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^{18}F-FDG PET/CT surveillance at 3–6 and 12 months for detection of recurrence and second primary cancer in patients with head and neck squamous cell carcinoma

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Background: Early detection of recurrence of head and neck squamous cell carcinoma (HNSCC), which is often obscured by surgical or radiotherapy-induced tissue distortion, is essential for proper patient management.

Methods: A total of 143 consecutive patients with previously untreated HNSCC were evaluated by whole-body fluorine 18-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) and regular clinical follow-up after curative treatment. The ^{18}F-FDG PET/CT was performed ~3–6 and 12 months after treatment and findings suspicious for recurrence or SPC were confirmed using histopathology.

Results: The sensitivities of 3–6- and 12-month PET/CT scans at patient level were 96% and 93%, respectively, and those of regular clinical follow-up were 11% and 19%, respectively (McNemar test, $P<0.001$). In patients with no clinical suspicion, PET/CT detected 95% and 91% of recurrent patients at 3–6 and 12 months, respectively. The sensitivity of PET/CT for the identification of SPC was 29% and 80% at 3–6 and 12 months, respectively. A positive interpretation of PET/CT was significantly associated with poor overall survival (log-rank test, $P<0.001$).

Conclusion: The ^{18}F-FDG PET/CT surveillance is beneficial for the detection of recurrence that may be missed by regular follow-up physical and endoscopic examinations of the head and neck area after curative treatment for HNSCC.

Head and neck cancer describes a group of tumours that arise in the upper aerodigestive tract including the larynx, pharynx, oral cavity, nasal cavity, and paranasal sinus, and the predominant histological type is squamous cell carcinoma. Head and neck squamous cell carcinoma (HNSCC) is the eighth most common cancer worldwide, with more than half a million patients diagnosed each year (Jemal *et al*, 2011). Tobacco and alcohol consumption increases the risk of developing HNSCC, and oncogenic human papilloma virus is associated with a high risk of oropharyngeal cancer (Pai and Westra, 2009). Approximately two-thirds of HNSCC patients are initially diagnosed with advanced-stage disease including regional lymph node metastasis. Patients with HNSCC are usually treated by a multidisciplinary approach involving surgery, radiotherapy, and chemotherapy (Argiris *et al*, 2008; Haddad and Shin, 2008).

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Despite the aggressive multimodal approach, the locoregional recurrence rate remains high in up to 54% of patients with advanced HNSCC, and distant metastases, which are less frequent, are reported in ~5% to 10% of HNSCC patients (Ang *et al*, 2001; Xu *et al*, 2011). Moreover, recurrence occurs predominantly within the first 2 years after curative treatment (Leemans *et al*, 1994). Early detection of recurrent disease or second primary cancers may provide a chance of cure by early salvage treatment, and potentially a survival benefit (Wong *et al*, 2003). However, postsurgical and radiation-induced changes in the normal tissues may interfere with the early detection of recurrence by regular standard examinations of the head and neck including physical examination, endoscopy, computed tomography (CT) and magnetic resonance imaging (MRI) (Lell *et al*, 2000).

The development of fluorine 18-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) or PET/CT has improved the post-treatment detection of residual or recurrent disease. The ^{18}F-FDG PET or PET/CT is capable of distinguishing post-treatment tissue changes from recurrence that is undetectable by routine clinical follow-up of physical examination, CT, or MRI (Salaun *et al*, 2007; Abgral *et al*, 2009; Krabbe *et al*, 2009; Zundel *et al*, 2011; Ho *et al*, 2013). Therefore, ^{18}F-FDG PET or PET/CT should be used after treatment as a sequential diagnostic tool regardless of the clinical suspicion of recurrence.

