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Original Research

Impact of ^{18}F-FDG PET/CT staging on management and prognostic stratification in head and neck squamous cell carcinoma: A prospective observational study

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Abstract ***Background:*** Accurate assessment of the extent of cancer is essential for appropriate treatment planning and outcome prediction. This study prospectively evaluated whether adding ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET)/computed tomography (CT) to the routine initial staging practice in head and neck squamous cell carcinoma (HNSCC) improved management and prognosis.

Methods: All consecutive patients with newly diagnosed HNSCC who presented in October 2010 – December 2012 underwent conventional workups (CWU) followed by PET/CT. The clinical stage and management plans before and after PET/CT were compared. PET/CT was deemed to have no/low, moderate, and high impact on management planning depending on whether PET/CT changed the treatment modality or goal. The appropriateness of PET/CT staging and management impact was confirmed by histopathology and clinical follow-up, and its association with survival was analysed.

Findings: Of the 248 patients, PET/CT changed the Tumour Node Metastasis (TNM) classification in 79 (31.9%). In the patients with discordant staging, PET/CT staging was significantly more sensitive and accurate than CWU staging (both $P < 0.001$). PET/CT had high or moderate impact on management in 39 (15.7%) patients. Patients with PET/CT upstaged disease had significantly worse progression-free survival (PFS) and overall survival (OS) than patients with no CWU-stage changes (3-year PFS = 56.8% versus 74.5%, $P = 0.043$; 3-year

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OS = 61.3% versus 85.3%, $P = 0.006$). Multivariate analyses revealed that PET/CT staging and second primary cancer were independent predictive factors for both PFS and OS ($P < 0.05$, each).
Interpretations: ^{18}F-FDG PET/CT added important staging information that improved management and prognostic stratification in HNSCC.

1. Introduction

Head and neck squamous cell carcinoma (HNSCC) accounts for 90% of head and neck cancers and 3–5% of all human malignancies [1,2]. A recent analysis of the Surveillance Epidemiology and End Results database indicated that, in 2005–2011, the overall 5-year survival rate for all HNSCC stages was ~60% [3,4]. The 5-year relative survival rate for patients with localised disease was ~80.0%. However, approximately two third of HNSCC patients are initially diagnosed with advanced stage disease, including regional lymph node metastasis [5]. In cases of nodal and distant metastasis, the 5-year relative survival decreases to 44.5% and 35.2%, respectively [3,4]. Although various clinicopathological factors correlate with HNSCC prognosis, the most significant factor is cancer stage at diagnosis [6]. Thus, precise cancer staging is essential as it allows clinicians to select the appropriate treatment strategies and predict the prognosis of the patients.

The conventional workups (CWU) for initial HNSCC staging include physical examination, endoscopy, computed tomography (CT), and/or magnetic resonance imaging (MRI) of the head and neck to evaluate the extent of the primary tumour and whether cervical lymph nodes are involved. CT scans of the chest are also usually included because the lung is the most common site of second or metastatic HNSCC cancer [7]. However, a more sensitive method that screens the whole body may be more accurate and less time consuming [8].

^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) was rapidly adopted in oncological practice over the past decade because it is an effective imaging modality that provides both functional and anatomical information [9]. Previous reports have demonstrated that adding ^{18}F-FDG PET/CT to CWU stages HNSCC more accurately than CWU alone and may alter the clinical management [10–13]. Recent studies also suggest that PET/CT detects regional or distant metastases and second primary cancers (SPCs) better than PET alone and CWU alone [14–16]. Nevertheless, the potential role of PET/CT in primary HNSCC staging has yet to be defined, and the clinical guideline only recommend PET/CT as an option for stage III–IV HNSCC [17]. The impact of the additional information provided by PET/CT on HNSCC management and prognosis also remains poorly understood [18,19]. We, therefore, evaluated whether ^{18}F-FDG PET/CT staging affects the management plan and prognostic stratification of patients with newly diagnosed HNSCC.

2. Materials and methods

2.1. Patients

This prospective study was approved by the institutional review board of our institution. Informed consent was obtained from all enrolled patients. The primary end-point was the clinical impact of PET/CT-induced change in CWU-determined stage on the CWU-based treatment plan. The secondary end-point was the prognostic value of incorporating PET/CT in the initial staging process.

All consecutive patients (≥18 years old) with pathologically confirmed untreated HNSCC of the oral cavity, oropharynx, larynx, or hypopharynx who underwent CWU for primary cancer staging within 3 weeks of the initial treatment between October 2010 and December 2012 were enrolled. All surviving patients were followed for at least 12 months. The exclusion criteria were patients with no available data of either pre-treatment CT/MRI or ^{18}F-FDG PET/CT ($n = 33$) and with no adequate follow-up information ($n = 21$). During the study period, a total of 248 eligible patients were included in this study.

2.2. Study design

CWU stage was determined on the basis of CWU before PET/CT. According to the protocol of our institution, CWU includes physical and endoscopic examinations, contrast-enhanced CT and/or MRI of the head and neck, CT of the chest, and flexible oesophagogastroduodenoscopy because synchronous cancers in HNSCC are predominantly located in the upper aerodigestive tract [20]. The CWU results are then reviewed for diagnostic quality during our institutional multidisciplinary head and neck oncology team meetings. The team consists of experienced surgical, medical, and radiation oncologists. The tumours are staged according to the *American Joint Committee on Cancer Staging Manual* (7th ed., 2010) [21].