Review Article

PET-CT imaging of Carcinoma of the Oesophagus: The Kwa-Zulu Natal perspective

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ABSTRACT

The introduction of computer software which enables assessment of various metabolic parameters has added value to the imaging, diagnosis and prognosis of oesophageal carcinoma (OC). Positron emission tomography/Computed tomography (PET/CT) is an imaging modality used for monitoring and follow-up of patients with flourodeoxyglucose (FDG) avid lesions in OC. The association of HIV with OC remains controversial, however in Kwa-Zulu Natal (KZN), where the incidence of this infection is high, the role of PET/CT in predicting the prognostic outcome of OC is important and may provide further information that may alter treatment.

Key words: *Oesophageal Cancer, PET-CT screening, Kwa-Zulu Natal, flourodeoxyglucose*

Most of the oesophageal carcinoma (OC) falls into 2 histological types that occur most frequently, these are squamous cell carcinoma and adenocarcinoma. Squamous cell carcinoma originates from the epithelium lining the oesophagus, while the malignant epithelial cells in adenocarcinoma are arranged in a glandular formation. In the past, squamous cell carcinoma occurred more frequently but, over the past couple of decades, an increase in adenocarcinoma of the oesophagus has been noted [1]. A patient's ethnicity plays an important role in the development of OC, which is illustrated by the drastic difference between the incidences of OC in Black and White ethnic groups [2]. OC in Black South Africans was very rare until the last couple of decades [3].

According to a case-control study performed in Soweto, South Africa, involving 200 OC patients and 391 hospital controls, pipe tobacco and the consumption of traditional beer were identified as risk factors for rural Black populations [4]. Patients who drink beer fermented from infected maize have also been found to be more likely to develop OC [5].

There has been an overwhelming shift in African People's health-seeking behavior with people opting for modern medicine such that, they prefer consulting a physician to a traditional healer. Therefore, the continuous increase in the OC incidence can be partly attributed to the improved diagnosis over the cumulative increased number of clients and patients consulting physicians in the region [6]. The diagnosis of OC is often made late, when screening is no longer beneficial. In countries with a high incidence of OC, such as China, population screening programmes may be employed. In Western countries, however, where the incidence is usually lower, these screening programmes are not always applied [7].

Screening for asymptomatic diseases, such as OC, in its early stages can reduce the burden of morbidity and mortality in all population groups. Few data are available on national screening rates in South Africa and how the data vary across the provinces [8]. The availability of data on screening and surveillance protocols of squamous cell carcinoma of the oesophagus in Kwa-Zulu Natal (KZN) is also limited.

In patients with early-stage malignancy at presentation, oesophagectomy is the treatment of choice and is potentially curative. Unfortunately, most patients have locally advanced disease at presentation, and 20%–30% have distant metastases. In patients with locally advanced disease without distant metastases, oesophagectomy is a potential treatment option after neoadjuvant chemotherapy and radiation therapy in those who do not develop distant metastases during therapy [9-12]. The main reason for the poor prognosis is that OC is largely asymptomatic in its early stages. Thus, most cases are diagnosed when the disease has become either locally advanced, with disease spreading to local draining lymph nodes, or distantly metastatic [13].

In all patients with potentially resectable disease, accurate staging at initial presentation and assessment of therapeutic response after neoadjuvant therapy are important in regard to optimal management.

DIAGNOSTIC EVOLUTION

Staging methods include upper endoscopic gastroduodenoscopy (EGD), endoscopic ultrasonography (EUS), and computed tomography (CT) of the thorax and abdomen. Metabolic assessment is difficult with conventional methods. Positron emission tomography (PET) is a non-invasive molecular imaging tool that provides tomographic images and quantitative parameters of perfusion, cell viability, proliferation and/or metabolic activity of tissues. These images result from the use of different substances of biological interest (sugars, amino acids, metabolic precursors, hormones) labelled with PET radionuclides). Fusion of the aforementioned important functional information with the morphological detail provided by CT as PET/CT provides clinicians with a sensitive and accurate one-step whole-body diagnostic and prognostic tool, which directs and changes patient management.

