National Comprehensive Cancer Network®

2026

NCCN Guidelines for Patients®

Cancer care recommendations from leading experts at the National Comprehensive Cancer Network® (NCCN®)

Esophageal Cancer



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NCCN Guidelines for Patients®

The essential guide for people facing cancer.

Based on care recommendations from leading cancer experts.

Explains high-quality cancer care provided at state-of-the-art cancer centers.

Reviewed and revised every year.

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Because cancer care is always evolving, NCCN develops and frequently updates evidence-based cancer care recommendations used by health care providers worldwide. These recommendations are known as the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®).

The NCCN Guidelines for Patients plainly explain these expert recommendations, so you can talk with your care team about the best care for you.

These NCCN Guidelines for Patients are based on the NCCN Guidelines® for Esophageal and Esophagogastric Junction Cancers, Version 3.2026 — June 3, 2026.

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ECAA is a 501(c)(3) all-volunteer non-profit organization with four mission goals: to raise public and professional awareness of esophageal cancer; to educate the public regarding the risks and symptoms of EC; to contribute to research into detection, treatment, and cure; and to provide personal support to patients, caregivers, and loved ones. 1.800.601.0613



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About esophageal cancer

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Esophageal cancer is cancer of the esophagus. This patient guideline provides you with the latest information on esophageal cancer testing, staging, and treatment to help you make informed decisions with your health care team.

What is esophageal cancer?

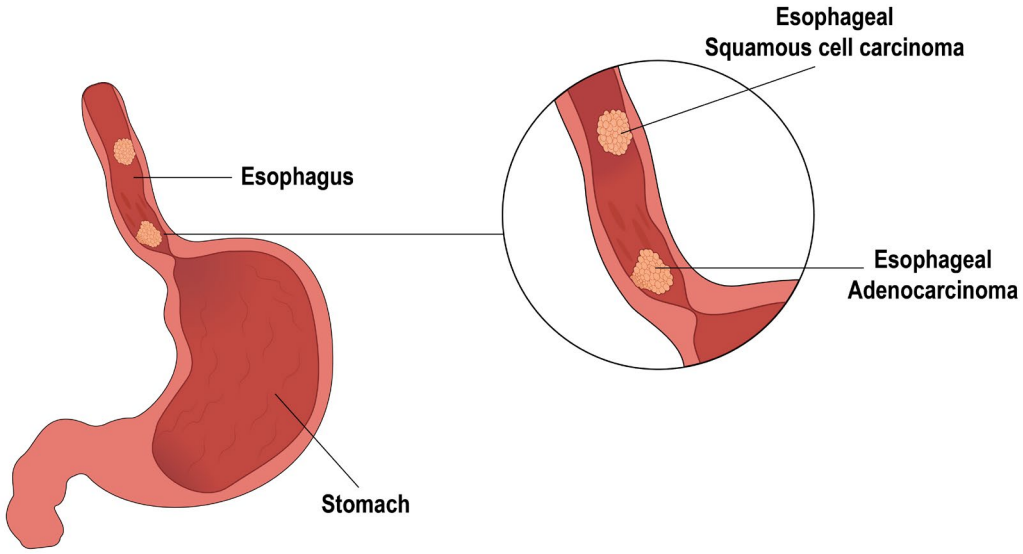
To understand what esophageal cancer is, it's helpful to know where it starts.

The esophagus is a long, muscular tube that moves food from the mouth and throat to the stomach. It's also known as the food pipe. Esophageal cancer starts when cells with damaged genes grow out of control and create a tumor in the innermost layer of the esophagus, called the mucosa. The tumor can grow in and through the layers of the esophagus and can spread to lymph nodes (small, bean-shaped, disease-fighting structures of the immune system) and other parts of the body. See the next chapter for an illustration of the layers of the esophagus.

There are 2 types of esophageal cancer:

- **Adenocarcinoma** starts in the mucus-making cells of the mucosa. Adenocarcinoma is often found in the lower esophagus but can occur in the middle esophagus as well. Today, adenocarcinoma is the most common type of esophageal cancer in North America and Europe.
- **Squamous cell carcinoma** starts in the thin, flat squamous cells of the mucosa. This type of cancer usually begins in the upper and middle esophagus but can occur in the lower esophagus as well. Squamous cell carcinoma is the most common type of esophageal cancer in the rest of the world.

Types of Esophageal Cancer



Barrett esophagus

A condition called Barrett esophagus (BE) is linked to adenocarcinoma. Chronic acid damage from reflux or gastroesophageal reflux disease (GERD) causes the cells that line the lower part of the esophagus to become abnormal (mutate). This can develop into Barrett esophagus. If left untreated, the cells can keep changing (mutating) and growing out of control, resulting in what's called dysplasia. Dysplasia is a pre-cancerous condition. In some cases, it can eventually become adenocarcinoma.

How does esophageal cancer spread?

Esophageal cancer tends to develop slowly over many years. Before it develops, pre-cancerous changes often occur in the inner lining (mucosa) of the esophageal wall. Cancers form tumors that grow outward (as well as up and down), through, and along the layers of the esophageal wall. Because these early changes rarely cause symptoms, they often go undetected.

As it grows, esophageal cancer can spread (metastasize) to nearby lymph nodes just outside of the esophagus. It can also spread much further to distant lymphatic vessels and lymph nodes, blood vessels, veins, arteries, and organs like the liver, bones, lungs, and brain, as well as other parts of the body.

What are the risk factors?

A risk factor increases the chances that you will develop a disease. The risk factors of esophageal cancer include smoking, drinking alcohol, or having a family member with esophageal cancer. If you have any of these risk factors, it doesn't mean you'll develop esophageal cancer. It just means it might be more likely because they increase the chance of damage to the cells in the esophageal lining.

These are the leading risk factors:

- Male sex assigned at birth
- Increased age (over 55 years)
- Tobacco use
- Heavy drinking
- GERD (chronic acid reflux)
- Barrett esophagus (for adenocarcinoma)
- Obesity
- Certain rare genetic conditions

What are the signs and symptoms?

In its early stage, esophageal cancer rarely causes symptoms. But when the cancer has progressed and grown to more advanced stages, the symptoms can include:

- Trouble with swallowing (called dysphagia)
- Painful swallowing
- New or worsening heartburn or indigestion
- Chest and back pain

- Chronic cough
- Coughing up blood
- Vomiting blood or passing blood in stools (dark stools)

Other symptoms

- Unintended weight loss
- Hoarseness or a change in voice
- Anemia (low red blood cell count that can make you feel weak and extremely tired)

How is esophageal cancer treated?

For treatment information, this guide is separated into the types of esophageal cancer: adenocarcinoma or squamous cell carcinoma. Read Chapter 6 if you have adenocarcinoma and Chapter 7 if you have squamous cell carcinoma. These 2 chapters also break down early-stage cancer and locally advanced cancer.

For more information about treatment for both types of cancer if it returns (called recurrence) or if it has spread far from the original site (metastasized), read *Chapter 8: Locally advanced recurrence or metastatic cancer*.

In general, treatment is based on the type, stage, tumor location, and depth of the esophageal cancer as well as the health of the person who has cancer.

Esophageal cancer is often treated with surgery, chemotherapy, or chemoradiation (chemotherapy and radiation combined). Chemoradiation is less common, but it depends on the cancer stage and how far it has spread. For example, because stage 4 esophageal cancer has spread far from the original site, surgery is not an option in the early phase of treatment, but chemoradiation or chemotherapy might be.

Stages of esophageal cancer can be grouped into 3 main categories, depending on how far the cancer has spread:

- **Early-stage** esophageal cancer has not grown beyond the inside of the esophagus. The tumor may be very small (2 centimeters or less, which is about the size of a peanut) and is not in any lymph nodes.
- **Locally advanced** esophageal cancer has invaded the esophageal wall and/or spread to nearby lymph nodes or organs, or is in direct contact with the esophagus.
- **Metastatic** esophageal cancer has spread to other parts of the body. The most common metastatic sites are the liver, distant lymph nodes, lungs, bones, and brain. For more information, see *Chapter 8: Locally advanced recurrence or metastatic cancer*.

How can I get the best care?

Advocate for yourself. You have an important role to play in your care. Many people feel more satisfied when they actively take part in planning their cancer care.

The NCCN Guidelines for Patients will help you play a larger role in your care. Discuss the recommendations in this guide with your care team. Ask questions about your options and share your goals and concerns.

Don't know what to ask? You're not alone. That's why we include suggested questions to ask at the end of chapters.

Keep reading to find the best care for you.

How this guide can help you

Making decisions about cancer care is stressful. There's a lot to learn, and you don't know what the future holds.

Use this guide to get the information and support you need.

Patients, doctors, and other health care professionals trust the NCCN Guidelines for Patients. This guide uses clear, everyday language to explain current cancer care recommendations made by respected experts in the field. Their recommendations are based on the latest research and practices at leading cancer centers.

Your health is unique to you, so your cancer care should be, too. As you read this guide, you'll learn which treatments are likely to provide the best results for you. And you'll be better prepared to talk with your care team.

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About the esophagus

10 How the esophagus works

10 The layers of the esophageal wall

11 Parts of the esophagus

13 Nearby lymph nodes

13 Key points

13 Questions to ask

Knowing how the esophagus works will help you better understand esophageal cancer. This chapter explains what you need to know.

How the esophagus works

The esophagus is located behind the trachea (windpipe) and in front of the spine. It's part of the digestive system. The digestive system takes in and breaks down food, absorbs nutrients, and removes digested food from the body. It includes the esophagus, stomach, liver, pancreas, small intestine, colon, rectum, and anus.

Food and drink enter the mouth and throat. They then move through the esophagus into the stomach. When you swallow, small contractions (called peristalsis), gravity, and pressure move food down the esophagus and into the stomach. Except during the act of swallowing, the esophagus is normally empty.

The esophagus is about 10 inches long and about 1 inch wide. It has 2 sphincters—circular muscles that are usually closed except during swallowing. One sphincter is located at the top of the esophagus and the other at the bottom, between the esophagus and the stomach.

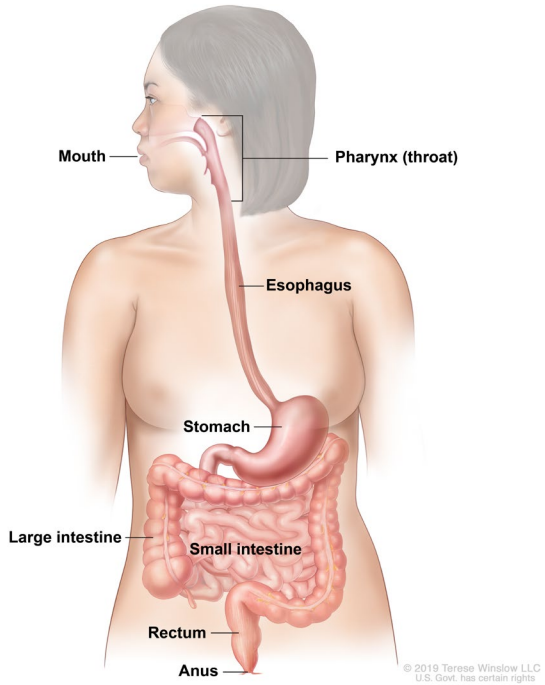
The layers of the esophageal wall

The esophagus is a hollow, muscular tube that connects the throat to the stomach. Its wall contains 4 layers:

1. **Mucosa** – Inner membrane that is in contact with food. The mucosa has 3 parts:

The digestive tract

The digestive or gastrointestinal (GI) tract is part of the digestive system. Food enters the mouth and passes through the esophagus into the stomach. After being broken down into a liquid, food enters the small intestine. Any unused food enters the large intestine and then is moved out of the body.



- Epithelium – Innermost lining normally made of flat, thin cells called squamous cells.
- Lamina propria – Thin layer of connective tissue under the epithelium.
- Muscularis mucosa – Very thin layer of muscle under the lamina propria.

2. **Submucosa** – Layer of connective tissue just below the mucosa that contains blood vessels, nerves, and lymphatic vessels. In some parts of the esophagus, this layer also includes glands that secrete mucus.

3. **Muscularis propria** – Thick layer of muscle under the submucosa. It contracts in a coordinated way to push food down the esophagus from the throat to the stomach (peristalsis).

4. **Adventitia** – Outermost layer, made of connective tissue.

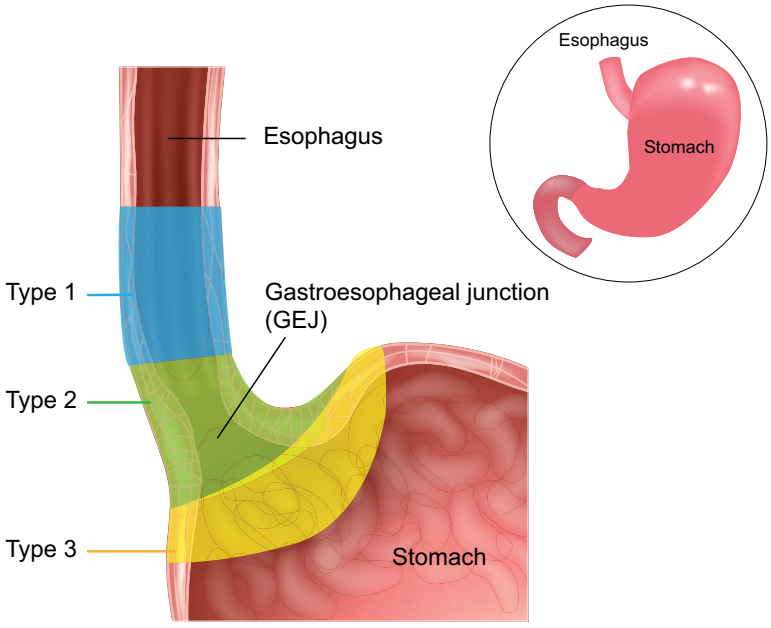
For an illustration of the esophageal wall, see *Chapter 4: Esophageal cancer staging*.

Parts of the esophagus

Where cancer develops in the esophagus is what dictates the type, staging, and kind of surgery as well as how easily the cancer spreads. Esophageal cancer can develop in any part of the esophagus but is most common in the upper and middle esophagus (squamous cell carcinoma) and lower esophagus (adenocarcinoma). Depending on the specific area where cancer develops in the gastroesophageal junction (GEJ), it could be treated as esophageal cancer or stomach cancer. Each part is explained ahead.

Siewert types

A Siewert type describes tumors located in the area of esophagus near the stomach. Siewert types 1 and 2 are treated as esophageal cancer. Siewert type 3 is treated as stomach cancer. There are some exceptions.



Upper esophagus (cervical esophagus)

This part is located in the neck and includes the area at the bottom of the throat (the pharynx) to the breastbone (thoracic inlet). The upper part of the esophagus is made of striated muscle. Striated muscle generates force and contracts. It's under your control (voluntary).

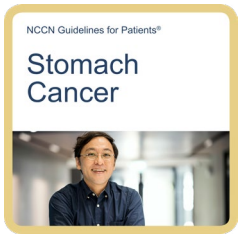
Middle esophagus (thoracic esophagus)

The middle part of the esophagus runs down behind the trachea (the windpipe) and heart and in front of the spine. It's a mixture of striated and smooth muscle.

Lower esophagus (GEJ)

This is the lower part of the esophagus. It consists only of smooth muscle. Smooth muscle isn't under your control. It's involuntary, like a reflex.

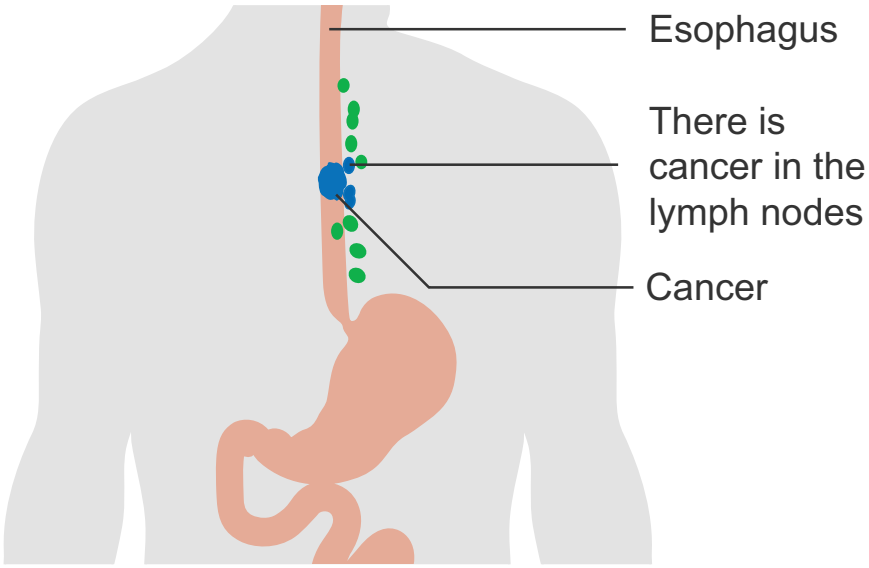
The gastroesophageal junction (GEJ), also referred to as the esophagogastric junction (EGJ), is where the stomach and the esophagus meet. The GEJ is found just beneath the diaphragm. It keeps stomach acid from entering the esophagus. Cancer of the GEJ is staged according to where the tumor is found using the Siewert classification system (see page 11). This determines if it's esophageal cancer or stomach cancer. Siewert types 1 and 2 are treated as esophageal cancer (specifically, adenocarcinoma). Siewert type 3 is treated as stomach cancer. For more information on stomach cancer, see *NCCN Guidelines for Patients: Stomach Cancer*, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Regional lymph nodes

A tumor can be found anywhere in the esophagus. Cancer may also be found in lymph nodes along the esophagus.

https://commons.wikimedia.org/wiki/File:Diagram_showing_oesophageal_cancer_in_the_lymph_nodes_(N_staging)_CRUK_174.svg



Nearby lymph nodes

There are hundreds of lymph nodes throughout your body. They're part of the immune system and filter out bacteria, viruses, and some cancer cells. Lymph, a clear fluid that contains infection-fighting white blood cells, flows through the lymphatic system. It drains from the esophageal wall into lymphatic vessels in the mucosa and submucosa. From there, it drains into lymph nodes outside of the esophagus. Several groups of nearby lymph nodes drain the wall of the esophagus.

Lymph nodes near the esophagus are called regional lymph nodes. Cancer in a regional lymph node is called lymph node metastasis and is considered regional spread or locally advanced cancer. This is different from distant metastasis, which is found far from the main tumor in the esophagus.

Key points

- The esophagus is located behind the trachea (windpipe) and in front of the spine. It's part of the digestive system.
- The esophageal wall has 4 main layers: mucosa, submucosa, muscularis propria, and adventitia.
- Where the cancer starts in the esophagus determines the type, staging, kind of surgery, and how easily the cancer spreads.
- Cancer can develop in any part of the esophagus but is most common in the upper and middle esophagus (squamous cell carcinoma) and lower esophagus (adenocarcinoma).
- Lymph drains from the esophageal wall into lymphatic vessels in the esophageal mucosa and submucosa.

Questions to ask

- How far into the esophageal wall does the cancer go?
- Has the cancer reached the lymph nodes outside of the esophagus?
- What kind of treatment will I have?
- What can I do to manage my current symptoms?

What's next

Now that you've learned about the esophagus and surrounding lymph nodes, you can better understand your cancer treatment. Read the next chapter for more information on what testing is needed before you start treatment.

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Testing for esophageal cancer

15 General health tests

17 Performance status

18 Nutrition assessment

18 Blood tests

18 Imaging tests

20 Endoscopy procedures

21 Biopsy

22 Genetic risk testing

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26 Questions to ask

You'll need testing to correctly identify the type and stage of esophageal cancer; to see if it has spread; and if so, how far. With that information, you and your care team will talk about treatment next steps. This chapter presents an overview of the tests you might receive and what to expect.

Results from different tests help guide esophageal cancer treatment. You won't need every test listed here, but you may need several tests before you start treatment. For possible tests, see **Guide 1**. More information on these tests is on the following pages.

