The Value of ^{18}F-FDG PET in the Detection of Stage M0 Carcinoma of the Nasopharynx

Tzu-Chen Yen, MD, PhD[1]; Joseph Tung-Chieh Chang, MD, MHA[2]; Shu-Hang Ng, MD[3]; Yu-Chen Chang, MD[1]; Sheng-Chieh Chan, MD[1]; Kun-Ju Lin, MD[1]; Wuu-Jyh Lin, PhD[4]; Ying-Kai Fu, PhD[4]; and Chen-Yu Lin[2]

[1]Department of Nuclear Medicine, Chang Gung Memorial Hospital and Chang Gung University, Taoyuan, Taiwan; [2]Department of Radiation Oncology, Chang Gung Memorial Hospital and Chang Gung University, Taoyuan, Taiwan; [3]Department of Radiology, Chang Gung Memorial Hospital and Chang Gung University, Taoyuan, Taiwan; and [4]Institute of Nuclear Energy Research, Taoyuan, Taiwan

Distant metastasis is an important issue for nasopharyngeal carcinoma (NPC). The potential value of PET using ^{18}F-FDG has not been well defined. This prospective study investigated the impact of ^{18}F-FDG PET in NPC patients with stage M0 disease. **Methods:** From April 2001 to June 2003, 140 NPC patients (118 primary and 22 primary recurrent) with stage M0 (negative results from chest radiography, liver sonography, and whole-body bone scanning) underwent ^{18}F-FDG PET to check for distant metastases. Confirmatory MRI or CT was performed if any abnormal ^{18}F-FDG uptake was found at distant sites. The distant lesion was confirmed pathologically, if feasible, and was followed up clinically and with imaging for at least 6 mo. **Results:** ^{18}F-FDG PET detected 26 true-positive metastatic sites in 18 (12.9%) of the 140 patients, among whom 14 had primary and 4 had recurrent tumors. The patient-based sensitivity and specificity of ^{18}F-FDG PET for distant metastases were 100% and 86.9%, respectively. Mediastinal lymph nodes (n = 8) were the most common sites, followed by lung, liver, and bone (n = 5 each) and by other lymph nodes (n = 3). In patients with primary tumors, advanced nodal status (N2–3) was a statistically significant variable associated with development of distant metastases (P = 0.044). For recurrent NPC, neither age, sex, initial tumor stage, grade of differentiation, nor nodal stage showed a statistically significant difference between patients with and patients without distant metastases. **Conclusion:** ^{18}F-FDG PET is valuable in avoiding aggressive locoregional radiotherapy in some NPC patients by the revelation of occult distant metastases, especially in patients with primary disease at a nodal stage of N2–3.

Key Words: ^{18}F-FDG; PET; nasopharyngeal carcinoma; M0

J Nucl Med 2005; 46:405–410

Nasopharyngeal carcinoma (NPC) is an epithelial malignancy occurring worldwide, with particularly high frequencies in southern China and parts of southeast Asia (*1*). With the use of CT and MRI for early detection, as well as modern radiotherapy techniques such as brachytherapy, 3-dimensional conformal radiotherapy, and intensity-modulated radiotherapy in combination with concurrent chemoradiotherapy, cure can be anticipated for most primary NPC and even for some recurrent disease (*2–4*). Unfortunately, about 5% of patients already have distant metastases at presentation (*1,5,6*), and up to 30% have distant recurrence after primary definitive radiotherapy (*7–9*). As well, radiotherapy and surgery are not harmless, and their major complications may cause considerable morbidity and even mortality (*10,11*). Because distant metastasis in NPC is not uncommon, it should be detected as early as possible to avoid ineffective treatment with curative intent.

Although the 5-y survival rate for overall NPC patients is high, around 90% of patients with distant metastases will die within 1 y (*5,7*). Thus, accurate staging and restaging of NPC are important for improving treatment and prognosis. In Taiwan, clinical staging comprises thorough physical examination and nasopharyngoscopy with biopsy sampling. CT or MRI of the head and neck is routinely done to assess the locoregional status, whereas chest radiography, liver sonography, and whole-body bone scanning are performed to exclude the possibility of distant metastasis. Previously, we have shown that MRI is superior to CT in determining the primary tumor extent, locoregional nodal metastases, and recurrent or residual tumors (*12–14*). Tempering this advantage is the reality that MRI is currently impractical for a whole-body survey in a single examination. Furthermore, the inadequate sensitivity of chest radiography, liver sonography, and whole-body bone scanning in discerning small lesions may cause distant metastases to be underestimated and some metastatic lesions to be missed when treatment is planned.

