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Chest radiography or chest CT plus head and neck CT versus ^{18}F-FDG PET/CT for detection of distant metastasis and synchronous cancer in patients with head and neck cancer

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ABSTRACT

Objectives: Current guidelines recommend chest computed tomography (CT) with locoregional CT/magnetic resonance imaging for patients with head and neck squamous cell carcinoma (HNSCC), and ^{18}F-fluorodeoxyglucose (FDG) positron-emission tomography (PET)/CT is suggested for stage III–IV patients. However, whole body screening with ^{18}F-FDG PET/CT may provide better detection of distant metastases and synchronous cancer than conventional imaging. We evaluated the utility of ^{18}F-FDG PET/CT in detecting distant metastasis and synchronous cancer.

Methods: This prospective study enrolled 740 consecutive patients with previously untreated HNSCC diagnosed between September 2010 and December 2015. Synchronous cancer was histologically confirmed and distant metastases were confirmed by biopsy or serial imaging follow-ups. McNemar test was used to compare the true-positive detection rates of chest radiography (CXR) + head and neck CT (hnCT) (A) versus ^{18}F-FDG PET/CT (C) and chest CT + hnCT (B) versus ^{18}F-FDG PET/CT.

Results: Distant metastases and synchronous cancer were found in 23 (3.1%) and 55 (7.4%) patients, respectively. A, B, and C detected distant metastases in 10 (1.3%), 19 (2.6%), and 21 (2.8%) patients, respectively. The absolute differences were 1.5% (A versus C, $P = 0.003$) and 0.3% (B versus C, $P = 0.687$). A, B, and C detected synchronous cancer in 15 (2.0%), 22 (2.9%), and 36 (4.9%) patients, respectively. The absolute differences were 2.8% (A versus C, $P < 0.001$) and 1.4% (B versus C, $P = 0.013$).

Conclusions: ^{18}F-FDG PET/CT detected more distant metastases and synchronous cancer than CXR + hnCT and more synchronous cancer than chest CT + hnCT.

Introduction

Integrated positron-emission tomography (PET) computed tomography (CT) using [^{18}F]-fluorodeoxyglucose (FDG) can provide more accurate tumour staging than conventional imaging modalities or PET alone [1]. Therefore, ^{18}F-FDG PET/CT is the primary tool for tumour staging and evaluating the therapeutic responses of solid tumours, including head and neck cancer [2–5], and is also being increasingly used to detect second primary cancers [6–8].

A tumour is defined as synchronous cancer if it is discovered in a different location than the index tumour within 6 months [9,10]. Synchronous cancer is observed in 1.2–18.2% of patients with head and neck squamous cell carcinoma (HNSCC) [11–13]. Because the development of second primary cancer is an unfavourable prognostic factor [14,15], detection at initial tumour staging is essential. However, the utility of ^{18}F-FDG PET/CT to identify synchronous or metachronous second primary cancer in HNSCC patients has largely been evaluated using retrospective studies [16,17].

Distant metastases are rarely found in HNSCC patients and are associated with extremely poor prognosis. The overall incidence of clinically detected distant metastasis in HNSCC patients is 2.8–23.8%, with the lung, bone, and liver being the most common sites [18–21]. There are no curative treatments for distant metastasis of HNSCC, and patients are offered only palliative treatment. Distant metastasis should

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be prevented or detected early to improve survival [22,23].

Current guidelines recommend chest CT with locoregional CT/magnetic resonance imaging (MRI) for HNSCC patients, and ^{18}F-FDG PET/CT should be considered for stage III–IV patients [24]. A recent study prospectively compared the true detection rate of distant metastases and synchronous cancer in 307 Danish HNSCC patients between different imaging modalities; detection was higher by ^{18}F-FDG PET/CT than chest radiography (CXR) plus head and neck MRI or chest CT plus head and neck MRI [25]. They also showed that the PET/CT-based upfront imaging strategy significantly changed the treatment intent [26]. The incidence and distribution of second primary cancer and distant metastases can vary by race and ethnicity [27,28]. More prospective studies are needed in other populations. Therefore, we evaluated the utility of ^{18}F-FDG PET/CT in detecting distant metastasis and synchronous cancer at diagnosis compared to CXR plus head and neck CT (hnCT) or chest CT plus hnCT.

