JBUON 2015; 20(2): 452-459
ISSN: 1107-0625, online ISSN: 2241-6293 • www.jbuon.com
E-mail: editorial_office@jbuon.com

ORIGINAL ARTICLE

Diagnosis of pancreatic cancer using ^{18}F-FDG PET/CT and CA19-9 with SUVmax association to clinical characteristics

Yunan Sun, Qiongyu Duan, Siliang Wang, Yuecan Zeng, Rong Wu
Department of Medical Oncology, Shengjing Hospital of China Medical University, Shenyang 110022, China.

Summary

Purpose: *To assess the ability of ^{18}F-FDG PET/CT alone or combined with CA19-9 to diagnose pancreatic cancer and to analyze the correlation between maximal standardized uptake value (SUVmax) and clinical characteristics.*

Methods: *Ninety-one patients diagnosed with pancreatic cancer using ^{18}F-FDG PET/CT before treatment were analyzed. Definite diagnosis was by histology or cytology. The SUVmax of the primary tumor was used for the statistical analysis and, using the best cutoff value, the patients were divided into 2 groups: a high SUVmax group (SUVmax>5.49) and a low SUVmax group (SUVmax≤5.49). Logistic regression analysis and receiver operating characteristic (ROC) analysis were applied to analyze the effects of SUVmax and/or CA19-9 on the diagnosis of pancreatic cancer.*

Results: *Of 91 patients, 80 had pancreatic cancer and 11 had benign conditions. The ROC curve analysis of the SUVmax yielded a best cutoff value of 5.49. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of ^{18}F-FDG PET/CT alone in the diagnosis of pancreatic cancer were 67.5, 72.73, 94.74, 23.53, and 68.13%, respectively, while these indices for ^{18}F-FDG PET/CT combined with CA19-9 increased to 96.25, 63.64, 95.06, 70, and 92.31%, respectively. The area under the curve (AUC) of the SUVmax combined with CA19-9 was 0.94, which was significantly higher than that of the SUVmax or CA19-9 alone ($p<0.05$). The SUVmax value and CA19-9 levels in pancreatic cancer patients were significantly higher than those with benign conditions ($p<0.05$). Only the SUVmax in the pancreatic cancer patient group was associated with tumor size ($p<0.05$).*

Conclusions: *^{18}F-FDG PET/CT is a common examination for diagnosing pancreatic cancer, and the SUVmax combined with the CA19-9 level can significantly improve the sensitivity and accuracy in the diagnosis of pancreatic cancer. SUVmax is merely indicative of the volume of pancreatic cancer.*

Key words: *CA19-9, diagnosis, ^{18}F-FDG PET/CT, pancreatic cancer, SUVmax*

Introduction

Pancreatic cancer accounts for only 2% of all tumors, but it is the fourth leading cause of tumor-related deaths [1]. The overall 5-year survival rate of pancreatic cancer is less than 5% [2]. Studies show that only 20% of affected patients undergo pancreatic cancer resection upon diagnosis, and 20% of these patients will survive for 5 years after surgery [2]. These low percentages are likely because by the time these patients present with clinical symptoms, more than 90% of them have already metastatic lesions [3]. Many prognostic factors for pancreatic cancer have been reported including age ≥65 years, physical status, increased fasting blood sugar, carbohydrate antigen 19-9 (CA19-9) level, carcinoembryonic antigen (CEA) level, tumor size, tumor location, grade of differentiation, vascular infiltration, venous infiltration, ascites cytology, lymph node metastasis, pancreatic intraglandular metastasis, distant metastasis, TNM stage, surgical margins, and ad-

Correspondence to: Rong Wu, MD, PhD. Department of Medical Oncology, Shengjing Hospital of China Medical University, 39 Huaxiang Road, Shenyang 110022, China. Tel: +86 24 96615-63211, Fax: +86 24 96615-63211, E-mail: wur@sj-hospital.org, 13709858148@163.com
Received: 10/10/2014; Accepted: 12/01/2014

juvant chemotherapy [2,4-9].

