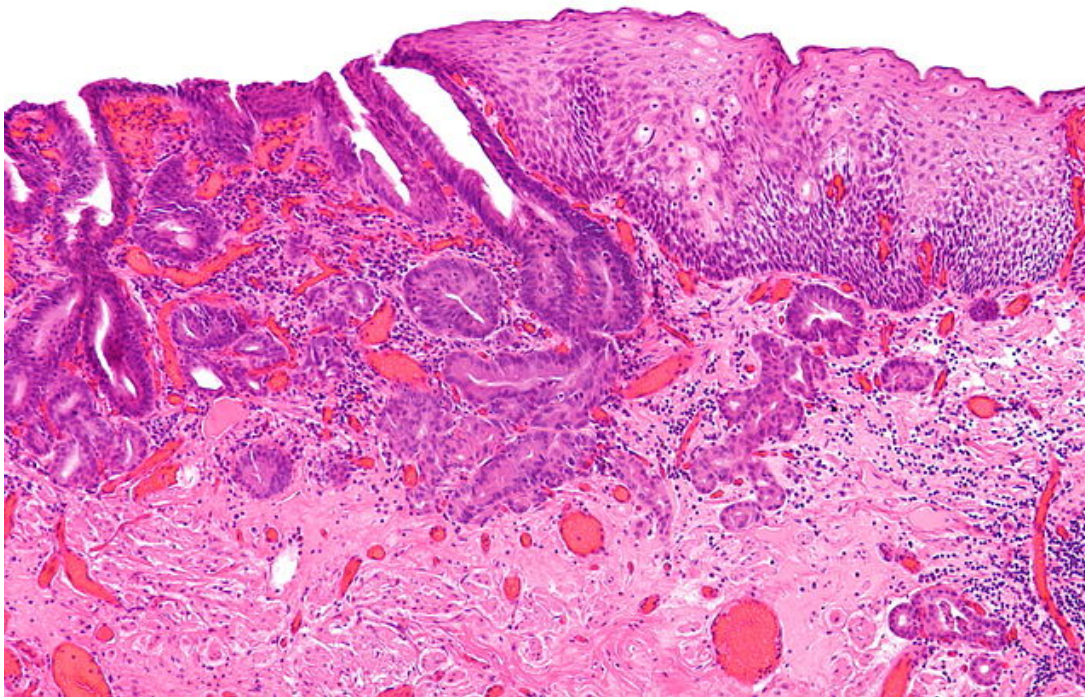


## Esophageal Cancer (Esophageal Carcinoma) — Classification, Staging, and Prognosis

[See online here](#)

**If diagnosed and treated on time, a patient with esophageal carcinoma can be cured. However, the symptoms are often non-specific and only appear once the tumor is already advanced. Therefore, it is all the more important not to overlook any relevant indications in clinical practice. Questions about esophageal carcinoma occasionally come up in exams, especially on etiology and clinical symptoms. Therefore, it pays to read on to learn more!**



### Definition and Clinical Pathology of Esophageal Carcinoma

#### Squamous cell and adenocarcinoma

Esophageal carcinoma describes a malignant tumor of the [esophagus](#) and is manifested most frequently as **squamous cell or adenocarcinoma**.

A squamous cell carcinoma primarily grows **endophytic-ulcerative**. It penetrates the esophageal wall and quickly infiltrates neighboring organs. Growth in the lumen of the esophagus is more likely to occur secondarily and at an advanced stage. Squamous cell carcinoma is found mostly in the area of 1 of 3 physiological **bottlenecks**: esophagus

entry (approx. 20%), aortic arch/left main bronchus (approx. 35%), and diaphragm constriction (approx. 45%).

It is also common for an **adenocarcinoma** to grow into the esophageal lumen. Almost always it is located in the **lower 3rd of the esophagus**.