Although previous reports indicated that ^{18}F-FDG PET is superior to CT or MRI in detecting nodal status or local recurrence of NPC (*15,16*), the role of ^{18}F-FDG PET in detecting distant metastatic NPC has not been addressed. We therefore conducted this prospective study to assess the efficacy of ^{18}F-FDG PET in detecting distant metastases in NPC patients, with M0 staging based on conventional imaging.

Received Mar. 31, 2004; revision accepted Sep. 30, 2004.

For correspondence or reprints contact: Tzu-Chen Yen, MD, PhD, Department of Nuclear Medicine, Chang Gung Memorial Hospital, Linkou Medical Center, 5 Fu-Shin St., Kueishan, Taoyuan 333, Taiwan.

E-mail: yen1110@adm.cgmh.org.tw

MATERIALS AND METHODS

Patients

The institutional review board of our hospital required written informed consent from all enrolled patients as a condition for approval of the study. To be eligible, patients needed to have histologically proven primary NPC and negative results from chest radiography, liver sonography, and whole-body bone scanning (M0) before treatment planning. As well, candidates needed to have completed primary definitive treatment lasting at least 3 mo, with subsequent negative results from chest radiography, liver sonography, and whole-body bone scanning (M0) during periodic surveillance at our outpatient clinics. All patients were evaluated through clinical history, physical examination, and direct fiberoptic endoscopy. Conventional imaging included chest radiography, MRI of the head and neck, whole-body bone scanning, and liver sonography. ^{18}F-FDG PET was performed within 1 wk of head-and-neck MRI. Patients who had evidence of distant metastasis ($n = 3$) on conventional images or a fasting serum sugar level of 200 ng/dL or higher ($n = 5$) were excluded.

PET Procedure

^{18}F-FDG PET images were obtained with an ECAT EXACT HR+ camera (CTI) using a full width at half maximum of 4.5 mm and a transaxial field of view of 15 cm. All patients fasted for at least 6 h before PET. Serum glucose level was measured and diazepam (5 mg orally) routinely given before the intravenous administration of 370 MBq (10 mCi) of ^{18}F-FDG. During imaging, patients kept their arms motionless over their head, aided by a headrest and a holding bar. Transmission scans were obtained with ^{68}Ge rod sources. The emission and transmission scans were obtained in an alternating sequence per bed position. Reconstruction of both transmission and emission scans used accelerated maximum-likelihood reconstruction and ordered-subset expectation maximization (*17,18*), which reduces image noise and avoids artifacts resulting from filtered backprojection reconstruction of data with low count densities.

Image Analysis

Three experienced nuclear physicians who were unaware of other imaging results and the clinical data analyzed the ^{18}F-FDG PET images using an interactive computer display. ^{18}F-FDG accumulation was scored using a 5-point scale: 0 = normal, 1 = probably normal, 2 = equivocal, 3 = probably abnormal, and 4 = definitely abnormal (*19*). An ^{18}F-FDG PET result of 3 or 4 was considered positive, and a grade of 0, 1, or 2 was considered negative. Interpretations were primarily based on visual analysis, using standardized uptake value as an accessory reference for abnormal ^{18}F-FDG uptake. The latter evaluation was based on a region-of-interest analysis that yielded the standardized uptake value. The region of interest was placed within an area of pathologically increased ^{18}F-FDG uptake on the attenuation-corrected image. The location of the edge of the region of interest was the contour for 75% of peak counts. Any difference of opinion was resolved by consensus.

Study Procedures and Determination of Lesion Status

All PET and conventional images were judged jointly by an NPC research team consisting of the nuclear medicine physicians, head-and-neck radiologist, otorhinolaryngologist, medical oncologist, and radiation oncologist. Confirmatory MRI or CT was performed to correlate the positive PET findings at the distant sites. CT-guided or sonography-guided biopsy was then performed to obtain a histopathologic diagnosis of distant lesions, if possible. If a biopsy of the lesion of interest was not feasible or yielded a negative result, follow-up MRI/CT or ^{18}F-FDG PET was performed 3–6 mo later. Any discordance among the results of ^{18}F-FDG PET, MRI/CT, and histopathologic studies were resolved by consensus.

