18 FDG PET/CT imaging in carcinoma cesophagus

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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%. Squamous cell carcinoma (SCC) is the most common pathological variant (50-70%) and tends to involve the middle and distal 1/3rd of oesophagus. 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. However, in the United States, AC has become the most common esophageal cancer (about 80%). Only 15% of oesophageal cancers involve proximal 1/3rd of the oesophagus.

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. 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.

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%. 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.

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

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

$^{18}$FDG 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 $^{18}$FDG PET/CT with EUS-guided nodal biopsy has significantly improved diagnostic yield of nodal metastasis prior to surgery. $^{18}$FDG PET/CT has a sensitivity and specificity of 51% and 94% for locoregional and 67% and 84% for distant staging, respectively. For primary tumor, $^{18}$FDG 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. Therefore, $^{18}$FDG 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, $^{18}$FDG PET/CT has a sensitivity of 22%, but specificity of 91% for nodal staging. Therefore, combining CT/EUS (having good sensitivity) with $^{18}$FDG PET/CT (having good specificity) would ensure high diagnostic accuracy for nodal staging. For distant metastasis, $^{18}$FDG PET/CT outperforms CT/EUS for being more sensitive (69% vs. 46%) and specific (93% vs. 74%). In clinical practice, $^{18}$FDG 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, $^{18}$FDG PET/CT has sensitivity and specificity similar to morphological imaging (CT/EUS).

However, use of $^{18}$FDG PET/CT in staging of early esophageal cancers has been questioned by some researchers, as well.

$^{18}$FDG PET/CT is also found to have good predictive value for response to chemotherapy or chemoradiation. $^{18}$FDG 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
SUVRmax (30 - 80%) is considered to have better survival. 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 18F-FDG PET/CT imaging. 18F-FDG is a sensitive but non-specific substrate having variable uptake in malignant and non-malignant (inflammatory and infection) lesions. Mild diffuse 18F-FDG uptake may be seen in patients with oesophagitis or lower oesophageal sphincter motility. Similarly, false-positive 18F-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 18F-FDG uptake in primary tumor may obscure perilesional nodal metastatic nodes. Detection of synchronous tumors is not commonly performed. It is important to be cognizant of pitfalls of 18F-FDG PET/CT imaging.

Oesophageal cancer is a biologically aggressive and metabolically active tumor with higher mortality. 18F-FDG PET/CT is useful for staging, restaging, prognostication, and assessing treatment response. 18F-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, 18F-FDG being a non-specific substrate may pose diagnostic challenge due to variable uptake in malignant and non-malignant (inflammatory and infection) lesions.

REFERENCES