According to Nuclear medicine guidelines in South Africa, fluoro-2-deoxyglucose (FDG) PET/CT imaging is not recommended in screening and diagnosis of OC. It is recommended in selecting cases for staging in patients being considered for radical therapy as well as in selecting cases for re-staging after neoadjuvant treatment in patients being considered for radical therapy. It is further recommended in selecting cases to detect recurrence when other imaging is negative or equivocal and may be considered for routine follow-up of patients given the high incidence of recurrence. It may be considered for radiotherapy planning as several studies have shown a good correlation between FDG-PET and pathology-based tumor length [14]. PET is an important component in the staging algorithm for patients with cancers of the oesophagus and gastro-oesophageal junction. At some centers, it is employed early in the staging pathway with all patients being assessed by this modality. In other centers, it features later in the staging pathway, only being utilized if CT and endoscopic ultrasound demonstrate potentially resectable tumor characteristics [15-16].

DISCUSSION

Accurate interpretation of PET/CT results in patients with OC, requires knowledge of the technical aspects of PET/CT image acquisition and the interpretative pitfalls that may be encountered. It also proves to be helpful, to understand how the disease manifests and disseminates, the staging criteria used, and the different management strategies available. The additional understanding of the role of metabolic parameters is also useful for the staging and prognosis of OC.

In the assessment of PET/CT scans, in previous studies quantification was conducted using only the mean or maximum Standard uptake value (SUVmax) of the primary tumor to evaluate disease status and prognosis. In considering the importance of whole-body tumor volume, a study performed with FDG PET determined that total metabolic tumour volume (MTV) was predictive of disease progression and obtained promising results [17].

Tumor lesion glycolysis (TLG) is the product of mean of SUV and MTV and was first introduced by Larson et al to evaluate therapeutic response. It combines the volumetric and metabolic information of FDG PET. Studies have shown the usefulness of TLG for evaluating treatment response in different tumors. Recent studies further demonstrated the predictive value of pretreatment of TLG in osteosarcoma, malignant mesothelioma, and nasopharyngeal cancer. The prognostic value of TLG in OC is unknown.

For the most accurate evaluation of prognosis, both tumor activity and tumor volume over the whole body should be considered. The summation of whole-body tumor glycolysis, embodied by whole-body tumor lesion glycolysis TLG may represent tumor burden and may be a good indicator of prognosis. TNM stage is primarily based on the tumor anatomic site and size, whereas whole-body TLG has the advantage that it reflects both the biologic information, such as biologic aggressiveness and whole-body total tumor volume.

The prognostic value of SUVmax in OC is unreliable in isolation. TLG is an independent prognostic factor for OC and is also a better predictor of survival than MTV and SUV in patients with locally advanced OC treated with radiotherapy [18-20]. The differences in SUV, MTV, and TLG between tumor histologies have not yet been investigated in OC. In lung cancer, the SUV of tumors with squamous cell histology are higher than that of adenocarcinomas. Differences in the SUV do not always

equate to differences in MTV and TLG. The differences in tumor histology may affect the different prognostic roles of MTV and TLG. Further large-scaled population-based analyses are warranted, including on the effect of tumor histology on metabolic parameters in OC [21].

Studies have found significant correlation between metabolic parameters and T stage in SUVmax in patients with initially diagnosed oesophageal squamous cell carcinoma (OSCC). T stage of the American Joint Committee on Cancer / Union for International Cancer Control's (AJCC/UICC) classification system describes the depth of invasion, whereas SUVmax has been associated with histological and immune histochemical markers of aggressiveness [22-24].

HIV & CA OESOPHAGOUS

Immunosuppressed people, such as people with HIV infection, have an increased risk of developing cancer compared with the general population. Among people with HIV, some of these cancers are directly associated with immunosuppression, the high prevalence of coinfections, and increased prevalence of other risk factors, such as tobacco smoking [25-26]. Whereas some studies have reported increased risks of oesophageal and stomach cancers in HIV-infected people, other studies have reported no associations [27-29]. The risks of these cancers, while elevated, are likely not high enough to justify cost-effective screening of the overall HIV population [30]. Utilizing imaging modalities such as FDG PET/CT as staging tools may provide additional clinical diagnostic and prognostic information that will redirect or alter treatment.

CONCLUSION

It is clear that PET/CT is a validated diagnostic tool in staging of OC. The value of TLG in prognosis has been demonstrated in various solid tumours. With the high incidence of HIV in KZN, the association with oesophagus ca in this population may further compound the prognosis of OC. Thus, the use of TLG in HIV OC patients may assist in more accurate prediction of outcome and should be further investigated.

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