Currently, no clear consensus exists regarding the interval and frequency of ^{18}F-FDG PET or PET/CT scans for post-treatment surveillance in HNSCC patients. A prospective study involving 48 oral and oropharyngeal SCC patients undergoing curative treatment recommended systematic ^{18}F-FDG PET scanning 3–6 months after treatment (Krabbe *et al*, 2009). Another prospective study that included 53 patients without clinically apparent recurrence proposed the systematic use of ^{18}F-FDG PET/CT at 12 months after treatment (Abgral *et al*, 2009). However, the use of post-treatment ^{18}F-FDG PET/CT in HNSCC patients needs to be further examined. In the present study, we evaluated the diagnostic value of ^{18}F-FDG PET/CT at 3–6 and 12 months after treatment for the detection of recurrence and second primary cancers in patients with HNSCC who underwent curative treatment. The early detection of recurrence is of value to guide clinicians in the management of these patients.

MATERIALS AND METHODS

Patients. Consecutive patients who were treated curatively for HNSCC from October 2009 to September 2010 at Asan Medical Center were reviewed. Inclusion criteria were previously untreated HNSCC, undergoing curative treatment, 3–6- or 12-month post-treatment imaging with whole-body ^{18}F-FDG PET/CT, and complete follow-up of at least 18 months after completion of treatment. Not eligible for inclusion were patients with distant metastasis at the initial staging and those treated with palliative intent. Tumours were staged according to the tumour–node–metastasis (TNM) staging system (7th edition, 2010) of the American Joint Committee on Cancer (AJCC) (Edge *et al*, 2010). Study protocols were reviewed and approved by the Institutional Review Board of Asan Medical Center and the informed consent required from each patient was waived.

Follow-up. After initial therapy with curative intent, patients were regularly followed by clinical examination and serial ^{18}F-FDG PET/CT scanning. All eligible patients were examined by palpation of all anatomic subsites of the head and neck and an endoscopic examination of the nasal and oral cavity, pharynx, and larynx at every clinic visit after curative treatment. The patients were scheduled for clinic visits every 1 to 2 months during the first year, every 2 to 4 months during the second and third years, and every 6 months during the fourth and fifth years. Regardless of the clinical suspicion of recurrence, a systematic follow-up protocol was established in our institution consisting of whole-body ^{18}F-FDG PET/CT with/without head and neck CT/MRI at ~3–6 and 12–18 months after curative therapy. Flexible esophagogastroduodenoscopy was performed annually.

The presence of clinical or imaging findings suggestive of local or regional recurrence, distant metastasis, or a second primary tumour was confirmed by biopsies. In cases of suspicious findings outside the head and neck region, the appropriate specialists examined the patient to confirm the lesions. Patients with confirmed recurrence or a second primary tumour were scheduled for salvage or palliative treatment. The positive results of regular follow-up or ^{18}F-FDG PET/CT scan were compared with the gold standard, namely the outcome of biopsies and imaging follow-up.

^{18}F-FDG PET/CT imaging and interpretation. The patients received whole-body ^{18}F-FDG PET/CT scans using a multi-slice PET/CT camera system (Biograph Sensation 16 and Truepoint 40, Siemens Medical System, Knoxville, TN, USA; or Discovery STE 8, GE Healthcare, Milwaukee, WI, USA) equipped with 16-, 40-, or 8-slice CT scanners. All patients fasted for at least 6 h before ^{18}F-FDG PET scanning and whole-blood glucose concentrations were $<150\,mg\,dl^{-1}$ before scanning. Whole-body image acquisition was started ~60 min after intravenous injection of 370–555 MBq. The ^{18}F-FDG/CT scanning without contrast enhancement was performed in spiral mode from the skull to the proximal thigh for attenuation correction and image fusion, followed by three-dimensional caudocranial PET scanning. The emission scan time per bed position was 2.5 min, and six or eight bed positions were used. The PET data were reconstructed using a standard iterative algorithm with attenuation correction based on the CT data.

A nuclear medicine physician with more than 15 years of experience interpreted the PET or PET/CT images by visual inspection. Foci with increased ^{18}F-FDG uptake in the primary tumours and metastatic nodes were evaluated and compared with the background and blood pool activities. Image interpretation was based on visual and semiquantitative analyses of abnormally increased focal ^{18}F-FDG uptakes but no strict standardised uptake value cutoffs were used. Local, regional, and distant sites were independently assessed and the presence of any primary site tumours, metastatic lymph nodes or soft tissues of the neck, and distant site of each patient was recorded.

