All About Laryngeal Cancer

What is the larynx?

The larynx, or voice box, is an area in the throat that contains both cartilage and muscles. It is responsible for producing our voice, and also performs other complex functions such as protecting our airway during swallowing. The larynx is divided into three separate regions: the supraglottis, the glottis, and the subglottis. The supraglottis is the space above the vocal cords that contains the epiglottis. The epiglottis is a flap of tissue that closes off the larynx when you swallow, which prevents food and fluids from entering your lungs. The supraglottis is protected in the front by the large thyroid cartilage, which can be felt as the “Adam's apple” in our neck. When you feel for your Adam's apple, directly under that large piece of firm cartilage is the voice box, or the glottis. The glottis is the portion of the larynx where the vocal cords are located. Below the vocal cords is the subglottic larynx, or subglottis. This area is the area of the throat and airway below the vocal cords but above the trachea. All three of these areas together are considered the larynx.

What is laryngeal cancer?

Normally, cells in the body will grow and divide to replace old or damaged cells in the body. This growth is highly regulated, and once enough cells are produced to replace the old ones, normal cells stop dividing. Tumors occur when there is an error in this regulation and cells continue to grow in an uncontrolled way. Tumors can either be benign or malignant. Although benign tumors may grow in an uncontrolled fashion sometimes, they do not spread beyond the part of the body where they started (metastasize) and do not invade into surrounding tissues. Malignant tumors, however, grow in such a way that they invade and damage other tissues around them. They also may spread to other parts of the body, usually through the blood stream or through the lymphatic system where the lymph nodes are located. Over time, the cells within a malignant tumor become more abnormal and appear less like normal cells. This change in the appearance of cancer cells is called the tumor grade. Cancer cells are described as being well-differentiated, moderately-differentiated, poorly-differentiated, or undifferentiated. Well-differentiated cells are quite normal appearing and resemble the normal cells from which they originated. Undifferentiated cells are cells that have become so abnormal that often we cannot tell what types of cells they started from.

Cancers are described by the types of cells from which they arise. A majority of laryngeal cancers develop from squamous cells, which are found in the epithelium of the larynx, which is the innermost layer lining the larynx. Therefore, they are referred to as squamous cell cancer of the larynx. Most squamous cell cancers start not as cancer, but as a pre-cancerous condition called dysplasia. Usually dysplasia does not turn into cancer. At times dysplasia can progress into cancer in which cancer cells are limited to the epithelium. This is called carcinoma in situ. There are also other very rare types of laryngeal cancer, including minor salivary gland cancer, sarcoma and melanoma.

What causes laryngeal cancer and am I at risk?

Approximately 13,150 people are diagnosed with laryngeal cancer each year. Of these cases, about 60% start in the glottis, 35% in the supraglottis and the rest develop in the subglottis or overlap more than one area. It is more common in men than women and most commonly diagnosed between the ages of 55-64. In the United States, it is most common in the African American population. There has been a steady decrease in the number of people diagnosed each year, which is thought to be related to the decrease in smoking rates.

Many risk factors have been associated with the development of laryngeal cancer. These include chronic irritation from laryngitis or voice abuse, chronic gastric reflux, and exposure to certain chemicals (like wood dust, nitrogen mustard, and asbestos), HPV, poor nutrition and some genetic syndromes (Fanconi anemia and Dyskeratosis congenital). However, the largest risk factor for the development of laryngeal cancer is smoking. Pipe smoking, cigar smoking, and cigarette smoking have all been strongly associated with the development of laryngeal cancer. There is also an association between heavy
alcohol intake and laryngeal cancer.

**How can I prevent laryngeal cancer?**

Since it is fairly uncommon for a non-smoker to be diagnosed with laryngeal cancer, smoking cessation is the best way to prevent laryngeal cancer. In fact, not using tobacco of any kind, either smoking or smokeless, is the healthiest thing anyone can do, both in terms of preventing laryngeal cancer, as well as the prevention of other throat cancers, lung cancers, and many other serious health problems.

