Clinical implications of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography at delayed phase for diagnosis and prognosis of malignant pleural mesothelioma

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Received August 31, 2011; Accepted October 3, 2011

DOI: 10.3892/or.2011.1520

Abstract. Malignant pleural mesothelioma (MPM) has a poor prognosis, and conventional imaging modalities do not reflect the prognosis of MPM. In this study, the clinical significance of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography fusion imaging (^{18}F-FDG PET/CT) was evaluated for the differential diagnosis, staging and prognosis in MPM patients. Ninety patients who underwent ^{18}F-FDG PET/CT scanning due to a clinical diagnosis or suspicion of MPM prior to therapy were reviewed. Of 90 patients, 31 were pathologically diagnosed as MPM. Maximum standardized uptake values (SUVmax) were semi-quantitatively obtained from PET/CT 60 min (early phase) and 120 min (delayed phase) after injection of ^{18}F-FDG, and the clinicopathological correlations with the level of SUVmax obtained from PET/CT were examined. The survival curves of MPM patients were plotted according to the methods of Kaplan-Meier. The prognostic implications of the level of SUVmax were estimated by t-test. PET/CT scan showed intense abnormal FDG uptake (SUVmax >2.0) in the pleural lesions of all 31 MPM patients at delayed phase, while it showed abnormal FDG uptake in 30 (97%) patients at early phase. In all 31 MPM patients, the values of SUVmax at delayed phase were higher than those at the early phase. PET/CT also indicated metastasis in the lymph node in 7 patients (23%) and in the systemic lesions in 8 patients (26%) with MPM. Twenty-three MPM patients with high SUVmax, whose prognosis was apparent, showed significantly poorer prognosis in both early and delayed phase (respectively, p=0.03 and p=0.01, t-test). The results showed that ^{18}F-FDG PET/CT at delayed phase is very useful for the diagnosis of pleural diseases, and SUVmax on PET/CT in the delayed phase is a more reliable prognostic factor than that in the early phase. High uptake of ^{18}F-FDG PET/CT may be a predictive factor of prognosis in MPM patients.

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Key words: malignant pleural mesothelioma, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography fusion imaging, prognosis

Introduction

The most common cause of pleural effusion is nonspecific pneumonia which can be successfully treated with proper antibiotic therapy. However, pleural effusion may persist and require further examinations in some cases in spite of proper therapy. Computed tomography (CT) provides detailed information on morphological changes, but on its own cannot differentiate between benign and malignant diseases. Also, invasive procedures are frequently required for a definitive diagnosis (1). Many studies have reported the value of ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET), a modality for imaging of glucose metabolism in cancer cells, for evaluation of pleural lesions (2,3). Recently, integrated ^{18}F-FDG PET/computed tomography fusion imaging (^{18}F-FDG PET/CT) has been shown to be capable of visualizing the anatomical location of hypermetabolic cancer lesions more accurately than ^{18}F-FDG PET alone (4-6). ^{18}F-FDG PET/CT would thus be more informative for diagnosis of pleural diseases than examination with^{18}F-FDG PET (7).

The incidence of malignant pleural mesothelioma (MPM) in many countries including Japan is rising, as predicted (8,9),

Table I. Pathological diagnosis and PET/CT finding.

	SUVmax at PET/CT[a]	
	>2.0 (early/delayed phase)	<2.0 (early/delayed phase)
Pathological diagnosis		
MPM[b]	30/31	1/0
Non-MPM	7/7	52/52

[a]Maximum standardized uptake values determined by ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography. [b]Malignant pleural mesothelioma.

but treatments for MPM remain limited and controversial. Radical surgery or extrapleural pneumonectomy (EPP) have contributed to comfortable survival, and are mostly offered together with chemotherapy and radiotherapy (10,11). Only a small number of patients with MPM are deemed suitable candidates for multimodality therapy which includes chemotherapy, surgery and radiotherapy. The usefulness of PET/CT may be characterized as a direct biopsy of pleural lesions, assessing the extent of tumor involvement, and surveillance of recurrence after therapy (12). Only a few studies have suggested that the level of ^{18}F-FDG uptake in MPM is associated with prognostic values, while some studies have reported the relationship between prognosis and PET/CT (13-15).