Positron emission tomography/computed tomography (PET/CT) is an important tool for tumor diagnosis, staging, treatment, and prognosis. ^{18}F-fluodeoxyglucose (FDG) PET/CT allows for ^{18}F-FDG uptake by lesions, which is closely correlated with tissue metabolism. Specifically, the metabolism of malignant cells becomes more active, indicating abnormal ^{18}F-FDG uptake [10]. SUVmax is the highest SUV measurement in the region-of-interest (ROI) and is the most commonly used value in clinical practice because it is least affected by partial volume effects [11]. The SUVmax measurement is the only non-invasive means for studying tumor biochemistry and metastasis [12]. To obtain an accurate diagnosis, in this study, we not only investigated the effect of SUVmax on the diagnosis of pancreatic cancer but also explored the diagnostic value of SUVmax and CA19-9. More importantly, we analyzed the correlation between SUVmax and the clinical characteristics in all the patients and in patients with pancreatic cancer. The clinical characteristics investigated included age, gender, fasting blood glucose, serum CA19-9 level, tumor location, tumor size, grade of differentiation, and clinical TNM stage.

Methods

General information from our hospital (January 2006-August 2013)

Ninety-one patients (56 male and 35 female) with suspected pancreatic cancer were retrospectively selected for analysis. All of the patients were evaluated using ^{18}F-FDG PET/CT before treatment. Serum CA19-9 levels and serum fasting blood glucose levels were also determined. The interval between the FDG-PET/CT evaluation and determining CA19-9 was no more than a week. The ^{18}F-FDG PET/CT images revealed pancreatic cancer with abnormal ^{18}F-FDG uptake in all of the patients. Benign pancreatic tumors included chronic pancreatitis, autoimmune pancreatitis, tuberculosis, benign cyst and benign acinar ductal epithelial cells. The final diagnosis depended on the pathological or cytological findings. Forty-eight patients who did not undergo contrast-enhanced CT/MRI or surgical resection were excluded from study, leaving 43 patients for study and analysis.

^{18}F-FDG PET/CT scanning and image analysis

Discovery ST 16 PET/CT (General Electric, USA, 2005) was used, with 16-slice multi-detector row CT scanner, with 120–140 kV and 160–240 mA. No intravenous contrast medium agents were used. The ^{18}F-FDG was synthesized by our hospital. The pH value range was controlled between 4.5 and 8.5, and the radiochemical purity was >98%. Patients fasted for at least 4 hrs before scanning, and fasting blood glucose levels were determined at less than 6.5 mmol/L. ^{18}F-FDG was injected via the cubital vein at a dosage of 5.55 MBq/kg. A pelvis to neck PET/CT imaging was conducted after 60±10 min of rest. The patient was instructed to breath slowly, and a mixture of milk and diatrizoate meglumine (10 ml/kg, diatrizoate meglumine titrated to a final concentration of approximately 1 g/100 ml) was consumed within 5 min. A total of 6±1 beds were scanned (each bed for 3 min at an interval of 25±5 min). Immediately following ingestion of milk and meglumine, a local pancreas area PET/CT scan (scanning 2 beds below the top of the diaphragm with 3D, each bed for 3 min) was performed using a Xeleris Functional Imaging Workstation (USA, 2006). The cross-sectional, sagittal, coronal, and fused images were obtained by the iterative reconstruction method after attenuation correction, with a slice thickness of 5 mm. The obtained fused images were read by 2 experienced radiologists. The images were assessed based on visual and semi-quantitative analyses.