Reducing alcohol intake may also be helpful in the prevention of laryngeal cancer, especially for people who smoke. You should also eat a healthy and balanced diet. Reducing other risk factors, such as chronic vocal irritation and gastroesophageal reflux (heartburn) may also be beneficial. A healthcare professional should be consulted for chronic health problems such as laryngitis or chronic heartburn.

**What are the signs of laryngeal cancer?**

Signs or symptoms of cancer of the larynx are somewhat dependent on where the cancer is growing (supraglottis, glottis, or subglottis). Patients with glottic cancer, or cancer that grows on the vocal cords, often present with the early sign of hoarseness. This occurs because even a slight interference with the vibrating function of the vocal cords can produce voice changes. Any long-standing hoarseness or voice changes should prompt a laryngeal examination. If hoarseness is ignored or if advanced disease occurs, airway obstruction, pain, or difficulty swallowing can result.

Supraglottic cancers usually do not produce early signs or symptoms, so supraglottic cancers are more often in advanced stage upon diagnosis. Hoarseness can also occur with supraglottic cancer, though usually after the cancer has progressed. Also, in patients with supraglottic cancer, voice changes referred to as "hot potato voice" can occur. This can be described as the type of voice someone would speak in if they had a piece of hot food (potato) in their mouth. In addition to voice changes, patients can also present with pain, problems swallowing, or even ear pain, which can result from the involvement of nerves in the throat by the tumor. Supraglottic cancers often spread to lymph nodes in the neck, and many patients notice a lump in the neck as the first sign of cancer. Any lump or bump in the neck that does not go away within a few days should be evaluated by a medical provider.

Subglottic cancers are fairly rare, but they also fail to produce early symptoms. Therefore, they also present in more advanced stages and patients can have signs of disease similar to that of supraglottic cancers.

Again, these signs and symptoms are nonspecific and could represent a variety of different conditions-both benign and malignant. However, if you have any of these symptoms, especially if they are longstanding or if you are a smoker, you should see your provider.

**How is laryngeal cancer diagnosed?**

If your provider suspects you have laryngeal cancer, he or she may start by doing a physical examination of your neck to check for any lumps or bumps. Your provider may send you to a doctor called an otolaryngologist who specializes in treatment of ear, nose and throat issues.

Clinical evaluation of a laryngeal cancer must include an evaluation of the inside of the throat. This can be done with a mirror, though it is more commonly done using a fiberoptic scope called a nasopharyngolaryngoscope. This is a camera attached to a long fiberoptic endoscope that is inserted into the patient's nose or mouth to view the throat. Medicine to numb the inside of a patient's nose or throat may be used before the procedure to maintain comfort during the exam. This exam is brief and is done in the provider's office. The entire throat down to the level of the vocal cords is evaluated with special attention to the surfaces of the throat and the movement of the vocal cords. Another, more thorough test that is used is called direct laryngoscopy, which is done in the operating room under anesthesia. Since the patient is sleeping during this examination, a more thorough exam can be done with biopsies being done at that time. A careful examination of the neck is also required to detect spread of tumor to the lymph nodes.

Other procedures are needed to determine the stage of the tumor. CT scans (CAT scans) or sometimes MRIs of the neck are...
done to further determine the extent of the disease, both in the throat and in the neck. A chest x-ray is also often ordered to rule out spread of tumor to the lungs. Blood tests are often done to insure that overall blood counts are within normal limits, and that a patient's liver, kidneys, and overall health are normal.

**How is larynx cancer staged?**

The staging of a cancer basically describes the extent of disease. Glottic cancer often produces hoarseness early, causing it to be diagnosed earlier. Unfortunately, supraglottic and subglottic laryngeal cancer often present as a more advanced disease because of being detected later, due mainly to the lack of specific symptoms. Before the staging systems are introduced, we will first discuss some background on how cancers grow and spread.