In this study, we investigated whether quantitative ^{18}F-FDG-PET/CT imaging added useful information to conventional clinical variables in the diagnosis of MPM and predicted the prognosis. Also, we showed that PET/CT imaging at delayed phase is more informative about the diagnosis and the prognosis of MPM than that at the early phase.

Patients and methods

This study was performed with the patients' informed consent and with approval by the ethics committees of Tokorozawa PET Diagnostic Imaging Clinic and other facilities which cooperated in this study, and was conducted in accordance with the ethical principles of the Declaration of Helsinki. The authors have no financial or personal relationships with other people or organizations that could inappropriately influence this work.

Patients. Between August 2005 and July 2010, at Tokorozawa PET Diagnostic Imaging Clinic, 19,320 clinical ^{18}F-FDG PET/CT scans were performed on patients with various types of human cancer. Ninety patients who underwent ^{18}F-FDG PET/CT scan due to a clinical diagnosis or suspicion of MPM were reviewed before initial therapy during these 5 years. Twelve patients were pathologically diagnosed as MPM before PET/CT and 19 patients were pathologically diagnosed as MPM after PET/CT.

^{18}F-FDG PET/CT and quantification of ^{18}F-FDG uptake in MPM. All patients underwent ^{18}F-FDG PET/CT scans at Tokorozawa PET Diagnostic Imaging Clinic. Patients fasted for at least 6 h before the PET/CT study. ^{18}F-FDG PET/CT scans were obtained with a Biograph Duo (Siemens CTI), as described in our previous study (16,17). One hour after intravenous administration of 3.7 Mbq/kg ^{18}F-FDG, 90 sec of transmission scan using CT was performed for attenuation correction and anatomical imaging. To determine semi-quantitative FDG uptake, regions of interest (ROIs) were placed over the lesion, including the highest uptake area (circular ROI, 1 cm in diameter), and the standardized uptake value (SUV) was calculated as decay-corrected tissue activity divided by the injected dose per patient body. Whole body scans were obtained by PET/CT 60 min (early phase) and 120 min (delayed phase) after the injection of ^{18}F-FDG, and maximum SUV (SUV max) was semi-quantitatively calculated in the primary pleural lesion and metastatic lesions at both early and delayed phase.

Relationship between SUVmax and clinicopathological parameters. Clinicopathological correlation with the level of SUVmax obtained from PET/CT was examined in 31 MPM patients. The survival curves of MPM patients were plotted according to the methods of Kaplan-Meier. The prognostic implications of the level of SUVmax were estimated by t-test in MPM patients.

Results

Differential diagnosis. The study subjects, 90 patients who underwent ^{18}F-FDG PET/CT scan as a clinical diagnosis or suspicion of MPM, were reviewed before initial therapy and during a 5-year period (between August 2005 and July 2010). Twelve patients were pathologically diagnosed as MPM before PET/CT, and intense abnormal FDG uptake (SUVmax >2.0) was observed in the pleural lesions in 11 out of 12 MPM patients at early phase and all 12 patients at delayed phase (Figs. 1-3).

Nineteen patients were pathologically diagnosed as MPM after PET/CT. At delayed phase, PET/CT showed significant intense uptake (SUVmax >2.0) in the pleura of 26 out of 78 patients with suspicion of MPM, and 19 of those 26 patients were pathologically diagnosed as MPM after PET/CT (Table I). The remaining 7 patients were diagnosed as follows: 2 tuberculous pleuritis, 1 pleuritis carcinomatosa, 4 non-specific inflammatory diseases. All 52 patients with suspicion