Statistical analysis. Any ^{18}F-FDG PET/CT findings suspicious for recurrence or a second primary cancer were confirmed by histopathology. Patients showing negative ^{18}F-FDG PET/CT results were regularly followed to confirm the absence of recurrence or new lesions by clinical and imaging examinations. The absence of evidence of recurrence or a second primary cancer at the indicated time points and subsequent early follow-up was considered when interpreting the negative ^{18}F-FDG PET/CT result at that time point.

Continuous variables were expressed as the median and range, and categorical variables were expressed as numbers and percentages. The sensitivity, specificity, accuracy, and predictive values of the imaging methods for assessing recurrence and secondary primary cancer were evaluated. Before referring to interpretation of ^{18}F-FDG PET/CT or other imaging, the clinicians recorded their clinical findings including endoscopic and physical examinations at the clinic visits. The diagnostic value of ^{18}F-FDG PET/CT was compared with that of regular clinical examination at the time points of ^{18}F-FDG PET/CT scans using the McNemar test. Estimates of survival functions for overall and disease-free survivals were generated by the Kaplan–Meier method and compared by the log-rank test. A two-tailed P-value of <0.05 was considered statistically significant. All statistical analyses were

performed using SPSS software version 21.0 (IBM, Armonk, NY, USA).

RESULTS

Patient characteristics and follow-up summary. A total of 143 patients, 113 men and 30 women with a median age of 63 years (range, 20 – 83 years), were included in the study. The characteristics of the patients are shown in Table 1. The primary tumours were most frequently detected in the larynx (27%) and the oral cavity (24%). At the time of initial staging, 41% of the patients were T3–4, 37% were N1–3, and 62% were overall TNM stage III or IV.

Follow-up data of patients after curative treatment are summarised in Table 2. Local or regional recurrence or distant metastases developed in 47 (33%) patients and second primary cancers occurred in 13 (9%) patients at a median of 12 months (range, 2–30 months). Considering the time points of post-treatment ^{18}F-FDG PET/CT scans, recurrences occurred in 27 patients at ~3–6 months (range, 2–9 months) and in 27 patients at 12 months (range, 9–20 months), of whom 12 had recurrences at both time points. Of 15 patients with late recurrences alone, 13 had negative PET/CT results at 3–6 months and 2 received no early PET/CT scans. All surviving patients were followed-up to a median of 30 months with a range of 18 to 45 months. At the last follow-up, 18 (13%) patients had died of HNSCC, 3 (2%) had died of other causes, 20 (14%) were alive with disease, and 102 (71%) had no evidence of disease. The 3-year overall and disease-free survival rates of all patients were 81% and 63%, respectively.

Value of ^{18}F-FDG PET/CT for post-treatment surveillance. The 3–6-month ^{18}F-FDG PET/CT was performed in 133 patients at a median of 5 months (range, 2–9 months), and the 12-month ^{18}F-FDG PET/CT was performed in 119 patients at a median of 13 months (range, 9–20 months) after curative therapy. Of the 143 study patients, 109 had the ^{18}F-FDG PET/CT scans at both time points. The diagnostic accuracy of ^{18}F-FDG PET/CT for the detection of post-treatment recurrence or second primary cancers is shown in Table 3. The sensitivity of the 3–6-month ^{18}F-FDG PET/CT for detecting local recurrence, regional recurrence, and distant metastasis was 100%, 92%, and 100%, respectively, and the specificity was 97%, 95%, and 99%, respectively. The sensitivity of the 12-month ^{18}F-FDG PET/CT for detecting local recurrence, regional recurrence, and distant metastasis was 83%, 100%, and 85%, respectively, and the specificity was 95%, 95%, and 100%, respectively. The 3–6- and 12-month ^{18}F-FDG PET/CT scans detected post-treatment recurrence in most cases despite the absence of clinical suspicion (Figure 1). Abnormal focal ^{18}F-FDG uptake read as false positive was reported in 10 patients on the 3–6-month PET/CT and in 5 patients on the 12-month PET/CT. However, the sensitivity of ^{18}F-FDG PET/CT for the identification of a second primary cancer was 29% and 80% at 3–6 and 12 months, respectively. Second primary cancers detected by 3–6- and 12-month ^{18}F-FDG PET/CT and later confirmed were 1 out of 4 (sensitivity, 25%) in the oesophagus, 1 out of 3 (33%) in the stomach, 1 out of 2 (50%) in the lung, 1 out of 1 (100%) in the thyroid gland, 1 out of 1 (100%) in the prostate gland, and 1 out of 1 (100%) in the nasopharynx.