Statistics

Using to the pathological results, the SUVmax cut-off value was calculated to distinguish between benign and malignant tumors. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the SUVmax and/or CA19-9 levels in the diagnosis of pancreatic cancer were analyzed using Cox logistic regression analysis and ROC analysis. The cut-off values of CA19-9 and CA19-9+SUVmax were used to calculate the diagnostic parameters. The Mann-Whitney nonparametric test was applied to compare the SUVmax differences in independent samples. Chi-square test and Fisher's exact test were used for the comparison of the frequencies between groups. Statistical analysis was performed using SPSS 19.0 software (SPSS Inc, Chicago, Ill, USA). MedCalc Statistical Package (MedCalc Software, Mariakerke, Belgium) was used to detect significant differences of the area under the ROC curve among different diagnostic methods. A p value of less than 0.05 was considered statistically significant.

Results

Demographic and baseline characteristics of the patients are shown in Table 1. Among the 91 patients, 80 (87.91%) were diagnosed with pancreatic cancer while 11 (12.09%) had benign tumors. The mean SUVmax value in the benign tumor patients was significantly lower than that in patients with cancer (4.91±0.64 vs 7.23±1.33, $p<0.05$). The CA19-9 levels in cancer patients were significantly higher than those in the benign tumor patients ($p<0.001$; Table 2). The sensitivity,

Table 1. Demographic and baseline characteristics of the patients

Characteristics	*Number of patients (N = 80)*	*%*
Age (years)		
Median (range)	56 (38-70)	
Sex		
Male	56	61.54
Female	35	38.46
Tumor size (cm)		
Median (range)	3.7 (1.0-11.1)	
Pathology		
Benign	11	12.09
Chronic pancreatitis	5	45.45
Tuberculosis	2	18.18
Autoimmune pancreatitis	2	18.18
Benign cyst	1	9.09
Benign acinar ductal epithelial cells	1	9.09
Malignant	80	87.91
Pancreatic duct adenocarcinoma	72	90.00
Pancreatic neuroendocrine carcinoma	4	5.00
Pancreatic mucinous carcinoma	2	2.50
Pancreatic adenosquamous carcinoma	1	1.25
Pancreatic carcinosarcoma	1	1.25
Histologic differentiation*		
Well (G1)	15	18.75
Moderate (G2)	50	62.50
Poor (G3)	15	18.75
Fasting blood glucose (mmol/L)		
≤ 6.11	55	60.44
> 6.11	36	39.56
CA19-9 (ng/ml)		
≤ 37	29	31.87
> 37	62	68.13
Tumor location		
Head	52	57.14
Body/tail	39	42.86
SUVmax		
Median (range)	6 (3-20.8)	
T stage		
T1-2	15	18.75
T3	61	76.25
T4	4	5.00
N stage		
N0	44	55.00
N1	36	45.00
M stage		
M0	42	52.50
M1	38	47.50

SUVmax: maximum standardized uptake value. * refers to UICC classification.

Table 2. SUVmax value and CA19-9 levels in benign and malignant tumor patients

Group	*SUVmax*	*CA19-9 (ng/ml)*
Benign tumor*	4.91 ± 0.64^{a}	23.48 ± 5.34^{c}
Malignant tumor	7.23 ± 1.33^{b}	801.70 ± 21.27^{d}

*comparison: a vs b, $p<0.05$; c vs d, $p<0.001$

specificity, positive predictive value, negative predictive value, and accuracy of CA19-9 in the diagnosis of pancreatic cancer were 75.00, 81.82, 96.77, 31.03, and 75.82%, respectively, and these indices for ^{18}F-FDG PET/CT were 67.50, 72.73, 94.74, 23.53, and 68.13%, respectively. These indices of ^{18}F-FDG PET/CT combined with CA19-9 increased to 96.25, 63.64, 95.06, 70, and 92.31%, respectively (Table 3).

ROC curve showed that the best cutoff value of SUVmax for distinguishing benign from malignant tumors was 5.49. The linear regression equation for SUVmax and CA19-9 was obtained by logistic regression analysis, as follows: y = -4.762 + 0.832 * SUVmax + 0.036 * CA19-9. The AUC of SUVmax combined with CA19-9 was larger than that of SUVmax or CA19-9 alone ($p<0.05$), but there was no significant difference regarding the AUC between CA19-9 and SUVmax taken separately ($p=0.30$; Figure 1, Table 3).