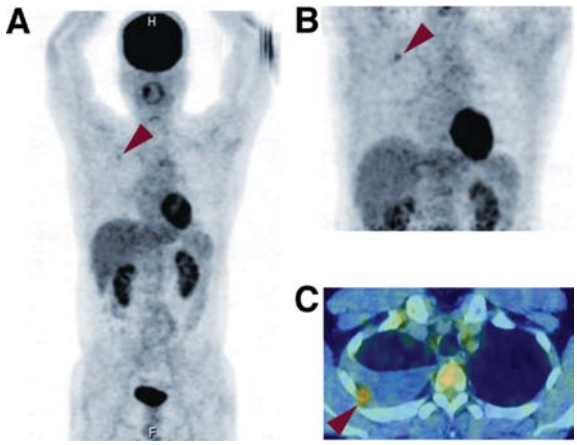

Figure 1. PET/CT findings of a localized MPM patient. Maximum intensity projection (MIP) PET imaging showed a faint level of abnormal FDG uptake (arrrowhead, SUVmax 2.7) in the right thorax at early phase (A) and more intense FDG uptake (SUVmax 3.0) at delayed phase (B). PET/CT showed intense FDG uptake in the right pleura with pleural effusion at delayed phase (C).

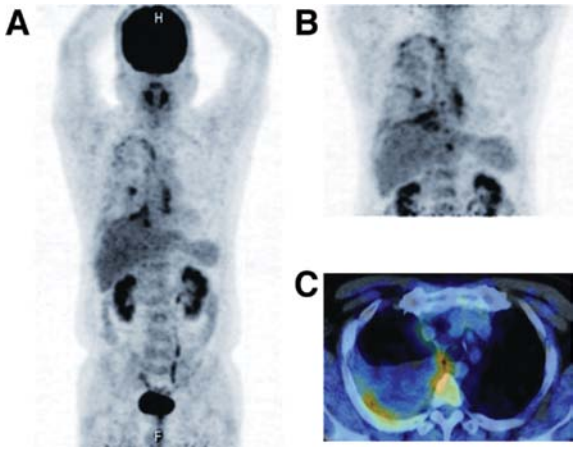

Figure 2. PET/CT findings of a typical MPM patient. MIP PET imaging showed an intense level of abnormal FDG uptake (SUVmax 5.1) in the right thorax at early phase (A) and more intense FDG uptake (SUVmax 5.4) with no metastasis at delayed phase (B). PET/CT showed diffuse FDG uptake in the right pleura with pleural effusion at delayed phase (C).

of MPM but who showed no significant FDG uptake by PET/CT were clinically and/or pathologically diagnosed with other diseases. The sensitivity at early phase and at delayed phase was 97 and 100%, respectively, while the specificity at early phase and at delayed phase was 88 and 88%, respectively.

Overall, PET/CT scan showed intense abnormal FDG uptake (SUVmax >2.0) in all 31 MPM patients at delayed phase and in 30 MPM patients (97%) at early phase.

Clinical findings in MPM patients. The thirty-one patients were 27 males and 4 females at mean age of 67 years (range: 47-79) (Table II). Pathological diagnosis of MPM was performed by biopsy (30 patients) and cytology (1 patient). Asbestos exposure was noted in 20 MPM patients, while no apparent asbestos exposure was noted in 11 patients. Twenty-five MPM patients were smokers or former smokers and the other 6 patients had never smoked.

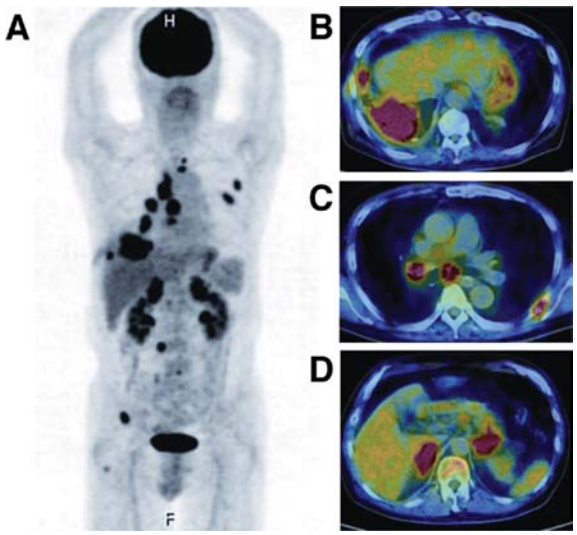

Figure 3. PET/CT findings of an advanced MPM patient. MIP PET imaging showed an intense level of abnormal FDG uptake in the right thorax (SUVmax 13.5) and other lesions at early phase (A). PET/CT showed very intense FDG uptake in the right pleural mass (B) with abnormal uptakes, suggesting metastasis to the lymph node and left rib (C), and metastasis to the bilateral aderenal glands (D).