General health tests

Medical history

A medical history, sometimes called a health history, is a record of all health issues and treatments you've had in your life. Be prepared to list all of your illnesses and injuries and when they happened.

Bring a list of old and new medicines and any over-the-counter medicines, herbals, or supplements you take. Some supplements interact and affect medicines your care team may prescribe.

Tell your care team about any symptoms you have. Your medical history can help decide which treatment is best for you.



What is your family cancer health history?

Some cancers and other diseases run in families—in other words, they are passed down through genes from biological parent to child. This information is called a family health history. Ask blood relatives about their health issues, like heart disease, cancer, and diabetes, and at what age they were diagnosed. For relatives who were diagnosed with cancer, ask them (or other relatives if they are no longer living) what type of cancer they had, if they died from the cancer, and at what age the cancer was diagnosed.

Start by asking your parents, siblings, and children. Next, talk to half-siblings, aunts and uncles, nieces and nephews, grandparents, and grandchildren.

Write down what you learn about your family history, and share this information with your health care provider.

Some of the questions to ask include:

- How old were you when each of these diseases and health conditions were diagnosed?
- What is your family's ancestry—from what countries did your ancestors originate?

Guide 1 Possible tests for esophageal cancer
Medical history and physical exam. Screen for family history
Upper GI endoscopy (also called EGD) and biopsy
CT of chest/abdomen with oral and IV contrast. CT of pelvis with contrast as needed
FDG-PET/CT evaluation (skull base to mid-thigh) if no evidence of metastatic cancer
Complete blood count (CBC) and comprehensive chemistry profile
Endoscopic ultrasound (EUS) if no evidence of metastatic unresectable cancer
Endoscopic resection (ER) is recommended for the accurate staging of early-stage cancers. Early-stage cancers can best be diagnosed by ER.
Biopsy of metastatic disease as needed
Testing for microsattelite instability (MSI) by polymerase chain reaction/next-generation sequencing (NGS) and testing for mismatch repair (MMR) by immunohistochemistry for all newly diagnosed patients
Testing for PD-L1 for all newly diagnosed patients
CLDN18.2 testing if advanced/metastatic adenocarcinoma is suspected
HER2 testing if advanced/metastatic adenocarcinoma is suspected
NGS testing should be considered
Bronchoscopy, if tumor is at or above the carina (the ridge at the base of the trachea) with no evidence of metastatic cancer
Nutrition assessment and counseling
Smoking cessation advice, counseling, and medicine as needed

Family history

Some cancers and other diseases can run in families. Your doctor will ask about the health history of family members who are blood relatives. This information is called a family history. Ask family members on both sides of your family about their health issues, like heart disease, cancer, and diabetes, and at what age they were diagnosed. It's important to know the specific type of cancer or where the cancer started, if it's in multiple locations, and if they had genetic testing.

Physical exam

During a physical exam, your doctor may:

- Check your temperature, blood pressure, pulse, and breathing rate
- Check your height and weight
- Listen to your lungs and heart
- Look in your eyes, ears, nose, and throat
- Feel and apply pressure to parts of your body to see if organs are of normal size, are soft or hard, or cause pain when touched
- Feel for enlarged lymph nodes in your neck, underarm, and groin

Performance status

Performance status is an estimate of a person's general level of fitness and ability to perform daily tasks. It's one factor taken into consideration when your doctors are deciding what intensity of treatment (for example, surgery and systemic therapy) you and your body can tolerate. Doctors use performance status to help determine if you're healthy enough for the treatment.

Performance status

Performance status is a person's ability to perform daily tasks.



Nutrition assessment

You should meet with a nutritionist before starting treatment because they can suggest the best foods and fluids for you. Esophageal cancer can make you lose your appetite or cause difficulty or pain when swallowing foods or liquids. You may also feel full after eating very little. These changes may cause you to lose too much weight or make you feel weak and tired.

It's important to receive adequate and sustained nutrition before you start treatment. You might receive food through a flexible, plastic feeding tube that's inserted into your stomach (called a gastrostomy tube, or G-tube) or small intestine (called a jejunostomy tube, or J-tube).

During and after treatment, your care team will check for weight loss and other signs you aren't getting enough nutrition.

Blood tests

Blood tests check for signs of disease and how well your organs are working. They require a sample of your blood, which is removed through a needle placed into your vein. Two blood tests are described next.

Complete blood count

A complete blood count (CBC) measures the levels of red blood cells, white blood cells, and platelets in your blood. Your doctor will want to know if you have enough red blood cells to carry oxygen throughout your body, white blood cells to fight infection, and platelets to control bleeding.

Comprehensive chemistry profile

A comprehensive chemistry profile provides important information about how well your kidneys and liver are working, among other things. It's usually part of a comprehensive metabolic panel (CMP). A CMP measures 14 different substances in your blood.

Imaging tests

Imaging tests provide pictures of the inside of the body. These images can show where the cancer started (the primary tumor) and find cancer in other parts of your body.

A radiologist, a doctor who interprets imaging tests, will write a report and send it to your health care provider. The report may also be sent directly to you through your patient portal, or patient access system. You should discuss these results with your doctor. Also, you won't have all of these imaging tests—this is just an overview.

Contrast material

Regardless of the imaging you receive, contrast material is sometimes used to help make the pictures of the inside of the body clearer. Contrast materials aren't dyes, but substances that help enhance and improve the images of organs and structures in the body. The contrast isn't permanent and leaves the body in your urine immediately after the test. The types of contrast vary and are different for CT and MRI.

Tell your care team if you've had allergic reactions to contrast in the past. This is important. You might be given medicines to avoid the effects of those allergies. Contrast

might not be used if you have a serious allergy or if your kidneys aren't working well.

CT scan

A computed tomography (CT or CAT) scan combines x-rays and computer technology to take detailed pictures of the inside of the body. A CT scan of your chest, abdomen, and/or pelvis may be one of the tests to look for cancer.

A CT scan takes many x-rays of the same body part from different angles. All the images are combined to make one detailed 3D picture.

A CT scan of your chest, abdomen, and/or pelvis may be one of the tests to look for cancer. Oral (by mouth) and IV (by a needle placed into a vein in your arm) contrast are often used together when testing for esophageal cancer.

PET scan

A PET scan uses a tracer. A tracer is a substance injected into a vein that makes cancer show up as bright areas on the scan. However, not all tumors appear on a PET scan, and not all bright spots are cancer. It's normal for the brain, heart, kidneys, and bladder to be bright on a PET scan. Inflammation or infection can also show up as a bright spot.

FDG-PET/CT

When a PET scan is combined with CT, it's called a PET/CT scan. It may be done with one or two machines depending on the cancer center. An FDG-PET/CT scan uses 18-fluorodeoxyglucose as its tracer.

CT machine

A CT machine is large and has a tunnel in the middle. During the test, you will lie on the table that moves slowly through the tunnel.



Ultrasound

An ultrasound uses high-energy sound waves to form pictures of the inside of the body. This is like a sonogram used for pregnancy. Ultrasound is painless and doesn't use x-rays. With esophageal cancer, an ultrasound (endoscopic) is used to guide a biopsy. See "Endoscopic ultrasound" below.

Endoscopy procedures

Some imaging tests are more invasive and use a thin, tube-shaped tool. This tool is called a scope, and it's inserted into the body to take pictures. One end of the scope has a small light and camera to see inside of your body. The scope is guided into the body through a natural opening, such as the mouth, nose, or anus. Or it may be inserted through a small surgical cut. The image is sent to a video monitor, so your doctor can view the inside of your internal organs to perform a biopsy, stent placement, or other tasks.

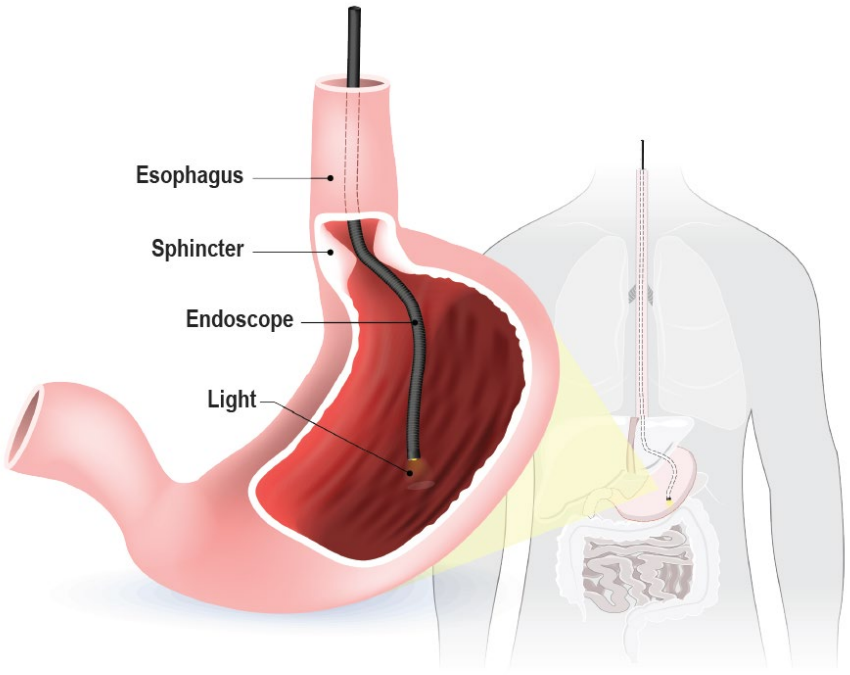
The type of scope often used for esophageal cancer is called an endoscope, and the procedure itself is known as upper gastrointestinal (GI) endoscopy. Endoscopy is an important tool in the diagnosis, staging, treatment, and care of people with esophageal cancer. Before an endoscopy, you'll be given medicine to help you relax or sleep during the procedure.

Upper GI endoscopy, or EGD

In upper GI (gastrointestinal) endoscopy (also known as esophagogastroduodenoscopy, or EGD), an endoscope is guided down the throat into the esophagus, stomach, and upper parts of the small intestine (duodenum). It's used to inspect the lining of these organs and to look for any signs of cancer or other abnormalities, such as enlarged blood vessels or ulcers. It

Upper GI endoscopy

Upper GI (gastrointestinal) endoscopy allows your doctor to see the inner wall of your stomach and esophagus. If ultrasound is used, your doctor will be able to see the deeper wall layers and nearby organs.



Through your cancer care, you might find measurements using the metric system (centimeters, millimeters, etc.). That is because your care team uses the metric system to measure many aspects of treatment.

can also perform biopsies and is the most common way for a biopsy to be taken for esophageal cancer. After the endoscopy, your throat may feel sore and swollen.

Endoscopic ultrasound

Endoscopic ultrasound (EUS) is an important part of cancer diagnosis and staging. It uses an endoscope with ultrasound to see how deep the tumor has grown into the esophageal wall. It can also detect signs of cancer in lymph nodes and other nearby organs.

You're most likely to have EUS if your care team suspects the cancer hasn't grown far into the esophageal wall (early-stage cancer), or to figure out whether the cancer is early stage or locally advanced.

Bronchoscopy

During a bronchoscopy, a device is inserted through the nose or mouth to examine the inside of your airway, including the trachea and bronchi. Bronchoscopy may be used to detect cancer from the esophagus or for some treatment procedures.

Laparoscopy

Laparoscopy (keyhole surgery) is a type of procedure that allows your surgeon to see inside of your abdomen. It uses a tool like an endoscope, called a laparoscope, that can introduce a camera or surgical instruments into the abdomen.

First, you'll be given general anesthesia to fall asleep, so you won't feel any pain. Then your surgeon will insert the laparoscope through a tiny cut in your esophagus (it's considered minimally invasive surgery).

Laparoscopy can be used to figure out the stage of disease and rule out metastasis. It can detect cancer spread that may have been missed on imaging scans. It can also be used to obtain biopsy samples. Laparoscopy is sometimes used to determine if you're a candidate for surgery.

Biopsy

A biopsy removes a sample of tissue or fluid that's tested for disease during an upper GI endoscopy. Several samples may be taken from the tumor, wall of your esophagus or stomach, and lymph nodes. The samples will be sent to a pathologist, an expert in examining cells under a microscope to find disease.

Other types of biopsies may include:

- **Fine-needle aspiration (FNA) or core biopsy (CB)** uses needles of different sizes to remove a sample of tissue or fluid. An EUS may guide the FNA for diagnosis.

- **Brushings or washings** involve removing tumors or cell samples with a small brush at the end of an endoscope.
- **Liquid biopsy** uses a sample of blood for testing.

Biopsy of metastases

Metastasis is the spread of cancer from where it started to another area of the body, such as the lung, liver, bone, or distant lymph nodes. A biopsy of the metastasis may be needed to confirm the presence of cancer. If there's more than one metastasis, each site may be biopsied. The type of biopsy used depends on the location of the suspected metastases and other factors.

Genetic risk testing

You may be thinking, "Why did I get cancer?" Most of the time, the answer is that one cell made a mistake when dividing and then a cancer formed. Some cells, however, have a predisposition (tendency) due to mutations (changes) in their DNA that makes them more likely to develop cancer. A genetic risk assessment will find if you have a cancer risk and if you could benefit from genetic testing, more screening, or preventive measures. Depending on the genetic risk assessment, you might have genetic testing and genetic counseling.

Genetic testing using blood or saliva (spitting into a cup) can show gene mutations inherited from your biological parents called germline mutations. Some mutations can put you at risk of more than one type of cancer and can be passed down to children. Also, family members might carry these mutations. Tell your care team if there's a family history of cancer.

Depending on your family history or other features of your cancer, your health care provider might refer you for hereditary genetic testing to learn more about your cancer. A genetic counselor will speak to you about the results.

Hereditary cancer predisposition syndromes

A syndrome is a set of symptoms or conditions that occur together and suggest the presence of a certain disease or an increased risk of the disease. Someone who has a genetic (inherited) cancer predisposition syndrome may have a greater risk of esophageal cancer.

Certain genetic (inherited) syndromes may put someone at risk of esophageal cancer. A syndrome is a group of signs or symptoms that occur together and suggest the presence or risk of a disease.

Hereditary syndromes most closely related to esophageal and GEJ cancers include:

- Esophageal cancer, tylosis with non-epidermolytic palmoplantar keratoderma (PPK), and Howel-Evans syndrome
- Familial Barrett esophagus (FBE)
- Bloom syndrome (BS)
- Fanconi anemia (FA)

What is the difference between genetic testing and biomarker testing?

Genetic testing looks for inherited gene changes (mutations) to determine your risk for a certain cancer.

Biomarker testing looks for tumor markers like genes and proteins in cancer cells to guide treatment.

Biomarker testing

A sample from a tumor biopsy may be tested to look for specific proteins and/or gene alterations (changes) or other molecular alterations. This is called biomarker testing, molecular testing, or tumor profiling. This information may be used to choose a more specific treatment for you. Biomarker testing is an umbrella term for any change or characteristic in your cancer that can affect your treatment.

Primary biomarkers are associated with the drugs that can be used. Additional information can be found through next-generation sequencing (NGS) on tumor tissue and/or blood. Also, genetic testing (mentioned above) can be done for inherited genetic mutations.

Biomarker testing includes tests of genes or their products (proteins). It shows the presence or absence of mutations (changes) as well as the presence of overexpression of certain proteins, both of which might suggest which treatment is needed.

Important biomarkers and tests to detect them for the treatment and management of metastatic esophageal cancer are explained next. Biomarker testing continues to expand, so ask your care team if other tests are needed.

Tumor mutation testing

Tumor mutation testing or tumor genomic aberration testing is a type of biomarker testing that uses a sample of your tumor or blood to see if the cancer cells have any specific DNA mutations. This information may be used to guide certain drug choices. This is a different type of DNA testing than the genetic testing for mutations you may have inherited from your biological parents. In tumor mutation testing, only the tumor is tested and not the rest of your body. Many mutations, such as *NTRK* gene fusions, can be targeted with specific therapies.

Specific biomarkers

HER2

Human epidermal growth factor receptor 2 (HER2) is a protein responsible for controlling normal cell growth. It's found on the surface of all epithelial cells. High amounts of HER2 cause cells to grow and divide. This is called HER2 positive (HER2+), overexpression, or amplification.

There might be higher amounts of HER2 in your esophageal cancer. If the tumor makes too much HER2, you might receive a targeted therapy called trastuzumab (Herceptin) or trastuzumab deruxtecan (Enhertu). These drugs target the HER2 protein and can help slow or stop the tumor from growing.

From the moment you get a cancer diagnosis, you are thrust into a world of new terms, many of them vital to understanding what is happening to you. It's important to understand what biomarkers are and even how these biomarkers can affect treatments."

MSI-H/dMMR mutation

Microsatellites are short, repeated strings of DNA. Sometimes errors or defects occur in these microsatellites. When this happens, they're usually fixed by mismatch repair (MMR) proteins.

But some cancer cells have DNA mutations that prevent MMR proteins from fixing these errors. This is called microsatellite instability (MSI) or mismatch repair deficiency (dMMR). When cancer cells have a high number of mutations in microsatellites, it's called MSI-H (microsatellite instability-high). MSI-H is often due to dMMR.

People with newly diagnosed esophageal cancer should be tested for MMR or MSI.

PD-L1

Programmed death ligand 1 (PD-L1) is one of the proteins that helps the body's immune system to function. But if this protein is present (expressed) on the surface of cancer cells, it can cause your immune cells to ignore the cancer and suppress the immune system's anti-tumor response.

If your cancer has this protein, you might have treatment that combines chemotherapy and an immune checkpoint inhibitor (ICI). This is designed to activate your immune system to better fight off the cancer cells.

Claudin 18 isoform 2

Claudin 18 isoform 2 (CLDN18.2) is a protein found on the surface of gastroesophageal (stomach and esophagus) cancer cells in advanced stages. If your cancer is suspected to be advanced adenocarcinoma and has a high level of CLDN18.2 (known as CLDN18.2 positive), you might be able to receive a type of immunotherapy called zolbetuximab-clzb (Vyloy).

Tumor mutational burden

Tumor mutational burden (TMB) is the total number of mutations (changes) found in the DNA of cancer cells. TMB is important because if a tumor has a high number of mutations (or errors), it's more visible to the immune system. And because of that, the tumor might be more likely to respond to ICIs. In esophageal cancer, ICIs target proteins called programmed cell death protein 1 (PD-1) and programmed death ligand 1 (PD-L1).

NTRK gene fusions

An *NTRK* gene fusion occurs when a piece of the *NTRK* gene merges (fuses) with a piece of another gene, which causes uncontrolled cell growth. Larotrectinib (Vitrakvi) and entrectinib (Rozlytrek) might be used to target advanced or metastatic cancer due to an *NTRK* gene fusion.

RET gene fusions

Rearranged during transfection *(RET)* gene mutation is related to cell growth (proliferation). Selpercatinib (Retevmo) might be used for cancer with a *RET* gene fusion.

BRAF V600E mutations

Mutations in the *BRAF* gene can cause normal cells to become cancerous. Dabrafenib (Tafinlar) and trametinib (Mekinist) might be used to treat tumors with *BRAF* V600E mutations.

Types of biomarker tests

NGS

Next-generation sequencing (NGS), also known as tumor mutation testing, uses a sample of your tumor or blood to see if the cancer cells have any specific DNA mutations (or changes). (It's a different type of DNA testing from the testing for mutations you may have inherited from your biological parents.)

Finding these changes can help guide the choice of therapies most likely to be effective. For example, certain tumor mutations, such as *NTRK* fusion, *RET* fusion, and *BRAF* V600E mutation, can be targeted with specific therapies. NGS also helps to determine if more biomarker testing is needed.

This method can only be used if enough tumor tissue remains after other biomarker testing has been completed. Tumor mutation testing is often done if the cancer is unresectable (not removable with surgery) or metastatic.

FISH

Fluorescence in situ hybridization (FISH) is a testing method that involves special dyes called probes that attach to pieces of DNA, the genetic material in a person's cells. This can tell how many copies of a gene are present in the cell. The cells are then studied using a fluorescence microscope.

PCR

Polymerase chain reaction (PCR) is a lab process that can make millions or billions of copies of your DNA (genetic information). This test is very sensitive. It can find 1 abnormal cell among more than 100,000 normal cells. These copies, called PCR product, might be used for NGS.