Table 1. Patient characteristics

Characteristic	*N*	%
Sex		
Male	113	79
Female	30	21
Age, years		
Median (range)	63 (20–83)	
Primary site		
Larynx	38	27
Oral cavity	34	24
Oropharynx	29	20
Hypopharynx	21	15
Nasopharynx	13	9
Nasal cavity, paranasal sinus	8	6
T classification		
T1–2	85	59
T3–4	58	41
N classification		
N0	90	63
N1–3	53	37
Overall TNM stage		
I	38	27
II	15	10
III	25	17
IVA–B	65	45
Primary treatment		
Surgery alone	44	31
Surgery + RT or CRT	34	24
RT alone	14	10
CRT	51	36

Abbreviations: CRT = chemoradiation therapy; RT = radiation therapy; TNM = tumour–node–metastasis stage (American Joint Committee on Cancer, 7th edition).

Table 2. Follow-up summary of patients after curative treatment

Characteristics	*N*	%
Recurrence site		
Local	29	20
Regional	17	12
Distant	21	15
Local and/or regional and/or distant	47	33
First recurrence		
Median time (range), months	11 (2–30)	
⩽12 months	31	22
>12 months	16	11
Second primary cancer		
Median time (range), months	5 (3–28)	
⩽12 Months	7	5
>12 Months	6	4
^{18}F-FDG PET/CT at ~3–6 months		
Number of patients scanned	133	93
Median (range) time after treatment, months	5 (2–9)	
^{18}F-FDG PET/CT at ~12 months		
Number of patients scanned	119	83
Median (range) time after treatment, months	13 (9–20)	

Abbreviations: CT = computed tomography; ^{18}F-FDG = fluorine 18-fluorodeoxyglucose; PET = positron emission tomography.

Table 3. Diagnostic value of ^{18}F-FDG PET/CT for the identification of recurrence or second primary cancers after curative treatment

	TP	FP	FN	TN	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
At 3–6 months ($n=133$)									
Local recurrence	17	4	0	112	100 (80–100)	97 (91–99)	97 (92–99)	81 (58–94)	100 (96–100)
Regional recurrence	11	6	1	115	92 (61–99)	95 (89–98)	95 (89–97)	65 (38–85)	99 (95–99)
Distant metastasis	6	1	0	126	100 (54–100)	99 (95–99)	99 (95–99)	86 (42–99)	100 (97–100)
Second cancer	2	4	5	122	29 (3–70)	97 (92–99)	93 (87–96)	33 (4–77)	96 (91–98)
At 12 months ($n=119$)									
Local recurrence	15	5	3	96	83 (63–95)	95 (91–97)	93 (87–97)	75 (56–86)	97 (93–99)
Regional recurrence	8	5	0	106	100 (63–100)	95 (89–98)	96 (90–98)	62 (31–86)	100 (96–100)
Distant metastasis	11	0	2	106	85 (54–98)	100 (96–100)	98 (94–99)	100 (71–100)	98 (93–99)
Second cancer	4	5	1	109	80 (28–99)	96 (90–98)	95 (89–98)	44 (13–78)	99 (95–99)

Abbreviations: CT = computed tomography; ^{18}F-FDG = fluorine 18-fluorodeoxyglucose; FN = false negative; FP = false positive; NPV = negative predictive value; PET = positron emission tomography; PPV = positive predictive value; TN = true negative; TP = true positive. Data in parentheses indicate the 95% confidence intervals.