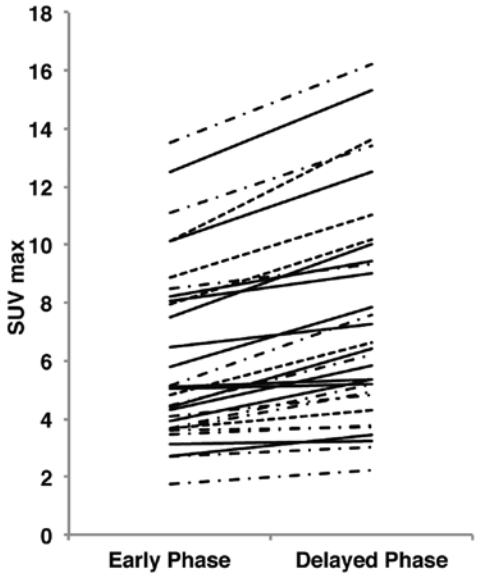

Figure 4. SUV max was determined by ^{18}F-FDG PET/CT. In all 31 MPM patients, the SUV max at delayed phase (2.2-16.2, mean: 7.5) was higher than that at early phase (1.7-13.5, mean: 6.1). Pathological subtype was epithelial type (14 cases, solid line), non-epithelial type (12 cases, broken line) and unknown (5 cases, dotted line).

^{18}F-FDG PET/CT findings in MPM patients. PET/CT scan showed intense abnormal FDG uptake (SUVmax >2.0) in the pleural lesions of all 31 MPM patients at delayed phase. In all 31 MPM patients, the SUVmax of delayed phase (2.2-16.2, mean: 7.5) was higher than that at the early phase (1.7-13.5, mean: 6.1) (Fig. 4). There was no significant relationship between SUVmax and clinical findings including age, gender, asbestos exposure and smoking. Localization of abnormal FDG uptake was noted in the right pleura in 20 patients and in the left pleura in 11. PET/CT scan also indicated metastasis in the lymph node in 7 patients (23%), and in systemic lesions

Table II. Patient characteristics.

Characteristics	
Total number of patients	(n=31)
Age	47-79 (mean: 67)
Gender	
Male	27
Female	4
Asbestos exposure	
Yes	20
No	11
Smoking status	
Yes	25
No	6
PET/CT findings	
Abnormal intense FDG uptake	(SUV max >2.0)
Early phase	
Yes	30
No	1
Delayed phase	
Yes	31
No	0
Localization	
Right	20
Left	11
Lymph node metastasis	
Yes	7
No	24
Systemic metastasis	
Yes (double count)	8
Lung	3
Bone	3
Adrenal gland	2
Muscle	1
No	23
Pathology	
Diagnostic method	
Biopsy	30
Cytology	1
Subtype	
Epithelioid	14
Sarcomatoid	4
Biphasic	6
Others	2
Unknown	5
Treatment (double count)	
Chemotherapy	19
Surgery	1
Radiation	0
[a]BSC	7
Unknown	5
Prognosis	
Alive	3
Death	20
Unknown	8

[a]Best supportive care.