Statistical Analyses

True and false imaging results were assessed on the basis of the histopathologic findings, when available, and on the posttreatment outcome. The χ^2 test, independent t test, and Fisher test were performed to compare the clinical characteristics and distant metastasis status for patient groups with primary and recurrent NPC. All statistical tests were 2-sided.

RESULTS

Figure 1 depicts the flowchart for this study. Between April 2001 and June 2003, 140 consecutive patients (97 male and 43 female; mean age, 49.4 ± 12.4 y; age range, 15–81 y) were enrolled. Of these, 118 (mean age, 49.7 ± 12.7 y) were patients with newly diagnosed NPC, whereas 22 (mean age, 48.1 ± 8.6 y) were patients with disease relapse. The NPC staging system in this study was based on the system of the International Union Against Cancer/American Joint Committee on Cancer (*20*). Of the 118 patients with primary NPC, the nodal stages were N0 in 16 patients (13.6%), N1 in 31 (26.3%), N2 in 53 (44.9%), and N3 in 18 (15.2%). The histopathology types were nonkeratinizing squamous cell carcinoma or poorly differentiated squamous cell carcinoma in 41 patients (34.7%) and undifferentiated carcinoma in 77 (65.3%). Of the 22 patients with locoregional recurrence, the histopathology types were nonkeratinizing squamous cell carcinoma or poorly differentiated squamous cell carcinoma in 11 patients (50%) and undifferentiated carcinoma in 11 (50%).

For 34 patients in this series, abnormally increased ^{18}F-FDG accumulation was visible on PET scans (47 sites; visual score ≥ 3). Among them, true-positive lesions were found in 15 patients, false-positive lesions were found in 16, and both true-positive and false-positive lesions were found in the other 3. In total, 26 sites were true-positive and 21 were false-positive. Of the 18 patients with true-positive distant metastases, 14 had primary disease and 4 had relapsed disease. Fourteen of the 26 true-positive distant lesions (53.8%) were confirmed pathologically, whereas the other 12 (46.2%) showed definite progression in clinical or imaging follow-up. Of these 26 metastatic sites, 8 occurred in mediastinal lymph nodes, 5 in lung, 5 in liver, 5 in bone (Fig. 2), and 3 in other distant lymph nodes. All true-positive lesions in the lung were small (0.5–1.0 cm) and so were not resolved on chest radiography. Of the other 19 patients with false-positive sites, 8 had primary disease and the other 11 had tumor relapse. Of the 21 false-positive sites, 6 were in mediastinal lymph nodes (Fig. 3), 4 in lung, 1 in liver, 5 in bone, 2 in other distant lymph nodes, and 3 in other soft tissues. Granulation tissue or an inflammatory