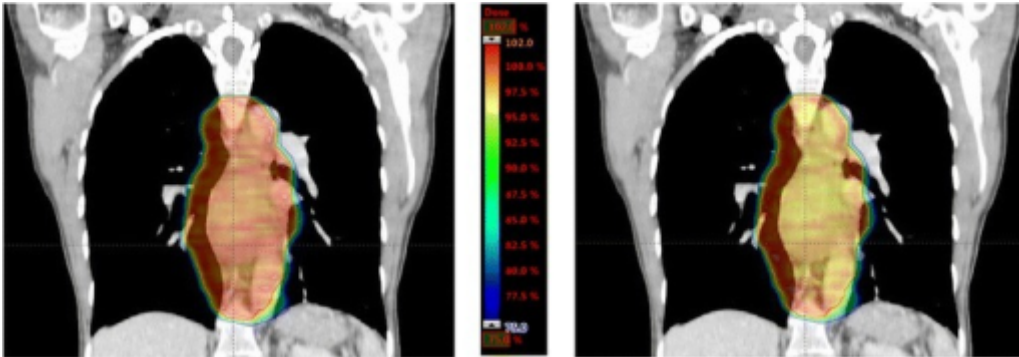


Image: "Comparison of dose distribution calculated using AAA and AXB dose calculation algorithms for mid-esophageal cancer," by Openi, License: [CC BY 4.0](https://creativecommons.org/licenses/by/4.0/)

## Epidemiology of Esophageal Carcinoma

### Esophageal cancer is significantly more common in men

In Europe, esophageal cancer is relatively rare with an **incidence** of 6/100,000 inhabitants. Compared to squamous cell carcinoma, adenocarcinoma is increasing in its frequency (about 60%) in Western industrialized countries. Squamous cell carcinoma, however, is reported more in other countries such as China, Turkmenistan, South Africa, and Japan. This underlines the assumption that dietary and environmental factors play an etiological role.

More men than women are affected (M:F = 5:1), and a peak age around the 6th and 7th decade of life can be established.

## Etiology of Esophageal Carcinoma

### Environmental influences and Barrett's esophagus as etiological factors

Triggering factors of squamous cell carcinoma are long-term consumption of highly concentrated alcohol and very hot foods and beverages, smoking, as well as **nitrosamines** and **aflatoxins**. Furthermore, scarring after burns or radiation, **achalasia**, **papillomaviruses** (HPV 16) and the **Plummer-Vinson syndrome** (in cases of chronic iron deficiency) can favor the formation of esophageal cancer. Vitamin deficiency and poor oral hygiene are also risk factors.

Adenocarcinoma, however, arises at the base of **Barrett's esophagus** in over 50% of the cases. Here, the esophageal squamous epithelium turns into **columnar epithelium**, in the course of chronic reflux esophagitis. Alcohol consumption and smoking are not considered abetting factors here!

**Note:** Esophageal adenocarcinoma usually arises in the course of Barrett's esophagus!

## Symptoms of Esophageal Carcinoma

### Dysphagia and B-symptoms

Esophageal tumors are often noticed late, as they display rather nonspecific symptoms:

- **Dysphagia:** In patients > 45 years, esophageal carcinoma is the most likely cause of progressive dysphagia!
- Retrosternal pain, possibly radiating to the back
- **Regurgitation**
- **Hiccoughs** in case of infiltration of the vagus nerve
- Hoarseness in case of infiltration of the recurrent laryngeal nerve
- **Hematemesis** (vomiting blood)
- **Cough and aspiration pneumonia** in case of **esophageal bronchial fistula**

Accompanying **B-symptoms** (weight loss, night sweats, and fever) may occur.

**Note:** Dysphagia only occurs at a luminal narrowing of more than 60%, which often occurs at a very late stage!

### Metastasis

Due to the lack of esophageal serosa coating, esophagus carcinoma metastasizes into adjacent organs and structures early on **per continuitatem**. For the same reason, the carcinoma also quickly spreads **lymphogenously** into regional, nuchal, cervical, and celiac lymph nodes. **Hematogenic metastasis** into the liver, lungs, and bones, however, occurs later and most patients don't experience it anymore.

## Differential Diagnosis of Esophageal Carcinoma

In terms of differential diagnosis, **esophageal diverticula**, stenoses after burns or inflammation, a cardia of the stomach or **benign esophagus tumors** has to be taken into consideration. Benign tumors of the esophagus are rare and often asymptomatic. They can grow in an **intramural** or **intraluminal** manner. They are diagnosed via esophageal bolus swallow test, endoscopy, and endoscopic ultrasonography. Small intraluminal tumors can usually be removed endoscopically with a **cautery snare** – larger ones are removed surgically.