Using the best cutoff value, all patients were divided into 2 groups: high SUVmax group (SUVmax >5.49) and low SUVmax group (SUVmax ≤ 5.49). In all patients, the clinical and pathological features did not correlate with high SUVmax or low SUVmax (Table 4). In pancreatic cancer patients, tumor size was found to correlate with the SUVmax value ($p<0.05$; Table 5).

Discussion

The majority of pancreatic cancer patients die 2 within years after diagnosis [3], and only 4% of the affected patients survive for 5 years after diagnosis despite advancements in the diagnostic methods and treatment of this disease [13]. Tumor resection is the only curative method, but 80-85% of the patients develop postoperative metastatic disease [13]. Late presentation of clinical symptoms prevents early pancreatic cancer detection [13]. Therefore, it is extremely crucial to find alternative detection methods to make a timely diagnosis and staging and select appropriate treatment.

^{18}F-FDG PET/CT is often used for pancreatic cancer diagnosis, staging, efficacy evaluation, and re-staging. ^{18}F-FDG PET/CT can be used to assess the biological activity of pancreatic cancer, which

Table 3. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of SUVmax and/or CA19-9 for the diagnosis of pancreatic cancer

Item	*Area under the ROC curve (%), (95% CI)*	*Sensitivity (%)*	*Specificity (%)*	*Positive predictive value (%)*	*Negative predictive value (%)*	*Accuracy (%)*
CA19-9	85.7 (77.1-94.2)#	75.00	81.82	96.77	31.03	75.82
SUVmax	75.9 (63.3-88.4)#	67.50	72.73	94.74	23.53	68.13
CA19-9+SUVmax	94.0 (89.0-99.0)	96.25	63.64	95.06	70.00	92.31

#comparison with CA19-9 + SUVmax, p < 0.05; comparison between CA19-9 and SUVmax, p=0.30

Table 4. Correlation between clinical characteristics and SUVmax value in all patients

Clinical characteristics	*SUVmax*		*p value*
	> 5.49	*≤ 5.49*	
Age (years)			0.372
> 65	26	18	
≤ 65	32	15	
Gender			0.228
Male	33	23	
Female	25	10	
Fasting blood glucose (mmol/L)			0.638
> 6.11	34	21	
≤ 6.11	24	12	
CA19-9 (ng/ml)			0.478
> 37	38	24	
≤ 37	20	9	
Tumor location			0.089
Head	37	15	
Body/tail	21	18	
Tumor size (cm)			0.087
> 3	22	8	
≤ 3	6	7	

Table 5. Correlation between clinical characteristics and SUVmax value in pancreatic cancer patients

Clinical characteristics	*SUVmax*		*p value*
	> 5.49	*≤ 5.49*	
Age (years)			0.347
> 65	25	14	
≤ 65	29	12	
Gender			0.178
Male	30	18	
Female	24	8	
Fasting blood glucose (mmol/L)			0.454
> 6.11	33	17	
≤ 6.11	21	9	
CA19-9 (ng/ml)			0.210
> 37	37	23	
≤ 37	15	5	
Tumor location			0.241
Head	33	13	
Body/tail	21	13	
Tumor size (cm)			0.040
> 3	20	6	
≤ 3	5	7	
Pathological grade			0.836
High	11	5	
Moderate	32	17	
Poor	11	4	
T stage			0.194
T1-2	8	7	
T3-4	46	19	
Lymph node metastasis			0.737
N0	29	15	
N1	25	11	
Distant metastasis			0.471
M0	29	13	
M1	25	13	
One	8	3	0.429
Multiple	17	10	

indirectly predicts tumor invasiveness, detects tumor proliferation and prognosis, retains the spatial resolution of CT scans, and assists surgical strategy design [14]. The maximum tumor diameter and the SUVmax value are easily measured and have been widely used [15,16]. Increasing evidence documented that SUVmax is regarded as an indicator for the diagnosis of pancreatic cancer and evaluation of prognosis.

