

Esophageal Cancer

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ABSTRACT

Esophageal cancer (EC) is a relatively rare malignancy occurring in the esophagus, the passage between the throat and stomach. Despite its infrequency, it ranks among the most aggressive gastrointestinal cancers, being the eighth most prevalent cancer type overall and the sixth leading cause of cancer-related deaths. Associated with a high mortality rate and often diagnosed at an advanced stage, it exhibits regional variations in incidence.

Risk factors for EC include socioeconomic status, tobacco and alcohol use, consumption of hot beverages, gastroesophageal reflux disease (GERD), obesity, exposure to nitrosamines, and Barrett's esophagus—a precancerous condition arising from GERD. Additionally, deficiencies in nutrients like folate, vitamin E, and vitamin C have been linked to its development.

Symptoms of EC encompass a dry cough, hoarse voice, swollen lymph nodes near the collarbone, difficulty and pain while swallowing, weight loss, and coughing up blood. Given its severity and prognosis, the importance of screening for early detection is expected to increase significantly.

Presently, no standardized methods exist for early detection. Diagnosis typically involves biopsy via an endoscope, a fiber optic camera. Treatment strategies depend on cancer stage, location, patient health, and preferences. Surgery may suffice for localized squamous-cell tumors, though often combined with chemotherapy and radiation for larger tumors. Palliative care becomes relevant for patients with advanced illness or when surgery isn't feasible.

Prevention and quality of life improvement efforts emphasize adopting a healthy diet and quitting smoking. These measures play a pivotal role in reducing EC risk and enhancing patient well-being.

INTRODUCTION

Cancer of the esophagus (esophageal cancer) is a tumor that is the least researched and deadliest type of cancer worldwide because of its aggressive nature and poor survival rate. It basically arises along

the lining of the esophagus and manifests as an uncontrolled growth in this lining gradually from the inner to the outer surface.

Due to the lack of serosa (the outer layer of tissue many organs have) and an extensive lymphatic drainage system, the disease can swiftly extend to neighboring mediastinal structures, facilitating tumor growth even in its initial stages. Typically, esophageal cancer spreads through lymphatics and direct extension.

In patients with advanced disease, the hematogenous spread is frequent, and hematogenous metastases to the lungs and liver are most frequent.[1].

There are basically two types of esophageal cancer are:

- **Adenocarcinoma** - Adenocarcinoma originates from the glandular cells located in the lower portion of the esophagus. It is frequently observed in developed nations.
- **Squamous cell carcinoma** – arises from the epithelial cells lining the esophagus. It is common in developing countries.
- In a few cases, lymphomas, leukemias, and sarcomas also potentially develop in esophageal cancer patients.
- **Barrett's esophagus** – usually progresses to adenocarcinoma in most of the cases. It is a premalignant condition that occurs as a complication of gastrointestinal reflux disease (a condition that occurs when stomach acid repeatedly flows back into the esophagus). It is usually asymptomatic but sometimes characterized by frequent heartburns and chest pain [2].

ETIOLOGY

The two types of liver cancer (squamous cell carcinoma and adenocarcinoma) has lot of differences in terms of etiology and risk factors associated with the disease. A few of them are listed below:

Esophageal cancer arises from DNA mutations acquired over a person's lifetime. There are two primary types: squamous cell carcinoma and adenocarcinoma. Squamous cell carcinoma typically originates from the uncontrollable growth of squamous cells lining the esophagus, with smoking and alcohol consumption being the main risk factors. Adenocarcinoma, more prevalent, is associated with Barrett's esophagus, a condition resulting from GERD, significantly elevating the risk of its development.

Additional risk factors for esophageal cancer include Helicobacter pylori infection, which paradoxically decreases the risk of adenocarcinoma, mutations in the BLM gene linked to Bloom syndrome, and

Fanconi anemia, an autosomal recessive disorder heightening the risk of squamous cell carcinoma. Oral bisphosphonates have also been implicated in the development of both squamous cell carcinoma and adenocarcinoma of the esophagus [3].