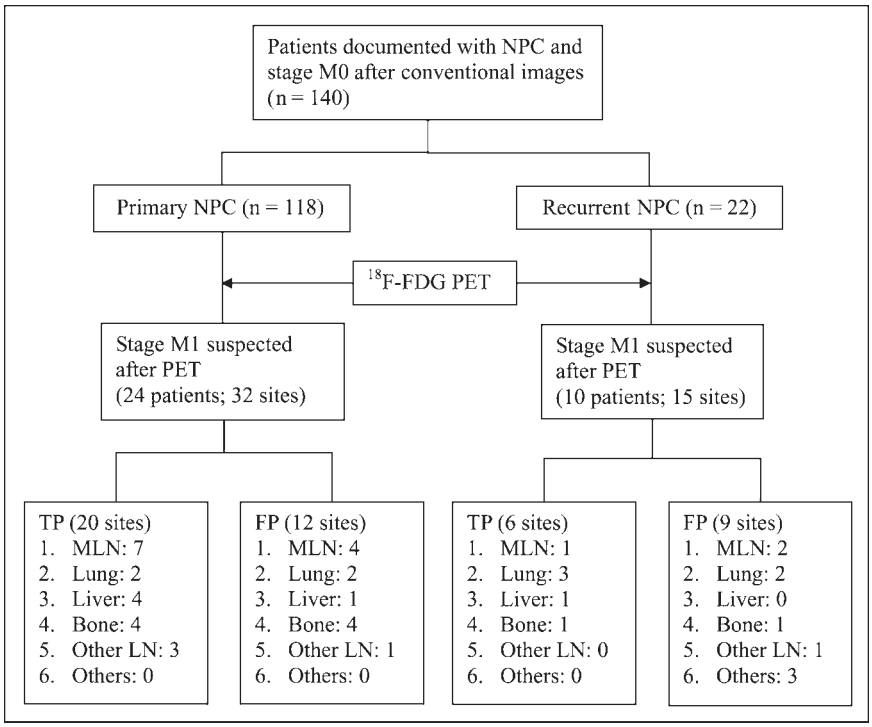

FIGURE 1. Flowchart of patients enrolled in this study. FP = false-positive; LN = lymph node; MLN = mediastinal lymph node; TP = true-positive.

change was the most common cause (12/21, or 57.1%) of false-positive findings, followed by degenerative bone disease or posttraumatic changes (5/21, or 23.8%). During follow-up (from 5 to 14 mo after PET) of patients with distant metastases, 4 patients (11.8%) died with the disease present, 15 patients (44.1%) remained alive with disease, and the other 15 patients (44.1%) were still alive and disease free. When calculated on a patient basis, the sensitivity and specificity of ^{18}F-FDG PET for distant metastases were 100% and 86.9%, respectively. With the help of ^{18}F-FDG PET, 18 patients (12.9%) were discovered to have distant metastases, and their treatment was changed from curative locoregional to systemic.

The relationships between the different variables (including age, sex, histologic type, and TNM stage) and development of distant metastases in patients with primary NPC and patients with recurrent NPC are shown in Tables 1 and 2, respectively. For patients with primary NPC, nodal stage was the only statistically significant variable related to the presence of distant metastases (P = 0.044). Primary NPC

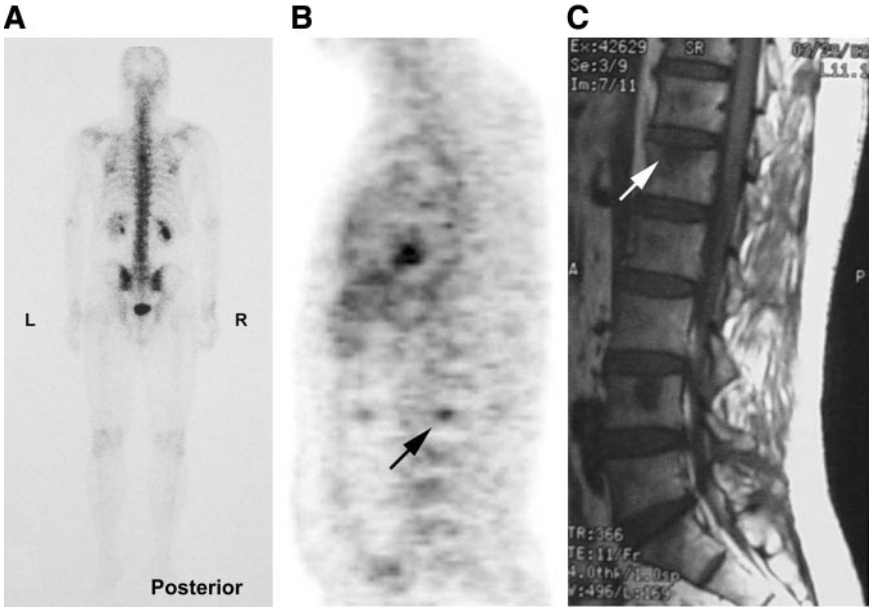

FIGURE 2. ^{18}F-FDG PET and MRI scans of 42-y-old male NPC patient (undifferentiated cell type) with initial clinical stage of T1 N3b M0. Result of whole-body bone scan was negative (A). Unexpected L1–2 spine metastatic lesion was found on whole-body ^{18}F-FDG PET scan (B, arrow) and later confirmed by MRI (C, arrow).