Investigation of PET is the current focus for diagnosis and staging of pancreatic cancer. Compared to CT and magnetic resonance (MR), PET has a better diagnostic value, which provides a sensitivity, specificity, positive predictive value, and negative predictive value of 85, 94, 94, and 85%, respectively [17]. Delbeke et al. [18] elucidated that FDG PET was more sensitive, specific, and accurate than CT, while Lemke et al. [19] found that FDG PET/CT enhanced the sensitivity of FDG PET. A meta-analysis showed that the sensitivity and specificity of PET for the diagnosis of

pancreatic cancer are 0.91 (95% CI: 0.88-0.93) and 0.81 (95% CI: 0.75-0.85), respectively [20]. These results suggest that PET is an effective means for diagnosing pancreatic cancer. Evidence from subsequent studies supported this conclusion [21,22]. Many authors summarized the SUVmax cutoff value to distinguish benign from malignant tumors [23-25]. However, the sensitivity of SUVmax in the diagnosis was relatively low in our study, possibly due to the high cutoff value of the SUVmax. To improve the diagnostic accuracy, we further analyzed SUVmax combined with CA19-9. The results of our study showed that the area under the ROC curve increased when SUVmax was combined with CA19-9 ($p<0.05$), and the sensitivity and accuracy were higher compared with SUVmax or CA19-9 alone, suggesting a better diagnostic value when the two tests are combined.

SUVmax values may overlap between benign and malignant tumors [26,27]. Regardless of benign and malignant solid pseudopaillary neoplasm of the pancreas, the SUVmax values were higher than 3, which makes it difficult to distinguish pancreatic cancer from neuroendocrine tumors [28]. Furthermore, malignant intraductal papillary-mucinous neoplasm of the pancreas has a significantly higher SUV than benign mucinous adenocarcinoma ($p=0.0011$) [29]. In this study, although SUVmax values overlapped, the SUVmax values measured were greater than 3 in all patients, showing significant differences between benign tumors and pancreatic cancer ($p<0.05$). This evidence suggested that PET/CT can provide some information for distinguishing benign from malignant pancreatic tumors, but the SUVmax cutoff value is not the only indicator for the diagnosis. Our findings were supported by Sampath et al. who demonstrated that FDG uptake was prone to malignant tumor diagnosis in suspected pancreatic cancer patients [25]. In addition, the same authors used the increase in FDG to diagnose ampullary and pancreatic cancer. In their study, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 93, 90, 95, 87, and 92%, respectively. However, when the SUVmax cutoff value was 2.8, the sensitivity and specificity reduced to 87.5 and 45%, respectively [25]. In contrast, Katsuhiko et al. did not find that FDG was elevated in pancreatic cancer and pancreatic masses but reported that the SUVmax at 1 hr was significantly higher in cases of pancreatic cancer than in pancreatitis [27]. Therefore, the changes in the SUVmax value at 1-2 hrs will help distinguish pancreatic cancer from mass-type pancreatitis. The SUVmax value was found to rise in 87% of pancreatic cancer patients during 1-2 hrs, while it decreased in the remaining 13% of patients. This value increased in 64% of mass-type pancreatitis patients, decreased in 27% patients after 1 hr, and remained unchanged in the remaining 9% of the patients during 1-2 hrs. The SUVmax values showed significant differences in pancreatic cancer patients at 1-2 hrs ($p=0.006$) compared with patients with focal pancreatitis ($p=0.312$) [27]. Nakamoto et al. demonstrated that the 2-hr SUVmax can be used to distinguish between benign and malignant pancreatic tumors [30]. However, delayed imaging data were not included in this study.