The disease displays a distinctive epidemiologic pattern compared to all other cancers. Globally, almost 4,50,000 people suffer from esophageal cancer every year, and the prevalence is rising. EC is more common in men, as compared to women. Squamous cell esophageal cancers account for 90% of all cases in the highest-risk region, known as the "esophageal cancer belt," which consists of parts of Northern Iran, southern Russia, Central Asian nations and Northern China. Adenocarcinoma is primarily seen in white men whereas Asians and Blacks have the greatest incidence rates of the squamous cell carcinoma variant of EC [4].

SYMPTOMS

Initially, patients with esophageal cancer (EC) may exhibit no symptoms, but dysphagia, difficulty in swallowing solid foods, emerges as a common clinical presentation due to tumor obstruction in the esophagus. As the disease progresses, dysphagia extends to liquid foods in advanced stages, leading to cachexia, a type of wasting syndrome, and gradual weight loss. Non-specific symptoms like retrosternal discomfort and throat burning may manifest early on, attributed to food regurgitation, along with breathing difficulties, fatigue, and pain akin to other cancers. Hematemesis, vomiting blood, melena, dark feces with blood, and anemia may occur due to gastrointestinal bleeding in some cases. Complications such as fistulas, laryngeal nerve paralysis, cough, and post-obstructive pneumonia may arise if the disease extends to the tracheobronchial wall. Immunocompromised patients may experience infectious esophagitis, with *Candida albicans*, herpes simplex, and cytomegalovirus contributing to esophageal cancer in these individuals [5].

DIAGNOSIS

Esophageal cancer is diagnosed based on the patient's clinical history and physical examination, as well as by the evaluation of endoscopic and other imaging studies. An initial step in diagnosing EC is the barium swallow test which confirms the presence of a tumor in the esophagus. Other diagnostic tests include various imaging modalities, endoscopy, routine blood investigations and biomarkers.

STANDARD OF CARE DIAGNOSTICS

PHYSICAL CLINICAL EXAMINATION

During a physical examination for esophageal cancer, there are no distinctive clinical markers specific to the disease. However, dysphagia (difficulty in swallowing) and weight loss are commonly observed symptoms. In advanced stages, hepatomegaly (enlarged liver) or lymphadenopathy, particularly involving supraclavicular nodes, may become apparent. [6].

IMAGING MODALITIES

Barium studies, computed tomography, positron emission tomography, and endoscopic ultrasound are the imaging tests that are used to assess esophageal cancer. Imaging offers crucial details on the local scope and regional spread of the disease, which in turn aids in choosing the best course of treatment for these individuals.

Barium swallow

In this technique, examination of the esophagus is done after the patient is orally administered high-density barium sulfate (200% w/v). Any defects in the esophagus are then identified with an esophagogram (x-ray of the esophagus). When compared to cross-sectional imaging techniques, it has the benefit of being inexpensive and easily accessible. The evaluation of dysphagia, gastroesophageal reflux, and other esophageal illnesses beyond the scope of endoscopies still begin with this barium swallow technique. An additional benefit of this technique over endoscopy and cross-sectional imaging is the examination of the structural and functioning aspects of the esophagus at the same time. It can be performed either in single or double-contrast [7].

Primary tumor (T)

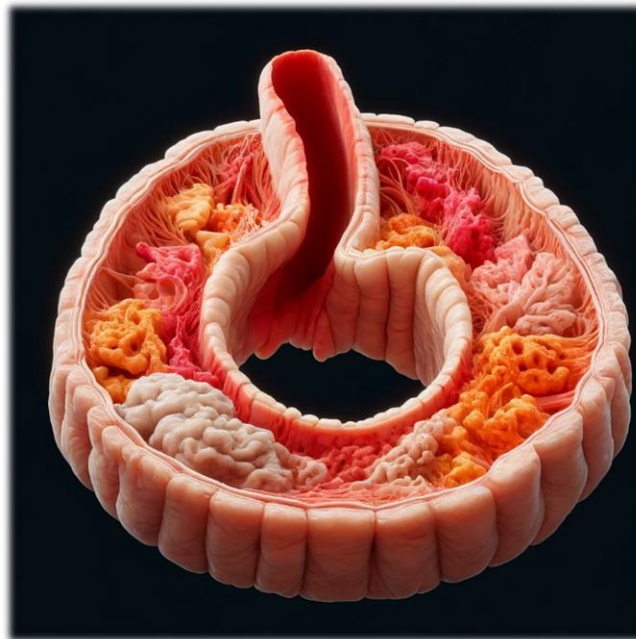
- T0- No evidence of primary tumor
- Tis- Carcinoma in situ
- T1- Tumor invades mucosa or submucosal
- T2- Tumor invades muscularis propria
- T3- Tumor invades adventitia
- T4- Tumor invades adjacent structures