Liquid biopsy

Some mutations can be found by testing circulating tumor DNA (ctDNA) in the blood. In a liquid biopsy, a sample of blood is taken to look for cancer cells or pieces of DNA from tumor cells. People who have metastatic or advanced esophageal cancer and are unable to undergo a traditional biopsy might have a liquid biopsy. Sometimes, traditional testing can quickly use up a tumor sample. In this case, a liquid biopsy might be a possibility.

Immunohistochemistry

Immunohistochemistry (IHC) is a special staining process that involves adding a chemical marker to cancer or immune cells. The cells are then studied under a microscope.

Key points

- Tests are used to find cancer, figure out the extent of cancer (staging), plan treatment, and check how well treatment is working.
- A medical history and physical exam inform your doctor about your overall health.
- Getting enough nutrition is important. You should meet with a nutritionist before starting treatment.
- Blood tests check for signs of disease and how well organs are working.
- Imaging tests look inside of the body through pictures. Images can be made with scanning machines or scoping tools.
- A biopsy removes a sample of tissue or fluid to be tested for cancer. One example is by using an upper gastrointestinal (GI) endoscopy biopsy tissue in the esophagus.
- Genetic testing might be done to look for gene mutations inherited from your biological parents.

Questions to ask

- What tests will I have?
- Do the tests have any risks?
- Will my insurance pay for them?
- Do I need to do anything to prepare for testing?
- Should I bring someone with me to the appointments?

What's next

Now that you understand the many tests that can help guide your treatment, read the following chapter to learn about staging, which is what happens after testing and how the cancer stage affects your treatment.



Knowledge is power. Do not settle if your questions and concerns are not properly addressed. Advocate for yourself and your needs."

4

Esophageal cancer staging

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Cancer staging is used to make treatment decisions. It describes the size and location (or extent) of the tumor; if the tumor has grown through the layers of the esophageal wall; and if cancer has spread to lymph nodes, organs, or other parts of the body. This chapter explains the stages of esophageal cancer.

Based on testing, your cancer will be assigned a stage. Staging signifies how much cancer is in your body, where it's located, and what subtype you have.

Whether your cancer is adenocarcinoma or squamous cell carcinoma, knowing the stage helps to predict the cancer's outlook (prognosis) and is needed to make treatment decisions. Read more for how the stages are determined and broken down for adenocarcinoma and squamous cell carcinoma.

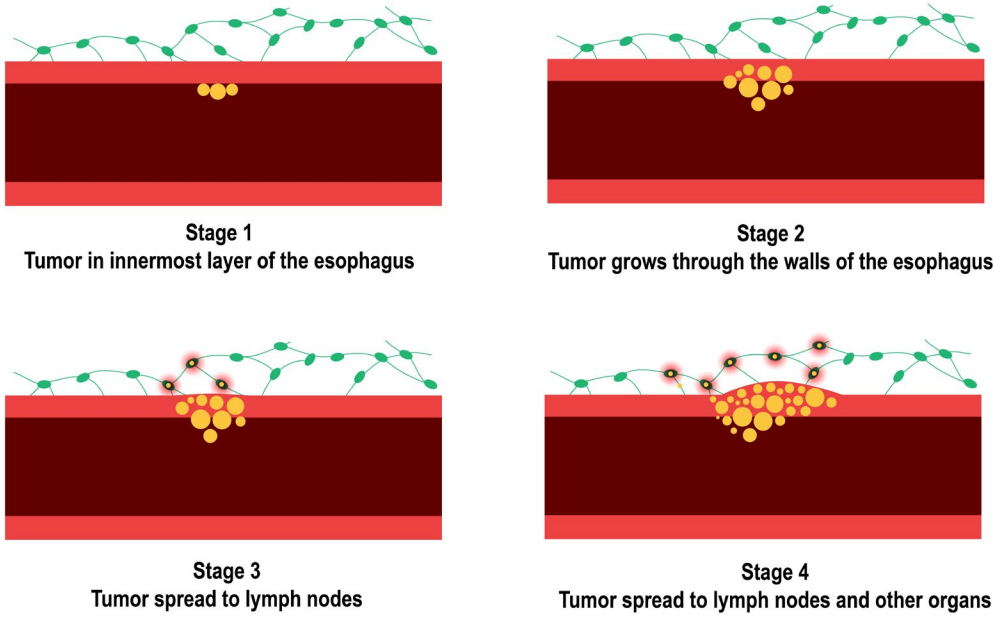
How esophageal cancer is staged

Following is the information gathered during staging for adenocarcinoma and squamous cell carcinoma:

- **Extent (size) of the tumor (T):** Has the cancer grown into nearby areas? How deep does it extend into the layers of the esophagus?
- **Spread to nearby lymph nodes (N):** Has the cancer spread to nearby lymph nodes? If so, how many? Where?
- **Spread (metastasis) to distant sites (M):** Has the cancer spread to distant organs, such as distant lymph nodes, lungs, bones, or liver?
- **Grade of the cancer (G):** How much do the cancer cells look like normal cells under the microscope?

Stages of esophageal cancer

These are 4 of the 5 stages of esophageal cancer. Stage 0 is not pictured. Most esophageal cancer is not found in Stage 0.



- **Biomarker testing:** Does the cancer have any genes, proteins, markers, or mutations that would make one kind of treatment work better?

Staging is based on a combination of information to reach a final numbered stage.

Stages range from stage 0 to stage 4, with 4 being the most advanced. They might be written by your care team with Roman numerals like stage 0, stage I, stage II, stage III, and stage IV.

Anatomical staging

The tumor, node, metastasis (TNM) system is part of what's used to stage esophageal cancer and is called the anatomical stage. In this system, the letters T, N, and M describe different areas of cancer growth. Based on cancer test results, your provider will assign a score or number to each letter. The higher the number, the larger the tumor or the more the cancer has spread. These scores are combined to assign the cancer a stage.

- **T (tumor)** – Depth and spread of the main (primary) tumor in the esophageal wall
- **N (node)** – If cancer has spread to nearby (regional) lymph nodes
- **M (metastasis)** – If cancer has spread to distant parts of the body, or metastasized

Ask your provider to explain any part of the staging that's unclear to you.

Often, not all information is available at the first evaluation. More information can be gathered as treatment begins.

Tumor grade

Grade is the way tumor cells look under a microscope. This information is part of what helps determine the stage. The lower the grade, the better the prognosis. Well differentiated (grade 1) means the cancer cells look similar to normal cells in the esophagus and grow slower than the higher grades. Moderately differentiated (grade 2) means the cancer cells look more abnormal and grow faster than grade 1. Poorly differentiated (grade 3) means the cancer cells look very different from normal esophageal cells and spread more quickly than grade 1 and grade 2 cells. Grade 3 is the highest grade for esophageal cancers.

Biomarker testing

Biomarkers may affect how some cancer treatments work. Results of biomarker testing help figure out if a treatment might work for a specific gene, protein, or mutation. Biomarkers that are tested for esophageal cancers include human epidermal growth factor receptor 2 (HER2), programmed death ligand 1 (PD-L1), microsatellite instability/mismatch repair (MSI/MMR) status, Claudin 18 isoform 2 (CLDN18.2), *NTRK* gene fusion, *RET* gene fusion, and *BRAF* V600 mutation.

Prognosis based on staging

Staging also includes what's known as prognostic information. A prognosis means the outlook for your cancer. This is the anatomical TNM plus tumor grade and the status of the biomarkers.

Stages are divided into clinical and pathological. Esophageal cancer staging is often done twice: once before surgery (clinical stage) and once after surgery (pathological stage). Staging after surgery provides more specific and accurate details about the size of the cancer, status of the lymph nodes (if the cancer has spread to the lymph nodes), and if the cancer has metastasized (spread to distant sites).

Clinical stage

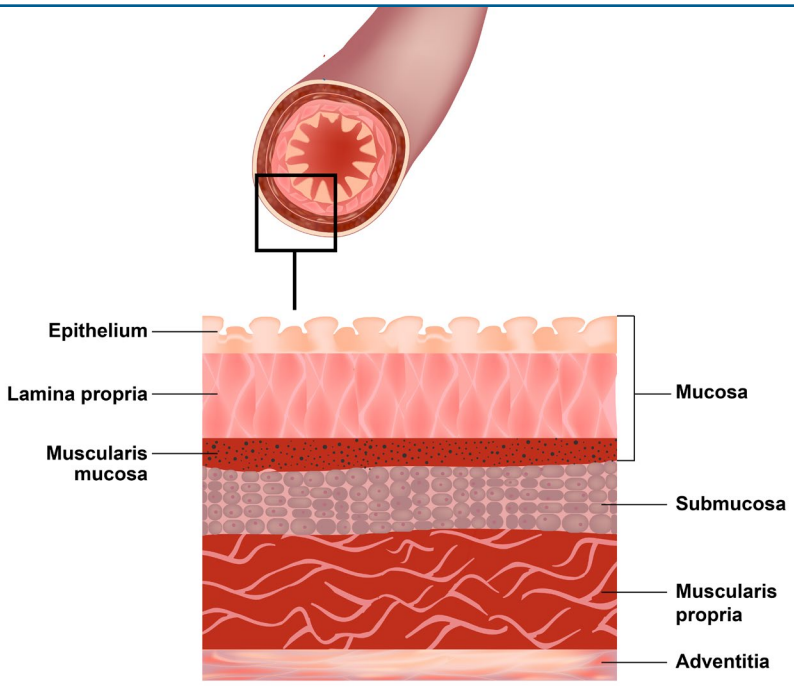
The clinical stage is the rating given before any treatment. It's assigned after you've had a physical exam, biopsy, and imaging tests. For example, in esophageal cancer, the clinical (before surgery) stage is based on the upper GI endoscopy (also called esophagogastroduodenoscopy, or EGD), imaging like CT or FDG-PET, biomarker testing, and biopsy results. Ask your provider to explain the clinical stage in a way you can understand.

Pathological stage

The pathological stage is determined by examining tissue removed during an endoscopic resection (ER) or surgery (and after preoperative therapy, if given) to remove all or part of the esophagus and nearby lymph nodes. This gives a more accurate picture of how far the cancer has spread and is used to determine your treatment options after surgery.

Layers of the esophagus

Pictured are the 4 layers of the esophagus: The mucosa, submucosa, muscularis propria, and adventitia.



Cancer stages explained

The stages of esophageal cancer may change after surgery—from the clinical stage to the pathological stage—because of the extra information provided by the tumor and tissue samples. The pathological (after-surgery) stages for adenocarcinoma and squamous cell carcinoma are as follows.

Adenocarcinoma

Below are the pathological stages for adenocarcinoma. For discussions of treatment based on the stages, see *Chapter 6: Adenocarcinoma* and *Chapter 8: Locally advanced recurrence or metastatic cancer*.

Stage 0

Stage 0 is also called high-grade dysplasia. This is pre-cancer with abnormal cells. It's found in the top layer of the mucosa, which is the epithelium. These cells can become cancer and spread to nearby tissue.

Stage 1

Stage 1 means cancer has grown from the esophageal lining into the deeper layers of the wall but hasn't reached any lymph nodes or distant organs.

Stage 1A

Stage 1A means cancer has formed in the mucosa layer of the esophagus. The grade of the cancer cells is either 1 or unknown.

Stage 1B

Stage 1B means cancer has spread to one of the following:

- Mucosa, and the grade of the cancer cells is 2.
- Submucosa (through the mucosa), and the grade of the cancer cells is 1, 2, or unknown.

Stage 1C

Stage 1C means cancer has spread to one of the following:

- Mucosa or submucosa layer of the esophageal wall, and the grade of the cancer cells is 3.
- Muscularis propria (outer muscle layer) of the esophageal wall (through the submucosa), and the grade of the cancer cells is 1 or 2.

Stage 2

Stage 2 means cancer has grown into the outer muscle layers (muscularis propria) of the esophagus and may have spread to one or two lymph nodes.

Stage 2A

Stage 2A means cancer has spread to the:

- Outer muscle layers of the esophageal wall (through submucosa), and the grade of the cancer cells is 3 or unknown.

Stage 2B

Stage 2B means the cancer cells could be any grade and have spread to one of the following:

- Last layer of the esophageal wall, called the adventitia.
- Mucosa layer or submucosa layer of the esophageal wall, and cancer is in 1 or 2 nearby lymph nodes.

Stage 3

Stage 3 is more advanced and means cancer has spread deeper into the esophageal wall and through the thicker muscle and outer layers. It may also have spread to nearby structures and involve regional lymph nodes.

Stage 3A

Stage 3A means the cancer cells could be any grade, and cancer has spread to one of the following:

- Mucosa layer or submucosa layer, with cancer found in 3 to 6 nearby lymph nodes.
- Muscularis propria (the thick muscle layer), with cancer found in 1 to 2 nearby lymph nodes.

Stage 3B

Stage 3B means the cancer cells could be any grade, and cancer has spread to one of the following:

- Muscularis propria, with cancer found in 3 to 6 nearby lymph nodes.
- Adventitia (the outer, deepest layer of the esophageal wall), with cancer found in 1 to 6 nearby lymph nodes.
- Diaphragm, azygos vein (blood vessel on the right side of the back of the chest), pleura (lining of the lungs), sac around the heart, or peritoneum (abdominal lining), with cancer found in 0 to 2 nearby lymph nodes.

Stage 4

Called metastatic cancer, stage 4 is the most advanced stage. Stage 4 cancer has spread to other parts of the body through the lymphatic system or blood and could affect distant lymph nodes and organs.

Stage 4A

Stage 4A means the cancer cells could be any grade and have spread to one of the following:

- Diaphragm, azygos vein, pleura, sac around the heart, or peritoneum, with cancer found in 3 to 6 nearby lymph nodes.
- Nearby organs, like the aorta, airway, or spine.
- Up to 7 or more nearby lymph nodes.

Stage 4B

Stage 4B means the cancer cells could be any grade, and cancer has spread to:

- Other parts of the body, like the liver, lungs, or bones, and could have spread to any number of lymph nodes.

“It's OK to have bad days but don't let yourself stay there. A positive attitude goes a long way."

Squamous cell carcinoma

Below are the pathological stages of squamous cell carcinoma. For discussions of treatment based on the stages, see *Chapter 7: Squamous cell carcinoma* and *Chapter 8: Locally advanced recurrence or metastatic cancer*.

Stage 0

Stage 0 is also called high-grade dysplasia. This is pre-cancer with abnormal cells. It's found in the top layer, which is the epithelium. These cells could become cancer and spread to nearby tissue.

Stage 1

Stage 1 means the cancer has grown from the esophageal lining into the deeper layers of the wall but hasn't reached any lymph nodes or distant organs.

Stage 1A

Stage 1A indicates the cancer has formed in the mucosa of the esophagus. The grade of the cancer cells is either 1 or unknown.

Stage 1B

Stage 1B means the cancer has spread to one of the following:

- Mucosa or the submucosa, and the cancer cells could be any grade or unknown.
- Muscularis propria (the thick muscle layer), and the grade of the cancer cells is 1.

Stage 2

Stage 2 is cancer that has spread further into the esophageal wall and may have spread to, but not further than, nearby lymph nodes.

Stage 2A

Stage 2A means the cancer has spread beyond one of the following:

- The submucosa to the muscularis propria. The grade of the cancer cells is either 2 or 3, or unknown.
- The muscularis propria and into the adventitia (the outer, deepest layer of the esophageal wall). The tumor is in the lower esophagus.
- The muscularis propria and into the adventitia, and the grade of the cancer cells is 1. The tumor is in the upper or middle esophagus.

Participating in a clinical trial may be an option. Be sure to ask your care team about it.



Stage 2B

Stage 2B indicates the cancer cells could be any grade, and cancer has spread to one of the following:

- The adventitia, and the grade of the cancer cells is 2 or 3. The tumor is either in the upper or middle esophagus.
- The adventitia, or it's not known where the tumor has formed in the esophagus, and the cancer grade is unknown.
- The mucosa layer or submucosa layer of the esophageal wall. Cancer is found in 1 or 2 lymph nodes near the tumor.

Stage 3

Stage 3 is cancer that has grown deeper into the esophageal wall and can involve nearby lymph nodes but not distant organs.

Stage 3A

Stage 3A means the cancer cells could be any grade, and the cancer has spread to one of the following:

- Mucosa or submucosa and is found in 3 to 6 nearby lymph nodes.
- Thick muscle (muscularis propria) and is found in 1 to 2 nearby lymph nodes.

Stage 3B

Stage 3B means the cancer cells could be any grade, and the cancer has spread to one of the following:

- Muscularis propria and is found in 3 to 6 nearby lymph nodes.
- Adventitia and is found in 1 to 6 nearby lymph nodes.
- Diaphragm, azygos vein (blood vessel on the right side of the back of the chest), pleura (lining of the lungs), sac around the heart, or peritoneum (abdominal lining) and is found in 0 to 2 nearby lymph nodes.

Stage 4

Called metastatic cancer, stage 4 is the most advanced stage. Stage 4 is cancer that has spread beyond the esophagus to nearby structures or lymph nodes or to distant organs and lymph nodes.

Stage 4A

Stage 4A means the cancer cells could be any grade, and the cancer has spread to one of the following:

- Diaphragm, azygos vein (blood vessel on the right side of the back of the chest), pleura (lining of the lungs), sac around the heart, or peritoneum (abdominal lining), and cancer is found in 3 to 6 nearby lymph nodes.
- Nearby structures, like the aorta, airway, or spine, and cancer is found in 0 to 6 nearby lymph nodes.
- 7 or more nearby lymph nodes.

Stage 4B

Stage 4B means the cancer has spread to one of the following:

- Distant parts of the body, such as the liver, lung, or bones, and to any number of lymph nodes.

Frequently used terms

Other terms might be used along with numbered cancer stages. This guide will use the following terms to describe esophageal cancer:

- **Resectable** – Tumor can be removed completely with surgery.
- **Unresectable** – Tumor can't be removed with surgery. The reasons a tumor can't be removed with surgery are because it might involve nearby blood vessels and arteries, making it unsafe to remove.
- **Locally advanced** – Tumor might be any size and could be in any layer of the esophagus. Cancer might be in the nearby lymph nodes, organs, and tissues.
- **Metastatic** – Cancer has spread to other parts of the body, including distant lymph nodes. The most common metastatic sites are the liver, distant lymph nodes, lungs, bones, and brain.

Your cancer stage is used to help guide your treatment. Be sure to ask your care team questions about your stage and any specifics about how your esophageal cancer will be treated.



Key points

- Staging helps to predict the prognosis (outlook) and is needed to make treatment decisions. A prognosis is the course your cancer will likely take.
- The tumor, node, metastasis (TNM) system is used to stage esophageal cancer.
- Esophageal cancer staging is often done twice: before and after surgery.
- Grade describes how abnormal tumor cells look under a microscope.
- Biomarker testing helps give more specific information on genes and proteins to help guide treatment.
- The clinical stage of esophageal cancer is based on the results of testing before any treatment.
- The pathological stage of esophageal cancer is based on the results of tissue examined during surgery.

Questions to ask

- What biomarker or genetic tests will I have?
- If biomarker testing is complete, what are the results?
- What stage is my cancer? What does that mean for treatment?
- How often does the clinical stage move to a higher pathological stage?
- Is my cancer resectable or unresectable? What does that mean?

What's next?

Now you know how cancer is staged, which is key to understanding the next steps of cancer care. Read the next chapter to learn all about the potential treatments for esophageal cancer.

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Types of treatment

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There's more than one treatment for esophageal cancer. This chapter describes treatment options and what to expect.

NCCN experts recommend that people with esophageal cancer seek treatment at cancer centers experienced in esophageal cancer. Also, it's important to know that treating esophageal cancer takes a team approach. Treatment decisions should involve a multidisciplinary care team. This is a team of health care providers from different professional backgrounds who have knowledge and experience in your type of cancer. This team is united with you in planning and carrying out your treatment.

Care team

Some members of your care team will be with you throughout cancer treatment, while others will only be there for parts of it. Get to know your care team and help them get to know you.

Depending on your diagnosis, your team might include the following specialists.