Methods

Study patients

This prospective study enrolled consecutive patients with head and neck cancer referred to our tertiary referral centre between September 2010 and December 2015. This study was conducted in accordance with good clinical practice and the Declaration of Helsinki. Study permission was granted from the Institutional Review Board of our hospital and informed consent was obtained from each patient. Eligible patients with previously untreated HNSCC and imaging evaluation were included in this study. Exclusion criteria were patients with non-squamous cell carcinoma, recurrent HNSCC, carcinoma of unknown primary site, and skin squamous cell carcinoma, and those not wanting chest CT or PET/CT. Patients with < 1 year follow-up or no follow-up imaging were also excluded. Patients with nasopharyngeal cancer of undifferentiated form were included. Tumours were staged using the tumour-node-metastasis staging system proposed by the American Joint Committee on Cancer (7th ed.). Patients underwent histological diagnoses and imaging evaluation, including CXR, contrast-enhanced hnCT, contrast-enhanced chest CT, and whole body ^{18}F-FDG PET/CT, prior to initial treatment. Patients also underwent flexible conventional white light esophagogastroduodenoscopy with narrow band imaging and Lugol chromoendoscopy.

Patients underwent primary surgery, radiotherapy, chemotherapy, or a combination, according to the consensus of our head and neck oncology team. Patients who received palliative or no treatments were included if they received follow-up imaging. After completion of initial treatment, patients were regularly followed with careful physical and endoscopic examinations at every clinic visit at regular intervals [29]. Chest radiography, hnCT, and ^{18}F-FDG PET/CT were performed postoperatively at 3–6 and 12 months [30] and when suspicious recurrent or new lesions or second primary cancers were identified [31,32].

Imaging techniques and interpretation

All study patients underwent ^{18}F-FDG PET/CT scanning using the Biograph Sensation 16 (BIO16)/TruePoint 40 (BIO40) system (Siemens Medical Systems, Knoxville, TN, USA) or Discovery STE 8 (DSTE)/Discovery 690 (D690) (GE Healthcare, Milwaukee, WI, USA). Serum glucose < 150 mg/dL was required before imaging. Whole-body PET images were obtained approximately 1 h after intravenous administration of FDG (370–580 MBq). PET attenuation correction and image fusion were obtained using non-contrast-enhanced CT scans (100 mAs, 120 kV, 5-mm section width, and 0.75-mm collimation). Caudocranial PET emission scans were obtained with 2-min (for BIO40, D690, and D710) or 2.5-min (for BIO16 and DSTE) acquisition times per bed position with 5–8 bed positions for the whole body and 5 min per bed position with 2 bed positions for the head and neck. PET data were reconstructed using CT-based attenuation correction, an iterative reconstruction algorithm (two iterations, 16 subsets for BIO16; three iterations, 21 subsets for BIO40; two iterations, 20 subsets for DSTE8; and 4 iterations, 18 subsets for D690 and D710), and a post-reconstruction smoothing Gaussian filter (full width at half-maximum = 4 mm). Images were reconstructed with a 168 × 168 matrix (pixel size = 5.3 mm). FDG PET/CT images were reviewed with a viewing platform (Syngo MMWP VE40A and Syngo VE32E; Siemens Medical Systems, Erlangen, Germany).

Contrast–enhanced hnCT was performed on a multi-detector CT scanner (Somatom Sensation 16; Siemens, Forchheim, Germany) or LightSpeed QX/I (GE Medical Systems, Milwaukee, WI, USA). Contrast-enhanced CT images were obtained 70 s after intravenous injection of a 150-mL bolus of nonionic iodinated contrast material (Optiray; Mallinckrodt Pharmaceuticals, Dublin, Ireland). Imaging was performed with the following parameters: section thickness, 3 mm; field of view, 20.9 cm; 120 kV; 200 mA; matrix, 256 × 256. Contrast-enhanced chest CT was also performed on a multidetector CT scanner or LightSpeed QX/I. The scanning parameters were: beam collimation, 16 × 0.75 mm, 32 × 0.6 mm, or 64 × 0.6 mm; beam pitch, 0.984:1; gantry rotation time, 0.5 s; field of view to fit, 120 kVp. Three-millimetre-thick images at 3-mm intervals without gaps were reconstructed in the axial planes. Coronal reformations were performed at a slice thickness of 5 mm. CXR was performed to departmental standards in full inspiration anteroposterior and lateral projections with 130–145 kV and automatic exposure control. FD-X hardware systems (Siemens Healthineers, Erlangen, Germany) were used, and studies were read using a Centricity RA1000 PACS workstation (GE Healthcare) with dual 3MP medical-grade monitors.