<p style="text-align: center;">Lymph nodes (N)</p> <p>N0- No regional nodes N1- Required nodal metastases</p>
<p style="text-align: center;">Distant metastases (M)</p> <p>M0- No distant metastases M1- Distant metastases</p>

Table 2: TNM staging for esophageal cancer [8].

Computed tomography (CT)

In patients with established esophageal cancer, the main goal of cross-sectional imaging studies is to stage the illness as precisely as possible to identify which patients may be candidates for surgical resection. In order to stage and monitor esophageal cancers, computed tomography (CT) is utilized in addition to the barium study. By displaying the degree of the tumor’s expansion, penetration of the esophagus wall, and its invasion into the peri-esophageal fat, a CT scan can be utilized to determine the local extent of the tumor. CT cannot consistently discriminate between T1 and T2 lesions because it is unable to define the distinct layers of the esophageal wall. In a CT scan, a T3 tumor is identified by the tumor infiltration into the peri-esophageal fat. Invasion of the tracheobronchial wall is also identified on CT scan by its wall thickening. CT is also helpful in identifying distant metastatic illness, which is frequently found in the liver and lungs [9].



3D color image representing a computed tomography (CT) scan of esophageal cancer. The image showcases an anatomically inspired representation of the esophagus, with areas affected by cancer highlighted in contrasting colors to clearly differentiate between healthy tissue and cancerous regions.

Magnetic resonance imaging (MRI)

The esophageal wall and esophagogastric junction can be identified using MRI, a non-irradiating and non-invasive technology. In terms of the regional and local staging of EC as well as the evaluation of therapy response, MRI has demonstrated positive capabilities. It is equally accurate in TNM staging of EC as 18F-FDG-PET/CT (18 Fluorodeoxyglucose– Positron emission tomography) and also provides the benefit of being used for repeated follow-ups without causing over-radiation risk to the patients, unlike other techniques. The limitation of MRI is that it is less accurate compared to CT in determining esophageal tumors as the distinct layers of the esophageal wall cannot be reliably distinguished by this technique, which is necessary for precise local staging [10].

18 Fluorodeoxyglucose –Positron emission tomography (18F-FDG-PET)

Patients with esophageal cancer are also staged using positron emission tomography (PET). These scans can be used to locate the main tumor, but their sensitivity in locating locoregional disease is restricted due to their overall spatial resolution. Whole body coverage is a benefit of this technique, and it has been demonstrated that when compared to traditional imaging, PET can identify EC at a very early stage. PET can identify metastases of EC in distant organs like the liver, lung, bone, adrenal, and other organs while eliminating the need for surgery and may influence the treatment choices [11].

Endoscopy

An endoscope is an instrument that helps to see inside an organ or other hollow body parts. Unlike many other types of imaging procedures in medicine, the endoscope is introduced directly into the specified organ. There exist various types of endoscopic procedures.

- Upper endoscopy - Examination of esophagus, stomach, and duodenum
- Colonoscopy - Examination of colon and rectum
- Sigmoidoscopy - Examination of sigmoid (lower part of colon)

Upper endoscopy is ideal in the diagnosis of EC. It can be either rigid or flexible. Flexible endoscopes are mostly used for diagnostic purposes, while rigid endoscopes are typically

employed for directing surgical operations. In endoscopy, the EC may appear as little round lumps or flat, elevated patches (known as plaques), and advanced tumors present as huge irregular areas which may lead to esophageal constriction [12].