Doctors who treat cancer

- **Gastroenterologists** are experts in diseases of the digestive tract.
- **Surgical oncologists** perform operations to remove cancer.
- **Medical oncologists** treat cancer in adults using systemic therapy.
- **Radiation oncologists** prescribe and deliver radiation therapy (RT) to treat cancer.
- **Pathologists** analyze the cells, tissues, and organs removed during a biopsy or surgery and provide cancer diagnosis, staging, and information about biomarker testing.

It's important to tell your care team about all side effects so they can be managed.

Other health care providers

- **Palliative care specialists** are doctors, nurses, or other health care providers trained in palliative medicine, which aims to reduce the pain and suffering of serious illness.
- **Nurse practitioners (NPs)** and **physician assistants (PAs)** are called advanced practice providers, or APPs. Some of your clinic visits may be done by a nurse practitioner or physician assistant.
- **Oncology nurses** provide hands-on care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects. Sometimes these experts are called nurse navigators.
- **Nutritionists and dietitians** provide guidance on what foods are most suitable for your condition.

- **Social workers** help people prevent and solve problems in their lives. They can also help navigate the complexities of financial and insurance stresses. People who are clinical social workers provide counseling and help for emotional issues.

Treatment for esophageal cancer can involve more than one therapy. For example, you may have surgery, then systemic therapy, and possibly palliative care. See **Guide 2** and keep reading for more information on each treatment.

Guide 2
Possible treatments for esophageal cancer

Endoscopic therapy
Surgery
Esophagectomy
Other procedures
Systemic therapy
Chemotherapy
Chemoradiation
Immunotherapy
Targeted therapy
Radiation therapy
Clinical trials
Supportive care

Endoscopic therapy

Some treatments use a thin, tube-shaped tool called an endoscope that's inserted into the body to take pictures. One end of the scope has a small light and camera lens to see inside your body. The image is displayed on a television monitor. This helps guide your doctor for a biopsy, treatment, or other tasks. An endoscope is often guided into the body through the mouth.

The goal of endoscopic therapy is to remove or destroy early-stage disease and Barrett esophagus (BE). Endoscopic resection (ER) with or without ablation is preferred for early-stage cancer.

Endoscopic resection

For people with early-stage esophageal cancer or BE, endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) is essential for accurate staging and diagnosis.

Early-stage esophageal cancer has not grown beyond the first layer (mucosa) of the esophageal wall. The tumor is often very small (2 centimeters or less) and is not in any lymph nodes.

- **Endoscopic mucosal resection (EMR)** is a procedure to remove pre-cancerous, early-stage cancer or other abnormal tissues (lesions) from the esophageal wall. During EMR, the endoscope is passed down your throat to reach the lesion or tumor in your esophagus. The lesion can be removed through suction or by cutting. Talk to your doctor to learn more.

- **Endoscopic submucosal dissection (ESD)** uses an endoscope to locate the tumor in the esophageal wall. A tool is inserted through the endoscope that injects fluid to help the tumor separate from the esophageal wall. Then a tool lifts and cuts the tumor from the esophageal wall.

Endoscopic resection is a minimally invasive procedure that uses an endoscope to remove precancerous and cancerous areas of the esophagus.

Ablation uses extreme cold or extreme heat, radio waves, microwaves, or chemicals to destroy cancer cells. It can destroy small tumors and metastases with little harm to nearby tissue. You might have multiple treatments to destroy the tumor or metastasis. Ablation might be used if you're not healthy enough for surgery.

There are many types of ablation used to destroy cancer cells. The most common types used to treat an esophageal tumor include:

- Cryotherapy or cryosurgery kills cancer cells by freezing them with a very cold substance.
- Radiofrequency ablation (RFA) kills cancer cells by heating them with high-energy radio waves.
- Photodynamic therapy (PTD) uses drugs that become active when exposed to light. These activated drugs may kill cancer cells.

Surgery

Surgery is an operation or procedure to remove cancer from the body. Surgery is often the main or primary treatment to remove cancer from the esophagus, but it might be just one part of a treatment plan.

When preparing for surgery, seek the opinion of an experienced surgeon. The surgeon should be an expert in performing your type of operation. Surgery for esophageal cancer should be done at a high-volume center that does at least 15 to 20 esophageal surgeries each year (as well as having a multidisciplinary team that has dedicated thoracic surgical, medical, and radiation oncologists). Hospitals that perform many surgeries tend to have

Nutrition matters

Esophageal cancer can make eating more challenging. A dietician or nutritionist can help you with any nutrition needs before, during, and after cancer treatment.



Surgery and endoscopic procedures are best performed by experienced surgeons and endoscopists in high-volume centers for esophageal cancer. High volume means performing dozens of procedures per year.

better results. You can ask for a referral to a hospital or cancer center that has experience in treating esophageal cancer.

Cancer removal through surgery can be done in different ways depending on the specific circumstances, such as the size and location of the tumor and if there's cancer in any surrounding organs and tissues. Your surgeon will choose an approach based on the safest and best way to remove the cancer.

Surgery can also ease pain or discomfort. This is called palliative surgery.

Open surgery

Open surgery may include incisions in the chest (thoracotomy), abdomen (laparotomy), or neck. These larger incisions let the surgeon directly view and access the tumor in your esophagus to remove it. Open surgery can take several hours or longer. After the surgery, you'll need to stay in the hospital for at least several days to recover.

Minimally invasive surgery

Minimally invasive surgery (keyhole surgery) uses a few small incisions. Small tools are inserted through each incision to perform the surgery. One of the tools, called a videoscope, is a long tube with a video camera at the end. The camera lets the doctor see your esophagus and other tissues inside your chest and abdomen. Other tools are used to remove the tumor.

Minimally invasive surgery, also called thoracoscopic and laparoscopic surgery, can be done using robotic arms to control the surgical tools. This is called robot-assisted or robotic surgery and is becoming increasingly more common.

Through a computerized console with a high-definition camera at the end of the scope, the surgeon operates the robot that performs the surgery. Robotic surgery also uses small incisions, which helps improve recovery times.

Minimally invasive surgery has the advantages of fewer complications and less pain than traditional, open surgery.

Tumor resection

Surgical removal of the tumor is called tumor resection. Imaging tests will be ordered first to see if your cancer is resectable (removable with surgery) or unresectable (not removable with surgery). Sometimes, imaging and scoping tests can't clearly show one way or the other.

Goal of surgery

The goal of surgery (tumor resection) is to remove all of the cancer. Sometimes a tumor can't be resected because not all of it can be removed, even if it's locally advanced. But the ultimate goal is to remove the tumor along with a portion of normal-looking tissue around its edge, called the surgical margin. The surgical margin may look normal during surgery, but cancerous cells may be found when later viewed under a microscope by a pathologist.

A clear or negative margin is when no cancer cells are found in the tissue around the edge of the tumor. (A negative margin is a good thing.)

In a positive margin, cancer cells are found in the normal-looking tissue around the tumor. (A positive margin may not be a good thing.) If there's a positive margin, you may require another surgery to try to remove the remaining tumor cells. Surgery also includes removal of lymph nodes. Or you might have radiation therapy if not given before.

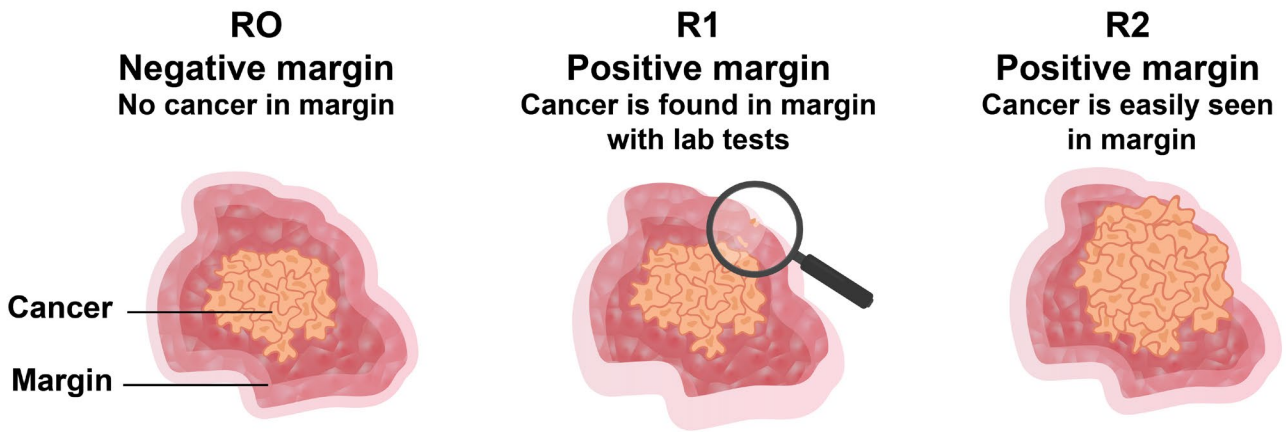
Surgical margins

The goal of surgery is to have a cancer-free surgical margin with a good functional outcome. This means it's ideal to remove the cancer as well as preserving your ability to perform daily tasks of living. After surgery, you may receive treatment, such as radiation, chemoradiation, or systemic therapy, to kill any remaining cancer cells.

- **In a clear, or negative, margin (known as R0)**, no cancerous cells are found in the tissue around the edge of the tumor.
- **In an R1 resection**, the surgeon removes all of the visible tumor, but the microscopic edges are still positive for tumor cells. Despite best efforts, this can happen.
- **In an R2 resection**, the surgeon is unable to remove all of the visible tumor or there's metastatic disease.

Surgical margin

The tumor will be removed, along with some normal-looking tissue around its rim. The normal-looking tissue is called the surgical margin. The surgical margin will be tested for cancer. Postoperative therapy is based on if there is cancer in the margins.



A negative margin (R0) is the best result. Your surgeon will look carefully for cancer not only along the surgical margin but also in other nearby areas. It's not always possible to find all of the cancer. Sometimes, surgeons can't safely remove the tumor with a cancer-free margin.

Surgeons often use an intraoperative pathology consultation. This is when a pathologist inspects the resected esophagus for cancer location and distance to surgical margins during the surgery. The pathologist will use a microscope to examine frozen sections of margins and possibly other metastases, such as liver. An intraoperative pathology consultation with the surgeon plays a key role in guiding the surgery. Sometimes the surgeon may stop the procedure if the consultation with the pathologist determines that the margins can't be made R0.

For more information about these results, ask your care team.

You may have more than one surgery. You may also have a wound drain placed to prevent fluid from collecting in the body after surgery. These drains are usually removed a few days after surgery.



If you smoke or vape, seek help to quit

Smoking or vaping nicotine greatly increases your chances of having side effects during and after surgery. Smoking and vaping can limit how well cancer treatment works and prevent wound healing. They also increase your chances of developing other cancers. Cannabis use might also affect the amount of anesthesia used during surgery.

Nicotine is the chemical in tobacco that makes you want to keep smoking and vaping. Nicotine withdrawal is challenging for most people who smoke or vape. The stress of having cancer may make it even harder to quit. If you smoke or vape, ask your care team about counseling and medicines to help you quit.

More information can be found in *NCCN Guidelines for Patients: Quitting Smoking*, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

For online support, try these websites:

- SmokeFree.gov
- CDC.gov/tobacco

Esophagectomy

An esophagectomy removes part, most, or all of the esophagus. This is a major operation even when the surgeon uses a minimally invasive technique. The surgery crosses 2 or 3 body cavities—abdomen, chest, and neck—and usually takes 4 to 6 hours.

Eating a healthy diet and exercising before surgery is important. When you're in your best possible physical condition before surgery, you're more likely to have a quicker and easier recovery after surgery.

There are 2 types of esophagectomy.

- **Transhiatal esophagectomy (THE)** is performed through creating an opening on the neck and abdomen. Typically, the stomach is joined to the esophagus in the neck.
- **Transthoracic esophagectomy (TTE)** is performed through creating an opening in the abdomen and the chest, and occasionally in the neck as well. The stomach may be joined to the esophagus in the chest or in the neck, depending on the location of the tumor.

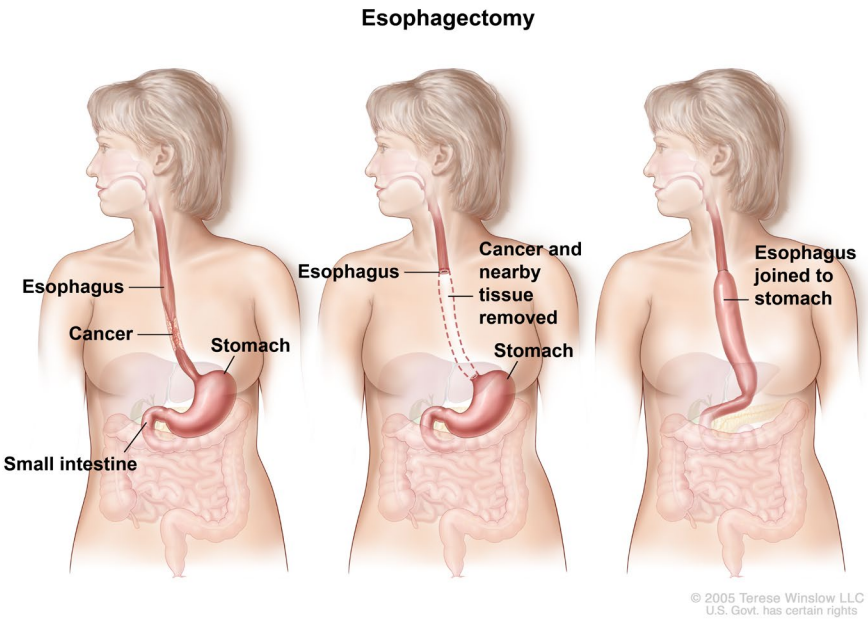
Minimally invasive laparoscopic and thoracoscopic or other robotic surgical approaches may be involved in an esophagectomy.

Reconstruction conduits

A conduit is a tube-shaped tissue, such as the stomach, colon, or small intestine, used to replace or reconstruct the part of the esophagus removed during an esophagectomy. A stomach (gastric) conduit is preferred and is the most commonly used conduit for esophageal reconstruction. The

Before and after an esophagectomy

These images show before and after an esophagectomy. In this case, a large portion of the esophagus has been removed. The stomach has been pulled up and joined with the esophagus. Sometimes, instead of the stomach, a piece of the small intestine or colon is used to replace the missing part of the esophagus.



stomach is a large, durable organ with an abundant blood supply.

The type of esophageal surgery is dictated by the location of the tumor, the choices available for conduit, and the surgeon's experience and preference, as well as your preference.

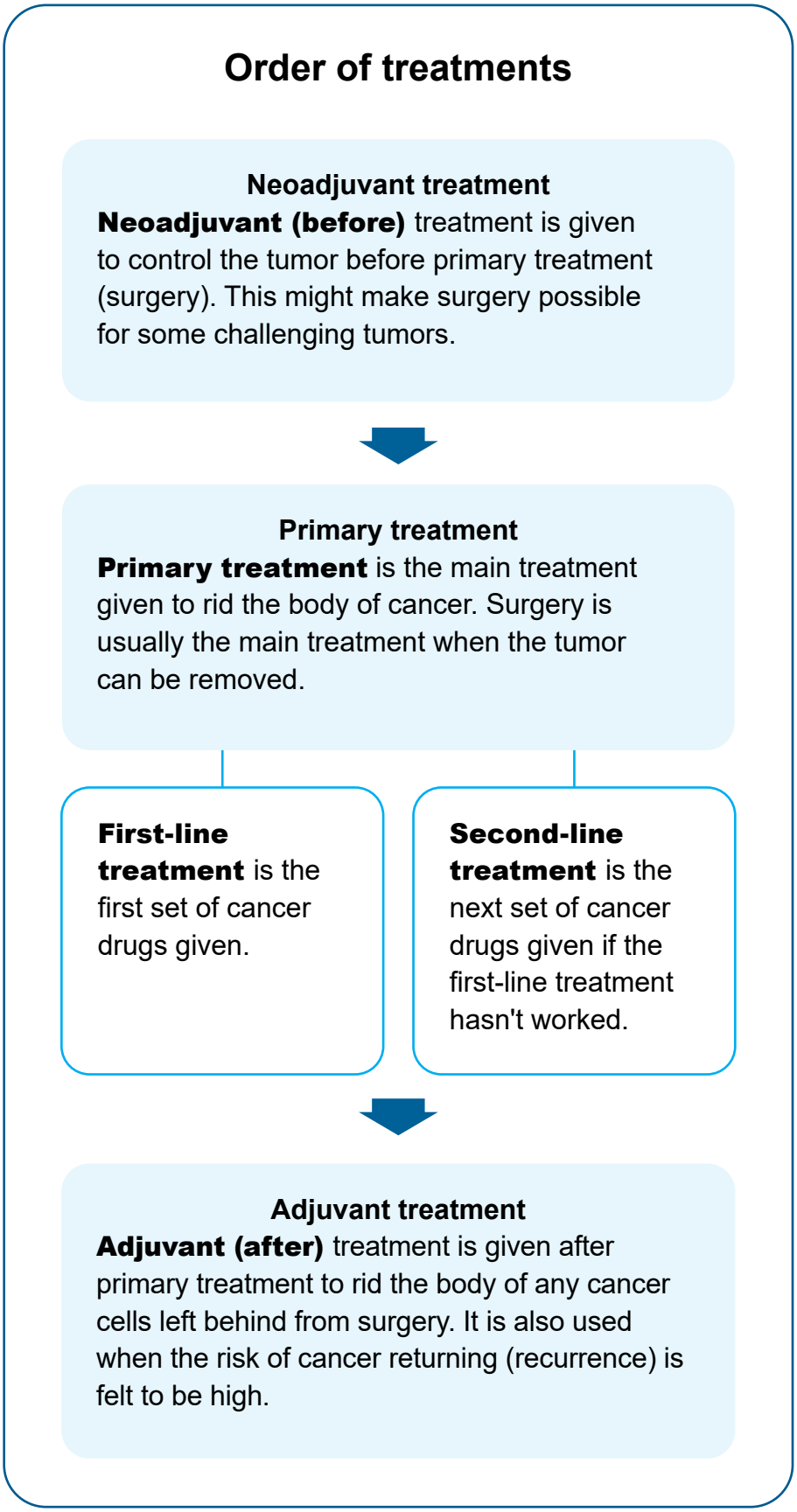
Other procedures

Esophagogastrectomy

In an esophagogastrectomy, the top part of the stomach and lower part of the esophagus are removed. A nutritionist or dietician provides guidance on what foods are most suitable for you before and after this surgery.

Lymph node dissection

Removal of lymph nodes or groups of lymph nodes is called lymph node or nodal dissection. It might be referred to as a lymphadenectomy. While at least 16 regional nodes should be removed and tested for cancer, NCCN experts recommend removal of more than 30 lymph nodes. The reason for additional lymph node removal is for more accurate staging as well as improved survival and reducing the risk of recurrence (cancer coming back).



Gastrostomy tube

A gastrostomy tube (G-tube) is a soft plastic tube inserted through the skin of the abdomen directly into the stomach. It allows air and fluid to leave the stomach and can be used to give medicines and fluids, including liquid food.

Giving food through a gastrostomy tube, also called a percutaneous endoscopic gastrostomy (PEG) tube, is known as enteral nutrition.

Jejunostomy tube

A jejunostomy tube (J-tube) is a flexible, plastic tube inserted into the skin of the abdomen and then into the midsection of the small intestine. The tube delivers food and medicine until you're healthy enough to eat by mouth.

Systemic therapy

Systemic therapy is treatment that works throughout the body. Types include chemotherapy, chemoradiation, targeted therapy, and immunotherapy. Systemic therapy might be used alone or with other therapies. The goals and side effects of systemic therapy should be discussed with your care team before you start treatment so that you're well informed on what you might experience.

Systemic therapy can be given at different times. The types and timing of these therapies are explained here:

- Systemic therapy or chemoradiation given before surgery is called **neoadjuvant** or **preoperative therapy**.
- Systemic therapy given before and after surgery is called **perioperative therapy**.
- Systemic therapy given after surgery is called adjuvant or **post-operative therapy**.
- Systemic therapy given for advanced disease may be a part of **palliative management**.