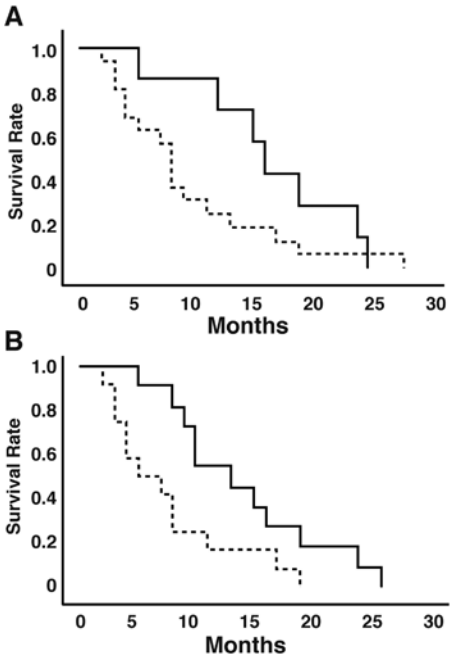

Figure 5. (A) The 16 patients (dotted line) who showed SUVmax values >3.65 had significantly poorer prognoses than the other 7 patients (solid line) with lower values in early phase PET/CT scan (p=0.03, t-test). (B) With delayed phase PET/CT scan, the 12 patients (dotted line) who had SUVmax values >6.0 had significantly poorer prognoses than the other 11 patients (solid line) with lower values (p=0.01, t-test).

including 3 cases of lung, 2 bone, 1 adrenal gland, 1 muscle and 1 bone plus adrenal gland in 8 patients (26%) with MPM. SUVmax of the primary lesion in the patients with lymph node metastasis was >4.45 at early phase and >6.18 at delayed phase. There was no significant difference in SUVmax of the primary lesion between the patients with lymph node metastasis and those without metastasis. SUVmax of the primary lesion in the patients with systemic metastasis was >3.61 at early phase and >4.82 at delayed phase. There was no significant difference in SUVmax of the primary lesion between the patients with systemic metastasis and those without metastasis. Not all but some metastatic lesions were confirmed by the pathological diagnosis.

Relationship between SUVmax and pathological subtype. The pathological features of the samples were classified according to the WHO histological criteria (18). The pathological subtypes of MPM were as follows: 14 epithelioid, 4 sarcomatoid, 6 biphasic, 2 variants and 5 unknown in detail. The SUVmax of 14 MPM patients with epithelioid subtype were 5.23±3.13 in early phase and 6.67±3.94 in delayed phase, respectively. The SUVmax value of 12 MPM patients with non-epithelioid subtype were 6.73±3.37 in early phase and 8.44±4.04 in delayed phases, respectively. The SUVmax value of 14 MPM patients with epithelioid subtype were lower than those of 12 patients with non-epithelioid subtype (4 sarcomatoid, 6 biphasic and 2 variants) in both early and delayed phase, but no significant difference was noted between these two groups.

Prognosis and SUVmax of PET/CT in MPM patients. Nineteen MPM patients were treated with chemotherapy (18 cisplatin and

pemetrexed, 1 cisplatin and gemcitabine hydrochloride), and only 1 of the 19 patients also underwent surgery. Seven patients were treated with best supportive care, no one was treated with irradiation, and 5 were unknown in detail. Twenty-three MPM patients, whose prognosis was apparent, were divided into two groups based on the SUVmax from PET/CT. The 16 patients with SUVmax >3.65 of had significantly poorer prognoses than the other 7 patients with lower values at the same phase of PET/CT scan (p=0.03, t-test, Fig. 5). The treatments for the high SUVmax group were 12 chemotherapy and 4 best supportive care, while those for the low SUVmax group were 1 surgery and chemotherapy combination, 4 chemotherapy only, and 2 best supportive care. There was no significant difference in therapy between these two groups. As for delayed-phase PET/CT scan, the 12 patients who has SUVmax >6.0 had significantly poorer prognoses than the other 11 patients with lower values (p=0.01, t-test). The treatments for the high SUVmax group were 9 chemotherapy and 3 best supportive care, while those for the low SUVmax group were 1 surgery and chemotherapy combination, 7 chemotherapy only, and 3 best supportive care. There was no significant difference with therapy between these two groups. However, more significant differences were noted at delayed phase of PET/CT in comparison to the early phase.