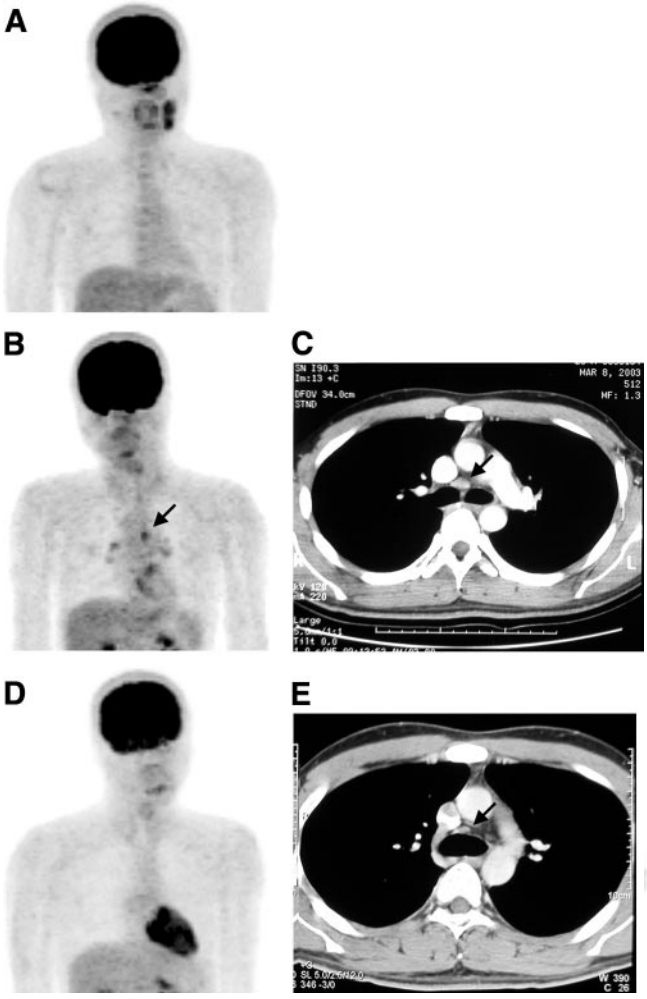

FIGURE 3. ^{18}F-FDG PET and CT scans of 29-y-old male NPC patient (poorly differentiated squamous cell type) with initial clinical stage of T3 N1 M0. Initial ^{18}F-FDG PET scan showed huge tumor in nasopharyngeal roof, with metastases to lymph nodes in left upper and lower neck. No definite evidence of mediastinal lymph node metastasis was noted (A). Three months after definitive concurrent chemoradiotherapy, follow-up ^{18}F-FDG PET showed complete remission of primary and metastatic lesions in left neck. However, equivocal mediastinal lymph node metastatic lesions were noted on both ^{18}F-FDG PET scans and chest CT scans (B and C). Further follow-up ^{18}F-FDG PET scans and chest CT scans showed no evidence of lymphadenopathy in mediastinal region (D and E). Findings shown in B can therefore be considered false-positive after concurrent chemoradiotherapy.

patients with a stage of N3 exhibited the greatest risk of distant metastases ($P = 0.008$), compared with those with a less advanced nodal status. For patients with recurrent NPC, the variables age, sex, histologic type, and TNM stage were not statistically significant for development of distant metastases.

DISCUSSION

NPC is exclusively a squamous cell carcinoma of the head-and-neck region. It is aggressive, with a high incidence of locoregional lymph node spread as well as distant metastasis at presentation (*5–9*). Yet, NPC is radiosensitive and is potentially curable. The 1-y mortality for NPC patients may be up to 90% when distant metastasis is found before treatment (*5,7*). Therefore, the presence of distant metastatic lesions greatly influences prognosis and treatment strategy. Treatment fails in a significant proportion of NPC patients because they already harbor distant metastatic lesions before the start of treatment (*1*). Also, some worrisome sequelae of radiotherapy, such as dry mouth, hearing impairment, and late neurologic complications, are major causes of morbidity and death (*10,11*). Therefore, the accurate assessment of distant metastases (M staging) for patients with primary or recurrent NPC is of paramount importance, not only for appropriate treatment planning but also for ensuring long-term survival and an acceptable quality of life.