The hnCT was evaluated by two experienced radiologists. CXR and chest CT were evaluated by experienced radiologists. PET/CT images were evaluated by two experienced nuclear physicians who were blinded to the biopsy results and information of hnCT, CXR, and chest CT. Synchronous cancer was verified by biopsy, and distant metastasis by biopsy or follow-up imaging (≤6 months after initial diagnosis). Metastatic disease and synchronous cancer were also characterized only in lesions fulfilling the RECIST and PERCIST criteria for progression of measurable lesions when using follow-up imaging as standard reference [33,34].

Sample size and outcome measurements

The sample size was estimated using an assumption of distant metastasis and synchronous cancer prevalence of 3–8%, including all early and advanced stages at diagnosis. The dropout rate was anticipated as 20%, and the detection rate of imaging modalities was anticipated as 2%. A sample size of 380–890 was calculated to meet a power of 0.8, an error of 0.05, and the detection rate. The main outcome measurement was the true-positive detection rates of distant metastasis and synchronous cancer by different imaging modalities at initial diagnosis. The prevalence or detection of diseases was expressed as number and percentage. Detection rates of distant metastasis and synchronous cancers were compared among the different combinations of imaging modalities: CXR plus hnCT versus ^{18}F-FDG PET/CT and chest CT plus hnCT versus ^{18}F-FDG PET/CT.

Statistical analysis

Continuous variables are expressed as median and interquartile range (IQR). The McNemar test was used to find differences in the paired proportions from different combinations of imaging modalities. The absolute difference in detection rates of distant metastasis and synchronous cancer was also assessed with 95% confidence interval. The comparison of imaging modalities was performed for subgroups, according to tumour site (larynx, oral cavity, and pharynx) and overall TNM stage (early I–II stage and advanced III–IV stage). All statistical