## Classification and Staging of Esophageal Carcinoma

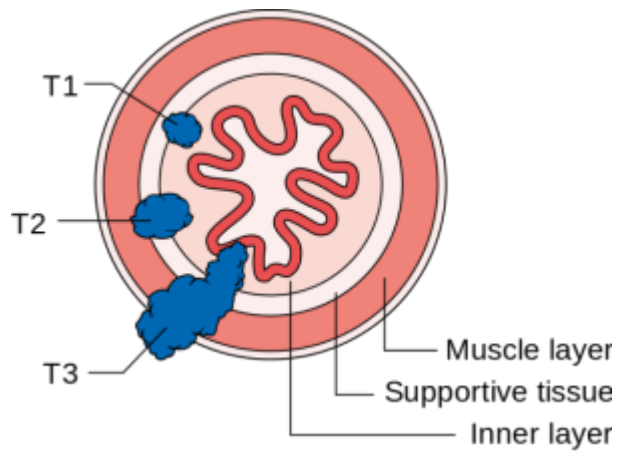


Image: "Diagram showing T1,T2, and T3 stages of esophageal cancer," by Cancer Research UK, License: [CC BY-SA 4.0](https://creativecommons.org/licenses/by-sa/4.0/)

Classification of the tumor stages is carried out according to general **TNM (Tumor-node-metastasis) classification**:

<b>TIS</b>	Carcinoma <i>in situ</i> (basement membrane is not crossed)
<b>T1a</b>	Infiltration of the lamina propria
<b>T1b</b>	Infiltration of the submucosa
<b>T2</b>	Infiltration of the muscularis propria
<b>T3</b>	Infiltration of the adventitia
<b>T4a</b>	Infiltration of neighboring structures (T4a: pleura, pericardium or diaphragm; T4b: other structures such as the aorta or vertebral bodies, etc.)
<b>N0</b>	Without regional lymph node metastasis
<b>N1</b>	1-2 regional lymph node metastases
<b>N2</b>	3-6 regional lymph node metastases
<b>N3</b>	≥ 7 regional lymph node metastases
<b>M0</b>	No remote metastasis
<b>M1</b>	Remote metastasis (hematogenous or non-regional lymph node metastases)

Resulting from this, is the UICC (Union for International Cancer Control) specified staging:

Stadium		TNM
1	1a	T1, N0, M0
	1b	T2, N0, M0
2	2a	T3, N0, M0
	2b	Until T2, N1, M0
3		T4, N0, M0
		From T3, N1, M0
		From N2, M0
4		M1

## Diagnostics of Esophageal Carcinoma

### Anamnesis as an indication of esophageal carcinoma

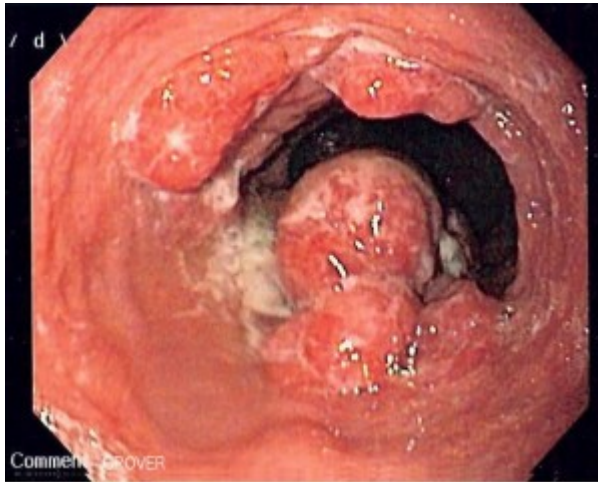
Whenever a patient complains about **dysphagia**, esophageal cancer always has to be ruled out, especially in elderly patients. One should specifically ask about the above-described symptoms. Unfortunately, however, patients often only have little discomfort,

even in advanced tumor stages.

## The esophageal bolus swallow test

By using an esophageal bolus swallow test, asymmetries, contour changes, stenoses or dilatations can be identified. The location, extent, and degree of functional limitation of the esophagus can also be judged.