The most common technique for all indications of upper endoscopy is known as “white-light endoscopy,” which refers to the utilization of all visible colors. It has become the gold standard for esophageal cancer detection and diagnosis. Those who exhibit symptoms like dysphagia and are likely to have tumors of a large size, can be traditionally identified by this white light endoscopy. However, the sensitivity of this endoscopic technique in detecting early lesions would be substantially reduced when the endoscopy was done as a screening or surveillance procedure.

To overcome this limitation from the early 2000s, **chromo endoscopy**, a modified GI endoscopy technique that uses stains, pigments, or dyes to find malignant spots in the mucosa lining of the esophagus has been used as the preferred screening tool in high-risk patients of EC. In healthy squamous epithelium, the agent stains to glycogen and emits a brown color which is visible under the white light endoscopy. But the mucosa will appear as unstained in epithelium with low glycogen levels, such as in dysplasia cases [13].

Narrow-band imaging (NBI) technology, which facilitates the endoscopic identification of gastrointestinal lesions was introduced in the early 2000s. The visibility of the mucosal surface and vascular pattern of the gastrointestinal system are improved by applying a filter with two distinct peak wavelengths (415 and 540 nm), enabling endoscopists to identify and classify abnormalities precisely. The technology is now integrated with the endoscopes and may now be readily activated by pressing a button. For the purpose of esophageal lesion screening, NBI technology can be employed in endoscopic procedures in two different manners- non magnifying endoscopy for lesion detection and a combination with magnifying endoscopy for the characterization of these lesions [14].

ROUTINE INVESTIGATIONS

All routine lab investigations such as complete blood picture, tests to detect levels of glucose in the blood, lipid profile, thyroid function tests, liver function tests (which detect the level of bilirubin, aspartate aminotransferase and alanine transaminase), urine analysis, and vitamin B₁₂

values to check for the deficiency can be done to understand the immune status of the patient and to identify the presence of any risk factors [15].

HISTOPATHOLOGICAL EXAMINATION

A tissue specimen is collected by biopsy (both excisional and incisional) and observed under the microscope. Esophageal squamous cell carcinoma is histologically identified by keratinocyte like cells with intercellular bridges or keratinization under a microscope. Adenocarcinoma on the other hand often has well or moderately-differentiated tumors with well-formed papillary or tubular characteristics [6].

BIOMARKERS

A biomarker refers to a natural substance found within a patient's blood, bodily fluids, or tissues. Blood biomarkers play a crucial role in the early detection, prognosis, and clinical management of different types of cancer. Desirable properties of a biomarker include:

- high sensitivity in general population screening.
- high specificity to a particular type of tumor, being detectable in early cancers.
- providing a lead-time over clinical diagnosis and correlating with the burden of a tumor.
- reflecting any tumor progression or regression.

There is not yet a perfect CM for EC, but there are many circulating biomarkers that are suggested for clinical use in esophageal cancer.

Type of biomarker	Example
Immunohistochemical markers	Epidermal growth factor receptor Vascular endothelial growth factor
Blood based biomarkers	Antibodies associated tumor-associated antigen (TAA)
MiRNA(microRNAS)	miR-129, miR-200

Table 3: Biomarkers in esophageal cancer [16].

ADVANCED DIAGNOSTICS

IMAGING

Sophisticated imaging methods are utilized to observe and measure the microstructure, blood flow, metabolites, and metabolic activity of lesions, focusing on obtaining more sensitive and pathophysiological diagnostic indicators of the disease. Such techniques encompass diffusion-weighted imaging (DWI), magnetic resonance (MR) spectroscopy, and other advancements in MRI technology.

- Diffusion-weighted imaging helps in the differentiation of low-grade esophageal cancer from high grade due to the difference in their diffusion coefficient.
- Fast spin echo magnetic resonance imaging can be employed in EC because of its fine matrix size that enhances spatial resolution. It can be used for screening purposes as well because it is inexpensive and non-invasive.
- Due to their enhanced image processing capabilities, emerging techniques such as vortex based morphometry (VMB), deformation-based morphometry (DBM), tensor-based morphometry (TBM), and pattern-based morphometry (PBM) can be utilized in addition to or as a substitute for magnetic resonance imaging [11].

