIIB (T3, N2, M0): It has spread to the nodes around the carina or in the mediastinum. The nodes are on the same side as the primary tumor but has not spread to distant parts of the body. It also meets one or more of the following criteria:
  - It is 5 to 7cm across.
  - It has grown into the chest wall, the parietal pleura, the phrenic nerve, or the parietal pericardium.
  - There are 2 or more nodules in the same lung lobe.

- Stage IIIB (T4, N2, M0): The cancer has spread to lymph nodes around the carina or in the mediastinum. The nodes are on the same side as the primary tumor. The cancer has not spread to distant parts of the body. It also must meet one or more of the following criteria:
  - It is larger than 7cm across.
  - It has grown into the mediastinum, the heart, the large blood vessels near the heart, the windpipe, the esophagus, the diaphragm, the backbone, or the carina.
  - There are 2 or more nodules in different lobes of the same lung.

- Stage IIIC (T3, N3, M0): The cancer has spread to lymph nodes near the collarbone on either side of the body and/or has spread to hilar or mediastinal nodes on the side opposite of the primary tumor. The cancer has not spread to distant parts of the body.
- Stage IIIC (T4, N3, M0): The cancer has spread to lymph nodes near the collar bone on either side of the body and/or has spread to hilar or mediastinal nodes on the opposite side of the primary tumor. It has not spread to distant parts of the body. It also must have one or more of the following criteria:
  - It is larger than 7cm across.
  - It has grown into the mediastinum, the heart, the large blood vessels near the heart, the windpipe, the esophagus, the diaphragm, the backbone, or the carina.
  - There are 2 or more nodules in different lobes of the same lung.

- Stage IVA (Any T, Any N, M1a): The cancer is any size and may or may not have grown into nearby structures and nearby lymph nodes. Also, one of these criteria must be met:
  - It has spread to the other lung.
  - Cancer cells are found in the fluid around the lung.
  - Cancer cells are found in the fluid around the heart.

- Stage IVA (Any T, Any N, M1b): The cancer can be any size. It may or may not have grown into nearby structures and lymph nodes. It has spread to a distant part of the body like nodes, the liver, bones, or brain.

- Stage IVB (Any T, Any N, M1c): The cancer is any size and may or may not have grown into nearby structures or lymph nodes. It has spread as more than one tumor outside the chest to areas like the nodes, liver, bones, or brain.

Depending on the stage of your cancer, your provider may want more tests to see if the cancer has spread to any other organs and nearby lymph nodes. Your providers will talk with you about what is needed to stage your cancer.

**How is carcinoid cancer treated?**

Treatment for carcinoid cancer depends on many factors, like your cancer stage, where the cancer is found, age, overall health, and testing results. Your treatment may include:

- Surgery.
- Chemotherapy.
- Radiation Therapy.
- Hormone Therapy.
- Other Medications
- Clinical Trials.

**Surgery**

The type of surgery you have depends on where your tumor is, if it has spread, and what side effects it is causing. Surgery may be done to remove part or all of the tumor, lymph nodes, and parts or all of organs affected by the cancer. In some cases, surgery can also help manage side effects. These side effects can include having a hard time breathing, blockage in the intestine, and secretion of hormones.

There is also a procedure called radiofrequency ablation (RFA). It can be used to destroy liver tumors. A probe that makes high-frequency radio waves is placed in the tumor. This heats and destroys the tumor. RFA is often done in an interventional radiology (IR) clinic.

**Chemotherapy**

Chemotherapy is the use of medications to treat cancer. They are given intravenously (IV, into a vein) or in pill form and can travel through the body to kill cancer cells. Chemotherapy can be used in some cases and clinical trials are being done to determine which medications work best. It is currently used to treat carcinoid tumors that have spread to other organs or are causing side effects that aren’t managed with other types of medications. Some of the chemotherapies that are being used are streptozocin, 5-fluorouracil, cisplatin, etoposide, and doxorubicin.

A directed form of chemotherapy, called chemoembolization, can be used to treat liver metastasis. A catheter (a hollow, flexible tube) is threaded through an artery that leads to the liver (intra-arterial therapy) and chemotherapy is put through the catheter to
the arteries that feed the tumor. A high dose of chemotherapy can then be given into the tumor while sparing the rest of the body from high doses of chemotherapy. Another form of intra-arterial therapy delivers a compound which blocks off the artery along with the chemotherapy. Chemoembolization allows the direct delivery of chemotherapy but also cuts off the blood supply to the tumor.

**Radiation**

Radiation is the use of high energy x-rays to kill cancer cells. Radiation is not often used to treat carcinoid tumors themselves, rather it is used to treat metastasis in the bones and other parts of the body. The radiation is used to relieve the symptoms caused by metastasis such as pain.

**Hormone Therapy**

Carcinoid syndrome is a group of symptoms caused by the release of substances in the body such as serotonin, histamine, and substance P. It most commonly affects those with carcinoid tumors in the small bowel. Symptoms can be brought on by certain foods. These foods include blue cheese and chocolate that contain tyramine, and wine and beer that contain ethanol. Carcinoid syndrome leads to:

- Flushing and Telangiectasia (collections of tiny blood vessels that develop close to the surface of the skin on the face).
- Diarrhea.
- Fast heart rate and lower blood pressure.
- Bronchospasm (closing of the airway making it hard to breathe).
- Pellagra (dry, scaly skin, dry cracked skin at the edges of the mouth, swollen tongue, diarrhea, and mental confusion).
- Right-sided heart disease or failure.

Hormone therapy can be used to control carcinoid syndrome by evening out the endocrine system and blocking the release of hormones causing the symptoms. These medications are called somatostatin analogs. Octreotide and lanreotide are examples. They don’t treat the cancer, only the side effects of carcinoid syndrome.

**Other Medications**

Other medications, such as interferons that boost the immune system, may help to slow tumor growth. Interferons are made by the body to fight viral and bacterial infections. They are given by injection and can sometimes help shrink tumors and reduce symptoms.

Cyproheptadine is an H1 antagonist that blocks histamine and serotonin. It can be used to treat the itching and flushing from carcinoid syndrome. You may be given more than one type of this medication and an H2 antagonist.

High levels of serotonin in the blood can cause problems with the heart valves and heart failure. Medications, such as octreotide and somatostatin, can be used to control serotonin levels and prevent further heart damage. Echocardiograms will be done to monitor your heart function.

**Clinical Trials**

You may be offered a clinical trial as part of your treatment plan. To find out more about current clinical trials, visit the [OncoLink Clinical Trials Matching Service](https://www.oncolink.org).

**Making Treatment Decisions**

Your care team will make sure you are included in choosing your treatment plan. This can be overwhelming as you may be given a few options to choose from. It feels like an emergency, but you can take a few weeks to meet with different providers and think about your options and what is best for you. This is a personal decision. Friends and family can help you talk through the options and the pros and cons of each, but they cannot make the decision for you. You need to be comfortable with your decision – this will help you move on to the next steps. If you ever have any questions or concerns, be sure to call your team.

You can learn more about carcinoid cancer at [OncoLink.org](https://www.oncolink.org).
medication that you have been prescribed, you should consult your health care provider.