## Esophagoscopy with biopsies



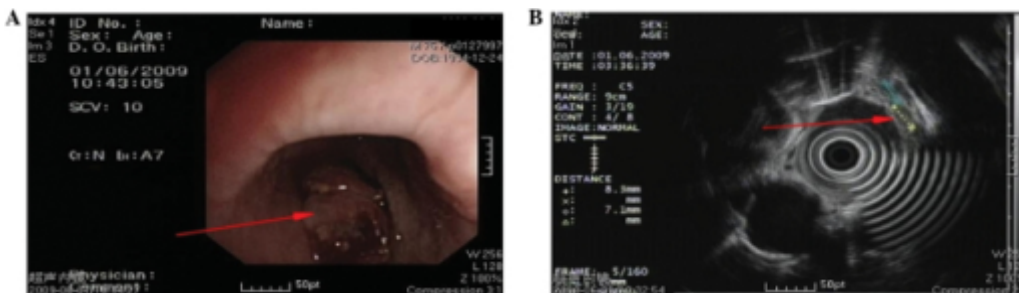
**Image:** "Endoscopic image of patient with esophageal adenocarcinoma seen at gastro-esophageal junction," by Samir, License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

A definitive diagnosis can only be made through histological results. For this purpose, an **esophagoscopy** is carried out and biopsies from at least 10 suspect areas are removed. In the case of a squamous cell carcinoma, the histological picture shows nests of **atypical keratinocytes** with lymphocytic infiltrates. Adenocarcinoma is typically presented by **metaplastic glandular tissue**, goblet cells, and the **columnar epithelium** (etiology: Barrett's esophagus).

## Staging of Esophageal Carcinoma

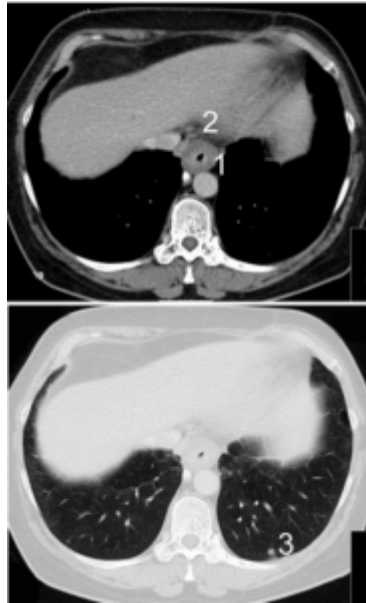
In order to assess the extent of the tumor, following investigations about the relevant issues are usually carried out:

- **Endosonography:** Depth of infiltration, regional lymph node involvement?



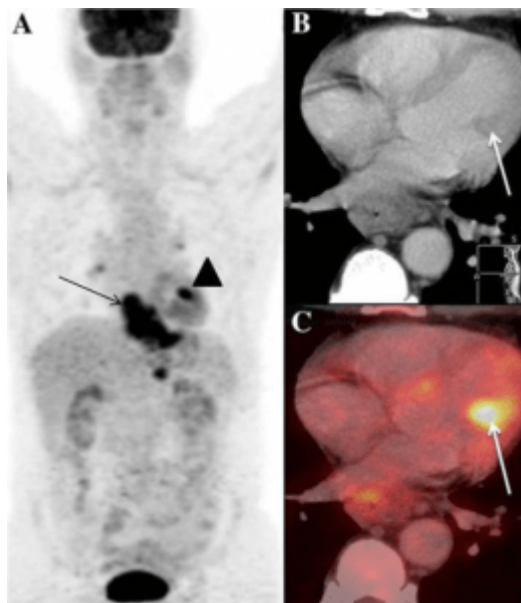
**Image:** "Endoscopic ultrasonography revealing (A) an esophageal neoplasm (indicated by the red arrow) and (B) multiple enlarged lymph nodes on the outside of the esophagus wall (indicated by the red arrow)," by Openi, License: [CC BY 3.0](https://creativecommons.org/licenses/by/3.0/)

- **Computed tomography (CT) and magnetic resonance imaging (MRI):** Assessment of anatomical relationships, remote metastases?



**Image:** "CT scan showing a circular esophageal cancer (1) with paraesophageal lymph node involvement (2) and small sarcoid lesions of the lung (3)," by Openi, License: [CC BY 2.0](https://creativecommons.org/licenses/by/2.0/)

- **Positron emission tomography (PET)/PET-CT:** Remote metastases (most sensitive detection method)?



**Image:** "Myocardial metastases from esophageal cancer. A- MIP image showing primary esophageal mass (arrow) with focal uptake in region of heart (arrowhead), B- Hypodense lesion in left ventricular myocardium (arrow) on axial CT images showing, C- FDG uptake on axial fused PET/CT images (arrow)," by Openi, License: [CC BY 4.0](https://creativecommons.org/licenses/by/4.0/)

- **Bone scintigraphy:** Bone metastases?