Discussion

Many studies have reported the value of ^{18}F-FDG PET in evaluating pleural lesions (2,3), and integrated ^{18}F-FDG PET/CT has been recently shown to be capable of visualizing the anatomical locations of cancer lesions more accurately than ^{18}F-FDG PET alone. Therefore, ^{18}F-FDG PET/CT would be more informative for diagnosis of pleural diseases than examination with^{18}F-FDG PET (7). Takeshima *et al* reported that the diagnostic accuracy for mesothelioma was 71.5% in a retrospective analysis of 328 Japanese MPM cases, and that it is very difficult to diagnose MPM accurately (9). The usefulness of PET/CT may be characterized as assessing the extent of tumor involvement of pleural lesions (12). PET/CT imaging also indicates the target of biopsy for patients in whom pleural effusion is noted by chest X-ray or CT scan. PET/CT scan is needed for an accurate pathological diagnosis of MPM. Yamamoto *et al* reported that although delayed SUV was significantly better than early SUV in MPM patients, the diagnostic performance with FDG PET at delayed phase was the same as that at the early phase (19). In our study, PET/CT at delayed phase showed intense abnormal FDG uptake in the pleura in all MPM patients with 100% sensitivity, while PET/CT at early phase showed no significant FDG uptakes in one of those MPM patients. This suggests that PET/CT at delayed phase provides more useful information for the differential diagnosis of pleural lesions than its conventional early phase. Some false positive were noted in this study, with 88% specificity, indicating a pitfall in the diagnosis of pleural lesion that PET/CT shows intense FDG uptake not only in MPM but also in inflammatory diseases and pleuritis carcinomatosa.

Our study showed that the SUVmax revealed by PET/CT at delayed phase was a more significant prognostic factor than that at the early phase. The prognostic value of tumor-node-metastasis (TNM) staging in MPM was not validated, since TNM staging may not accurately reflect the burden of disease in MPM. A small number of studies have suggested that the level of ^{18}F-FDG uptake in MPM is associated with prognostic values (13,20). Flores *et al* reported that SUVmax >10 was associated with poor prognosis (13). We found that semi-quantitative SUVmax (>3.65 at early phase and >6 at delayed phase) were associated with poor prognosis. In this study, most of the therapy was chemotherapy, and only one patient was treated in combination with surgical operation. Pemetrexates (Alimuta) was expected to improve the prognosis of MPM. Combination chemotherapy has led to modest survival improvements (21), while trimodal therapy with neoadjuvant pemetrexates plus cisplatin is feasible (22). More effective chemotherapy using new drugs will be required to improve the prognosis of MPM. ^{18}F-FDG PET/CT may be a good tool to evaluate the effectiveness of such new therapies for MPM (23).

Sarcomatoid histology is known to be an indicator of poor prognosis in MPM patients (24,25), but no significant difference in SUVmax was noted between epithelioid and other subtypes (including sarcomatoid) in this study. Nowak *et al* noted that FDG-PET parameters are more predictive of survival than tumor-node-metastasis staging in MPM patients with non-sarcomatoid disease (14). Randomized clinical trials in MPM should stratify patients by histology. However, most MPM patients do not have a pure sarcomatoid histology, and prognosis is also valuable for patients with non-sarcomatoid histology. Hence, the prognostic model needs to distinguish between those with good and poor prognosis. PET/CT may be a useful candidate to assess the prognosis of MPM patients with various histologies.

Some studies have reported the staging of MPM by ^{18}F-FDG-PET/CT, and Otsuka *et al* reported that PET/CT is useful for detecting distant metastasis and for evaluating activity in supraclavicular or abdominal lymph nodes (26). Sørensen *et al* showed that non-curative surgery is avoided in 29% out of 42 MPM patients by preoperative PET/CT (27). In this study, there was only one surgical case and the pathological diagnosis of metastasis was insufficient to evaluate the staging of MPM by PET/CT.

In conclusion, PET/CT at delayed phase provides more useful information for the differential diagnosis of pleural diseases. Moreover, a high uptake of ^{18}F-FDG PET/CT may be a predictive factor of prognosis in MPM patients, and SUVmax at delayed phase is a more reliable prognostic factor than that at the early phase.

Acknowledgements

We thank Mr. Kenji Kawai for excellent technical assistance.