Cancers cause problems because they spread and can disrupt the functioning of normal organs. One way larynx cancers can spread is by local extension. Local extension is invasion of the cancer through the normal structures in the throat and into adjacent structures in the neck. These include the vocal cords themselves, the structures controlling voice and swallowing, the epiglottis (which is needed to prevent choking when swallowing), and even the cartilage and muscles surrounding the larynx. All cancers can spread via local extension, though this method of spread is particularly important in larynx cancer and other cancers of the throat. Tumor growth by local extension in the larynx can cause a patient's airway to be compromised or the swallowing function to be interrupted (which leads to problems eating and subsequent malnutrition), as well as causing the loss of the protection of the airway during swallowing, leading to choking and infection. Keep in mind that larynx cancers, when spreading via local extension, often spread from one subsite to the other (for example, glottis cancers can spread locally to involve the supraglottis). Sometimes, if cancers are locally advanced, it can be difficult to tell from which part of the larynx they originally grew.

Larynx cancer can also spread by accessing the lymphatic system. The lymphatic circulation is a complete circulation system in the body (somewhat like the blood circulatory system) that drains into various lymph nodes and organs. When cancer cells access this lymphatic circulation, they can travel to lymph nodes and start new sites of cancer. This is called lymphatic spread. Larynx cancers differ in their propensity to spread, again based on the site of the larynx that the tumor involves. Supraglottic cancers have spread to the lymph nodes in over 50% of patients by the time a diagnosis has been made. This is in contrast to a pure glottic cancer (one that has not spread to the supraglottis or other sites within the throat by local extension), which spreads to the lymph nodes in less than 5% of patients upon diagnosis. However, keep in mind that once a cancer spreads from the glottis (the true vocal cords) to another subsite, it can spread to lymph nodes just as much as a cancer that originated in that other subsite. The first lymph nodes that cancer cells spread to are the “jugular chain” of lymph nodes, which are found along the side of the neck. They can be found in front of the large muscles on either side of the neck that contract when the head is turned from side to side. Tumor cells that spread to the jugular lymph nodes can then spread to the “supraclavicular” lymph nodes (found behind the collar bone) and to other lymph nodes in the neck.

Larynx cancers can also spread through the bloodstream. Cancer cells gain access to distant organs via the bloodstream. The tumors that arise from this travel to other organs are called metastases. Cancers of the larynx generally spread locally or to lymph nodes before spreading distantly through the bloodstream. Hence, the incidence of distant metastases is thought to be 10% or less. Although this increases with extent of disease in the throat and neck and is more common with supraglottic (and subglottic) tumors, distant metastases are still found in only a small number of patients diagnosed with laryngeal cancer (15% or less). If spread through the bloodstream does occur, the lungs are the most common site of metastasis, followed by the bones.

The staging system used in larynx cancer is designed to describe the extent of disease in both the throat itself and the neck (with spread to the lymph nodes). Both are important for treatment and need to be considered somewhat separately. The staging system used to describe laryngeal tumors is the “TNM system”. The TNM system has three components: T-describing the extent of the “primary” tumor (the tumor in the throat itself); N-describing the spread to the lymph nodes; M-describing the spread to other organs (i.e.-metastases). Since the different subsites of the larynx have different structures, the “T” portion (or local extent of disease) is described separately for each. Your healthcare provider will use the results of the diagnostic work up to assign the TNM result and combine these to get a stage from 0 to IV.

Though complicated, these staging systems help physicians determine the extent of the cancer, and therefore make treatment decisions regarding a patient's cancer. The stage of cancer, or extent of disease, is based on information gathered through
How is laryngeal cancer treated?

Typically the goal of treatment for laryngeal cancer is not only to remove the cancer but also to preserve the patient’s ability to speak and swallow. The options for treating cancer of the larynx are primarily surgery, radiation and chemotherapy. Your treatment plan will depend upon where your cancer is and if it has spread. It is important to work with your care team to create a plan that works best for you and your lifestyle.