^{18}F-FDG PET/CT has some limitations in the diagnosis of pancreatic cancer. For example, FDG-PET/CT is poorly sensitive to lymph node metastasis [17] and generated false-negative results when the mass diameter was less than 1 cm [31]. FDG-PET failed to detect islet cell tumors with a diameter of 1.5-8mm [32] and liver/peritoneal metastatic tumor with a diameter of less than 1 cm [23]. Many authors suggest that the impact of PET analyses on staging needs further studies [17,20-22,33,34].

This study showed that SUVmax levels were associated with tumor size in pancreatic cancer patients, rather than other clinical characteristics and histological findings. Statistical analysis showed that SUVmax had no correlation with any clinical characteristics or pathological findings in any of the patients. Moon et al. obtained similar results, showing that the correlation of the SUVmax value and tumor size can be interpreted by the effect of tumor cellularity, although no GLUT-1 expression in pancreatic tumor cells was observed [15]. *In vitro* studies have shown that FDG uptake largely depended on the number of active tumor cells, rather than on the proliferative activity of tumor cells [35]. This evidence may explain our findings, but fundamental limitations remain since we are still unable to determine a positive correlation between tumor size and the number of active tumor cells or to account for differences between *in vitro* and *in vivo* samples. In addition to tumor invasion (>3 cm; $p<0.001$), high SUVmax values were significantly correlated with T stage in TNM staging system ($p=0.003$) and CA19-9 levels (>100 U/mL; $p=0.002$) [36]. SUVmax was also used in the TNM staging of pancreatic cancer and lymph node metastasis [37]. However, Choi et al. reported no association of SUVmax with clinical characteristics, grade of differentiation, overall sur-

vival and disease-free survival, or tumor size [2].

FDG uptake may be affected by blood glucose levels due to competitive inhibition [38]. In a study by Xu et al., blood glucose levels were less than 8 mmol/L in each patient undergoing a PET/CT examination. In addition, multivariate analysis showed that plasma glucose concentrations had no impact on the prognostic value of SUVmax [37]. Diabetes mellitus and blood glucose levels were not related to SUVmax values [10]. In our study, all the patients underwent ^{18}F-FDG PET/CT examination, and plasma glucose concentrations were <6.5 mmol/L. Fasting blood glucose on admission was only collected for statistical analysis, and elevated blood glucose was not correlated with the SUVmax value.

Neither the maximum tumor diameter nor the SUVmax value reflect tumor burden or tumor biology because SUVmax can be affected by many factors [39-41]. For example, tumor shape is diverse and asymmetric, and tumor cells, necrotic tissue, and fibrous scars interfere with ^{18}F-FDG uptake [15,16]. The exact volume of the tumor and metastatic lesions can be determined only after resection surgery. ^{18}F-FDG PET/CT is not sufficient to define the prognostic factors.

^{18}F-FDG PET/CT combined with CA19-9 is more expensive than CA19-9 alone. However, the combination yields significantly higher sensitivity and accuracy for the diagnosis of pancreatic cancer than ^{18}F-FDG PET/CT or CA19-9 alone. Speeding up diagnosis not only allows for the treatment to start much earlier and increases the chance of patients receiving effective treatment but also reduces the hospitalization time, which may reduce the patient's expenses and avoid unnecessary surgery costs. PET/CT significantly improves patient selection and is cost-effective [42]. In addition, compared with puncture and surgery, this non-invasive examination can reduce the patient's physiological pain, especially for those patients who have contraindications or refuse invasive examination. Moreover, patients with cancer need a comprehensive evaluation to assess distant metastases. ^{18}F-FDG PET/CT is capable of imaging the whole body [19], thus avoiding the time and money spent in itemized inspection. Therefore, the combination of ^{18}F-FDG PET/CT and CA19-9 is a cost-effective examination.

Nevertheless, our study has some limitations. First, this study is retrospective, involving a small sample size, and all patients were selected from our hospital. Second, the lymph node metastasis, distant metastasis, and clinical stage in some patients were determined based on the results of ^{18}F-FDG PET/CT imaging, thus affecting the accuracy of the experimental results. Therefore, a multi-center, large-sample prospective study is urgently needed to further evaluate the diagnostic and prognostic value of ^{18}F-FDG PET/CT.