ADVANCES IN ENDOSCOPY - Conventional endoscopic techniques are modified by adding advancements like auto fluorescence imaging, confocal laser endomicroscopy, and endocytoscopy (novel ultra-high magnification endoscopic technique to provide an excellent in vivo assessment of lesions found in the GI tract) for getting better image quality in EC diagnosis [17].

Artificial intelligence (AI), commonly called computer-assisted diagnosis (CAD) is the technology that enables machines to process information and function at, or even above human level. It helps in endoscopic imaging research, and it is of two types- deep learning (DL) and machine learning

(ML). Deep learning replicates the learning process of the brain to replicate high dimensional data in larger volumes which is similar to endoscopic image recognition [18].

GENETIC TESTING

According to the literature, most frequently mutated genes in esophageal cancer are **TP53 (tumor protein)**, followed by NOTCH1 (neurogenic locus notch homolog protein), EP300 (histone acetyltransferase p300), and KMT2C (lysine methyltransferase 2).

Early prediction of esophageal cancer can be facilitated by detecting specific gene mutations, indirectly aiding in the diagnosis of the condition. Even though advanced genome sequencing technology helps to identify these genes in EC, genetic screening to detect esophageal cancer is still an emerging field that needs further study before it can be used as a conventional diagnostic procedure [19].

MANAGEMENT

In esophageal cancer, there are different treatment options that were decided based on the grade of the tumor. Surgery alone is frequently used to treat stage 0 and stage I illness. Whereas in stage II or stage III, surgery is performed with or without neoadjuvant therapy. Stage IV on the other hand, is treated with nonsurgical modalities such as neoadjuvant therapy, stents, photodynamic therapy, targeted therapy, or immunotherapy which may help to decrease the progression of tumors in some patients [20].

STANDARD OF CARE THERAPEUTICS

SURGERY & RECONSTRUCTION

Numerous surgical procedures are employed in the treatment of esophageal cancer (EC), selected based on tumor position and size. Two primary techniques include transhiatal esophagectomy (THE) and transthoracic esophagectomy. In THE, a midline supraumbilical incision is utilized, while transthoracic esophagectomy employs approaches like the Ivor Lewis technique or McKeown modification. Lymph node dissection is crucial, with retrieval rates influenced by surgical exposure and operator skill. Various techniques for esophageal reconstruction exist,

including interposition grafts from the stomach, colon, or jejunum, as well as free flaps such as pedicled, local, radial forearm, anterolateral thigh (ALT), and jejunal [21, 22].

RADIOTHERAPY

Radiation therapy employs high-energy rays, such as X-rays or gamma rays, to either reduce the size of cancerous tumors or eliminate cancer cells altogether. These rays penetrate the body and target the cancer cells, damaging their DNA and preventing them from multiplying. This technique is frequently used with chemotherapy before and after surgery, and for incurable esophageal cancers, local radiation is frequently utilized to treat both distant and local illnesses. Radiation therapy may result in side effects such as skin toxicity, rib fractures, primary tumor necrosis with or without underlying infections, telangiectasia (dilatation of capillaries), dryness, and ulcers. The types of radiation therapy used in EC are:

External beam radiation therapy – This technique is frequently used to treat EC. Typically; it is administered every day for several weeks. With intensity- modulated radiation therapy (IMRT), the radiation can be concentrated on the cancerous tissues, to reduce the damage to the healthy tissues.

Proton beam radiation therapy - In addition to x-rays, proton beam radiation can also be used to treat cancer. Even though it has potential advantages over IMRT, it is not used as an effective alternate treatment for IMRT.

Intraoperative radiation therapy (IORT) - It involves giving the patient a single high dose of radiation after the tumor has been removed but before the wound is closed. This way, radiation can reach the area that has to be treated without destroying much of the good tissues [23].