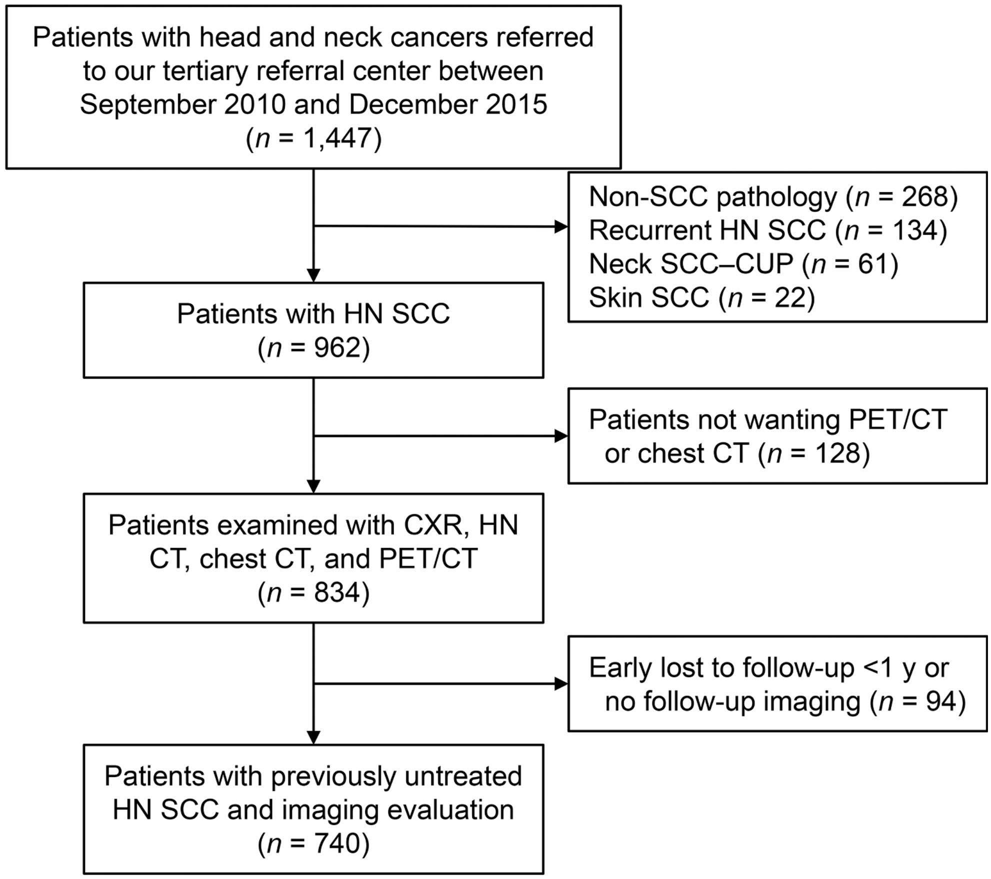

Fig. 1. Flowchart showing study patients. CXR = chest radiography; CUP = carcinoma of unknown primary; HN = head and neck; PET/CT, whole body ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography; SCC = squamous cell carcinoma.

analyses were performed using IBM SPSS version 24.0 (IBM Corp., Armonk, NY, USA).

Results

Patient characteristics

A total of 1447 patients were admitted to our department for histologically verified malignancies of the head and neck. Fig. 1 shows the excluded and included patients. This study included 740 patients, including 605 men (81.8%) and 135 women (18.2%), with a median age of 60 (IQR, 53–68) years (Table 1). Primary tumours were found in the larynx (*n* = 212, 28.6%), oral cavity (*n* = 210, 28.4%), oropharynx (*n* = 155, 20.9%), hypopharynx (*n* = 96, 13.0%), nasopharynx (*n* = 50, 6.8%), and nasal cavity (*n* = 17, 2.3%). Three hundred ninety-six (53.5%) and 436 (58.9%) patients were heavy smokers (> 20 pack-years) and heavy drinkers (≥1 drink/day), respectively. Advanced T3–T4 tumours, nodal positivity, and distant metastasis at presentation were found in 287 (38.8%), 350 (47.3%), and 23 (3.1%) patients, respectively. Overall advanced III–IV stage was found in 446 patients (60.3%). Previous (non-HNC) and synchronous second cancers were found in 82 (11.1%) and 55 (7.4%) patients, respectively. Primary surgery and radiotherapy-based non-surgical treatment were performed in 518 (70%) and 203 (27.4%) patients, respectively. Chemotherapy alone or no treatment was performed in 19 (2.6%) patients.

Incidence and site distribution of distant metastasis and synchronous cancer

Distant metastasis at diagnosis was found in 23 patients (3.1%); the most frequent sites were the lung, bone, and liver (Supplementary Table S1). Distant metastasis was most frequently found in patients with nasopharynx cancer (14.0%), followed by those with primary tumours in the hypopharynx (7.3%), oropharynx (3.2%), oral cavity (1.0%), and larynx (0.9%) (χ^2 test, $P < 0.001$). Synchronous cancers were most frequently found in the oesophagus, lung, stomach, thyroid, other head and neck sites, and colon (Supplementary Table S2). Synchronous cancers were most frequently found in patients with primary tumours in the hypopharynx (22.9%), larynx (9.0%), oropharynx (5.8%), nasopharynx (2.0%), and oral cavity (1.9%) (χ^2 test, $P < 0.001$; Supplementary Table S3).

