18FDG PET/CT Imaging in Carcinoma Oesophagus

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Carcinoma of oesophagus is relatively rare malignancy and constitutes about 10% of all gastrointestinal malignancies. The 5-year survival ranges between 14 - 20%.[1,2] Squamous cell carcinoma (SCC) is the most common pathological variant (50-70%) and tends to involve the middle and distal 1/3rd of oesophagus.[3] Smoking and alcohol consumption are considered important risk factors. While 30-50% cases are adenocarcinoma (AC), which involves distal oesophagus associated with Barrett's transformation.[4] However, in the United States, AC has become the most common esophageal cancer (about 80%).[5] Only 15% of oesophageal cancers involve proximal 1/3rd of the oesophagus.[3]

Oesophageal cancer has notorious behaviour with dismal outcome in most of the patients. As oesophagus does not have serosa, it has the tendency to involve neighbouring structures. Since oesophagus has a rich vascular and lymphatic supply, therefore, it has the tendency for an early nodal and distant metastasis. About 20-30% of patients with carcinoma of oesophagus present with nodal and (or) distant metastasis at the time of presentation.[6] Early-stage disease is usually asymptomatic; but in the late stage, dysphagia is the most common presenting complaint. The severity of dysphagia correlates with a degree of luminal obstruction by primary tumor itself and/or perilesional nodal metastasis. TNM (tumor, node, metastasis) staging is commonly performed by the American Joint Committee on Cancer (AJCC - 8th Edition) staging system.[7]

Fifty-four to sixty-nine percent (54-69%) of patients with carcinoma of oesophagus are eligible for surgery; however, median survival after surgery is only 13-19%.[8] Neoadjuvant chemotherapy and external beam radiation therapy are gaining acceptance in recent years due to promising results. Conventional diagnostic workup including fluoroscopy, tomography (CT), MRI and endoscopy ultrasound (EUS) play a pivotal role in diagnosis and staging of the disease.[9]

In the hybrid imaging era, PET/CT using 18-fluorodeoxyglucose (18FDG) is gaining acceptance in staging, restaging, response evaluation and prognostication in carcinoma of oesophagus.

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SCC and AC of oesophagus have similar metabolic signatures and concentrate intense 18FDG uptake. However, the mucinous type of AC, near the gastro-oesophageal junction, may have slightly less 18FDG uptake than SCC. The majority of literature supports the notion that intensity of 18FDG uptake correlates with survival; and tumors with standardised uptake value <3 (SUVmax <3) are associated with better outcome.[10] However, other prognostic indicators like length of hypermetabolic primary tumor, regional nodes, and distant metastasis are strong indicators of survival.

18FDG PET/CT being a part of diagnostic paradigm in carcinoma oesophagus has significantly improved detection of distant hypermetabolic metastasis and also specificity of nodal staging. Combining 18FDG PET/CT with EUS-guided nodal biopsy has significantly improved diagnostic yield of nodal metastasis prior to surgery. 18FDG PET/CT has a sensitivity and specificity of 51% and 94% for locoregional and 67% and 84% for distant staging, respectively.[11] For primary tumor, 18FDG PET/CT has an overall sensitivity of 80% which reaches up to 100% for T3 and T4 tumors. However, sensitivity declines to 43% for T1 tumors and fails to detect tumors *in situ* and T1a tumors.[11] Therefore, 18FDG PET/CT has significantly weaker role in determining T-staging than morphological imaging like CT, MRI and EUS. For nodal staging, CT/EUS has a sensitivity of 83% but specificity of 45%. On the other hand, 18FDG PET/CT has a sensitivity of 22%, but specificity of 91% for nodal staging. Therefore, combining CT/EUS (having good sensitivity) with 18FDG PET/CT (having good specificity) would ensure high diagnostic accuracy for nodal staging. For distant metastasis, 18FDG PET/CT outperforms CT/EUS for being more sensitive (69% *vs.* 46%) and specific (93% *vs.* 74%).[11] In clinical practice, 18FDG PET/CT has been found to change staging in 14% of the patients and can detect distant hypermetabolic metastasis in additional 5-8% patients, which were not evident on CT/EUS. However, in patients with recurrence, 18FDG PET/CT has sensitivity and specificity similar to morphological imaging (CT/EUS).[11] However, use of 18FDG PET/CT in staging of early esophageal cancers has been questioned by some researchers, as well.[12]

18FDG PET/CT is also found to have good predictive value for response to chemotherapy or chemoradiation.[13] 18FDG PET/CT performed two weeks after chemotherapy or chemoradiation can be used to categorise patients as responder and non-responder, based on metabolic changes (change in SUVmax pre- and post-therapy scans). Using PET emission response criteria in solid tumor (PERCIST), significant decline in

SUVmax (30 - 80%) is considered to have better survival.[13] However, due to limited special resolution of PET images, minimal residual disease cannot be excluded as there is higher incidence of recurrence within 1-2 years despite significantly reduced SUVmax.

It is important to be cognizant of pitfalls of [18]FDGPET/CT imaging. [18]FDG is a sensitive but non-specific substrate having variable uptake in malignant and non-malignant (inflammatory and infection) lesions.[14] Mild diffuse [18]FDG uptake may be seen in patients with oesophagitis or lower oesophageal sphincter motility. Similarly, false-positive [18]FDG uptake may be seen over hiatus hernia, benign strictures after dilatation, post-biopsy sites, and oesophageal leiomyomas. Small intra-capsular nodal metastases have a higher possibility of false negative results. Intense [18]FDG uptake in primary tumor may obscure perilesional nodal metastatic nodes. Detection of synchronous tumors is not uncommon (5.5 - 8%) in patients with carcinoma oesophagus undergoing [18]FDG PET/CT study for staging workup.[14]

Oesophageal cancer is a biologically aggressive and metabolically active tumor with higher mortality. [18]FDG PET/CT is useful for staging, restaging, prognostication, and assessing treatment response. [18]FDG PET/CT has good specificity for loco-regional nodal metastases; and being whole-body technique, has good diagnostic accuracy for distant metastatic disease in patients with oesophageal cancers. However, [18]FDG being a non-specific substrate may pose diagnostic challenge due to variable uptake in malignant and non-malignant (inflammatory and infection) lesions.

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