References

1. Kramer H, Pieterman RM, Slebos DJ, Timens W, Vaalburg W, Koëter GH and Groen HJ: PET for the evaluation of pleural thickening observed on CT. J Nucl Med 45: 995-998, 2004.
2. Flores RM, Akhurst T, Gonen M, Larson SM and Rusch VW: Positron emission tomography defines metastatic disease but not locoregional disease in patients with malignant pleural mesothelioma. J Thorac Cardiovasc Surg 126: 11-16, 2003.
3. Schaffler GJ, Wolf G, Schoellnast H, Groell R, Maier A, Smolle-Jüttner FM, Woltsche M, Fasching G, Nicoletti R and Aigner RM: Non-small cell lung cancer: evaluation of pleural abnormalities on CT scans with 18F FDG PET. Radiology 231: 858-865, 2004.

4. Ueda S, Tsuda H, Asakawa H, Shigekawa T, Fukatsu K, Kondo N, Yamamoto M, Hama Y, Tamura K, Ishida J, Abe Y and Mochizuki H: Clinicopathological and prognostic relevance of uptake level using 18F-fluorodeoxyglucose positron emission tomography computed tomography fusion imaging (18F-FDG PET/CT) in primary breast cancer. Jpn J Clin Oncol 38: 250-258, 2008.
5. Weiler-Sagie M, Bushelev O, Epelbaum R, Dann EJ, Haim N, Avivi I, Ben-Barak A, Ben-Arie Y, Bar-Shalom R and Israel O: (18)F-FDG avidity in lymphoma readdressed: a study of 766 patients. J Nucl Med 51: 25-30, 2010.
6. Abe Y, Tamura K, Sakata I, Ishida J, Fukuba I, Matsuoka R, Shimizu S, Murakami H and Machida K: Usefulness of ^{18}F-FDG positron emission tomography/computed tomography for diagnosis of pyothorax-associated lymphoma: A report of three cases. Oncol Lett 1: 833-836, 2010.
7. Orki A, Akin O, Tasci AE, Ciftci H, Urek S, Falay O and Kutlu CA: The role of positron emission tomography/computed tomography in the diagnosis of pleural diseases. Thorac Cardiovasc Surg 57: 217-221, 2009.
8. Mak V, Davies E, Putcha V, Choodari-Oskooei B and Møller H: The epidemiology and treatment of mesothelioma in South East England 1985-2002. Thorax 63: 160-166, 2008.
9. Takeshima Y, Inai K, Amatya VJ, Gemba K, Aoe K, Fujimoto N, Kato K and Kishimoto T: Accuracy of pathological diagnosis of mesothelioma cases in Japan: clinicopathological analysis of 382 cases. Lung Cancer 66: 191-197, 2009.
10. Weder W, Kestenholz P, Taverna C, Bodis S, Lardinois D, Jerman M and Stahel RA: Neoadjuvant chemotherapy followed by extrapleural pneumonectomy in malignant pleural mesothelioma. J Clin Oncol 22: 3451-3457, 2004.
11. Flores RM: The role of PET in the surgical management of malignant pleural mesothelioma. Lung Cancer 49 (Suppl 1): 27-32, 2005.
12. Tan C, Barrington S, Rankin S, Landau D, Pilling J, Spicer J, Cane P and Lang-Lazdunski L: Role of integrated 18-fluorodeoxyglucose position emission tomography-computed tomography in patients surveillance after multimodality therapy of malignant pleural mesothelioma. J Thorac Oncol 5: 385-388, 2010.
13. Flores RM, Akhurst T, Gonen M, Zakowski M, Dycoco J, Larson SM and Rusch VW: Positron emission tomography predicts survival in malignant pleural mesothelioma. J Thorac Cardiovasc Surg 132: 763-768, 2006.
14. Nowak AK, Francis RJ, Phillips MJ, Millward MJ, van der Schaaf AA, Boucek J, Musk AW, McCoy MJ, Segal A, Robins P and Byrne MJ: A novel prognostic model for malignant mesothelioma incorporating quantitative FDG-PET imaging with clinical parameters. Clin Cancer Res 16: 2409-2417, 2010.