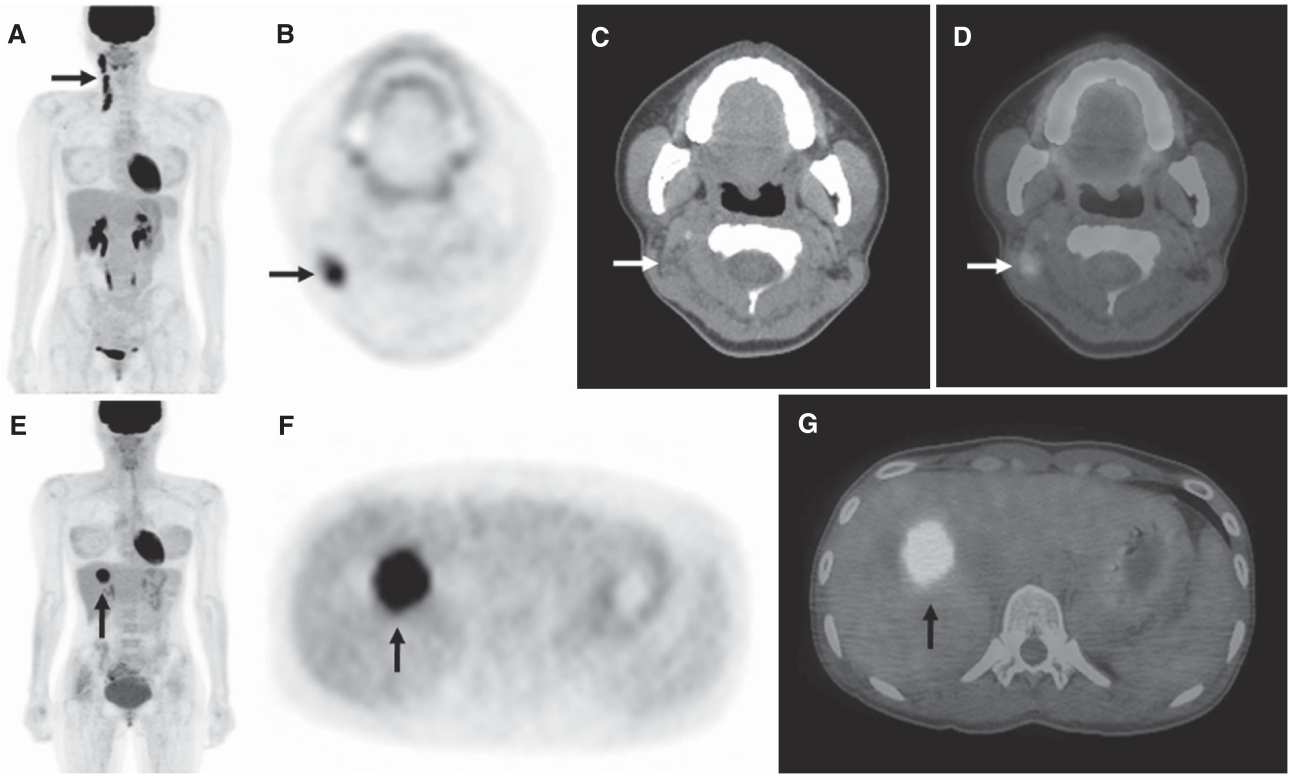

Figure 1. The ^{18}F-FDG PET/CT images showing true-positive foci (arrows) of post-treatment recurrence. Whole-body ^{18}F-FDG PET/CT scans correctly detected lymph node recurrence on the right neck at 3 months (**A–D**) and hepatic metastasis at 10 months (**E–G**) after chemoradiotherapy for oropharyngeal carcinoma. (**A**, **B**, **E**, and **F**) The ^{18}F-FDG PET images; (**C**) axial CT image; (**D** and **G**) fused ^{18}F-FDG PET/CT images.