Why some therapies are preferred

All treatments listed in this guide are recommended and appropriate. When helpful, NCCN experts also assign a level of preference to their recommendations for systemic therapies:

- **Preferred therapies** have the most evidence they may work better and be safer than other therapies.
- **Other recommended therapies** can provide effective results but may have less evidence, more side effects, or may not work quite as well as preferred therapies.
- **Therapies used in certain cases** work best for individuals with specific cancer features or health circumstances.

Chemotherapy

Chemotherapy kills fast-growing cells throughout the body, including cancer cells and some normal cells. When chemotherapies are combined, it's called multi-agent or combination chemotherapy. Chemotherapy might be used before and after surgery. It might be used with radiation (called chemoradiation).

Some examples of chemotherapies include, in alphabetical order:

- Capecitabine (Xeloda)
- Carboplatin
- Cisplatin
- Docetaxel (Taxotere)
- Fluorouracil
- Irinotecan (Camptosar)
- Oxaliplatin (Eloxatin)
- Paclitaxel (Taxol)

Chemoradiation

Treatment that combines chemotherapy with radiation therapy is called chemoradiation. Chemotherapy may improve how well radiation works, and that's why they are sometimes given together. Chemoradiation may be used to control symptoms caused by a tumor, to shrink the tumor before surgery, to prevent the return of cancer after surgery, or as the primary (main) treatment for the tumor. It can be done in 2 ways: sequentially (1 treatment after the other) or concurrently (both chemotherapy and radiation given at the same time).

Immunotherapy

The immune system has many on and off switches. Tumors take advantage of off switches, such as programmed cell death protein 1 (PD-1) and CTLA4. Immunotherapy is a type of systemic treatment that tries to turn the immune system back on to destroy tumor



Warnings about supplements and drug interactions

You might be asked to stop taking or avoid certain herbal supplements when on a systemic therapy. Some supplements can affect the ability of a drug to do its job. This is called a drug interaction.

It is critical to speak with your care team about any supplements you may be taking. Some examples include:

- Turmeric
- Ginkgo biloba
- Green tea extract
- St. John's Wort
- Antioxidants

Certain medicines can also affect the ability of a drug to do its job. Antacids, heart or blood pressure medicine, and antidepressants are just some of the medicines that might interact with a systemic therapy or supportive care medicines given during systemic therapy. Therefore, it is very important to tell your care team about any medicines, vitamins, over-the-counter (OTC) drugs, herbals, or supplements you are taking.

Bring a list with you to every visit.

cells. Immune checkpoint inhibitors (ICIs) are one type of immunotherapy.

Immunotherapy can be given alone or with other types of treatment. Some examples of immunotherapy for esophageal cancer are, in alphabetical order:

- Dostarlimab-gxly (Jemperli)
- Durvalumab (Imfinzi)
- Ipilimumab (Yervoy)
- Nivolumab (Opdivo)
- Pembrolizumab (Keytruda)
- Tislelizumab-jsgr (Tevimbra)
- Tremelimumab (Imjudo)

More information on ICIs and immunotherapy side effects is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Targeted therapy

Targeted therapy focuses on specific or unique features of cancer cells. Targeted therapies seek out how cancer cells grow, divide, and move in the body. These drugs stop or inhibit the action of molecules that help cancer cells grow and/or survive.

Chemotherapy and systemic therapy are not the same. Systemic therapy includes chemotherapy, targeted therapy, and immunotherapy.

Targeted therapies for esophageal cancer include:

- Ramucirumab (Cyramza) targets VEGF (vascular endothelial growth factor) receptors.
- Entrectinib (Rozlytrek) and larotrectinib (Vitrakvi) are examples of TRK inhibitors used for *NTRK* gene fusion-positive tumors.
- Trastuzumab (Herceptin) or trastuzumab deruxtecan (Enhertu) target HER2 overexpression-positive tumors.

Radiation therapy

Radiation therapy (RT) uses high-energy radiation from x-rays, photons, protons, electrons, and other sources to kill cancer cells and shrink tumors. RT can be given alone or with other treatments. Unlike how drug therapy travels throughout the whole body to treat a tumor, radiation is a precisely targeted beam on individual areas. It can be targeted on the area of the esophagus containing the tumor, the lymph nodes containing the tumor, and nearby areas that may have hidden tumor cells.

RT can be used as the primary treatment for esophageal cancer. It can also be given before or after surgery to treat or slow the growth of cancer, especially if the surgical margins have cancer cells. RT may be used to treat a tumor that has spread (metastasized) to other parts of your body. RT can also be used as supportive care or palliative care to help ease pain or discomfort caused by cancer, or to control bleeding caused by a tumor.

Types of RT

- **External beam radiation therapy (EBRT)** uses a machine outside of the body to aim radiation at the tumor(s) or areas of the body.
- **Internal radiation** is placed inside the body as a solid like seeds. This is called brachytherapy.

You won't feel radiation treatments while you're receiving them, but side effects in the targeted area may develop over time. Discuss the risks and side effects with your care team.

Clinical trials

Another treatment option at any stage of disease is participating in a clinical trial. A clinical trial is a type of medical research study. After being developed and tested in a lab, potential new ways of fighting cancer need to be studied in people.

If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. FDA.

Everyone with cancer should carefully consider all of the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your doctor about whether a clinical trial may make sense for you.

Ask your care team what treatment options are available and if a clinical trial might be right for you.



Phases

Most cancer clinical trials focus on treatment and are done in phases.

- **Phase 1** trials study the safety and side effects of an investigational drug or treatment approach.
- **Phase 2** trials study how well the drug or approach works against a specific type of cancer.
- **Phase 3** trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase 4** trials study the safety and benefit of an FDA-approved treatment.

Who can enroll?

It depends on the clinical trial's rules, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. They ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Informed consent

Clinical trials are managed by a research team. This group of experts will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss it with people you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.



Finding a clinical trial

In the United States

NCCN Cancer Centers
NCCN.org/cancercenters

The National Cancer Institute (NCI)
cancer.gov/about-cancer/treatment/clinical-trials/search

Worldwide

The U.S. National Library of Medicine (NLM)
clinicaltrials.gov

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS)
1.800.4.CANCER (1.800.422.6237)
cancer.gov/contact

"My doctor encouraged me to seek additional medical opinions to ensure I was comfortable with my treatment decision. Only after I made up my mind did she share her thoughts."

Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It is common to receive either a placebo with a standard treatment, or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

Are clinical trials free?

There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. But you may need to pay for other services, like transportation or childcare, due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is often covered by insurance.

Supportive care

Supportive care is available at any time in your cancer treatment. Supportive care is health care given to prevent, reduce, and relieve symptoms and side effects and to improve your quality of life while you're undergoing cancer treatment. It might include pain relief, emotional or spiritual support, home care, medical equipment, financial aid, or family counseling. Tell your care team how you're feeling and about any treatment side effects so they can be managed.

It's very important to take care of yourself by eating well, drinking plenty of fluids, exercising, and doing things that make you feel energized.

Strength is needed to sustain you during treatment. For more information on supportive care, see *Chapter 9: Supportive care*.

Supportive care and palliative care: Are they the same?

You might hear the terms supportive care and palliative care and think they mean the same thing. While they both aim to improve your quality of life, they have slightly different meanings.

Palliative care (also called palliative management) can be a part of supportive care. Palliative care aims to relieve major symptoms like pain, bleeding, blockages, or nausea and vomiting, in advanced cancer.

Supportive care is more of a broad type of care that is available at any time in your cancer journey. It is intended to support you and your family to help you feel better tolerate treatment. For more information, see *Chapter 9: Supportive care*.

Key points

- Surgery is a main or primary treatment for esophageal cancer.
- A resectable tumor can be removed with surgery. An unresectable tumor can't be removed with surgery.
- Systemic therapy works throughout the body. It includes chemotherapy, targeted therapy, and immunotherapy.
- Targeted therapies can block the ways cancer cells grow, divide, and move in the body.
- Immunotherapy uses your body's natural defenses to find and destroy cancer cells.
- Radiation therapy (RT) uses high-energy radiation from x-rays, gamma rays, protons, photons, and other sources to kill cancer cells and shrink tumors.
- A clinical trial is a type of research that studies a treatment to see how safe it is and how well it works.

Questions to ask

- What is your experience treating esophageal cancer? What else do you treat?
- What are my treatment options?
- What is the stage of my disease?
- Is a clinical trial an option for me?
- I'd like a second opinion. Is there someone or a resource to find one that you can recommend?

What's next?

Now that you've read about all of the treatment possibilities, as well as staging, you can find more specific treatment information for your type of cancer in *Chapter 6: Adenocarcinoma*, *Chapter 7: Squamous cell carcinoma*, or *Chapter 8: Locally advanced recurrence or metastatic cancer*.

6
Adenocarcinoma

54 Early stage

56 Locally advanced

60 After esophagectomy

62 Follow-up care

63 Key points

63 Questions to ask

Treatment for esophageal adenocarcinoma is based on the size and location of the tumor and your overall health. This chapter is for people diagnosed with early-stage or locally advanced adenocarcinoma.

Esophageal adenocarcinoma starts in the mucus-making cells of the esophagus. This type of cancer is often found in the lower part of the esophagus. Because esophageal cancer symptoms tend to show up once cancer has advanced, it's not as common to be diagnosed at the early stage as the locally advanced stage.

Early stage

You've probably already received a diagnosis of early-stage adenocarcinoma after having various imaging tests and a biopsy, and/or you've had an endoscopic resection (ER) that determined your diagnosis.

But understanding your diagnosis may not be straightforward. Early-stage adenocarcinoma includes both the clinical stages and pathological stages. Imaging and biopsy determine the clinical stage, and that information plus an ER determine the pathological stage.

ER is known to be accurate for staging early-stage cancers because it can give more detailed information on the tumor growth than an endoscopic ultrasound (EUS), which can be used after an upper GI endoscopy for staging. As long as it's a small, early tumor, ER can remove the tumor, which will then be examined under the microscope. EUS is less invasive but still can show detailed images of the layers of the esophageal wall, the growth of a tumor, and lymph nodes. EUS is more helpful when combined with a biopsy for other stages of disease.

For details on staging and an illustration of the esophageal wall, see *Chapter 3: Esophageal cancer staging*.

ER doesn't just help stage early cancer, it can also help remove it. For types of treatments, see **Guide 3**.

Here's how the stages break down once you receive your diagnosis:

Clinical

- Stage 1: The tumor has invaded the submucosa
- Stage 2: The tumor has spread to the muscularis propria

Guide 3
Possible treatments for early-stage adenocarcinoma

Esophagectomy
Endoscopic resection
Ablation

Pathological

- Stage 0: Abnormal cells are found in the epithelial layer of the mucosa. This could be called dysplasia or Barrett esophagus with high-grade dysplasia.
- Stage 1A: The tumor invades the lamina propria or the muscularis mucosa.
- Stage 1B: The tumor spreads to the second layer of the esophageal wall (the submucosa).

Before you start treatment, your care team should meet to discuss it. They might recommend laparoscopy (minimally invasive surgery) if there's no evidence of metastases (spread) and the tumor is at the esophagogastric junction (EGJ). They might also advise that you receive liquid nutrition through an enteric feeding tube to help you get enough nutrients before any treatment.

Your treatment will be based on the size, grade, depth, and location of the tumor as well as your overall health.

If you're healthy enough for surgery and don't have any other serious health issues that prevent surgery, then an esophagectomy might be an option. For people who don't want or can't have surgery, chemoradiation might be an option.

If endoscopic therapy or surgery is an option

Early-stage adenocarcinoma is less likely to have spread to the lymph nodes, so treatment with a less-invasive endoscopic therapy, like ER, may be an option. But if the cancer has spread to the second layer (the submucosa), you might have an esophagectomy.

Clinical stage 1 or stage 2

If you haven't received an ER and the tests and biopsies diagnosed your cancer at clinical stage 1 or 2, your treatment option is:

- Esophagectomy (see "After esophagectomy" for what comes next).

Pathological stage 0, stage 1A, stage 1B, or stage 1C

If you had the ER before diagnosis, you might need additional therapies that could include another ER to remove any remaining cancerous areas.

In other words, if you're healthy enough, then you could have:

- ER with or without ablation.
- Ablation.
- Esophagectomy (see "After esophagectomy" for what comes next).

If surgery is not an option

A tumor that can't be completely removed with an esophagectomy is called unresectable. For people who have an unresectable tumor, aren't healthy enough to tolerate major surgery, or don't want surgery, then treatment will be ER and/or ablation. Treatment might be followed by chemoradiation.

Pathological stage 0

For pathological stage 0, if you're not healthy enough for surgery or you don't want surgery, then treatment may include:

- ER with or without ablation.
- Ablation.

Pathological stage 1A, stage 1B, or stage 1C

For pathological stage 1A ,1B, or 1C, your treatment option is:

- ER with or without ablation.

Chemoradiation might be an additional treatment if your cancer has more advanced features like lymphovascular invasion (LVI), a higher grade, positive margins, or larger size (2 centimeters or bigger).

Surveillance

The surveillance step will start about 6 weeks or more after endoscopic therapy. Surveillance looks for and treats any signs that cancer has returned, called recurrence. This means having an upper GI endoscopy every 3 months for the first year, every 6 months for the second year, and then annually. This will check for signs of thickening in the esophageal wall. It will also look for Barrett esophagus or recurrent dysplasia.

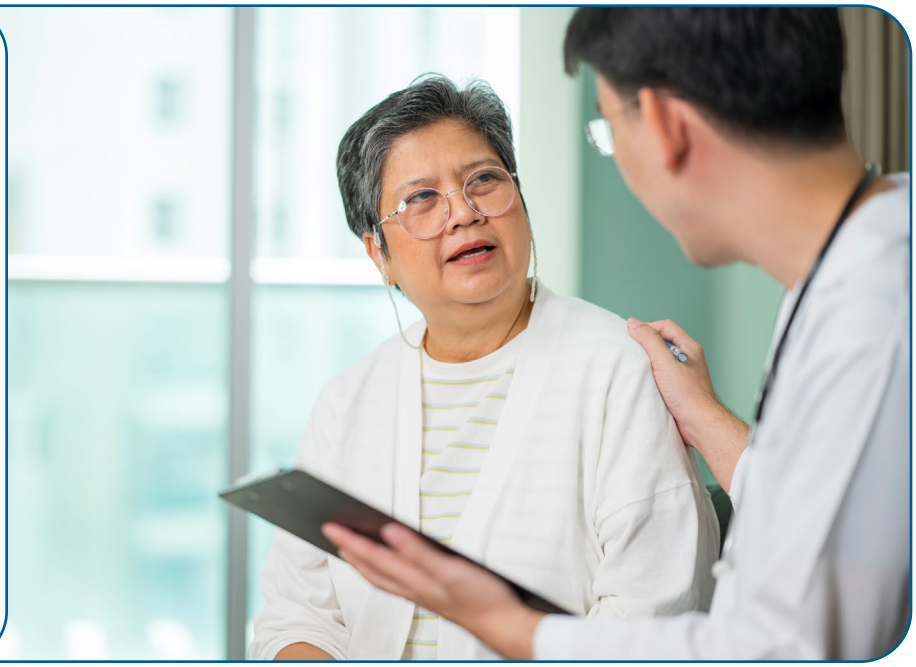
Locally advanced

In locally advanced (also called locoregional) adenocarcinoma, the tumor has grown into other layers of the esophagus and may or may not have spread to nearby lymph nodes. It's cancer that has spread but not metastasized (spread far from original site).

Locally advanced adenocarcinoma is often diagnosed and treated from the clinical stage. This is when the stage is based on information from the endoscopic ultrasound (EUS) and other imaging or biopsy results.

One of the most important markers of more advanced esophageal cancer is the presence of lymphovascular invasion (LVI). This means that even if no cancer is found in the lymph nodes, cancer cells are more aggressive and have spread to lymphatic vessels or blood vessels in or near the tumor. It could also mean the cancer has spread to lymph nodes not found in the original biopsy. If LVI is found

Your preferences about treatment are always important. Talk to your care team and make your wishes known.



when the pathologist examines the biopsy, then there's a higher chance of it spreading to the lymph nodes.

Before you start treatment, your care team might recommend that you receive liquid nutrition through a feeding tube that goes directly to your stomach or small intestine. If it's determined that you can have an esophagectomy, see below. If you're not able to have the surgery, see "If surgery is not an option."

For types of treatments, see **Guide 4**.

If surgery is an option

Clinical stage 1 or stage 2A

At these stages, an esophagectomy might be an option if the tumor is less than 3 centimeters (cm), it has not grown beyond the third layer (muscularis propria) of the esophageal wall, and there's no cancer in the lymph nodes. Treatment after an esophagectomy will be based on the surgical margin results. See "After esophagectomy."

Guide 4
Possible treatments for locally advanced adenocarcinoma

Esophagectomy
Chemoradiation
Chemotherapy
Systemic therapy
Palliative management
Palliative radiation therapy
Observation

Clinical stage 2B or stage 3

For tumors 3 cm or larger, cancer is found in the lymph nodes, or tumors that have grown into or beyond the third layer (muscularis propria) of the esophageal wall, treatment options include:

- **Perioperative (around the time of surgery) systemic therapy** (preferred) followed by imaging tests and upper GI endoscopy with biopsy to check on the status of the cancer.
  - If no cancer is found or if it's found but considered local, then your treatment will be an esophagectomy. Even if no cancer is found, this surgery might be needed to prevent the cancer from recurring. See "After esophagectomy" to read what's next.
  - If you don't want surgery or you have unresectable cancer (not removable with surgery), then the option is chemoradiation alone followed by follow-up care. See "Follow-up care."
  - If you're found not to be healthy enough to tolerate surgery after the systemic therapy and imaging, then you have the options of chemoradiation alone followed by follow-up care or palliative management. (See Chapter 8 and Chapter 9 for more information on palliative management).
  - If the cancer has spread to distant sites (is metastatic), then your option is palliative management.

- **Preoperative chemoradiation** can be an option if the tumor is potentially resectable (removable) to help shrink the tumor before surgery. If you receive preoperative chemoradiation, you'll have imaging tests and upper GI endoscopy with biopsy to check on the status of the cancer. Chemoradiation is also an if you're not healthy enough for surgery or chemotherapy.
  - If no cancer is found, then you'll have an esophagectomy (preferred). Even though no cancer was found, this surgery might be needed to prevent the cancer from recurring. Another option is observation in follow-up care. See "Follow-up care."
  - If there's still cancer and it's considered local, you'll have an esophagectomy (preferred) or palliative management.
  - If the cancer is considered unresectable or it's become metastatic, then your option is palliative management.
- **If the tumor has microsatellite instability-high or mismatch repair deficiency (MSI-H/dMMR)**, your care team should meet to determine next steps. You might have an immune checkpoint inhibitor (ICI) before (preoperatively) and around the time of surgery (perioperatively). After that treatment, you'll receive imaging tests and upper GI endoscopy and biopsy to check on the status of the cancer.
  - If no cancer is found, you'll go to observation in follow-up care (see "Follow-up care") or have an esophagectomy (see "After esophagectomy") to help prevent recurrence and with long-term survival.
  - If there's still cancer and it's considered local, then you'll have an esophagectomy (preferred) or palliative management.
  - If new metastatic disease is found, you'll receive palliative management.
- **Chemoradiation alone** (also called definitive chemoradiation) is an option for people who don't want to have surgery. If you receive chemoradiation, then you'll move to observation in follow-up care. See "Follow-up care."

The term palliative management means any and all treatments to reduce pain and suffering. The term palliative care is more specific. See Chapters 8 and 9 for more information.

For systemic therapy options, see **Guide 5**.