In case of relevant suspicion:

- **Laryngoscopy/bronchoscopy:** infiltration of the airways?

## Therapy of Esophageal Carcinoma

The stage of the esophageal carcinoma determines the treatment

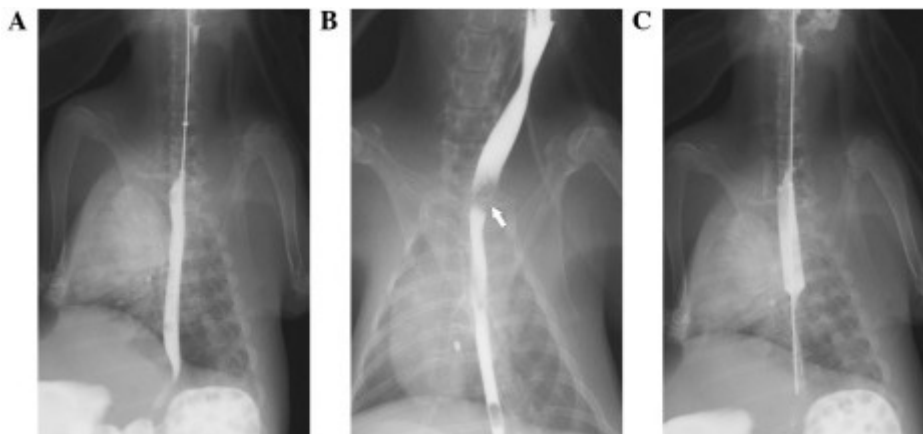
**Early adenocarcinomas (T1a):** These are treated with endoscopic **mucosal resection**. The cure rate is very high. In the course of the intervention, a frozen section diagnosis is always carried out. If this shows that the tumor has already infiltrated the submucosa, a subtotal esophagectomy will be carried out.

**From TNM stage T1b to UICC stage 2A: Subtotal esophagectomy** with radical lymphadenectomy with curative intent (R0 resection) is carried out. The resected esophagus is replaced with a gastric pull-up ('gastric tube') or **colon interponate**. It is a 2-cave-procedure (thoracoabdominal access path) with high surgery mortality (about 5%). The postoperative complications include anastomotic leakage, interponate necrosis, stenosis, bleeding, chylothorax (injury of the thoracic duct), and hoarseness (injury of the recurrent laryngeal nerve). Especially in the case of adenocarcinoma, **perioperative chemotherapy** with **5-FU** and **cis-platinum** increase the chance of survival.

**Stage 2B and 3:** Downstaging using **neoadjuvant chemoradiation** (cisplatin, 5-FU) can be attempted to subsequently perform curative surgery.

In inoperable patients, or for squamous cell carcinoma in the area of the upper esophagus, only curative radiation chemotherapy may be considered. However, adenocarcinomas do not respond to radiotherapy!

**Palliative: From T4 or M1** curative treatment is no longer possible. Palliative care aims to maintain the passage of food. This can be achieved through irradiation or laser therapy. In most cases, however, a **metal stent** has to be placed endoscopically. The timely use of a **PEG** (percutaneous endoscopic gastrostomy) **tube** usually prolongs survival time significantly, as many patients otherwise mostly succumb to the complications of cancer cachexia.



**Image:** "Rabbit esophageal tumor featured by barium meal and stent implant. (A) Normal rabbit esophagus. (B) Rabbit esophageal cancer. (C) Implantation of the stent. Arrow, tumor location," by

## Prognosis of Esophageal Carcinoma

### Esophageal cancer carries a high mortality rate

The overall prognosis is poor. The 5-year survival rate of all patients is less than 10%. Palliative patients usually survive less than a year, while the 5-year survival rate of R0-resected patients is approx. 40%.

The problem is the late diagnosis: in 90% of patients, a locally advanced stage (at least T3, N1) is found.

## Prevention of Esophageal Carcinoma

### Esophageal cancer can be avoided

The above-mentioned risk factors (in particular alcohol consumption and smoking) should be avoided. Patients at increased risk (e.g., known Barrett's esophagus) should regularly receive esophagoscopy check-ups.

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