Surgery

Surgery plays a key role in the treatment of laryngeal cancer. The goal of surgery is to remove all of or as much of the cancer as possible while causing minimal damage to the remaining tissue. In some instances you will be treated with surgery and chemotherapy or radiation. There are a number of surgical options to treat cancer of the larynx. The type of surgery that your team will suggest will depend upon where the cancer is and if it has spread or not. Here is a list of possible surgical treatments:

- **Vocal Cord Stripping**: The superficial layers of tissue on the vocal cords are stripped away using a long surgical instrument. The purpose of vocal cord stripping is to biopsy or to treat carcinoma in situ (Stage 0). After recovery, the normal speaking voice is usually maintained.
- **Cordectomy**: In a cordectomy either part or all of your vocal cords are removed and is used to treat superficial glottic cancers. The effect on your speech is dependent upon how much of the vocal cord is removed. If only part of the vocal cord is removed you may experience hoarseness; if both cords are removed you will not have normal speech.
- **Laryngectomy**: There are a number of different types of laryngectomies, all with the goal of removing as much cancer as possible while sparing healthy tissue.
  - **Partial Laryngectomy**: In a partial laryngectomy only a portion of the larynx is removed. There are two types. In a supraglottic laryngectomy the portion of the larynx above the vocal cords known as the supraglottis is removed. You will be able to speak normally after surgery. The second is a hemilaryngectomy and in this procedure only one of the vocal cords is removed. After this procedure some speech will remain.
  - **Total Laryngectomy**: The entire larynx is removed because of how advanced the cancer is. Because the entire larynx is removed, the windpipe (trachea) will be brought up through the skin on the front of the neck creating a hole (stoma) that you will now breathe through, rather than through your nose or mouth. This is known as a tracheostomy. You will not be able to speak normally. After recovery from the surgery you should be able to swallow normally.
- **Laser Surgery**: In laser surgery, an endoscope is placed into your mouth and down into your throat to find the tumor and then vaporize or cut out (excise) the tumor using the laser that is on the tip of the endoscope. If this technique is used to remove part of the vocal cord, it can result in a hoarse voice.
- **Lymph Node Dissection**: If it is suspected that the cancer has spread to the lymph nodes then your surgeon may choose to do a lymph node dissection or removal. There are several types of dissections, which can range from the removal of one or a few lymph nodes to the removal of nodes, nerves and muscle. Your surgeon will determine the extent of dissection needed based on the size and location of the original tumor and if the nodes were enlarged on previous imaging tests.

If your voice or swallowing is affected by the surgery you had you will be referred to work with a speech therapist. A speech therapist will be able to teach you techniques and give you tools to improve your speech and swallowing. If you are unable to swallow efficiently enough to maintain proper nutrition after surgery, you may have a gastrostomy tube placed. This is a tube that is placed directly through the skin and into the stomach with a port to infuse liquid nutrition into. This will likely be temporary until your swallowing improves enough to maintain proper nutrition. You may also need reconstructive surgery depending upon how much normal tissue was removed. Skin may need to removed from one part of your body to replace skin and tissues removed during surgery.

Radiation Therapy

Radiation therapy can be used as the only treatment or in combination with surgery or chemotherapy to treat laryngeal cancer. Radiation comes in the form of high energy x-rays that are delivered to the patient only in the areas at highest risk for cancer.
These x-rays are similar to those used for diagnostic x-rays, but they are of a much higher energy. The higher energy of x-rays in radiation therapy results in damage to the DNA of cells. Cancer cells divide faster than healthy cells, and so their DNA is more likely to be damaged than that of normal cells. Additionally, cancer cells are generally less able to repair damaged DNA than normal cells are, so cancer cells are killed more easily by radiation than normal cells are.

In early stages of the disease, laryngeal cancer may be treated with radiation alone. This can preserve better voice quality for some patients. When radiation is used with surgery it is called adjuvant therapy. It is used as a treatment after surgery to kill any remaining cancer cells and to lower the chance of recurrence. Radiation may also be the course of treatment for patients who cannot tolerate surgery or whose cancer is so advanced that the goal is to manage symptoms, such as pain and bleeding. Radiation therapy is generally given daily, five times a week. It can result in side effects such as skin irritation and it can affect nearby glands and tissues.

