

ESOPHAGEAL CANCER: EPIDEMIOLOGY, PATHOGENESIS, AND MODERN APPROACHES TO MANAGEMENT

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Abstract: Esophageal cancer (EC) is the seventh most common cancer worldwide and the sixth leading cause of cancer-related deaths. It is characterized by late diagnosis, aggressive progression, and poor prognosis. The two major histological types—squamous cell carcinoma (ESCC) and adenocarcinoma (EAC)—differ in epidemiology, etiology, and geographic distribution. Advances in diagnostic techniques, multimodal treatment, and targeted therapies have improved survival, yet outcomes remain unsatisfactory. This review summarizes current knowledge on epidemiology, risk factors, pathogenesis, diagnostic strategies, and modern treatment approaches for esophageal cancer.

Key words: Esophageal cancer, squamous cell carcinoma, adenocarcinoma, chemotherapy, immunotherapy, surgical management.

1. Introduction

Esophageal cancer accounts for approximately 604,000 new cases and 544,000 deaths annually (GLOBOCAN 2020). It predominantly affects men, with a male-to-female ratio of nearly 3:1. The disease has a poor 5-year survival rate, ranging from 15–25% globally, due to late-stage detection.

2. Epidemiology

Geographic distribution: ESCC is more common in Asia and Africa, while EAC predominates in Western countries.

Age: Most cases occur after age 50.

Gender: Higher prevalence in males.

Table 1. Global Incidence of Esophageal Cancer

Region	Predominant Type	Incidence (per 100,000)	Mortality (per 100,000)
East Asia	ESCC	20–30	18–28
North America	EAC	6–8	5–7
Sub-Saharan Africa	ESCC	12–18	11–16
Western Europe	EAC	7–10	6–9

3. Etiology and Risk Factors

3.1 Squamous Cell Carcinoma

- ✓ Tobacco smoking
- ✓ Alcohol consumption
- ✓ Nitrosamine-rich diet
- ✓ Hot beverage intake
- ✓ Human papillomavirus (possible role)

3.2 Adenocarcinoma

- ✓ Barrett's esophagus

- ✓ Gastroesophageal reflux disease (GERD)
- ✓ Obesity
- ✓ High-fat diet
- ✓ Male gender

4. Pathogenesis

ESCC develops due to chronic mucosal irritation leading to dysplasia and carcinoma, while EAC follows progression from GERD to Barrett's esophagus, dysplasia, and adenocarcinoma. Molecular pathways include p53 mutations, EGFR amplification, HER2 overexpression, and PD-L1 expression.

5. Diagnosis

- ✓ Endoscopy with biopsy: Gold standard.
- ✓ Endoscopic ultrasound (EUS): Tumor depth and nodal status.
- ✓ CT, PET-CT, MRI: Staging and metastasis detection.
- ✓ Molecular markers: HER2, PD-L1, and MSI for targeted therapy eligibility.

6. Treatment Approaches

6.1 Early-Stage Disease

Endoscopic mucosal resection (EMR) or submucosal dissection (ESD).

6.2 Locally Advanced Disease

Neoadjuvant chemoradiotherapy (CROSS regimen: carboplatin + paclitaxel). Esophagectomy (transthoracic or transhiatal). Minimally invasive and robotic-assisted techniques are gaining popularity.

6.3 Advanced/Metastatic Disease

Systemic chemotherapy: Platinum-based regimens. Targeted therapy: Trastuzumab (HER2-positive EAC). Immunotherapy: PD-1 inhibitors (nivolumab, pembrolizumab).

Table 2. Treatment Modalities and Outcomes

Stage	Treatment	5-Year Survival Rate
Early (T1a)	EMR/ESD	80–90%
Locally advanced	Chemoradiotherapy + surgery	35–45%
Metastatic	Chemotherapy ± immunotherapy	5–10%

7. Prognosis

Prognosis depends on stage at diagnosis. Lymph node metastasis is the most important prognostic factor. Early detection through screening in high-risk populations is essential.

8. Future Directions

Development of molecular-targeted therapies, biomarker-driven personalized treatment, wider use of immunotherapy in earlier stages, and liquid biopsy for early detection and monitoring.

9. Conclusion

Esophageal cancer remains a global health burden with poor prognosis. Advances in multimodal management, particularly the integration of targeted therapies and immunotherapy, offer hope for improved survival. Early detection and prevention strategies remain the cornerstone of reducing mortality.

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