Clinical stage 4A

For a tumor that has grown through the layers of the esophageal wall into nearby structures, treatment options are:

- Chemoradiation alone
- Chemotherapy alone if cancer is found in the trachea (windpipe), large vessels, or heart

Guide 5
Systemic therapy options

Preoperative (before surgery) chemoradiation	**Preferred** • Paclitaxel and carboplatin • Fluorouracil and oxaliplatin **Other recommended** • Fluorouracil and cisplatin • Irinotecan and cisplatin • Paclitaxel and fluoropyrimidine
Preoperative or perioperative (around the time of surgery) immunotherapy	**Used in some cases** Only for MSI-H/dMMR tumors • Dostarlimab-gxly for neoadjuvant therapy only • Nivolumab and ipilimumab followed by nivolumab • Pembrolizumab • Tremelimumab and durvalumab for neoadjuvant therapy only
Perioperative systemic therapy	**Preferred** • FLOT (fluorouracil, leucovorin, oxaliplatin, and docetaxel) - For PD-L1 positive tumors, FLOT plus durvalumab - For clinically node-negative tumors, FLOT plus durvalumab - For diffuse-type GEJ adenocarcinoma tumors, FLOT plus durvalumab **Other recommended** • Fluorouracil and cisplatin • Fluoropyrimidine and oxaliplatin
Definitive chemoradiation	**Preferred** • Paclitaxel and carboplatin • Fluorouracil and oxaliplatin **Other recommended** • Fluorouracil and cisplatin • Cisplatin with docetaxel or paclitaxel • Irinotecan and cisplatin • Paclitaxel and fluoropyrimidine
Postoperative (after surgery) systemic therapy	**Preferred** • Nivolumab only after preoperative chemoradiation with R0 • resection and residual disease **Other recommended** • Capecitabine and oxaliplatin26 • Fluorouracila and oxaliplatin • Fluoropyrimidine (infusional fluorouracila or capecitabine) before and after fluoropyrimidine-based chemoradiation

But if you receive chemoradiation, after that treatment you'll have imaging tests and upper GI endoscopy with biopsy to see if any cancer remains. If no cancer is found, you'll enter observation (preferred) or have an esophagectomy. If you have the surgery, see "After esophagectomy."

If cancer is found but it's local and not metastatic, your options are an esophagectomy (preferred) or palliative management. If you have surgery, then see "After esophagectomy."

Clinical stage 4B is metastatic cancer. For more information on how it's treated, see *Chapter 8: Locally advanced recurrence or metastatic cancer*.

If surgery is not an option

Not everyone is healthy enough for or wants surgery. Regardless of the stage, chemoradiation is an option for people who don't want surgery or are not healthy enough for it. For people who can't tolerate chemoradiation, palliative radiation therapy or palliative care are options.

After esophagectomy

The goal of surgery (esophagectomy) is to remove the tumor and any remaining cancer. Your treatment after surgery depends on whether, during surgery, the cancer is found to be R0, R1, or R2 (explained below).

But the next step matters if you didn't receive treatment before your surgery. See the next section. If you did receive treatment, see "If you received chemoradiation or systemic therapy before surgery."

Keep a positive outlook and accept the love of those around you who are concerned. Always believe that you are going to be okay.



If you didn't receive chemoradiation or systemic therapy first

If you had an esophagectomy and didn't have chemoradiation or systemic therapy before it, then your cancer will be staged with the new, more detailed tissue samples taken during surgery.

R0 resection

In a clear, or negative, resection margin (R0), no cancer cells are found in the tissue around the edge of the tumor. If the lymph nodes also showed no signs of cancer, called node negative, then you'll enter observation in follow-up care. This would be pathological stage 0, stage 1, or stage 2A or 2B. See "Follow-up care."

If the cancer is now a pathological stage 3B or 4A, or your lymph nodes tested positive at any stage, then your options include:

- Chemotherapy
- Chemoradiation with fluoropyrimidine (chemotherapy)
- Observation

After treatment, you'll enter follow-up care. See "Follow-up care."

R1 resection

An R1-positive margin means the surgeon removed all of the visible tumor, but microscopic cancer remains in the margin. This cancer can't be seen with the human eye, but it can be seen under a microscope. For treatment, you'll receive chemoradiation with fluoropyrimidine (chemotherapy).

R2 resection

An R2 resection means that the surgeon was unable to remove all of the visible tumor, or there's cancer in the surgical margin that can be seen with the human eye. The remaining cancer after surgery may be near where the primary tumor was and in the lymph nodes or at distant sites (metastatic). Your treatment will be either:

- Chemoradiation with fluoropyrimidine (chemotherapy)
- Palliative management

If you received chemoradiation or systemic therapy before surgery

If you had an esophagectomy but received chemoradiation or systemic therapy first, then your cancer will be restaged with the new, more detailed tissue samples taken during the esophagectomy.

R0 resection

If you had no cancer in the margins and your cancer is now a pathological stage 1, then your options include:

- Systemic therapy, if received around the time of surgery (perioperatively)
- Observation, if you're not healthy enough for systemic therapy

If no cancer was found in the margins and your cancer is now a pathological stage 1, 2, 3A, 3B, 4A, or 4B, then your options are:

- Systemic therapy, if you received it around the time of surgery (perioperatively)
- Immunotherapy with nivolumab, if you received preoperative chemoradiation

- Observation, if you're not healthy enough for more systemic therapy

After treatment, you'll move to follow-up care (see "Follow-up care"). Follow-up care should include upper GI endoscopy with biopsy (endoscopic ultrasound, if needed) every 12 weeks for 2 years, and then every 6 months until year 5.

R1 resection

Separately, if your cancer is an R1 resection, meaning there's still cancer in the surgical margins, you'll receive:

- Chemoradiation with fluoropyrimidine (chemotherapy), only if radiation therapy wasn't received preoperatively
- Observation in follow-up care
- Possibly another surgery

R2 resection

An R2 resection means that the surgeon was unable to remove all of the visible tumor, or there's cancer in the surgical margin that can be seen with the human eye. The remaining cancer after surgery may be near where the primary tumor was and in the lymph nodes, or at distant sites (metastatic). Your treatment options include:

- Chemoradiation with fluoropyrimidine (chemotherapy), only if radiation therapy wasn't received preoperatively
- Palliative management

Follow-up care

After treatment, you'll receive follow-up care to watch for signs that cancer has returned, called recurrence. For more information on recurrence, read *Chapter 8: Locally advanced recurrence or metastatic cancer*.

If the tumor was treated with surgery or endoscopic resection (ER), then follow-up care should include:

- Medical history and physical exam every 3 to 6 months for 1 to 2 years, then every 6 to 12 months for 3 to 5 years
- Complete blood count (CBC) and chemistry profile, as needed
- Imaging as needed for signs or symptoms of cancer
- Upper GI endoscopy with biopsy as needed for signs or symptoms of cancer
- Dilatation for anastomotic stenosis (a minimally invasive surgery that widens the esophagus after an esophagectomy)
- Nutrition counseling

Key points

- Treatment is based on the size, depth, and location of the tumor, as well as your overall health.
- Very small, early-stage tumors are staged using a biopsy sample from an endoscopic resection. This is called the pathological stage.
- Locally advanced cancer is staged before surgery. This is called the clinical stage. It's based on the endoscopic ultrasound (EUS) and other imaging or biopsy results.
- Your tumor and lymph nodes removed during an esophagectomy will be tested and staged before starting the next treatment.
- Chemoradiation might be given before (preoperative) or after (postoperative) surgery, or as definitive (only) treatment.
- Palliative management means any and all treatments to relieve pain and suffering.
- After treatment, you'll receive follow-up care. It's important to stay on top of your health and keep any doctor visits and imaging test appointments.

Questions to ask

- What stage is my esophageal cancer and why?
- What is the postoperative period like at the hospital?
- How long will it take for me to heal from surgery?
- Is there cancer in the lymph nodes? If so, what does that mean for me?
- I'd like to get a second opinion. Can you suggest someone?

What's next

After your treatment and as mentioned above, you'll receive regular exams and imaging. In the meantime, be sure to contact your doctor if you have any new or worsening symptoms. See *Chapter 10: Survivorship* for what you might expect.

Be your own advocate. Talk to someone who has gone through the same thing as you. Ask a lot of questions, even the ones you are afraid to ask. You have to protect yourself an densure you make the best decisions for you, and get the best care for your particular situation."

7
Squamous cell carcinoma

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Treatment for esophageal squamous cell carcinoma is based on the size and location of the tumor and your overall health. This chapter is for people diagnosed with early-stage or locally advanced squamous cell carcinoma.

Esophageal squamous cell carcinoma starts in the thin, flat cells found in the inner lining of the esophagus, known as the epithelium. Squamous cell carcinoma is often found in the middle and upper part of the esophagus. Because esophageal cancer symptoms tend to show once cancer has advanced, it's not as common to be diagnosed at the early stage as at the locally advanced stage.

Early stage

You've probably already received a diagnosis of early-stage adenocarcinoma after having various imaging tests and a biopsy, and/or you've had endoscopic resection (ER) that determined your diagnosis.

Still, understanding your diagnosis may not be straightforward. Early-stage squamous cell esophageal cancer includes both the clinical and pathological stages. It's a clinical stage if the imaging and biopsy determined the stage, and it's a pathological stage if that information plus an ER determined the stage.

Basically, ER is known to be accurate for staging early-stage cancers because it can give more detailed information on the tumor growth than an endoscopic ultrasound (EUS), which can be used after an upper GI endoscopy for staging.

As long as it's a small, early tumor, ER can be used to remove the tumor and then it is examined under a microscope. EUS is less invasive but still can show detailed images of the layers of the esophageal wall, the growth of a tumor, and lymph nodes. It's more helpful when combined with a biopsy for other stages of disease. For details on staging and an illustration of the esophageal wall, see *Chapter 3: Esophageal cancer staging*.

For types of treatment for early-stage squamous cell carcinoma, see **Guide 6**.

Following is a description of the stages of early squamous cell carcinoma.

Clinical stages

- Stage 1: The tumor invades the submucosa
- Stage 2: The tumor spreads to the muscularis propria

Guide 6
Possible treatments for early-stage squamous cell carcinoma

Esophagectomy
Endoscopic resection
Ablation

Pathological stages

- Stage 0: Abnormal cells are found in the epithelial layer of the mucosa
- Stage 1A: The tumor invades the lamina propria or the muscularis mucosa
- Stage 1B: The tumor spreads to the second layer of the esophageal wall (the submucosa)

Your care team should meet to discuss your treatment before starting. They might decide that you should be given liquid nutrition through an enteric feeding tube to help you get enough nutrients before treatment.

Endoscopic therapy or surgery as an option

Early-stage squamous cell esophageal cancer is less likely to have spread to the lymph nodes, so treatment might be a less-invasive endoscopic therapy, like ER. But if the cancer has spread to the second layer (the submucosa), you might have surgery, known as an esophagectomy.

Clinical stage 1 or stage 2

If you haven't received an ER and the tests and biopsies diagnosed your cancer at clinical stage 1 or 2, your treatment option is:

- Esophagectomy, if the tumor is in the noncervical esophagus (not in the neck region). (See "After esophagectomy" for what comes next.)

If the tumor is in the neck region, surgery is usually avoided at the early stage because of the long-term impact on surrounding organs like the windpipe (trachea), the voice box (larynx), and parts of the throat (pharynx).

Pathological stage 0, stage 1A, stage 1B

If you had ER before diagnosis, you might need additional therapies that could include another ER to remove any remaining cancerous areas.

In other words, if you're healthy enough, then you could have:

- ER with or without ablation (preferred)
- Ablation (preferred)
- Esophagectomy (see "After esophagectomy" for what comes next)

If surgery is not an option

If you have early-stage cancer but are not healthy enough or don't want surgery, then treatment may include:

- ER with or without ablation
- Ablation

For pathological stage 1B (more advanced), your treatment option is:

- ER with or without ablation

Chemoradiation might be an additional treatment if your cancer has more advanced features like lymphovascular invasion (LVI), a higher grade, positive margins, or a larger tumor size: 2 centimeters (cm) or bigger.

Surveillance

About 6 or more weeks after endoscopic therapy, the next step is surveillance to look for and treat any signs the cancer has returned, called recurrence. This means having an upper GI endoscopy done every 3 months for the first year, then every 6 months for the second year,

and then annually. This will check for signs of thickening in the esophageal wall. It will also look for recurrent dysplasia.

Locally advanced

In locally advanced (also called locoregional) squamous cell carcinoma, the tumor has grown into other layers of the esophagus and may or may not have spread to nearby lymph nodes.

Locally advanced esophageal cancer is often diagnosed and treated from the clinical stage. This is when the stage is based on information from the EUS and other imaging or biopsy results.

One of the most important markers of more advanced esophageal cancer is the presence of LVI. This means that even if no cancer is found in the lymph nodes, the cancer cells are more aggressive and have spread to lymphatic vessels or blood vessels in or near the tumor. It could also mean the cancer has spread to lymph nodes not found in the original biopsy. If LVI is found when the pathologist examines the biopsy, then there's a higher chance of it spreading to the lymph nodes.

Before you start treatment, your care team might recommend that you receive liquid nutrition through a feeding tube that goes directly to your stomach or small intestine. This will help you get the nutrients you'll need for treatment. If it's determined that you can have surgery (an esophagectomy), see below. If you're not able to have surgery, see "If surgery is not an option."

For types of treatments, see **Guide 7**.

If surgery is an option

Clinical stage 1 (more advanced) or stage 2

If you're healthy enough for surgery, then you might have an esophagectomy. But an esophagectomy will only be done if the tumor is not in the cervical esophagus (the neck region), is less than 3 cm, and hasn't grown beyond the second layer (submucosa) of the esophageal wall.

If the tumor is in the neck region, surgery is usually avoided because of the long-term impact on surrounding organs like the windpipe (trachea), the voice box (larynx), and parts of the throat (pharynx).

Treatment after an esophagectomy is based on the surgical margin results (see "After esophagectomy" below).

Guide 7
Possible treatments for locally advanced squamous cell carcinoma

Esophagectomy
Chemoradiation
Chemotherapy
Palliative management
Palliative radiation therapy
Observation

Clinical stage 2 or stage 3

For tumors 3 cm or bigger considered high risk and have LVI, or tumors that have grown into or beyond the third layer (muscularis propria) of the esophageal wall, options include:

- Preoperative chemoradiation followed later by an esophagectomy (preferred)
- Chemoradiation alone (also called definitive chemoradiation)

After preoperative chemoradiation, you'll have imaging tests as well as an upper GI endoscopy with biopsy to see if any cancer remains. If none remains, then you'll have either an esophagectomy or enter observation in follow-up care (see "Follow-up care"). Even if no cancer was found, this surgery might be needed to prevent the cancer from recurring and to help with long-term survival. See "After esophagectomy" to read what's next.

If cancer is found after preoperative chemoradiation and its spread is considered local, then your options are:

- Esophagectomy (preferred). See "After esophagectomy" for what's next.
- Palliative management

If your cancer is considered unresectable (not removable with surgery) or metastatic (has spread to distant areas), then your option is palliative management.

If you received chemoradiation only, then you'll move to follow-up care.

The term palliative management means any and all treatments to reduce pain and suffering. The term palliative care is more specific. See Chapters 8 and 9 for more information.

Clinical stage 4

For a **clinical stage 4A** tumor that has grown through the layers of the esophageal wall into nearby structures, treatment options are:

- Chemoradiation alone
- Chemotherapy alone if cancer is found in the trachea (windpipe), large vessels, or the heart

After chemoradiation, you'll have imaging tests and upper GI endoscopy with biopsy to see if any cancer remains. If no cancer remains, then you'll enter observation in follow-up care (see "Follow-up care") or have an esophagectomy (see "After esophagectomy"). Even if no cancer was found, this surgery might be needed to prevent the cancer from recurring and to help with long-term survival.

If cancer is found after chemoradiation and it's spread is considered local, your options are:

- Esophagectomy (preferred). See "After esophagectomy" for what's next.
- Palliative management

If after chemoradiation and imaging the cancer is found to be unresectable or metastatic (has spread to distant areas), then your option is palliative management.

If you had chemotherapy alone, then you'll also have palliative management.

Clinical stage 4B is metastatic cancer. For more information on how it's treated, see *Chapter 8: Locally advanced recurrence or metastatic cancer*.

If surgery is not an option

If you aren't able to have or don't want surgery, then your options depend on if you can tolerate chemoradiation or not.

If you can tolerate chemoradiation, then you'll have chemoradiation alone.

If you can't tolerate chemoradiation, then you'll have:

- Palliative radiation therapy
- Palliative care

See "Follow-up care" for what happens next.

After esophagectomy

The goal of surgery (esophagectomy) is to remove the tumor and any remaining cancer. The tumor and lymph nodes removed during surgery will be tested and staged. So treatment after an esophagectomy is based on pathology results—if any cancer cells remain in the surgical margin. Your treatment after surgery depends on whether, during surgery, the cancer is found to be R0, R1, or R2, explained below.

If you didn't receive chemoradiation before surgery

If you had an esophagectomy but didn't have chemoradiation first, then your cancer will be staged with the new, more detailed tissue samples taken during the surgery.

R0 resection

In a clear, or negative, resection margin (R0), no cancer cells are found in the tissue around the edge of the tumor. The next step is observation in follow-up care. See "Follow-up care."

If there's anything you don't understand about your treatment plan, don't hesitate to ask your care team.



R1 resection

An R1-positive margin means the surgeon removed all of the visible tumor, but microscopic cancer remains in the margin. This cancer can't be seen with the human eye, but it can be seen under a microscope. For treatment, you'll receive chemoradiation with fluoropyrimidine (chemotherapy).

R2 resection

An R2 resection means that the surgeon was unable to remove all of the visible tumor, or there's cancer in the surgical margin that can be seen with the human eye. The remaining cancer after surgery may be near where the primary tumor was and in the lymph nodes or at distant sites (metastatic). Your treatment will be either:

- Chemoradiation with fluoropyrimidine (chemotherapy)
- Palliative management

If you received chemoradiation before surgery

If you had an esophagectomy but received chemoradiation first, then your cancer will be restaged with the new, more detailed tissue samples taken during the surgery, which is the pathological stage.

R0 resection

If you had no cancer in the margins and your cancer is now a pathological stage 1, then you'll receive observation in follow-up care (see "Follow-up care").

If you had no cancer in the margins and your cancer is now a pathological stage 2, 3A, 3B, or 4A, then you will be treated with the systemic immunotherapy, nivolumab. After treatment, you'll move to follow-up care.

Follow-up care should include upper GI endoscopy with biopsy (EUS, if needed) every 12 weeks for 2 years, and then every 6 months until year 5.

R1 or R2 resection

Separately, if your cancer is an R1 or R2 resection, meaning there's cancer in the surgical margins that could have metastasized (pathological stage 4B), you'll receive:

- Observation in follow-up care
- Palliative management

Follow-up care

After treatment, you'll receive follow-up care to watch for signs that cancer has returned, called recurrence. For more information on recurrence, read *Chapter 8: Locally advanced recurrence or metastatic cancer*.

If the tumor was treated with surgery or ER, then follow-up care should include:

- Medical history and physical exam every 3 to 6 months for 1 to 2 years, then every 6 to 12 months for 3 to 5 years
- Complete blood count (CBC) and chemistry profile, as needed
- Imaging as needed for signs or symptoms of cancer
- Upper GI endoscopy and biopsy as needed for signs or symptoms of cancer
- Dilatation for anastomotic stenosis (a minimally invasive surgery that widens the esophagus after an esophagectomy)
- Nutrition counseling

It helps to ask questions to learn all you can. It will give you a more active role in your care and may help you feel a sense of control.

Key points

- Treatment is based on the size, depth, and location of the tumor, as well as your overall health.
- Very small, early-stage tumors have not grown beyond the second layer (submucosa) of the esophageal wall. These are staged using a biopsy sample from an endoscopic resection (ER). This is called the pathological stage.
- Locally advanced disease is staged before surgery. This is called clinical stage, and it's based on endoscopic ultrasound (EUS) and other imaging or biopsy results.
- Your tumor and lymph nodes removed during an esophagectomy will be tested and staged before the next treatment is started.
- Palliative management means any and all treatments to relieve pain and suffering.
- Chemoradiation might be given before (pre-operative) or after (post-operative) surgery, or by itself (called definitive chemoradiation).
- After treatment, you'll receive follow-up care. It's important to stay on top of your health and keep any doctor visits and imaging test appointments. Contact your doctor if you have any new or worsening symptoms.