Chemotherapy

Chemotherapy is the use of medications that treat cancer. Chemotherapy is known as a "systemic" treatment, which means that it goes throughout the entire body. These medications may be given through a vein (IV, intravenously) or by mouth, as pills. There are two different methods of giving chemotherapy for the treatment of laryngeal cancer, conventional chemotherapy and chemoradiation. Conventional chemotherapy is useful in treating the cancer if it has metastasized (spread) or if the cancer was not completely removed during surgery. The chemotherapy medications commonly used to treat laryngeal cancer include: cisplatin, carboplatin, fluorouracil, docetaxel, paclitaxel and cetuximab. Cetuximab, a targeted therapy, can be used in combination with chemotherapy or radiation to treat laryngeal cancer. Your chemotherapy regimen, created by your provider, may consist of a single medication or a combination of medications.

Chemoradiation is chemotherapy that is given at the same time as radiation. Chemoradiation tends to be more effective than using radiation or chemotherapy alone. The medication of choice for chemoradiation is cisplatin and in some cases cetuximab.

Clinical Trials

There are clinical research trials for most types of cancer, and every stage of the disease. Clinical trials are designed to determine the value of specific treatments. Trials are often designed to treat a certain stage of cancer, either as the first form of treatment offered, or as an option for treatment after other treatments have failed to work. They can be used to evaluate medications or treatments to prevent cancer, detect it earlier, or help manage side effects. Clinical trials are extremely important in furthering our knowledge of this disease. It is through clinical trials that we know what we do today, and many exciting new therapies are currently being tested. Talk to your provider about participating in clinical trials in your area. You can also explore currently open clinical trials using the OncoLink Clinical Trials Matching Service.

Follow-Up Care and Survivorship

After you have completed treatment for laryngeal cancer, your care team will follow you closely to monitor for recurrence of cancer and to help you manage any side effects you may encounter from the treatment you received. Visits to your provider will be frequent during the first couple of years after completion of treatment. During the first year you will see your provider about every other month. At these appointments your provider will examine your neck and may do a laryngoscopy. Your provider may also order chest x-rays and other imaging tests. The longer you are cancer free, the longer the time will be between appointments.

If you were treated with radiation that included your thyroid gland, you will have regular blood tests to check the functioning of your thyroid gland. Radiation may also include the salivary glands in the field, which causes dry mouth, which can affect speech, swallowing and lead to tooth decay. Your provider may suggest more frequent trips to the dentist and preventive oral care to manage these side effects.

Patients who were treated with surgery or surgery and radiation often have issues with swallowing and speech after treatment. You will be referred to work with a speech therapist. A speech therapist will be able to teach you techniques and supply you with tools to improve or regain your speech. A speech therapist can also assist you with swallowing. You may need to adjust your eating habits to better suit your needs after treatment. You may also be referred to a nutritionist to help you manage your nutritional goals and needs. You may temporarily need a feeding tube placed into your stomach until your swallowing
improves.

Patients who were treated with a total laryngectomy are left with a tracheostomy, also known as a stoma. A tracheostomy, done through a surgical procedure, is a hole in the front of the throat that is used to breathe, rather than the nose or mouth. The mouth and nose moisten and remove particles from the air that is then introduced into our lungs. Because the air being transferred through a stoma will be drier and cooler, it can cause buildup of thick mucous, making it difficult to breathe. Patients with stomas will be instructed in how to care for their stoma and how to use a humidifier to moisten the air they are taking in to prevent the buildup of mucous. Your provider and home care nurses will teach you how to care for and protect your stoma.

Difficulty with speech and swallowing, changes in appearance, sexuality, fear of recurrence, financial impact of cancer treatment, employment issues and coping strategies are common emotional and practical issues experienced by laryngeal cancer survivors. Your healthcare team can identify resources for support and management of these practical and emotional challenges faced during and after cancer.

Cancer survivorship is a relatively new focus of oncology care. With some 15 million cancer survivors in the US alone, there is a need to help patients transition from active treatment to survivorship. What happens next, how do you get back to normal, what should you know and do to live healthy going forward? A survivorship care plan can be a first step in educating yourself about navigating life after cancer and helping you communicate knowledgeably with your healthcare providers. Create a survivorship care plan today on OncoLink.

### Resources for More Information

**International Association of Laryngectomees (IAL)**
This site offers education, support and information on suppliers of care products for patients with laryngectomies.