Impact of ^{18}F-FDG PET/CT on patient management. The diagnostic performance of ^{18}F-FDG PET/CT for the detection of post-treatment recurrence was compared with that of regular clinical follow-up at patient level and the results are shown in Table 4. The sensitivities of 3–6- and 12-month ^{18}F-FDG PET/CT scans at patient level were 96% and 93%, respectively, and those of regular follow-up were 11% and 19%, respectively, showing statistically significant differences ($P<0.001$). In patients with no clinical suspicion, recurrence was detected by PET/CT at 3–6 months in 23 (95%) patients and at 12 months in 20 (91%) patients. The detection of recurrence by follow-up ^{18}F-FDG PET/CT contributed to patient management for salvage or palliative treatment. However, patients with a positive detection of recurrence by ^{18}F-FDG PET/CT had overall poorer survival outcome than those with negative results ($P<0.001$; Figure 2). A positive PET/CT interpretation was associated with an eight-fold increase in the relative risk of overall death (8.60, 95% CI 3.32–22.29).

DISCUSSION

The National Comprehensive Cancer Network (NCCN, 2013) guidelines for follow-up care in head and neck cancer patients recommend post-treatment baseline imaging within 6 months after

Table 4. Comparison of the diagnostic performance of ^{18}F-FDG PET/CT and regular clinical follow-up[a] at the patient level for the detection of recurrence

	TP	FP	FN	TN	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
At 3–6 months ($n=133$)									
^{18}F-FDG PET/CT	26	10	1	96	96 (81–99)	91 (83–95)	92 (85–95)	72 (54–85)	99 (94–99)
Clinical follow-up	3	8	24	98	11 (2–29)	92 (85–96)	76 (67–82)	27 (6–60)	80 (72–86)
At 12 months ($n=119$)									
^{18}F-FDG PET/CT	25	5	2	87	93 (75–99)	95 (87–98)	94 (88–97)	83 (65–94)	98 (92–99)
Clinical follow-up	5	4	22	88	19 (6–38)	96 (89–98)	78 (69–85)	56 (21–86)	80 (71–87)

Abbreviations: CT = computed tomography; ^{18}F-FDG = fluorine 18-fluorodeoxyglucose; FN = false negative; FP = false positive; NPV = negative predictive value; PET = positron emission tomography; PPV = positive predictive value; TN = true negative; TP = true positive . Data in parentheses indicate the 95% confidence intervals.
[a]Clinical follow-up included inspection, palpation and endoscopy of the head and neck region.

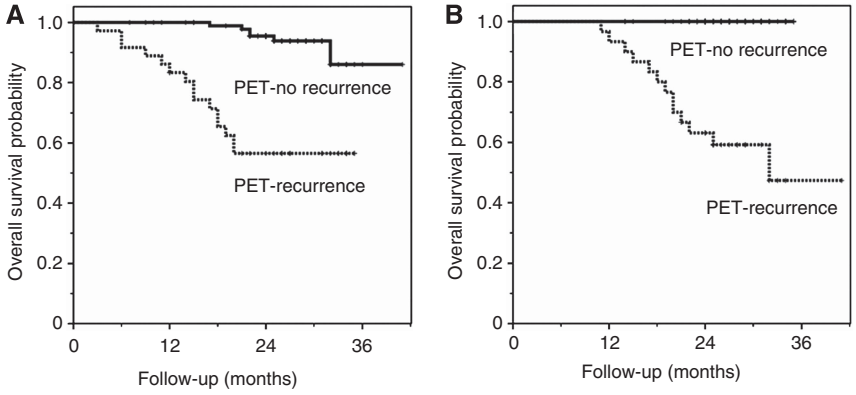

Figure 2. Kaplan–Meier estimates of overall survival according to the interpretation of ^{18}F-FDG PET/CT performed at ~3–6 months (**A**) and 12 months (**B**) after curative treatment. Log-rank test, $P<0.001$.

initial treatment for cancers of the oropharynx, hypopharynx, larynx, and nasopharynx in patients with T3–4 or N2–3 disease only, and further re-imaging is not recommended except in clinically suspected patients. However, post-treatment recurrence may occur in patients negative for disease on clinical follow-up (Salaun *et al*, 2007). Tissue fibrosis, oedema, necrosis, and anatomic changes after RT and/or surgery can interfere with early detection of residual viable tumour or recurrence by the usual sequential physical and endoscopic examinations of the head and neck (Lell *et al*, 2000; Zundel *et al*, 2011). In the present study, ^{18}F-FDG PET/CT was significantly more effective at detecting recurrence than clinical follow-up examination, suggesting that the inclusion of ^{18}F-FDG PET/CT as a sequential diagnostic tool is beneficial regardless of the presence or absence of clinical findings suggestive of recurrence.