15. Gerbaudo VH, Mamede M, Trotman-Dickenson B, Hatabu H and Sugarbaker DJ: FDG PET/CT patterns of treatment failure of malignant pleural mesothelioma: relationship to histologic type, treatment algorithm, and survival. Eur J Nucl Med Mol Imaging 38: 810-821, 2011.
16. Abe Y, Tamura K, Sakata, I, Ishida J, Mukai M, Ohtaki M, Nakamura M and Machida K: Unique intense uptake demonstrated by ^{18}F-FDG positron emission tomography/computed tomography (PET/CT) in primary pancreatic lymphoma: A case report. Oncol Lett 1: 605-607, 2010.
17. Ozeki Y, Abe Y, Kita H, Tamura K, Sakata I, Ishida J and Machida K: A case of primary lung cancer lesion demonstrated by F-18 FDG positron emission tomography/computed tomography (PET/CT) one year after the detection of metastatic brain tumor. Oncol Lett 2: 621-623, 2011.
18. Travis WD, Brambilla E, Muller-Hermelink HK, *et al*: World Health Organization Classification of Tumours: Pathology and Genetics of Tumours of the Lung, Pleura, Thymus and Heart. IARC Press, Lyon, pp125-136, 2004.
19. Yamamoto Y, Kameyama R, Togami T, Kimura N, Ishikawa S, Yamamoto Y and Nishiyama Y: Dual time point FDG PET for evaluation of malignant pleural mesothelioma. Nucl Med Commun 30: 25-29, 2009.
20. Krug LM, Pass HI, Rusch VW, Kindler HL, Sugarbaker DJ, Rosenzweig KE, Flores R, Friedberg JS, Pisters K, Monberg M, Obasaju CK and Vogelzang NJ: Multicenter phase II trial of neoadjuvant pemetrexed plus cisplatin followed by extrapleural pneumonectomy and radiation for malignant pleural mesothelioma. J Clin Oncol 27: 3007-3013. 2009.
21. Vogelzang NJ, Rusthoven JJ, Symanowski J, Denham C, Kaukel E, Ruffie P, Gatzemeier U, Boyer M, Emri S, Manegold C, Niyikiza C and Paoletti P: Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma. J Clin Oncol 21: 2636-2644, 2003.
22. Lee HY, Hyun SH, Lee KS, Kim BT, Kim J, Shim YM, Ahn MJ, Kim TS, Yi CA and Chung MJ: Volume-based parameter of 18F-FDG PET/CT in malignant pleural mesothelioma: prediction of therapeutic response and prognostic implications. Ann Surg Oncol 17: 2787-2794, 2010.
23. Veit-Haibach P, Schaefer NG, Steinert HC, Soyka JD, Seifert B and Stahel RA: Combined FDG-PET/CT in response evaluation of malignant pleural mesothelioma. Lung Cancer 67: 311-317, 2010.
24. Edwards JG, Abrams KR, Leverment JN, Spyt TJ, Waller DA and O'Byrne KJ: Prognostic factors for malignant mesothelioma in 142 patients: validation of CALGB and EORTC prognostic scoring systems. Thorax 55: 731-735, 2000.
25. Fennell DA, Parmar A, Shamash J, Evans MT, Sheaff MT, Sylvester R, Dhaliwal K, Gower N, Steele J and Rudd R: Statistical validation of the EORTC prognostic model for malignant pleural mesothelioma based on three consecutive phase II trials. J Clin Oncol 23: 184-189, 2005.
26. Otsuka H, Terazawa K, Morita N, Otomi Y, Yamashita K and Nishitani H: Is FDG-PET/CT useful for managing malignant pleural mesothelioma? J Med Invest 56: 16-20, 2009.
27. Sørensen JB, Ravn J, Loft A, Brenøe J and Berthelsen AK; Nordic Mesothelioma Group: Preoperative staging of mesothelioma by 18F-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography fused imaging and mediastinoscopy compared to pathological findings after extrapleural pneumonectomy. Eur J Cardiothorac Surg 34: 1090-1096, 2008.