BRACHYTHERAPY - Tiny radioactive particles are inserted in catheters (very thin, soft tubes), which will be inserted into the surgical cavity during operation. The use of brachytherapy alone or in conjunction with external beam radiation therapy can have favorable effects. However, side effects include hemorrhage, mediastinal fistula development, arrhythmias, hypotension, bronchospasm, necrosis, or bronchial stenosis [25].

CHEMOTHERAPY

Chemotherapy involves giving anticancer medications to the patient to eradicate cancer cells. It is given as a sole treatment for EC or in advanced cases it is given along with surgery. Typically, neoadjuvant chemotherapy (given before the surgery to shrink the tumor) is recommended in EC, and it is continued postoperatively. The following are the drugs that are used in the chemotherapy of EC:

- Capecitabine
- Ipilimumab
- Pembrolizumab
- Nivolumab
- Nivolumab
- Capecitabine
- Ipilimumab
- Paclitaxel
- Vinorelbine

While prescribing these medications, drug interactions should be considered and given appropriately. Although the tumor in EC shrinks after the use of these drugs, their usage will involve several side effects such as nausea, vomiting, dry mouth, and loss of appetite. Severe adverse effects include persistent infections that occur because of the reduced red blood cell count (due to the destruction of hemopoietic stem cells) [24].

ADVANCED THERAPEUTICS

ENDOSCOPIC MUCOSAL RESECTION

Endoscopic mucosal resection is a minimal surgical invasive technique that uses an endoscope (small camera) and surgical instruments to remove the tumor from the esophagus. This technique is proposed for tumor resection to limit overall incision size, spread of infection to other organs, and to reduce tissue trauma. Therefore, it reduces postoperative pain and preserves respiratory

mechanics and esophageal structure. Although it is a minimally invasive technique it is associated with several complications like acute intraprocedural bleedings, perforations, stricture formation, and delayed bleedings. Apart from this technique, the following treatments are performed with the help of an endoscope:

- **Endoscopic dilatation:** The esophagus is widened by this procedure. If the tumor recurs, it might need to be done again.
- **Insertion of a stent:** A stent is placed in the esophagus during this procedure using an endoscopy. It is a mesh device made up of metal (esophageal stent) and it is expanded to maintain the esophagus open.
- **Electro coagulation:** In this type of palliative care, electric current is delivered through the endoscope and cancer cells are destroyed by the heat generated from this electric current. Even though the removal of a tumor blockage is brought on by this method, it is occasionally used to assist in discomfort relief.
- **Cryotherapy:** An endoscope with a probe affixed that can freeze and remove tumor tissue is used in this kind of palliative care.
- **Laser therapy & photodynamic therapy:** These less popular methods include In photodynamic therapy, a photo sensitizer is injected intravenously and an endoscope is then inserted to aim a laser which will destroy the esophageal tumors. In laser therapy, a laser is directly used to burn esophageal tumors [25].

OTHER ADVANCEMENTS

Immunotherapy and targeted therapy can also be advocated for esophageal cancer. Commonly used immunotherapeutic drugs in esophageal cancer are pembrolizumab, camrelizumab and nivolumab. They target the PDL-1 expression which is involved in the pathogenesis of EC. They are approved by FDA and indicated in both types of esophageal cancers. They can be given alone or in combination with chemotherapy and targeted therapy [26]. Targeted therapy employs drugs such as trastuzumab, larotininib (which targets epidermal growth factor) and ramucirumab (which targets the angiogenesis pathway). According to the literature, this targeted therapy is given in combination with the chemotherapeutic agent paclitaxel in recurrent EC patients. Another advancement used in EC is CAR (chimeric antigenic receptor) and TCR (T-cell receptor) T-cell therapy, where specific proteins implicated in the pathogenesis of this disease will be targeted by T-cells [27].

QUALITY OF LIFE

Esophageal cancer patients reported having a lower quality of life (QoL) in terms of their overall and physical health, as well as their emotional condition. QoL is subordinate in EC patients as compared to the general population. As a result, in addition to treating the illness, the treatment of EC should emphasize on maintaining the quality of life.