Comparison of imaging detection for distant metastasis and synchronous cancer

CXR + hnCT detected distant metastases in 10 (1.3%) patients, chest CT + hnCT in 19 (2.6%), and ^{18}F-FDG PET/CT in 21 (2.8%). CXR + hnCT detected synchronous cancer in 15 (2.0%) patients, chest CT + hnCT in 22 (2.9%), and ^{18}F-FDG PET/CT in 36 (4.9%). ^{18}F-FDG PET/CT had significantly higher detection rates of distant metastasis and synchronous cancers than CXR + hnCT ($P = 0.003$ and $P < 0.001$, respectively) (Table 2). In subgroup analyses, ^{18}F-FDG PET/CT had better detection of distant metastasis in patients with pharyngeal tumours ($P = 0.012$) and N1–N3 tumours ($P = 0.006$) and of synchronous cancers in patients with laryngeal ($P = 0.016$) or pharyngeal ($P = 0.001$) tumours and N1–N3 tumours ($P < 0.001$). Moreover, ^{18}F-FDG PET/CT detected significantly more synchronous cancer (4.9% vs 2.0%, $P = 0.013$) (Table 3), but not distant metastasis (2.8% vs 2.6%, $P = 0.687$) than chest CT + hnCT. In subgroup analyses, the detection rates of ^{18}F-FDG PET/CT were significantly higher in pharynx tumours ($P = 0.021$) and overall III–IV stage ($P = 0.004$). However, there were significant false-negative results of ^{18}F-FDG PET/CT (11/20, 55%) and chest CT + hnCT (16/20, 80%) for detection of synchronous cancer in

Table 1
Patient characteristics (N = 740).

Variable	Patients	%
Age (y), median (IQR)	60 (53–68)	
Sex		
Male/female	605/135	81.8/18.2
Tumour site		
Larynx	212	28.6
Oral cavity	210	28.4
Oropharynx	155	20.9
Hypopharynx	96	13.0
Nasopharynx	50	6.8
Nasal cavity	17	2.3
Smoking, pack-years		
> 20/ ≤ 20	396/344	53.5/46.5
Alcohol, drinks/day		
≥1/ < 1	436/304	58.9/41.1
TNM stage		
T1/T2/T3/T4	294/159/92/195	39.7/21.5/12.4/26.4
N0/N1/N2/N3	390/93/242/15	52.7/12.6/32.7/2.0
M0/M1	717/23	96.9/3.1
Overall stage I/II/III/IV	234/60/104/342	31.6/8.1/14.1/46.2
Second cancers		
Previous	82	11.1
Synchronous	55	7.4
Treatment modality		
None	3	0.4
Surgery only	271	36.6
Surgery + RT	181	24.5
Surgery + CRT	66	8.9
RT only	62	8.9
CRT	141	19.0
Chemotherapy only	16	2.2

Abbreviations: CRT, chemoradiotherapy; IQR, interquartile range; RT, radiotherapy; TNM, tumour-node-metastasis stage proposed by the American Joint Committee on Cancer (7th edition, 2010).

the oesophagus or stomach (Supplementary Table S2).

Discussion

We found that ^{18}F-FDG PET/CT could detect more distant metastases and synchronous cancer than CXR + hnCT. ^{18}F-FDG PET/CT also detected more synchronous cancer than chest CT + hnCT, but failed to increase the detection rate of distant metastases over chest CT + hnCT. This might be because the most common site of distant metastasis was the chest, and the majority of hepatic parenchyma was visible by chest CT. Increased detection of synchronous cancer by ^{18}F-FDG PET/CT compared to chest CT + hnCT was found in pharynx tumours and overall stage III–IV tumours. Therefore, our study supports the current guideline recommending chest CT with locoregional hnCT for HNSCC patients and consideration of ^{18}F-FDG PET/CT for stage III–IV patients [24].

The rates of distant metastases and synchronous cancer were 3.1% and 7.4%, respectively, at initial staging, which are within the reported ranges of 2.8–23.8% for distant metastasis [18–21] and 1.2–18.2% for synchronous cancer [11–13]. Our previous retrospective studies reported rates of distant metastasis of 1.2% at initial staging and 7.5% at a median follow-up of 12 months [22]. The site distribution of distant metastasis was similar to that in previous reports, most commonly occurring in the lung (80.6%), bone (38.9%), and liver (11.1%) [18–21]. In a previous review of HNSCC patients, the cumulative incidence of second primary cancer was 7.2% at 6 months, 17.9% at 5 years, and 23.1% at 10 years [35]. However, the distribution of synchronous cancers in this study was different from that of previous reports, with synchronous cancer mainly in the lung and other head and neck sites [18–21]. The present and our previous findings, including HNSCC patients of a single ethnic group residing in South Korea [35], showed a considerable proportion of synchronous cancers in the oesophagus and stomach. It is possible that there are relatively high incidences of oesophageal, gastric, and hepatic cancers in East Asia [27].