Distant metastases of NPC, before and after primary definitive radiotherapy, are not uncommon (*1,7–9*). However, a detailed whole-body survey with MRI is generally impractical for tumor staging. Lack of a sensitive examination method may cause subtle and distant metastatic lesions to be missed at the time of diagnosis and result in undertreatment.

Recent retrospective analyses have supported the potential of ^{18}F-FDG PET for the early identification of both tumor recurrence and lymph node metastases in NPC (*15,16*). As yet, the efficacy of ^{18}F-FDG PET in the detection of unexpected distant metastases has not been studied. In the present study, ^{18}F-FDG PET disclosed distant metastases in 13% of NPC patients with an initial stage of M0. Such an incidence of distant metastasis is higher than previously reported (*1,5,6*). Our results show that the sensitivity of ^{18}F-FDG PET in detecting distant metastasis is higher than that of the conventional chest radiography, liver sonography, or bone scanning methods used to date.

The present study included patients with both primary and recurrent NPC. For those with primary NPC, N2–3 status was found to be an independent risk factor for distant metastasis (odds ratio, 3.27; 95% CI, 1.48–27.52) regardless of age, sex, cell type, and initial tumor stage. ^{18}F-FDG PET scans revealed unexpected distant metastases in 11.9% (14/118) of patients with primary disease and 18.2% (4/22) of patients with tumor recurrence. Although the incidence of distant metastasis in the latter group was higher, the difference did not reach statistical significance ($P = 0.486$). Mediastinal lymph nodes were the most common sites for distant metastasis, followed by lung, liver, and bone. The distribution of distant metastases in our NPC patients differed from that found in previous studies, which showed that bone was the most common site, followed by the liver (*5,21*). Such a difference may stem from the fact that the previous studies assessed distant metastases by conventional imaging instead of ^{18}F-FDG PET or CT, leading to underestimation of mediastinal lymph node or lung metastases. Although a previous study showed that conventional chest CT cannot provide adequate sensitivity to detect mediastinal lymph node metastases (*1*), modern CT techniques such as spiral CT or even multislice CT are better able to detect small

TABLE 1
Comparison of Demographics and Disease Characteristics Between Primary NPC Patients With Distant Metastasis and Their Counterparts Without Distant Metastasis

Characteristic	Patients with distant metastasis (n = 14)	Patients without distant metastasis (n = 104)	All patients (n = 118)	P
Age (y)	53.07 ± 11.66	49.22 ± 12.8	49.68 ± 12.68	0.288*
Sex				0.221†
Male	12	68	80	
Female	2	36	38	
Cell type (n = 91)§				1.000†
Nonkeratinized or poorly differentiated carcinoma	5	36	41	
Undifferentiated carcinoma	9	68	77	
Tumor stage				0.923‡
T1–2	8	58	66	
T3–4	6	46	52	
Nodal stage				0.044†
N1 or less	2	45	47	
N2 or greater	12	59	71	
				0.008†
N2 or less	8	92	100	
N3	6	12	18	

*Independent t test.
†Fisher exact test.
‡χ^2 test.
§One patient with adenoid cystic carcinoma is excluded.

lesions (*22,23*). Considering the rationale for the use of PET to detect distant metastases in NPC patients, our observation of the relatively higher overall detection rate for distant metastasis in recurrent than in primary NPC patients prompts us to suggest that PET should be performed on patients with recurrent NPC. The problematic (cost/benefit) but not less judicious indication is primary NPC, particularly if the incidences are not significantly different. Of note, in light of our data showing that a total of 80 NPC patients with N2–3 disease had a significantly higher risk of distant metastasis, primary NPC patients in such high-risk groups (nodal stage ≥ 2) will benefit substantially from early detection of distant metastases by the use of PET.