STANDARD OF CARE QUALITY OF LIFE MANAGEMENT

POST-OPERATIVE REHABILITATION

Post-operative rehabilitation treatment might be necessary, depending on the tumor position and any post-operative deficits. The majority of patients are undergoing endoscopic resection for removal of the tumors, which results in minimal post-operative recovery care needs and a shorter hospital stay. Routine wound inspection, infection control procedures, and stringent hygiene (particularly hand cleanliness and prompt removal of clips, sutures, drains and foreign items) decrease the risk of wound infection following surgery. However, those who have surgical site infections frequently experience discomfort, erythema, dehiscence, redness, and swelling. These patients should undergo the necessary diagnostic evaluations, and quick-acting antibiotic medication should be prescribed as early as possible [28].

SUPPORTIVE AND PALLIATIVE THERAPY

Supportive and palliative therapy includes modification of diet to softer meals and small foods to get relief from dysphagia. Consumption of liquids also help to some extent. Medication management of dysphagia is marginally effective. Commonly prescribed medications for dysphagia include antacid medications, anti-emetics, promotility agents, and anti-spasmodic agents. However, it is important to note that these medications do not address the root cause of dysphagia. This supportive therapy can be provided with the help of caregivers.

The caregiver (family members or friends) can provide physical, practical, and emotional support to the patient. Caregivers can provide care and encouragement to the patients, give medications on time, help patients to manage symptoms and side effects, and also caregivers can talk to the healthcare team about the patient's symptoms and side effects [29].

Enhancing cardiopulmonary performance and managing pulmonary complications after esophagectomy are important tasks for physiotherapists in EC patients. Traditionally, physiotherapy focused on post-operative care, but the role is evolving to include surgical pre-habilitation and enhanced recovery after surgery. The primary post-operative physiotherapy goals in esophageal cancer patients are:

- Preservation of respiratory function to maintain adequate gas exchange.
- Primarily avoidance of post-pulmonary complications and minimizing effects when they occur.
- Early mobilization and return to physical function [30].

SUPPORTIVE GROUPS

There are many resources available for coping with these issues, including therapy, support groups, social media, and community resources. In order to provide cancer patients with comprehensive care that fully addresses all their requirements, psychosocial oncology social workers evaluate and handle the financial and logistical needs of cancer patients. A live, online support group for EC patients is called post treatment **esophageal cancer survivorship support group**. It gives them the chance to talk about problems that might come up throughout their treatment, to share their own stories, and to support one another emotionally and practically [31].

<https://www.mskcc.org/event/esophageal-cancer-support-group>

<https://www.smartpatients.com/communities/esophageal-cancer>

ADVANCED QUALITY OF LIFE MANAGEMENT

COGNITIVE BEHAVIORAL AND RELAXATION THERAPY

Following treatment for esophageal cancer, patients may encounter cognitive difficulties such as memory loss and attention issues, impacting their daily functioning and potentially affecting their work performance. Cognitive behavioral therapy (CBT) is utilized to equip patients with new coping strategies to address these challenges positively. While complete resolution of these issues may not be achievable, they can be effectively managed to some extent.

Additionally, the emotional toll of living with uncertainty, fear, anxiety, and sadness due to disease progression or recurrence is a significant concern for individuals with esophageal cancer. Relaxation therapy serves as a complementary approach to conventional medical interventions, offering relief from these negative emotions. Techniques such as progressive relaxation, muscle contractions, and various forms of meditation, whether spiritual or non-spiritual, can be integrated into the overall treatment plan to promote emotional well-being and resilience [32].

COMPLEMENTARY AND INTEGRATIVE THERAPIES:

A person's physical, emotional, mental, social, spiritual, and environmental variables all have an impact on their health. A wide range of complementary treatments are included in integrative medicine, including family systems therapy, nutritional therapy, and psychotherapy for esophageal cancer. These therapies are employed to treat a broad range of physical and mental health issues as well as to enhance interactions, experiences, and quality of life in patients with esophageal cancer [33].