Questions to ask

- What stage is my esophageal cancer and why?
- What is the post-operative period like at the hospital?
- How long will it take for me to heal from surgery?
- Is there cancer in the lymph nodes? If so, what does that mean for me?
- I'd like to get a second opinion. Can you suggest someone?

What's next

After your treatment and, as mentioned above, you'll receive regular exams and imaging. In the meantime, be sure to contact your doctor if you have any new or worsening symptoms. See *Chapter 10: Survivorship* for what you might expect.

8

Locally advanced recurrence or metastatic cancer

73 Palliative management

74 Locally advanced recurrence

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80 Key points

80 Questions to ask

This chapter discusses treatment options for recurrent or metastatic esophageal cancer for both adenocarcinoma and squamous cell carcinoma. Recurrence is the return of cancer. Metastatic cancer is cancer that has spread far from its original site after being diagnosed or after treatment.

When cancer returns near the esophagus, it's called locally advanced (or locoregional) recurrence. Cancer might be in regional lymph nodes or in another nearby organ. Surgery might be an option for people with a locally advanced resectable (removable) tumor and for those who are healthy enough for surgery. Other treatments like palliative care might also be an option.

Esophageal cancer that has spread to distant sites in the body is called metastatic cancer. It might be referred to as stage 4 cancer. The most common metastatic sites are the liver, distant lymph nodes, lungs, bones, and brain. The goal of treatment is to reduce the amount of cancer, called cancer burden, and to prevent the further spread of cancer.

For unresectable locally advanced recurrence or metastatic disease, or if you aren't healthy enough for surgery, treatment may focus on palliative care. Systemic therapy might also be given. Options are based on biomarker testing status and looking at your overall health: level of fitness and ability to perform daily tasks. See **Guide 8** for available treatments.

If you have a cancer recurrence or it's metastatic and you're feeling overwhelmed, don't hesitate to reach out to your care team to let them know. They may be able to direct you to extra support or programs that can help you manage your feelings. You are not alone.

Palliative management

In recurrent and metastatic esophageal cancer, the term palliative management refers to ways to reduce pain and suffering. It means you have different options. These options can include treatments like chemoradiation, systemic therapy, or simply palliative care (which is any of the treatments available to reduce swallowing difficulty, bleeding, pain, blockages, as well as nausea and vomiting). According to NCCN experts, relieving major symptoms of esophageal cancer may extend life, which is why they encourage many approaches.

Guide 8
Possible treatments for locally advanced recurrence or metastatic cancer

Esophagectomy
Concurrent chemoradiation
Systemic therapy
Palliative care
Surgery

Locally advanced recurrence

It's possible to have cancer return in the remaining esophagus. Locally advanced recurrence is cancer that has returned to or near the esophagus. Cancer might also be in regional lymph nodes.

If you had an esophagectomy before, but not chemoradiation, palliative management treatment options include:

- Concurrent chemoradiation—when chemotherapy and radiation are given at the same time (preferred)
- Surgery
- Systemic therapy
- Palliative care

After these treatments, you'll have imaging again to check the status of the cancer. After that, if tests show cancer is still present, you'll receive palliative management.

But if you had chemoradiation before but not an esophagectomy, the tumor is resectable, and you're healthy enough for surgery, you might have an esophagectomy. After that, you'll have imaging again to check on the status of the cancer. If cancer is found, you'll receive palliative management.

Unresectable locally advanced or metastatic cancer

If the tumor is considered unresectable (not removable with surgery) or metastatic but you're healthy enough for more treatment, you might receive biomarker testing. For squamous cell esophageal cancer, you'll receive microsatellite and programmed death ligand 1 (PD-L1) testing, if not done before. For adenocarcinoma, you'll receive microsatellite, PD-L1, HER2, and CLDN18.2 testing if not done before.

For either cancer type, your treatment options could include:

- Systemic therapy
- Palliative care

If you aren't healthy enough for systemic therapy, or you don't want it, then treatment will focus on palliative care.

Palliative care

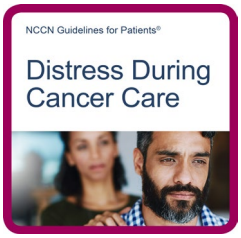
The goal of palliative care is to prevent and relieve pain and discomfort and provide the best quality of life for you. It's part of palliative management and can include treatments like systemic therapy and chemoradiation, as well as other therapies for trouble swallowing, bleeding, blockages, pain, nausea, and vomiting.

Receiving palliative care is still treatment. You're actively choosing care to help yourself feel better. While the goal is different (relieving pain and discomfort), your wishes and opinions are just as important as they are with other treatment options.

If you have any questions about what your palliative care options are, don't hesitate to ask your care team. For more information, see *Chapter 9: Supportive care*. More on the topic can be found in *NCCN Guidelines for Patients: Palliative Care*. For more information on dealing with the feelings and emotions that come with cancer care, see *NCCN Guidelines for Patients: Distress During Cancer Care*.

Both are available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.





For systemic therapy options for adenocarcinoma, see **Guide 9** and **Guide 10**.

For systemic therapy options for squamous cell carcinoma, see **Guide 11** and **Guide 12**.

Guide 9
Adenocarcinoma first-line therapy options: Unresectable, locally advanced recurrence, or metastatic disease

Preferred options	For HER2-positive tumors: • Fluoropyrimidine (fluorouracil or capecitabine), oxaliplatin, and trastuzumab • Fluoropyrimidine, oxaliplatin, trastuzumab, and pembrolizumab • Fluoropyrimidine, cisplatin, and trastuzumab • Fluoropyrimidine, cisplatin, trastuzumab, and pembrolizumab
	For HER2-negative tumors: • Fluoropyrimidine, oxaliplatin, and nivolumab • Fluoropyrimidine, oxaliplatin, and pembrolizumab • Fluoropyrimidine, oxaliplatin, and tislelizumab-jsgr • Fluoropyrimidine and oxaliplatin • Fluoropyrimidine, cisplatin, and pembrolizumab • Fluoropyrimidine, cisplatin, and tislelizumab-jsgr • Fluoropyrimidine and cisplatin
	Microsattelite instability-high/mismatch repair deficient (MSI-H/dMMR) tumors (independent of PD-L1 status): • Pembrolizumab • Dostarlimab-gxly • Nivolumab and ipilimumab • Fluoropyrimidine, oxaliplatin, and nivolumab • Fluoropyrimidine, oxaliplatin, and pembrolizumab
Other recommended	• Fluorouracil and irinotecan • Paclitaxel with or without carboplatin or cisplatin • Docetaxel with or without cisplatin • Fluoropyrimidine (fluorouracil or capecitabine) • Docetaxel, cisplatin or oxaliplatin, and fluorouracil

Note: Leucovorin might be added to fluorouracil-based regimens.

Guide 10
Adenocarcinoma next-line therapy options: Unresectable, locally advanced recurrence, or metastatic disease

Preferred options	• Ramucirumab and paclitaxel • Fam-trastuzumab deruxtecan-nxki for HER2-positive tumors • Docetaxel • Paclitaxel • Irinotecan • Fluorouracil and irinotecan • Trifluridine and tipiracil for third-line or subsequent therapy for esophagogastric junction (EGJ) adenocarcinoma
Other recommended	• Ramucirumab • Irinotecan and cisplatin • Fluorouracil and irinotecan with ramucirumab (leucovorin might be added) • Irinotecan and ramucirumab • Docetaxel and irinotecan
Used in some cases	• Entrectinib, larotrectinib, or repotrectinib for *NTRK* gene fusion-positive tumor • For MSI-H/dMMR tumors, pembrolizumab, nivolumab and ipilimumab, or dostarlimab-gxly • Pembrolizumab for tumor mutational burden-high (TMB-H) tumors • Dabrafenib and trametinib for *BRAF* V600E mutated tumors • Selpercatinib for *RET* gene fusion-positive tumors

Note: Systemic therapy options are based on prior therapy and performance status.

Guide 11
Squamous cell carcinoma first-line therapy options: Unresectable, locally advanced recurrence, or metastatic disease

Preferred options	• Fluoropyrimidine (fluorouracil or capecitabine), oxaliplatin, and nivolumab • Fluoropyrimidine, oxaliplatin, and pembrolizumab • Fluoropyrimidine, oxaliplatin, and tislelizumab-jsgr • Oxaliplatin, paclitaxel, and tislelizumab-jsgr • Fluoropyrimidine and oxaliplatin • Fluoropyrimidine, cisplatin, and nivolumab • Fluoropyrimidine, cisplatin, and pembrolizumab • Fluoropyrimidine, cisplatin, and tislelizumab-jsgr • Cisplatin, paclitaxel, and tislelizumab-jsgr • Fluoropyrimidine and cisplatin • Nivolumab and ipilimumab
	Microsattelite instability-high/mismatch repair deficient (MSI-H/dMMR) tumors (independent of PD-L1 status) • Pembrolizumab • Dostarlimab-gxly • Nivolumab and ipilimumab • Fluoropyrimidine, oxaliplatin, and nivolumab • Fluoropyrimidine, oxaliplatin, and pembrolizumab
Other recommended	• Fluorouracil and irinotecan • Paclitaxel with or without carboplatin or cisplatin • Docetaxel with or without cisplatin • Fluoropyrimidine • Docetaxel, cisplatin or oxaliplatin, and fluorouracil

Notes: Oxaliplatin is preferred over cisplatin because of lower toxicity.

Leucovorin might be added to fluorouracil-based regimens.

Guide 12
Squamous cell carcinoma next-line therapy options: Unresectable, locally advanced recurrence, or metastatic disease

Preferred options	• Nivolumab • Pembrolizumab in some cases • Docetaxel • Paclitaxel • Irinotecan • Tislelizumab-jsgr • Fluorouracil and irinotecan (leucovorin might be added)
Other recommended	• Irinotecan and cisplatin • Docetaxel and irinotecan
Used in some cases	• For *NTRK* gene fusion-positive tumor, entrectinib or larotrectinib • For MSI-H/dMMR tumors, pembrolizumab, nivolumab and ipilimumab, or dostarlimab-gxly • For tumor mutational burden-high (TMB-H) tumors, pembrolizumab • For *BRAF* V600E mutated tumors, dabrafenib or trametinib • For *RET* gene fusion-positive tumors, selpercatinib

Note: Systemic therapy options are based on prior therapy and performance status.

Key points

- Cancer may return in the remaining esophagus or may recur in another organ.
- Locally advanced recurrence is cancer that's returned to or near the esophagus. Cancer might be in nearby lymph nodes.
- Esophageal cancer that has spread to distant sites in the body is called metastatic disease. It might be referred to as stage 4 cancer.
- Esophageal cancer most commonly metastasizes (spreads) to the liver, distant lymph nodes, bones, and lungs.
- The goal of treatment is to reduce the amount of cancer, called cancer burden, and to prevent further spread.
- An unresectable tumor can't be completely removed with surgery.
- Treatment for unresectable and/or metastatic disease is palliative care with or without systemic therapy, depending on your overall health.

Questions to ask

- What should I expect from treatment this time? What are the side effects?
- How much pain will I have? What will be done to manage it?
- What will my recovery look like?
- Should I bring someone with me to all of my treatments?
- Can you direct me to emotional support resources?

9
Supportive care

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You can receive supportive care at any point during your treatment for esophageal cancer. Supportive care can enhance your quality of life, help lessen symptoms, and promote your comfort.

Supportive care is an important part of cancer care. The goal is to improve your quality of life during and after cancer treatment. Supportive care is for everyone with cancer and their families, not just for those at the end of life.

Supportive care includes a wide range of services. Supportive care prevents or manages the symptoms of cancer and the side effects of cancer treatment, like pain and cancer-related fatigue. It also addresses the mental, social, emotional, and spiritual concerns faced by people with cancer.

Supportive care provides help with additional needs, such as:

- Making treatment decisions
- Coordinating your care
- Paying for care
- Planning for advance care and end of life

See the related supportive care *NCCN Guidelines for Patients* at the end of this chapter.

Help with physical symptoms

When it comes to esophageal cancer, part of supportive care is palliative care, which can relieve major symptoms and side effects and may even extend life. This is especially true when a multidisciplinary care team is involved throughout your cancer care. It's also why NCCN experts encourage palliative care.

Below are some signs and symptoms of esophageal cancer and side effects of treatment that palliative care can help prevent, reduce, and/or relieve.

Trouble swallowing

The medical name for difficulty or discomfort in swallowing is dysphagia. It's the most common symptom of esophageal cancer and may be caused by the tumor or the treatment you receive. It happens from the tumor growing and narrowing the esophagus, which makes swallowing more challenging. Sometimes an esophageal stent is used to help open up the passageway. An esophageal stent is a flexible tube that widens the esophagus so food can pass into the stomach.

But if you're about to have surgery or you're receiving chemoradiation therapy, NCCN experts don't recommend an esophageal stent because it could interfere with either treatment.

One other option could be palliative radiation therapy to help shrink the tumor to open the esophagus and help with swallowing.

Bleeding

Bleeding is common in people with esophageal cancer. It may be caused by the tumor or a result of treatment. Stopping it can help people with cancer feel better. Bleeding is considered either acute (sudden bleeding that lasts a short time) or chronic (bleeding that lasts a long time).

Bleeding can be stopped in the following ways:

- **Endoscopic treatment**: For acute bleeding, treatment with an endoscope to reach the bleeding area can be used in some cases. Known as electrocoagulation, this technique stops bleeding by sealing the tissue with heat or ionized gas.
- **External beam radiation therapy (EBRT)**: Used to control chronic bleeding, radiation is targeted at the bleeding area.

Blocked esophagus

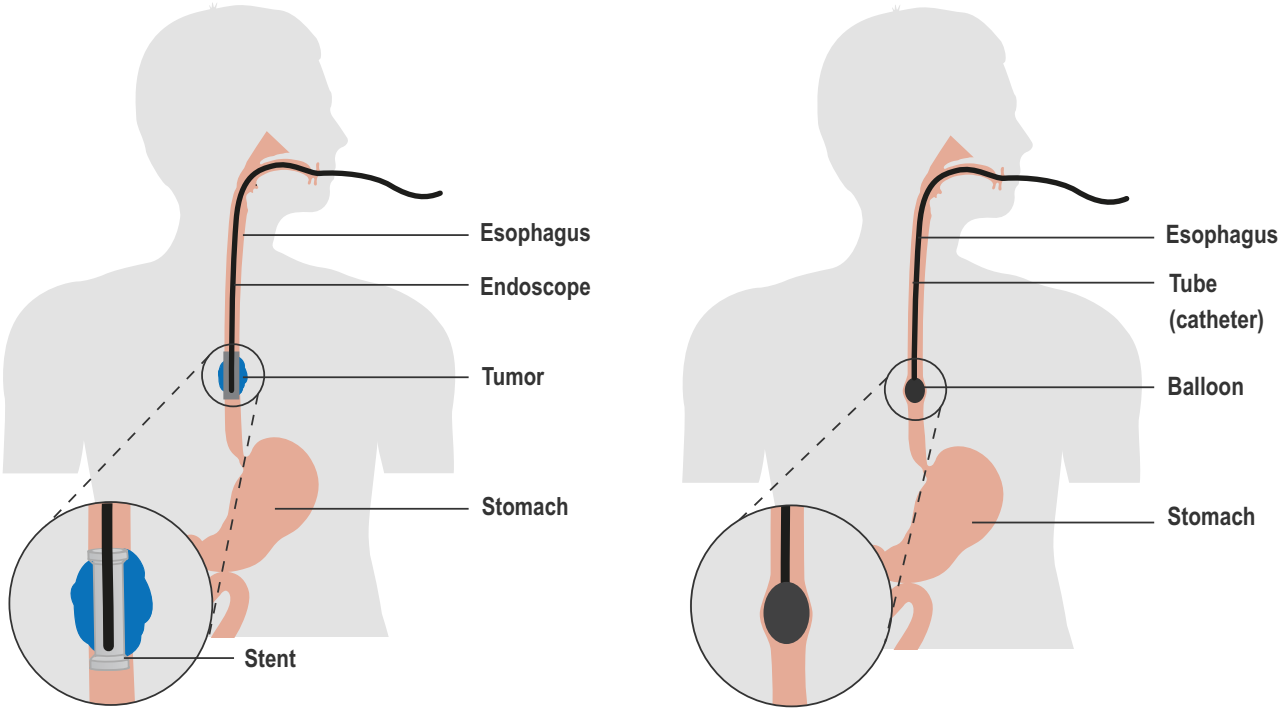
When there's a blockage (obstruction) in the esophagus from the tumor, palliative care can be in the form of:

- Endoscopic treatment
- EBRT

Blocked esophagus

An esophageal stent is a tube that widens the esophagus so food can pass into the stomach (image on left). Special expanding (dilating) balloons or bougies can relieve a blockage or a narrowing of the esophagus (image on right).

Left: https://commons.wikimedia.org/wiki/File:Diagram_showing_an_oesophageal_stent_being_put_in_CRUK_495.svg. Right: https://commons.wikimedia.org/wiki/File:Diagram_showing_how_a_balloon_is_used_to_stretch_the_oesophagus_CRUK_492.svg



- Brachytherapy, given in experienced centers
- Chemotherapy
- Surgery, used only in some cases
- Photodynamic therapy: Minimally invasive treatment that uses a laser light to help open the throat
- Balloons or bougies: Special expanding (dilating) balloons or bougies can relieve a blockage caused by a tumor or treatment-related narrowing (stricture) of the esophagus

Pain

Tell your care team about any pain or discomfort. Treating pain can be complicated. You might meet with a palliative care specialist or with a pain specialist to manage it.

Pain is common in people with a tumor causing a blockage, or for metastatic esophageal cancer. Sometimes pain is treated with around-the-clock medicine, such as morphine or other opioids (narcotics). Sometimes, non-narcotic medicines are used to treat pain. As a result, you might meet with a palliative care specialist or a pain specialist to manage your pain.

Integrative medicine programs at hospitals and cancer centers can be personalized to help with your specific pain problems. These programs use complementary therapies, like massage, to help with pain. Ask your care team about them.

Treatment side effects

All cancer treatments can cause unwanted health issues. Such health issues are called side effects. Side effects depend on many factors. These factors include the drug type and dose, length of treatment, and the person.

Some side effects may be harmful to your health. Others may just be unpleasant.

Ask for a complete list of side effects of your treatments. Also, tell your treatment team about any new or worsening symptoms. There may be ways to help you feel better. There are also ways to prevent some side effects.

Supportive care is available at any stage of cancer treatment. It can involve help with physical, emotional, financial, and end-of-life planning. Your care team is there to help you through it all.



Tube feeding

Also called enteral nutrition, tube feeding is when a tube inserted into the stomach or small intestine directly transports a liquid nutrition mixture of protein, carbohydrates, fats, and vitamins. You'll likely have tube feeding after surgery to allow your esophagus to heal. The tube is temporary and will be removed. However, some people need tube feeding for longer periods to maintain weight or if they have pain or difficulty swallowing.

Liquid nutrition might be given through:

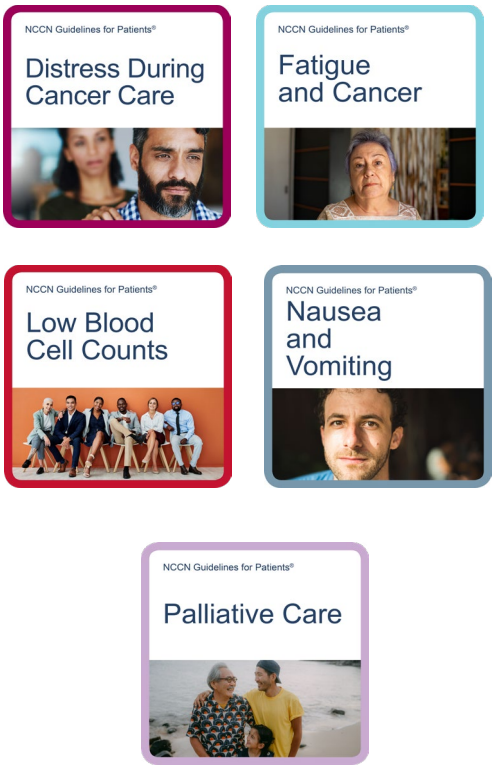
- **A nasogastric tube (NG tube)** inserted through the nose.
- **A gastrostomy tube (G-tube)** placed through the skin of the abdomen directly into the stomach. It's also called a percutaneous endoscopic gastrostomy (PEG) tube.
- **A jejunostomy tube (J-tube)** placed through the skin of the abdomen into the small intestine.