Our study showed similar detection rates of distant metastasis between ^{18}F-FDG PET/CT and chest CT + hnCT, which did not differ among different tumour sites, tumour classification, or nodal positivity. Distant metastasis from HNSCC is mostly confined to the chest. Multiple site metastases also commonly included lung metastasis. A recent study showed a significant difference between ^{18}F-FDG PET/CT and chest CT + head and neck MRI in detecting distant metastasis and synchronous cancer [25]; however, there are some differences from our study in terms of tumour sites and incidence and site distribution of synchronous cancer. That study included a 9.4% distant metastatic rate, consisting of 147 (47.9%) oral cavity cancers, 103 (33.6%) pharynx cancers, and 57 (18.6%) larynx cancers. Synchronous cancer was found in 31 (10.1%) patients, with a similar incidence in tumour sites. In our study, synchronous cancers were most frequent in the larynx and hypopharynx. These might explain the different significance of ^{18}F-FDG PET/CT.

^{18}F-FDG PET and PET/CT are the primary diagnostic modalities for the detection and staging of distant metastases and second primary cancer of various malignancies, including HNSCC [7,36]. The sensitivity of ^{18}F-FDG PET in detecting synchronous cancer is 100% [36], and the sensitivity of ^{18}F-FDG PET/CT in detecting both synchronous cancer and distant metastases is 91% [7]. Here, however, the sensitivity

Table 2
Detection rates of distant metastasis and synchronous cancer for CXR + hnCT versus ^{18}F-FDG PET/CT.

Patients (n = 740)	PET/CT	CXR + hnCT	Absolute difference (95% CI)	P[a]
Distant metastasis	21 (2.8%)	10 (1.3%)	1.5% (0%–3.1%)	0.003
Larynx (n = 212)	2 (0.9%)	2 (0.9%)	0% (− 2.5%–2.5%)	1.000
Oral cavity (n = 210)	2 (1.0%)	0	0% (− 1.0%–3.4%)	–
Pharynx (n = 301)	17 (5.7%)	8 (2.7%)	3.0% (− 0.3%–6.5%)	0.012
T1–T2 (n = 453)	6 (1.3%)	1 (0.2%)	1.1% (− 0.1%–2.7%)	0.063
T3–T4 (n = 287)	15 (5.2%)	9 (3.1%)	2.1% (− 1.3%–5.6%)	0.070
N0 (n = 390)	1 (0.3%)	0	0.3% (− 0.7%–1.4%)	–
N1–N3 (n = 350)	20 (5.7%)	10 (2.9%)	2.9% (− 0.2%–6.1%)	0.006
Synchronous cancer	36 (4.9%)	15 (2.0%)	2.8% (1.0%–4.8%)	< 0.001
Larynx (n = 212)	11 (5.2%)	4 (1.9%)	3.3% (− 0.4%–7.3%)	0.016
Oral cavity (n = 210)	3 (1.4%)	3 (1.4%)	0 (− 2.9%–2.9%)	1.000
Pharynx (n = 301)	22 (7.3%)	8 (2.7%)	4.7% (1.2%–8.4%)	0.001
Stage I–II (n = 294)	9 (3.1%)	7 (2.4%)	0.7% (− 0.2%–3.6%)	0.688
Stage III–IV (n = 446)	27 (6.1%)	8 (1.8%)	3.4% (1.0%–5.9%)	< 0.001

Abbreviations: CI, confidence interval; CXR, chest radiography; CT, computed tomography; ^{18}F-FDG, ^{18}F-fluorodeoxyglucose; hnCT, contrast-enhanced head and neck CT; PET, positron emission tomography.

[a] McNemar test, $P < 0.05$.

Table 3
Detection rates of distant metastasis and synchronous cancer for chest CT + hnCT versus ^{18}F-FDG PET/CT.