Conclusions

This study demonstrated that both SUVmax and CA19-9 are effective in distinguishing between benign and malignant pancreatic tumors. The combination of the two methods improved the sensitivity and accuracy in the diagnosis of malignant tumors, and it is a cost-effective regimen. A high SUVmax value indicates malignancy, but it is not absolutely diagnostic.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (No. 81201803).

References

1. Faria SC, Tamm EP, Loyer EM et al. Diagnosis and staging of pancreatic tumors. Semin Roentgenol 2004;39:397-411.
2. Choi HJ, Kang CM, Lee WJ et al. Prognostic value of 18F-fluorodeoxyglucose positron emission tomography in patients with resectable pancreatic cancer. Yonsei Med J 2013;54:1377-1383.
3. Muniraj T, Jamidar PA, Aslanian HR. Pancreatic cancer: comprehensive review and update. Dis Mon 2013;9:368-402.
4. Lim JE, Chien MW, Earle CC. Prognostic factors following curative resection for pancreatic adenocarcinoma: a population-based, linked database analysis of 396 patients. Ann Surg 2003;237:74-85.
5. Sohn TA, Yeo CJ, Cameron JL et al. Resected adenocarcinoma of the pancreas – 616 patients: results, outcomes, and prognostic indicators. J Gastrointest Surg 2000;4:567-579.
6. Ueda M, Endo I, Nakashima M et al. Prognostic fac-

tors after resection of pancreatic cancer. World J Surg 2009;33:104-110.

