

Table 1. TNM categories and clinical staging of oesophagus and oesophagogastric junction cancer, according to AJCC Cancer Staging Manual, 8th edition [3].

Category	Criteria		
T category			
TX	Tumor cannot be assessed		
T0	No evidence of primary tumor		
Tis	High-grade dysplasia, defined as malignant cells confined by the basement membrane		
T1	Tumor invades the lamina propria, muscularis mucosae, or submucosa		
T1a	Tumor invades the lamina propria or muscularis mucosae		
T1b	Tumor invades the submucosa		
T2	Tumor invades the muscularis propria		
T3	Tumor invades the adventitia		
T4	Tumor invades adjacent structures		
T4a	Tumor invades the pleura, pericardium, azygos vein, diaphragm, or peritoneum		
T4b	Tumor invades other adjacent structures, such as the aorta, vertebral body, or trachea		
N category			
NX	Regional lymph nodes cannot be assessed		
N0	No regional lymph node metastasis		
N1	Metastasis in 1–2 regional lymph nodes		
N2	Metastasis in 3–6 regional lymph nodes		
N3	Metastasis in ≥7 regional lymph nodes		
M category			
M0	No distant metastasis		
M1	Distant metastasis (including non-regional lymph node metastasis)		
Clinical stage groups (cTNM) Squamous Cell Carcinoma		Clinical stage groups (cTNM) Adenocarcinoma	
cStage 0	Tis N0 M0	cStage 0	Tis N0 M0
cStage I	T1 N0-1 M0	cStage I	T1 N0 M0
cStage II	T2 N0-1 M0 T3 N0 M0	cStage IIA	T1 N1 M0
cStage III	T3 N1 M0 T1-3 N2 M0	cStage IIB	T2 N0 M0
cStage IVA	T4a-T4b N0-3 M0 T1-T4b N3 M0	cStage III	T3-T4a N0 M0 T2-T4a N1 M0
cStage IVB	AnyT AnyN M1	cStage IVA	T4b N0-3 M0 T1-T4b N2-3 M0
		cStage IVB	AnyT AnyN M1

Table 2. Comparing the ECOG Performance Status and the Karnofsky Performance Status Scales.

ECOG Performance Status	Karnofsky Performance Status
0: Fully active, able to carry on all pre-disease performance without restriction.	100%: Normal, no complaints; no evidence of disease. 90%: Able to carry on normal activity; minor signs or symptoms of disease.
1: Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.	80%: Normal activity with effort, some signs or symptoms of disease. 70%: Cares for self but unable to carry on normal activity or to do active work.
2: Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours.	60%: Requires occasional assistance but is able to care for most of personal needs. 50%: Requires considerable assistance and frequent medical care.
3: Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours.	40%: Disabled; requires special care and assistance. 30%: Severely disabled; hospitalization is indicated although death not imminent.
4: Completely disabled; cannot carry on any selfcare; totally confined to bed or chair.	20%: Very ill; hospitalization and active supportive care necessary. 10%: Moribund.
5: Dead.	0%: Dead.

Table 3. Some tools examples for patient’s fitness-for-surgery assessment.

Variable	Assessment tool	Description
Performance status [27]	ECOG (Eastern Cooperative Oncology Group) scale	Clinician-assessed prospectively. Categorical (0-5): scores 0, 1, 2 or >2
	Karfnofsky score	Clinician-assessed prospectively Categorical rating (100-0%): 100-80%, 80-70%, 60-50% or <50%
Frailty [27]	GO2 Frailty Score	Measured prospectively by assessing impairment in 9 frailty domains. Categorical: Not frail (0–1/9 domain impaired), Mildly frail (2/9 domains impaired), Severely frail (≥3/9 domains impaired)
	mCFS (“Modified” Clinical Frailty Scale)	7-point scale derived retrospectively by feedback expert review. Categorical (score 1-7): Fit (1–2), Pre-frail (3–4), Frail (5+)
	G8 (Geriatric-8)	8-item questionnaire collected prospectively. Total score of 0–17 Categorical: >14 (‘normal’), ≤14 (‘abnormal’)
Quality of life [27,28]	EORTC QLQ-C30	Generic score questionnaire for cancer patients. It contains 5 functioning scales, 8 symptom scales, financial impact, and overall quality of life. Linear range from 0 to 100.
	FACT-E (Functional assessment of cancer therapy- esophagus)	Health-related quality-of-life (HRQOL) instruments comprised of a general component (physical, functional, social and emotional well-being) and an oesophageal cancer sub-scale (eating, swallowing, enjoyment of food, voice, dry mouth, appetite, cough, choking, and pain). Patient-reported measure. Higher scores denote better quality of life.
Comorbidity [29]	International ESODATA Group Risk Prediction Model of 90-day Mortality after Esophagectomy	On the basis of 10 preoperative variables. 5 risk groups: very low risk (score 1; 90-day mortality, 1.8%), low risk (score 0; 90-day mortality, 3.0%), medium risk (score –1 to –2; 90-day mortality, 5.8%), high risk (score –3 to –4; 90-day mortality, 8.9%), and very high risk (score –5; 90-day mortality, 18.2%).
Cardiopulmonary assessment [30]	Functional capacity by METs (metabolic equivalents)	1 MET = the basal oxygen consumption of a 40-year-old man weighing 70 kg Categorical functional assessment: excellent (>10 METS), good (7–10 METS), moderate (4–6 METS), poor (<4 METS)
	Plasma natriuretic peptide concentration: NT-proBNP and BNP	High negative predictive value, particularly helpful when classifying patients at low risk of cardiovascular complications.
	CPET (Cardiopulmonary Exercise Test)	Provides information about real cardiopulmonary reserve by evaluating maximum oxygen consumption (VO _{2max}). Categorical cardiopulmonary risk assessment: low (VO _{2max} >20 mL/kg/min), intermediate (VO _{2max} between 15 to 20 mL/kg/min) or high risk (VO _{2max} <15 mL/kg/min)

Table 4. Biological and targeted agents, and checkpoint inhibitors under assessment for oesophageal cancer.

Anti-HER-2	Trastuzumab Pertuzumab
Anti-PD-1	Nivolumab Pembrolizumab Tislelizumab Toripalimab Camrelizumab Sintilimab
Anti-PD-L1	Atezolizumab Avelumab Durvalumab SHR-1316 Socazolimab
Anti-CTLA-4	Ipilimumab Tremelimumab
Anti-VEGF	Bevacizumab
Tyrosine-kinasa inhibitors	Lenvatinib Apatinib Sotigalimab
Anti-EGFR	Nimotuzumab

HER-2: Human Epidermal Growth Factor Receptor-2; PD-1: programmed cell death receptor 1; PD-L1: programmed cell death ligand 1; CTLA-4: cytotoxic T-lymphocyte-associated antigen 4; VEGF: vascular endothelial growth factor; EGFR: epidermal growth factor receptor.