Of the 26 true-positive sites in this study, 14 were proven histologically and 12 were unequivocally established by lesion progression on follow-up imaging. Of the 21 false-

TABLE 2
Comparison of Demographics and Disease Characteristics Between Relapsed NPC Patients With Distant Metastasis and Their Counterparts Without Distant Metastasis

Characteristic	Patients with distant metastasis (n = 4)	Patients without distant metastasis (n = 18)	All patients (n = 22)	P
Age (y)	45.0 ± 8.87	48.72 ± 8.68	48.05 ± 8.62	0.448*
Sex				0.535†
Male	4	13	17	
Female	0	5	5	
Cell type				0.586†
Nonkeratinized or poorly differentiated carcinoma	3	8	11	
Undifferentiated carcinoma	1	10	11	
Initial tumor stage				0.582†
T1–2	1	8	9	
T3–4	3	7	10	
Initial nodal stage				0.616†
N1 or less	3	10	13	
N2 or greater	1	8	9	

*Independent t test.
†Fisher exact test.

positive sites in this study, 5 showed benign changes histologically, and all showed no progression during clinical or imaging follow-up of more than 6 mo. The presence of granulation or inflammation was the most common cause of false-positive findings (12/21, or 57.1%), followed by degenerative bone disease or posttraumatic changes (5/21, or 23.8%). Because of the still relatively high number of false-positive findings, every distant ^{18}F-FDG–avid area should be viewed with caution and considered for further cross-sectional imaging and, if feasible, histopathologic study for confirmation.

With the introduction of dual-modality PET/CT, the inherent limitation of ^{18}F-FDG PET—poor anatomic resolution—has been overcome. The sensitivity and specificity of this dual system are better than those of PET alone. The superiority of PET/CT to whole-body MRI in overall TNM staging (*24*) supports the usefulness of ^{18}F-FDG PET/CT as a possible first-line modality for whole-body tumor staging. We did not use whole-body CT in staging NPC. Currently, chest radiography, liver sonography, and bone scanning are still the primary modalities for detecting distant NPC metastases in endemic areas, including France, Hong Kong, Taiwan, and Singapore. In a recent study from Singapore, chest radiography, bone scanning, and liver sonography were suggested only for node-positive patients (*25*). For node-negative and stage I patients, liver sonography was not suggested. However, with the increased availability of multidetector CT in such endemic areas, CT of the neck and chest should be included as part of the workup of NPC patients, especially those with N2–3 disease.

CONCLUSION

PET has made a major impact on the detection of distant metastases in NPC patients with primary lesions and stage M0 disease, especially those who also have stage N2–3 disease. Because of the higher incidence of distant metastases in patients with recurrent NPC than in those with primary tumors, ^{18}F-FDG PET is also recommended for assessing recurrent NPC before embarking on salvage therapy. However, the cost of ^{18}F-FDG PET and the occurrence and rate of false-positive uptake are still problematic. With the technologic advances in multislice CT and whole-body MRI, these may be alternatives. The most important contribution of ^{18}F-FDG PET for patients with NPC is the ability to reveal occult distant metastases on chest radiography, liver sonography, and conventional bone scanning. Hence, unsuccessful therapy with curative intent or comorbidity induced by radiotherapy can be avoided and effective systemic therapy can be given without delay.

ACKNOWLEDGMENTS

This research was supported by grants NSC 92-2314-B-182A-089 from the National Science Council, Taiwan, and CMRPG32034 from the Chang Gung Memorial Hospital and University.