[www.Theial.com](http://www.Theial.com)

**Support for People with Oral and Head and Neck Cancer, INC. (SPOHNC)**
Free support for survivors and their families including: resources, referrals, product information and "survivor-to-survivor" network.

[www.spohnc.org](http://www.spohnc.org)

**WebWhispers Nu-Voice Club**
A free internet-based laryngectomy resource for those who have questions about larynx cancer treatment, surgery, recovery and life after laryngectomy.

[www.webwhispers.org](http://www.webwhispers.org)

### Appendix: Complete Laryngeal Cancer Staging

**American Joint Committee on Cancer (7th ed., 2010)**

<table>
<thead>
<tr>
<th>Primary Tumor (T)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
</tbody>
</table>

**T**  

<table>
<thead>
<tr>
<th>T</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumor limited to one subsite of supraglottis with normal vocal cord mobility</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis without fixation of the larynx.</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor limited to the larynx with vocal cord fixation and/or invades any of the following: postcricoid area, pre-epiglottic space, paraglottic space, and/or inner cortex of thyroid cartilage.</td>
</tr>
<tr>
<td>T4a</td>
<td>Moderately advanced local disease. Tumor invades through the thyroid cartilage and/or invades tissues beyond the larynx</td>
</tr>
<tr>
<td>-----</td>
<td>---------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>T4b</td>
<td>Very advanced local disease. Tumor invades pre-vertebral space, encases carotid artery, or invades mediastinal structures</td>
</tr>
</tbody>
</table>

### T1
- **Glottis** - T
  - **Description**
  - **T1**: Tumor limited to the vocal cord(s) with normal mobility
  - **T1a**: Tumor limited to one vocal cord
  - **T1b**: Tumor involves both vocal cords
  - **T2**: Tumor extends to supraglottis and/or glottis, and/or with impaired vocal cord mobility
  - **T3**: Tumor limited to the larynx with vocal cord fixation and/or invasion of the paraglottics space, and/or inner cortex of the thyroid cartilage
  - **T4a**: Moderately advanced local disease. Tumor invades through the outer cortex of the thyroid cartilage and/or invades tissues beyond the larynx
  - **T4b**: Very advanced local disease. Tumor invades pre-vertebral space, encases carotid artery, or invades mediastinal structures.

### T1
- **Subglottis** - T
  - **Description**
  - **T1**: Tumor limited to the subglottis
  - **T2**: Tumor extends to vocal cord(s) with normal or impaired mobility
  - **T3**: Tumor limited to the larynx with vocal cord fixation
  - **T4a**: Moderately advanced local disease. Tumor invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx
  - **T4b**: Very advanced local disease. Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures.

### NX
- **Regional Lymph Nodes (N)**
  - **Description**
  - **NX**: Regional lymph nodes cannot be assessed
  - **N1**: Metastasis in a single ipsilateral lymph node, 3cm or less in greatest dimension
  - **N2**: Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
  - **N2a**: Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension
  - **N2b**: Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
  - **N2c**: Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
  - **N3**: Metastasis in a lymph node, more than 6 cm in greatest dimension
## Distant Metastasis (M)

<table>
<thead>
<tr>
<th>M</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>

## Anatomic Stage

<table>
<thead>
<tr>
<th>Anatomic Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage II</td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage III</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>T4a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4a</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4a</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IVB</td>
<td>T4b</td>
<td>Any N</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IVC</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

## Histologic Grade (G)

<table>
<thead>
<tr>
<th>G</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>GX</td>
<td>Grade cannot be assessed</td>
</tr>
<tr>
<td>G1</td>
<td>Well differentiated</td>
</tr>
<tr>
<td>G2</td>
<td>Moderately differentiated</td>
</tr>
<tr>
<td>G3</td>
<td>Poorly differentiated</td>
</tr>
<tr>
<td>G4</td>
<td>Undifferentiated</td>
</tr>
</tbody>
</table>

OncoLink is designed for educational purposes only and is not engaged in rendering medical advice or professional services. The information provided through OncoLink should not be used for diagnosing or treating a health problem or a disease. It is not a substitute for professional care. If you have or suspect you may have a health problem or have questions or concerns about the medication that you have been prescribed, you should consult your health care provider.