Patients (n = 740)	PET/CT	Chest CT + hnCT	Absolute difference (95% CI)	P^a
Distant metastasis	21 (2.8%)	19 (2.6%)	0.3% (− 1.4%–2.0%)	0.687
Larynx (n = 212)	2 (0.9%)	2 (0.9%)	0% (− 2.5%–2.5%)	1.000
Oral cavity (n = 210)	2 (1.0%)	2 (1.0%)	0% (− 2.6%–2.6%)	1.000
Pharynx (n = 301)	17 (5.7%)	15 (5.0%)	0.7% (− 3.1%–4.4%)	0.625
T1–T2 (n = 453)	6 (1.3%)	6 (1.3%)	0% (− 1.7%–1.7%)	1.000
T3–T4 (n = 287)	15 (5.2%)	13 (4.5%)	0.7% (− 3.0%–4.4%)	0.625
N0 (n = 390)	1 (0.3%)	0	0.3% (− 0.7%–1.4%)	–
N1–N3 (n = 350)	20 (5.7%)	19 (5.4%)	0.3% (− 3.2%–3.8%)	1.000
Synchronous cancer	36 (4.9%)	22 (2.9%)	1.9% (− 0.1%–4.0%)	0.013
Larynx (n = 212)	11 (5.2%)	7 (3.3%)	1.9% (− 2.2%–6.1%)	0.219
Oral cavity (n = 210)	3 (1.4%)	3 (1.4%)	0.5% (− 2.2%–3.3%)	1.000
Pharynx (n = 301)	22 (7.3%)	12 (4.0%)	3.3% (− 0.4%–7.2%)	0.021
Stage I–II (n = 294)	9 (3.1%)	9 (3.1%)	0% (− 3.0%–3.0%)	1.000
Stage III–IV (n = 446)	27 (6.1%)	13 (2.9%)	3.1% (0.4%–6.0%)	0.004

Abbreviations: CI, confidence interval; CT, computed tomography; ^{18}F-FDG, ^{18}F-fluorodeoxyglucose; hnCT, contrast-enhanced head and neck CT; PET, positron emission tomography.
[a] McNemar test, $P < 0.05$.

of ^{18}F-FDG PET/CT for identifying synchronous cancer was only 65.5%, much lower than that reported previously [7,36]. This was mainly due to a high false-negative rate (11 of 20 lesions) in detecting synchronous oesophageal and gastric cancers. Early-stage or superficial second primary cancer of the oesophagus and stomach may be undetected by ^{18}F-FDG PET or PET/CT [37,38], which may explain why previous studies showed very low sensitivity for ^{18}F-FDG PET (8%) and PET/CT (17%) in detecting synchronous oesophageal cancer [16,39]. The low sensitivity of ^{18}F-FDG PET/CT for detecting oesophageal synchronous cancer is most apparent in patients with Tis- or T1-stage disease [16,37,38]. It may be difficult to detect superficial or early-stage simultaneous cancers in the upper gastrointestinal tract using ^{18}F-FDG PET/CT or to differentiate malignant tumours from physiologic uptake or benign lesions. Systematic endoscopic examination of the upper digestive tract is required in addition to ^{18}F-FDG PET/CT screening for the proper detection of second primary cancer in East Asian HNSCC patients.

Although many studies have evaluated the usefulness of ^{18}F-FDG PET and PET/CT for detecting distant metastasis and synchronous cancer, this study prospectively evaluated the diagnostic values between different imaging modalities. Unlike the results of a similar prospective study [25], our study failed to show a diagnostic advantage of ^{18}F-FDG PET/CT over chest CT + hnCT in detecting distant metastasis. ^{18}F-FDG PET/CT showed modestly increased detection of synchronous cancer over chest CT + hnCT when compared to the results of a recent report [25]. This might result from the different patterns of second primary cancer occurrence in East Asian and Western HNSCC patients [27,28].

Conclusions

Our study shows that ^{18}F-FDG PET/CT can detect more distant metastases and synchronous cancer than CXR + hnCT, and more synchronous cancers but not more distant metastasis than chest CT + hnCT. Distant metastases and synchronous cancer were found in 3.1% (23/740) and 7.4% (55/740) of patients, respectively. However, a significant proportion of synchronous cancer, particularly in the oesophagus or stomach, was undetected by either ^{18}F-FDG PET/CT or chest CT + hnCT. This should be compensated by endoscopic screening of the upper digestive tract for staging workups in HNSCC patients, which may require future randomized studies.

Conflicts of interest

The authors have declared no conflicts of interest.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.oraloncology.2018.11.026.

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