REFERENCES

1. Vokes EE, Liebowitz DN, Weichselbaum RR. Nasopharyngeal carcinoma. *Lancet.* 1997;350:1087–1091.
2. Chang JT, See LC, Tang SG, Lee SP, Wang CC, Hong JH. The role of brachytherapy in early stage nasopharyngeal carcinoma. *Int J Radiat Oncol Biol Phys.* 1996;36:1019–1024.
3. Lee N, Xia P, Quivey JM, et al. Intensity-modulated radiotherapy in the treatment of nasopharyngeal carcinoma: an update of the UCSF experience. *Int J Radiat Oncol Biol Phys.* 2002;53:12–22.
4. Oh JL, Vokes EE, Kies MS, et al. Induction chemotherapy followed by concomitant chemoradiotherapy in the treatment of locoregionally advanced nasopharyngeal cancer. *Ann Oncol.* 2003;14:564–569.
5. Teo PM, Kwan WH, Lee WY, Leung SF, Johnson PJ. Prognosticators determining survival subsequent to distant metastasis from nasopharyngeal carcinoma. *Cancer.* 1996;77:2423–2431.
6. Sham JST, Cheung YK, Chan FL, Choy D. Nasopharyngeal carcinoma: pattern of skeletal metastases. *Br J Radiol.* 1990;63:202–205.
7. King WWK, Ku PKM, Mok CO, Teo PML. Nasopharyngectomy in the treatment of recurrent nasopharyngeal carcinoma: a twelve-year experience. *Head Neck.* 2000;22:215–222.
8. Lee AWM, Law SCK, Foo W, et al. Retrospective analysis of patients with nasopharyngeal carcinoma treatment during 1976–1985: survival after local recurrence. *Int J Radiat Oncol Biol Phys.* 1993;26:773–782.
9. Vikram B, Mishra UB, Strong EW, Manolatos S. Patterns of failure in carcinoma of the nasopharynx: failure at distant sites. *Head Neck Surg.* 1986;8:276–279.
10. Lee AWM. Complication. In: Van Hasselt CA, Gibb AG, eds. *Nasopharyngeal Carcinoma.* Hong Kong: The Chinese University Press; 1991:221–234.
11. Lee AWM, Law SCK, Ng SH, et al. Retrospective analysis of nasopharyngeal carcinoma treated during 1976–1985: late complications following megavoltage irradiation. *Br J Radiol.* 1992;65:918–928.
12. Ng SH, Chang TC, Ko SF, et al. Nasopharyngeal carcinoma: MRI and CT assessment. *Neuroradiology.* 1997;39:741–746.
13. Ng SH, Chang TC, Ko SF, Wan YL, Tang LM, Chen WC. MRI in recurrent nasopharyngeal carcinoma. *Neuroradiology.* 1999;41:855–862.
14. Ng SH, Wan YL, Ko SF, Chang JT. MRI of nasopharyngeal carcinoma with emphasis on relationship to radiotherapy. *J Magn Reson Imaging.* 1998;8:327–336.
15. Kao CH, ChangLai SP, Chieng PU, Yen RF, Yen TC. Detection of recurrent or persistent nasopharyngeal carcinomas after radiotherapy with 18-fluoro-2-deoxyglucose positron emission tomography and comparison with computed tomography. *J Clin Oncol.* 1998;16:3550–3555.
16. Kao CH, Hsieh JF, Tsai SC, et al. Comparison of 18-fluoro-2-deoxyglucose positron emission tomography and computed tomography in detection of cervical lymph node metastases of nasopharyngeal carcinoma. *Ann Otol Rhinol Laryngol.* 2000;109:1130–1134.
17. Smith RJ, Karp JS, Muehllehner G, et al. Single transmission scans performed post-injection for quantitative whole body PET imaging. *IEEE Trans Nucl Sci.* 1997;44:1329–1335.
18. Meikle SR, Hutton BF, Bailey DL, Hooper PK, Fulham MJ. Accelerated EM reconstruction in total-body PET: potential for improving tumor detectability. *Phys Med Biol.* 1994;39:689–1704.
19. Anzai Y, Carroll WR, Quint DJ, et al. Recurrence of head and neck cancer after surgery or irradiation: prospective comparison of 2-deoxy-2-[F-18]fluoro-D-glucose PET and MR imaging diagnoses. *Radiology.* 1996;200:135–141.
20. American Joint Committee on Cancer. *AJCC Cancer Staging Manual.* 2nd–5th eds. Philadelphia, PA: Lippincott-Raven; 1983, 1988, 1992, and 1997.
21. Fandi A, Bachouchi M, Azli N, et al. Long-term disease-free survivors in metastatic undifferentiated carcinoma of nasopharyngeal type. *J Clin Oncol.* 2000;18:1324–1330.
22. Leung S, Cheung H, Teo P, Lam WW. Staging computed tomography of the thorax for nasopharyngeal carcinoma. *Head Neck.* 2000;22:369–372.
23. Diederich S, Wormanns D, Semik M, et al. Screening for early lung cancer with low-dose spiral CT: prevalence in 817 asymptomatic smokers. *Radiology.* 2002;222:773–781.
24. Antoch G, Vogt FM, Freudenberg LS, et al. Whole-body dual-modality PET/CT and whole body MRI for tumor staging in oncology. *JAMA.* 2003;290:3199–3206.
25. Kumar MB, Lu JJ, Loh KS, et al. Tailoring distant metastatic imaging for patients with clinically localized undifferentiated nasopharyngeal carcinoma. *Int J Radiat Oncol Biol Phys.* 2004;58:688–693.