CLINICAL TRIALS (RECRUITING)

Title	Intervention	Short summary	NCT	Dates
1. Study of larotininib in unresectable or advanced esophageal cancer[34]	Drug: larotininib Drug: Irinotecan/Tegafur	This randomized controlled phase 3 study was conducted over 416 participants to know the efficacy of larotininib in advanced esophageal cancer. Participants are openly labeled and parallelly assigned.	NCT04415853	Start date: January 2021 Completion date: August 2023
2. Study of Docetaxel or Vinorelbine plus Cisplatin in neoadjuvant Chemoradiotherapy for Esophageal cancer [35]	Drug: Docetaxel, Cisplatin Radiation therapy	The primary objective is to compare docetaxel plus cisplatin (DP) versus vinorelbine plus cisplatin (NP) in neoadjuvant chemoradiotherapy, in terms of the overall survival and toxicity in patients with Stage IIB or III squamous cell esophageal carcinoma. This is a randomized controlled study conducted over 610 patients.	NCT02465736	Start date: July 2015 Completion date: July 2023
3. Trastuzumab and Pertuzumab in HER + 2 esophageal cancer [36]	Drug: Trastuzumab, Pertuzumab, Carboplatin Paclitaxel,	This is a phase 3 interventional study where 376 participants are randomly assigned to know the effect of adding trastuzumab and Pertuzumab to neoadjuvant chemo	NCT05188313	Start date: March 2022 Completion date: February 2027

4. Study of epigallocatechin-3gallate(EGCG) for supportive and symptomatic management in patients with esophageal cancer[37]	Other: EGCG	This single group assessment study is conducted over 15 patients to know the efficacy of EGCG in improving airway obstruction in esophageal cancer.	NCT05039983	Start date: August 2021 Completion date: October 2021
5. DCF combined with camrelizumab in the treatment of esophageal cancer[38]	Camrelizumab DCF (Docetaxel, Cisplatin, Fluorouracil)	This is a single group assessed interventional study conducted over 50 participants to evaluate the safety and feasibility of DCF in the treatment of locally advanced esophageal cancer.	NCT05050760	Start date: September 2021 Completion date: December 2023
6. Effectiveness of a rehabilitation program in improving quality of life in patients with esophageal cancer [39]	Exercise and dietary education, weekly telephone consultations concerning exercise and diet.	This study will investigate the effectiveness of rehabilitation program in improving sleep quality, emotional distress, and quality of life in patients with esophageal cancer in 175 patients.	NCT03161535	Start date: September 2017 Completion date: July 2023
7. Investigating the association between microbiota and esophageal cancer/oropharyngeal cancer[40]	Diagnostic test: oral swab test	This study compares the oral/esophageal microbiota composition between oropharyngeal cancer and esophageal cancer cases in 60 participants where patients are randomly allocated.	NCT05412628	Start date: March 2022 Completion date: February 2023
8. Dyadic yoga intervention in improving physical performance and quality of life in patients with Stage I-IV non-small cell lung or esophageal cancer in patients undergoing radiotherapy and their caregiver [41]	Other: Educational intervention, quality of life assessment, questionnaire administration Procedure: Yoga	This phase 3 randomized interventional parallel assigned study is conducted over 400 participants to know how well yoga procedure improves the quality of life in esophageal cancer patients.	NCT03948100	Start date: December 2018 Completion date: June 2023
		radiation in esophageal cancer.		

Table 4 Recruiting clinical trials of esophageal cancer [34-41]

CONCLUSION

EC must be properly diagnosed and treated because it is one of the most prevalent chronic illnesses with a rising prevalence. Proper care should be taken to avoid the occurrence of co-morbid diseases and other serious complications associated with EC. Better management of the disease will yield optimistic outcomes in terms of improvement in the control of symptoms and the QOL of the patients. During the last decade, there has been a paradigm shift in the treatment of esophageal cancer. While there is still a long way to go, due to the advancements in novel therapies, the future seems promising for the treatment of EC.

Acknowledgement: For a list of our contributing authors please visit

www.curescience.org/publications/writers.

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