The results of our study indicated that ^{18}F-FDG PET/CT is a useful tool for the detection of recurrent tumours at ~3–6 and 12 months after curative treatment. However, the recommended intervals and frequencies of post-treatment ^{18}F-FDG PET/CT are controversial. The ^{18}F-FDG PET or PET/CT is highly effective for distinguishing persistent disease from nonviable tumours or treatment sequelae, with potential to guide therapeutic decision making, but the timing of post-treatment ^{18}F-FDG PET or PET/CT has a significant impact on its diagnostic accuracy (Isles *et al*, 2008; Ong *et al*, 2008; Gupta *et al*, 2011). Because of its limited accuracy within 2 months after treatment, ^{18}F-FDG PET/CT at 3 months after treatment is now accepted as a standard method of post-treatment surveillance at many institutions (Isles *et al*, 2008; Gupta *et al*, 2011). Furthermore, in a recent retrospective study that included 388 HNSCC patients with definitive chemoradiation therapy, 45% of the observed asymptomatic recurrences were detected during the first 6 months of surveillance (Beswick *et al*, 2012). A prospective study recommended one systematic ^{18}F-FDG PET/CT at 3–6 months after treatment as the optimal timing (Krabbe *et al*, 2009), which was confirmed by our data showing the sensitivity of a 3–6-month ^{18}F-FDG PET/CT scan for the detection of early recurrence.

Moreover, further re-imaging with ^{18}F-FDG PET/CT may be necessary to properly detect later recurrence. In this regard, few systematic studies have been conducted to assess the use of repeated routine post-treatment ^{18}F-FDG PET/CT scans. The results of a prospective study suggested that ^{18}F-FDG PET/CT scanning at 12 months improves the detection of HNSCC recurrence with 90% overall accuracy in patients with clinically unsuspected disease (Abgral *et al*, 2009). However, retrospective studies showed that patients with negative results on 3–6-month imaging had limited benefit from subsequent ^{18}F-FDG PET/CT surveillance (Périé *et al*, 2007; Ho *et al*, 2013). In this patient cohort, considerable numbers of the recurrent patients had recurrences later than 9 months. This may be a discrepancy with other published data showing that negative 3–6-month PET/CT scans were a prognostic predictor (Ho *et al*, 2013). The results of our study showed that ^{18}F-FDG PET/CT at 12 months detected recurrence in 25 of 27 patients (93%), supporting the use of ^{18}F-FDG PET/CT at 12 months after treatment for the accurate detection of recurrence that may occur >9 months after treatment. In the present study, systematic ^{18}F-FDG PET/CT scans at 12 months in addition to 3–6 months after treatment may also significantly impact salvage treatment planning. Our results showed that ^{18}F-FDG FDG PET is a highly sensitive method for the detection of recurrence of HNSCC, thus providing important prognostic information for survival outcomes, as a positive PET

interpretation was associated with an eight-fold increase in the relative risk of patient death.