Help with other supportive care areas

More information on the physical, emotional, financial, and end-of-life aspects of supportive care can be found in related NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

Supportive care resources

More information on supportive care is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Key points

- Palliative care is part of supportive care and can help with physical symptoms like trouble swallowing, bleeding, blockages, pain, as well as nausea and vomiting.
- Emotional support is also part of supportive care. All you need to do is ask your care team about it.
- Cancer and its treatment can be expensive. Supportive care can help you find programs that might be able to pay for some of these costs.

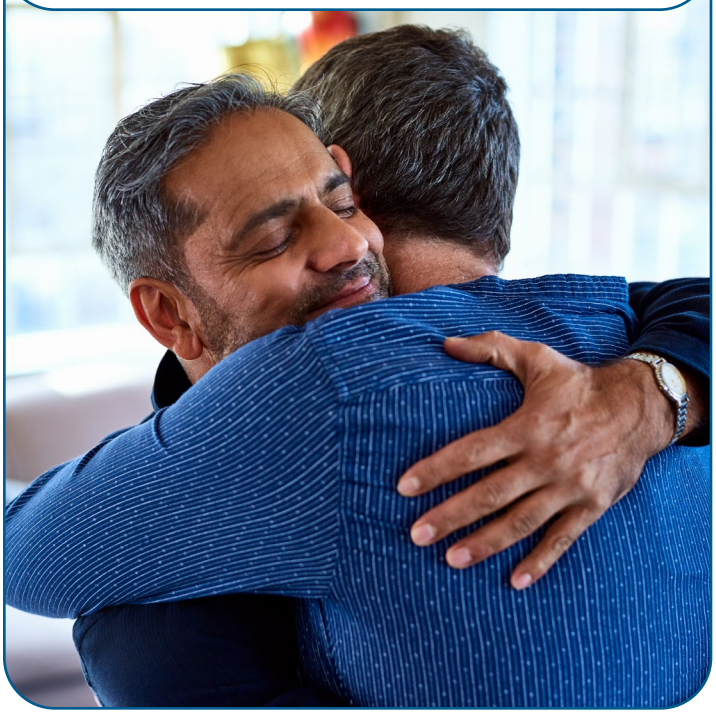
Questions to ask

- Can you tell me about all of my supportive care options (both physical and emotional)?
- Is there one care team member whom I should call first about supportive care?
- If I need transportation to and from appointments, can you suggest any programs that might help?
- What supportive care resources at my health care facility might help me?
- What online resources can you recommend?

What's next?

Understanding that supportive care is there for you throughout your cancer care, and asking for it, could make a big difference. But after you finish your treatment, you're in what's called survivorship. Read the next chapter for more information on what you might expect after treatment.

If you need support while dealing with your diagnosis, ask about a nearby in-person or online cancer support group.



10 Survivorship

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After treatment, you'll be monitored for any new or ongoing health issues. It's important to keep follow-up doctor visits and imaging test appointments to stay on top of your health.

A person is a cancer survivor from the time of diagnosis until the end of life. When treatment leads to remission (also called no evidence of disease), you'll need follow-up or survivorship care for long-term side effects. Entering survivorship is viewed in different ways by different people. Cancer and its treatment can be a long journey, so survivorship may be viewed as a new, positive chapter, or as an extended chapter of cancer. Either way, it's a new normal, so it's important to know what to expect in this next phase of your life.

Monitoring

In addition to monitoring for the possible return of cancer, called recurrence (see "Follow-up care" at the end of treatment chapters), you should seek reliable routine medical care, including regular doctor visits for preventive care and cancer screening. Routine esophageal cancer-specific tests, such as imaging, endoscopy, or tumor tests, are not recommended after 5 years. Be sure to keep follow-up doctor visits and imaging test appointments.

Physical and mental health

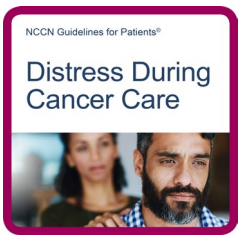
People with esophageal cancer are monitored for long-term side effects that can often be managed.

Overall, you're encouraged to:

- Maintain a healthy body weight.
- Adopt a physically active lifestyle. The goal is at least 30 minutes of moderate-intensity activity most days of the week.
- Eat a mostly plant-based diet.
- Limit alcohol use.
- If you smoke or vape, seek help to quit.
- Get necessary vaccines and any other preventive health measures.

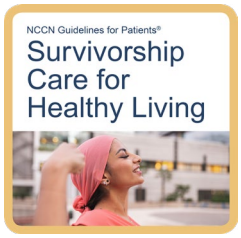
Be sure to talk to your doctor about how you're feeling both physically and mentally. If you're not feeling like yourself, you might benefit from talking to someone else who's been there. Seek out peer support groups, either online or in person, to help manage your feelings and emotions. Ask your cancer center about a patient-to-patient peer support program.

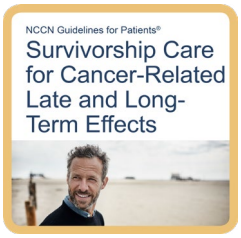
For more information on dealing with feelings and emotions that come with cancer care, see *NCCN Guidelines for Patients: Distress During Cancer Care*, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



You might also find it helpful to talk to your care team about survivorship resources in your area.

More information on survivorship is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.





Specific symptoms

Some of the most common symptoms you might experience in survivorship include the following:

Diarrhea

Diarrhea is frequent and watery bowel movements. Your care team will tell you how to manage diarrhea and may recommend medicines to stop it. It's important to drink lots of fluids to prevent dehydration (losing too much fluid or water from your body). Changes to your diet might help, too.

Difficulty swallowing

Dysphagia, or difficulty swallowing, may be a result of the cancer or an esophagectomy. Esophagectomy can cause an anastomotic stricture from the scar tissue left after the surgery. This is a narrowing of the esophagus that can be managed with endoscopic dilation, which helps stretch the area.

Dumping syndrome

Dumping syndrome is when food travels from the stomach and empties into the small intestine too quickly. It's a common side effect of stomach surgery. It may happen within 30 minutes after eating a meal (early dumping syndrome) or within 2 to 3 hours of eating (late dumping syndrome).

Symptoms of early dumping syndrome include heart racing/pounding, diarrhea, nausea, and cramps. Late dumping syndrome tends to cause dizziness, hunger, cold sweats, and feeling faint.

To help manage the symptoms of dumping syndrome:

- Eat often throughout the day
- Avoid drinking fluids with meals
- Eat a diet high in protein and fiber and low in simple carbohydrates and sugars

Fatigue

Fatigue is feeling extremely tired and having no energy to do things you'd like to do. Let your care team know if fatigue is affecting your quality of life. Eating a balanced diet, exercise, yoga, acupuncture, and massage therapy can help. You might be referred to a nutritionist or dietitian to help manage your fatigue.

Fullness after meals and eating issues

Eat small portions and eat more often to cope with feeling full after meals. Also avoid drinking fluids with meals because it can make you feel fuller. Continue to drink fluids between meals.

Heart issues

Because of the location of the esophagus, radiation therapy for esophageal cancer may cause heart issues. Work with your primary care doctor to monitor your blood pressure, cholesterol, blood sugar, and weight.

Indigestion

Indigestion is pain or discomfort in the upper abdomen (belly) after eating. It can feel like fullness, bloating, gassiness, heartburn, or nausea.

To prevent indigestion, avoid foods that increase acid production, such as citrus juices, tomato sauces, and spicy foods.

Neuropathy

Neuropathy results from damage to the nerves. It feels like prickling, tingling, numbness, and pain. Neuropathy caused by chemotherapy is called chemotherapy-induced neuropathy. You might be given medicines or referred to occupational therapy and/or physical therapy.

Reflux

Reflux is the backward flow of liquid from the stomach into the esophagus. Some ways to help include:

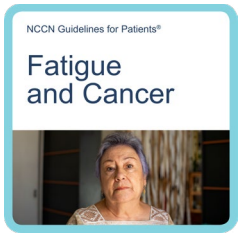
- Avoid lying flat after eating.
- Use a foam wedge (triangular) pillow in bed and sleep in a slightly upright position at night.
- Talk to your doctor before taking any over-the-counter (OTC) medicine.
- Don't eat within 2 hours of bedtime.

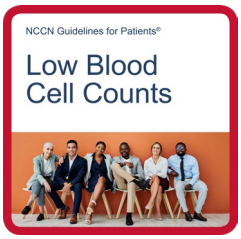
Weight loss

Your weight will be monitored for changes. You might lose weight after an esophagectomy. In fact, weight loss is expected in the first 6 months after surgery. You'll also be monitored to make sure you are getting enough nutrition and your body is absorbing the nutrition from the food you eat.

Healthy eating is important after treatment. This includes eating a balanced diet, eating the right amount of food, and drinking enough fluids. Eat often and avoid fluids with meals. A registered dietitian, who's an expert in nutrition and food, can help if you have trouble eating or maintaining weight.

More information on fatigue and anemia is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.





Cancer screening

Schedule cancer screenings as recommended by your doctor based on your age, risk, and other factors.

Screenings for cancer include:

- Breast
- Colorectal
- Lung
- Prostate

Key points

- A person is a cancer survivor from the time of diagnosis until the end of life.
- Surgery and other treatments for esophageal cancer can cause health issues, so your health will be monitored regularly.
- A nutritionist or dietician provides guidance on what foods are best for your condition.
- Continue to see your primary health care provider on a regular basis and have preventive cancer screenings as recommended.
- Eat often throughout the day (graze) and avoid drinking liquids with meals.
- Eat a mostly plant-based diet high in protein and fiber and low in simple carbohydrates and sugars.
- Limit alcohol use.
- If you smoke or vape, seek help to quit.

Questions to ask

- What are some of your best recommendations for handling my survivorship?
- What health care provider will I rely on most in survivorship?
- What other cancer screenings can you recommend?
- What about the emotional side of survivorship? Do you have any recommendations for help with mental health?
- Can you recommend any support groups?



Take our survey and help make the NCCN Guidelines for Patients better for everyone!

NCCN.org/patients/comments

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Other resources

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Want to learn more? Here's how you can get additional help.

What else to know

This guide helps you know your options so you can make informed decisions and improve your cancer care. But it's not the only resource that you have.

Ask for as much information and help as you need. Many people are interested in learning more about:

- The details of their esophageal cancer treatment and its side effects
- Being a part of a care team
- Getting financial help
- Finding a cancer care professional who's an expert in their field
- Coping with other health problems

What else to do

Your health care center can help you with next steps. It often has on-site resources to help meet your needs and find answers to your questions. Health care centers can also inform you of resources in your community.

In addition to help from your providers, the resources listed in the next section provide support for many people like yourself.

Where to get help

Look through the list below and visit the provided websites to learn more about these organizations.

Bone Marrow & Cancer Foundation
bonemarrow.org

Cancer*Care*
cancercare.org

Cancer Hope Network
cancerhopenetwork.org

ECAN Esophageal Cancer Action Network
ecan.org

Esophageal Cancer Awareness Association dba EC Aware
ecaware.org

Esophageal Cancer Education Foundation
fightec.org

GRACE
cancergrace.org

Imerman Angels
imermanangels.org

Triage Cancer
triagecancer.org

Questions to ask

- Who can I talk to about help with housing, food, and other basic needs?
- What assistance is available for transportation, childcare, and home care?
- How much will I have to pay for treatment?
- What help is available to pay for medicines and other treatment?
- What other services are available to me and my caregivers?



Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.
NCCN.org/patients/response



Words to know

abdomen
The belly area between the chest and pelvis.

adenocarcinoma
A type of cancer that forms in the glandular cells of the esophagus. These cells line the lower esophagus and make mucus.

adventitia
The outermost layer of the esophageal wall.

anastomotic stricture (or stenosis)
Narrowing of the esophagus after an esophagectomy.

Barrett esophagus (BE)
A condition in which the cells lining the lower part of the esophagus change or are replaced with abnormal cells that could lead to cancer of the esophagus.

biopsy
A procedure that removes fluid or tissue samples to be tested for a disease.

brachytherapy
A treatment with radiation from an object placed near or in the tumor. Also called internal radiation.

bronchi
The two airways extending from the windpipe into the lungs.

bronchoscope
A device guided through the nose or mouth to examine the inside of the trachea, bronchi, and lungs.

cancer grade
A rating of how much cancer cells look like normal cells.

cancer stage
A rating of the growth and spread of cancer. The extent of cancer.

chemoradiation
Treatment that combines chemotherapy with radiation therapy.

chemotherapy
Drugs that kill cancer cells by damaging or disrupting the making of the genetic code.

clinical stage
Rating the extent of a tumor based on tests before treatment.

clinical trial
Research on a test or treatment to assess its safety or how well it works.

colon
The longest part of the large intestine.

complete blood count (CBC)
A test of the number of blood cells.

comprehensive chemistry profile
A panel of tests that gives information about the health and functions of the kidneys and the liver. Usually ordered as part of a comprehensive metabolic panel (CMP).

computed tomography (CT)
A test that uses x-rays to view body parts.

conduit
Tube-shaped tissue, such as the stomach or part of the colon or small intestine, that replaces the part of the esophagus removed during an esophagectomy.

contrast
A substance put into your body to make clearer pictures during imaging tests.

core biopsy
Removal of tissue sample with a hollow needle.

diaphragm
The thin muscle below the lungs and heart that separates the chest from the abdomen and helps a person to breathe.

digestive system
A set of organs that breaks down food for the body to use.

digestive tract
Tube-shaped organs that break down food for the body to use. Part of the digestive system.

duodenum
First part of the small intestine.

dysphagia
Difficult or painful swallowing.

endoscope
A thin, long tube fitted with tools guided down the mouth and through the throat.

endoscopic mucosal resection (EMR)
Removal of early tumors with a snare guided down the throat.

endoscopic resection (ER)
Treatment that removes early tumors with a tool guided down the throat.

endoscopic submucosal dissection (ESD)
Removal of early tumors with a special knife guided down the throat.

endoscopic ultrasound (EUS)
A device to make pictures using sound waves guided down your throat.

epithelium
Cells that line the esophageal wall.

esophagectomy
Surgery that removes all or part of the esophagus.

esophagogastroduodenoscopy (EGD)
Use of an endoscope guided down the throat into the esophagus and stomach. Also called an upper endoscopy or upper gastrointestinal (GI) endoscopy.

esophagogastrostomy
Surgery that removes the esophagus and some of the stomach.

esophagus
The tube-shaped organ between the throat and stomach.

external beam radiation therapy (EBRT)
Radiation therapy received from a machine outside the body.

fine-needle aspiration (FNA)
Removal of a tissue sample with a thin needle.

gastroenterologist
A doctor who's an expert in digestive diseases.

gastroesophageal junction (GEJ)
The area where the esophagus and stomach connect. Also known as the esophagogastric junction (EGJ).

gastrointestinal (GI) tract
The group of organs through which food passes after being eaten. Also called the digestive tract.

gastrostomy tube (G-tube)
A feeding tube inserted through a cut in the skin of the abdomen directly into the stomach. Also called a percutaneous endoscopic gastrostomy (PEG) tube.

general anesthesia
Complete loss of feeling and awareness that feels like a very deep sleep.

hereditary
Passed down from birth parent to child through coded information in cells.

high-grade dysplasia (HGD)
Abnormal cells that are likely to become cancer cells.

human epidermal growth factor receptor 2 (HER2)
A protein on the surface of a cell that sends signals for the cell to grow.

jejunostomy tube (J-tube)
A feeding tube inserted through a cut into the middle intestine (jejunum).

jejunum
The middle part of the small intestine.

imaging
A test that makes pictures (images) of the inside of the body.

immune system
The body's natural defense against infection and disease.

immunotherapy
Treatment with drugs that help the body find and destroy cancer cells.

infection
An illness caused by germs.

intestine
The organ that food passes through after leaving the stomach.

intravenous (IV)
A method of giving drugs by a needle or tube inserted into a vein.

lamina propria
Connective tissue in the mucosa of the esophageal wall.

laparoscopy
Use of a thin tool inserted through a cut made into the belly area.

lymph
A clear fluid containing white blood cells.

lymph node
A small group of special disease-fighting cells located throughout the body.

lymph node dissection
A type of surgery that removes some disease-fighting structures called lymph nodes.

medical oncologist
A doctor who's an expert in cancer drugs.

metastasis
The spread of cancer cells from the first (primary) tumor to a new site.

microsatellite instability (MSI)
Microsatellites are short, repeated sequences of DNA. Instability is errors made in small, repeated DNA parts during the copy process because of an abnormal repair system.

microsatellite instability-high (MSI-H)
Mutations in 30% or more microsatellites.

minimally invasive procedure
A procedure that places tools through small incisions or an opening of the body to reduce damage to body tissue.

mucosa
The first, inner layer of the esophageal wall. It's made of 3 layers: epithelium, lamina propria, and muscularis mucosa.

muscularis mucosa
A thin layer of muscle separating the mucosa from the submucosa of the esophageal wall.

muscularis propria
The third layer of the esophageal wall made mostly of muscle.

mutation
An abnormal change.

nasogastric tube (NG tube)
A tube inserted through the nose and into the stomach to provide liquid nutrition.

observation
A period of monitoring and testing for changes in cancer status while not receiving treatment.

palliative care
Care to improve quality of life and help reduce suffering.

pathological stage
A rating of the extent of cancer based on additional tissue samples and microscopic review after surgery.

pathologist
A doctor who’s an expert in examining tissue and cells to find disease.

pelvis
The area of the body between the hip bones.

percutaneous endoscopic gastrostomy (PEG)
A procedure that inserts a feeding tube into the stomach through a small cut in the skin.

positron emission tomography-computed tomography (PET/CT)
A test that uses radioactive material and x-rays to see the shape and function of body parts.

primary treatment
The main treatment used to rid the body of cancer.

primary tumor
The first mass of cancer cells.

radiation oncologist
A doctor who’s an expert in radiation treatment.

radiation therapy (RT)
Treatment that uses high-energy rays.

radiologist
A doctor who's an expert in imaging tests.

recurrence
The return of cancer after a cancer-free period.

resectable
Cancer that can be removed with surgery.

side effect
An unhealthy or unpleasant physical or emotional response to treatment.

small intestine
The digestive organ that absorbs nutrients from eaten food.

squamous cell carcinoma
A type of cancer that starts in the thin, flat cells that line the surface of organs like the esophagus.

stricture
Narrowing of the esophagus. Might be caused by a tumor or treatment.

submucosa
The second layer of the esophageal wall made mostly of connective tissue, blood vessels, and nerve cells.

subtype
A smaller group within a type of cancer based on certain cell features.

supportive care
Health care that includes symptom relief and support services but is not cancer treatment.

surgical margin
The normal-looking tissue around the edge of a tumor removed during surgery.

surgical oncologist
A surgeon who's an expert in performing surgical procedures in people with cancer.

surveillance
Testing after treatment ends to check for the return of cancer.

targeted therapy
Drugs that stop the growth process specific to cancer cells.

trachea
The airway between the throat and airway into the lungs. Also called the windpipe.

tumor marker
A substance found in body tissue or fluid that may be a sign of cancer.

ultrasound (US)
A test that uses sound waves to take pictures of the inside of the body.

unresectable
Cancer that can't be removed by surgery.

upper endoscopy
Use of a thin tool guided down the throat into the esophagus and stomach. Also called an upper gastrointestinal (GI) endoscopy or esophagogastroduodenoscopy (EGD).



We want your feedback!

Our goal is to provide helpful and easy-to-understand information on cancer. Take our survey to let us know what we got right and what we could do better.
NCCN.org/patients/feedback

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Esophageal and Esophagogastric Junction Cancers, Version 3.2026. It was adapted, reviewed, and published with help from the following people:

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