Systemic reviews have been conducted on the role of ^{18}F-FDG PET or PET/CT in the follow-up of head and neck cancer patients. A meta-analysis of 51 trials involving 2335 patients showed that the pooled sensitivity and specificity of post-treatment ^{18}F-FDG PET or PET/CT for the primary site were 80% and 88%, respectively, and those for the neck were 73% and 88%, respectively (Gupta *et al*, 2011). In 27 of 1871 identified studies evaluating ^{18}F-FDG PET or PET/CT for the detection of residual or recurrent HNSCC after RT or CRT, the pooled sensitivity and specificity of ^{18}F-FDG PET or PET/CT were 94% and 82%, respectively, whereas those of CT were lower (67% and 78%, respectively) (Isles *et al*, 2008). The positive predictive value (PPV) and negative predictive value (NPV) of ^{18}F-FDG PET or PET/CT were 75% and 95%, respectively. Several studies analysing the diagnostic performance of post-treatment ^{18}F-FDG PET or PET/CT for the detection of HNSCC recurrence report sensitivities of 89–100%, specificities of 64–100%, PPVs of 64–100%, NPVs of 92–100%, and overall accuracy of 88–91% (Wong *et al*, 2002; Kitagawa *et al*, 2003; Salaun *et al*, 2007; Abgral *et al*, 2009; Kao *et al*, 2009; Krabbe *et al*, 2009; Kim *et al*, 2011; Zundel *et al*, 2011; Ho *et al*, 2013). The diagnostic value of ^{18}F-FDG PET/CT determined in the present study was comparable to those of the previous reports. The NPV of ^{18}F-FDG PET remained exceptionally high (99%), whereas its PPV was somewhat suboptimal (72%). This implies that a negative post-treatment scan is highly suggestive of the absence of recurrence. The low sensitivity and PPV of clinical examination may result from the potential difficulty in detection of distant metastases or early small-volume recurrences because of postsurgical and radiation-induced changes in both primary sites and the neck (Lell *et al*, 2000).

In the present study, we examined the role of ^{18}F-FDG PET/CT in the detection of second primary cancers after treatment. The 3–6- and 12-month ^{18}F-FDG PET/CT scans correctly identified 6 of 12 (50%) second primary cancers. The relatively low sensitivity of ^{18}F-FDG PET/CT for the detection of post-treatment second primary cancers could be attributed to its low detection rate (29%) in the oesophagus or the stomach. The ability of ^{18}F-FDG PET or PET/CT to detect superficial or early-stage second primary cancers in the upper gastrointestinal tract is limited (Little *et al*, 2007; Shoda *et al*, 2007). These can be better diagnosed using systematic endoscopic screening (Petit *et al*, 2001; Takenaka *et al*, 2009). However, because the anatomic site and incidence of second primary cancers may differ among different ethnic groups, the follow-up protocols for detecting second primary cancers should be examined in further studies. In addition, because second primary cancers can arise after initial presentation of index HNSCC at an annual rate of 2.8% (Jovanovic *et al*, 1994), the efficacy and timing of the diagnostic methods for detecting second primary cancers need to be further examined.

Our study has revealed the potential role of post-treatment ^{18}F-FDG PET/CT surveillance for early detection of recurrences. However, there is no clear evidence of any survival benefit of treating as asymptomatic recurrence compared with symptom-directed recurrences. This may be from a lack of prospective studies on the issues and small number of inclusion patients. This needs to be elucidated by further prospective studies with large HNSCC population. Furthermore, the cost effectiveness of ^{18}F-FDG PET/CT for routine post-treatment surveillance *vs* for clinically suspected recurrence should be determined. In addition, the 3–6- and 12-month ^{18}F-FDG PET/CT showed a relatively wide range of 2–9 and 9–20 months, respectively. This might result from the retrospective nature of our study despite a systematic follow-up protocol established in our institution consisting of whole-body ^{18}F-FDG PET/CT at ~3–6 and 12–18 months after curative therapy.

In conclusion, ^{18}F-FDG PET/CT showed high sensitivity and NPV for the detection of recurrence after curative treatment in HNSCC patients. Our data indicated that ^{18}F-FDG PET/CT surveillance is beneficial for the detection of recurrence that may be missed by regular physical and endoscopic examinations of the head and neck area. In addition, follow-up ^{18}F-FDG PET is important to provide clinicians with information on patient survival. The results of our study indicate that systematic ^{18}F-FDG PET/CT scanning at 3–6 months and at 12 months after treatment is beneficial for the early detection of recurrence and may facilitate proper salvage intervention in these patients. Although this study shows a benefit to ^{18}F-FDG PET/CT surveillance, further studies are needed to optimise frequency and timing.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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