7. Oguro S, Shimada K, Ino Y et al. Pancreatic intraglandular metastasis predicts poorer outcome in postoperative patients with pancreatic ductal carcinoma. Am J Surg Pathol 2013;37:1030-1038.
8. Wang DS, Wang ZQ, Zhang L et al. Are risk factors associated with outcomes in pancreatic cancer? PLoS One 2012;7:e41984.
9. Weber A, Kehl V, Mittermeyer T et al. Prognostic factors for survival in patients with unresectable pancreatic cancer. Pancreas 2010;39:1247-1253.
10. Moon SY, Joo KR, So YR, et al. Predictive value of maximum standardized uptake value (SUVmax) on 18F-FDG PET/CT in patients with locally advanced or metastatic pancreatic cancer. Clin Nucl Med 2013;38:778-783.
11. Ikushima H1, Dong L, Erasmus J et al. Predictive value of 18F-fluorodeoxyglucose uptake by positron emission tomography for non-small cell lung cancer patients treated with radical radiotherapy. J Radiat Res 2010;51:465-471.
12. Gambhir SS. Molecular imaging of cancer with positron emission tomography. Nat Rev Cancer 2002;2:683-693.
13. Vincent A, Herman J, Schulick R et al. Pancreatic cancer. Lancet 2011;13:607-620.
14. Lococo F1, Cesario A, Okami J et al. Role of combined 18F-FDG-PET/CT for predicting the WHO malignancy grade of thymic epithelial tumors: a multicenter analysis. Lung Cancer 2013;82:245-251.
15. Henson JW, Ulmer S, Harris GJ. Brain tumor imaging in clinical trials. AJNR Am J Neuroradiol 2008;29:419-424.
16. Sorensen AG, Patel S, Harmath C et al. Comparison of diameter and perimeter methods for tumor volume calculation. J Clin Oncol 2001;19:551-557.
17. Kauhanen SP, Komar G, Seppänen MP et al. A prospective diagnostic accuracy study of 18F fluorodeoxyglucose positron emission tomography/computed tomography, multidetector row computed tomography, and magnetic resonance imaging in primary diagnosis and staging of pancreatic cancer. Ann Surg 2009;250:957-963.
18. Delbeke D, Rose DM, Chapman WC et al. Optimal interpretation of FDG PET in the diagnosis, staging and management of pancreatic carcinoma. J Nucl Med 1999;40:1784-1791.
19. Lemke AJ, Niehues SM, Hosten N et al. Retrospective digital image fusion of multidetector CT and 18F-FDG PET: Clinical value in pancreatic lesions -A retrospective study with 104 patients. J Nucl Med 2004;45:1279-1286.
20. Wang Z, Chen JQ, Liu JL et al. FDG-PET in diagnosis, staging and prognosis of pancreatic carcinoma: a meta-analysis. World J Gastroenterol 2013;19:4808-4817.
21. Strobel K, Heinrich S, Bhure U et al. Contrast-enhanced 18FFDG PET/CT: 1-stop-shop imaging for assessing the resectability of pancreatic cancer. J Nucl Med 2008;49:1408-1413.
22. Wang X, Yu LJ. 18F-FDG PET/CT in detection of pancreatic cancer: Value of synthetic analysis interpretation. Zhongguo Yixue Yingxiang Jishu 2007;23:1709-1712.
23. Diederichs CG, Staib L, Vogel J et al. Values and limitations of 18F-fluorodeoxyglucose-positron-emission tomography with preoperative evaluation of patients with pancreatic masses. Pancreas 2000;20:109-116.
24. van Kouwen M, Jansen JB, van Goor H et al. FDG-PET is able to detect pancreatic carcinoma in chronic pancreatitis. Eur J Nucl Med Mol Imag 2005;32:399-404.
25. Santhosh S, Mittal BR, Bhasin D et al. Role of (18) F-fluorodeoxyglucose positron emission tomography/computed tomography in the characterization of pancreatic masses: experience from tropics. J Gastroenterol Hepatol 2013;28:255-261.
26. Asagi A, Ohta K, Nasu J et al. Utility of contrast-enhanced FDG-PET/CT in the clinical management of pancreatic cancer: impact on diagnosis, staging, evaluation of treatment response, and detection of recurrence. Pancreas 2013;42:11-19.
27. Kato K, Nihashi T, Ikeda M et al. Limited efficacy of (18)F-FDG PET/CT for differentiation between metastasis-free pancreatic cancer and mass-forming pancreatitis. Clin Nucl Med 2013;38:417-421.
28. Guan ZW, Xu BX, Wang RM et al. Hyper accumulation of (18)F-FDG in order to differentiate solid pseudopapillary tumors from adenocarcinomas and from neuroendocrine pancreatic tumors and review of the literature. Hell J Nucl Med 2013;16:97-102.
29. Tomimaru Y, Takeda Y, Tatsumi M et al. Utility of 2-[18F] fluoro-2-deoxy-D-glucose positron emission tomography in differential diagnosis of benign and malignant intraductal papillary-mucinous neoplasm of the pancreas. Oncol Rep 2010;24:613-620.
30. Nakamoto Y, Higashi T, Sakahara H et al. Delayed(18) F-fluoro-2-deoxy-D-glucose positron emission tomography scan for differentiation between malignant and benign lesions in the pancreas. Cancer 2000;89:2547-2554.
31. Delbeke D, Pinson CW. Pancreatic tumors: role of imaging in the diagnosis, staging, and treatment. J Hepatobiliary Pancreat Surg 2004;11:4-10.
32. Nakamoto Y, Higashi T, Sakahara H et al. Evaluation of pancreatic islet cell tumors by fluorine-18 fluorodeoxyglucose positron emission tomography: comparison with other modalities. Clin Nucl Med 2000;25:115-119.
33. Asagi A, Ohta K, Nasu J et al. Utility of contrast-enhanced FDG-PET/CT in the clinical management of pancreatic cancer: impact on diagnosis, staging, evaluation of treatment response, and detection of recurrence. Pancreas 2013;42:11-19.
34. Nakata B, Nishimura S, Ishikawa T et al. Prognostic and predictive value of 18F-fluorodeoxyglucose positron emission tomography for patients with pancreatic cancer. Int J Oncol 2001;19:53-58.
35. Higashi K, Clavo AC, Wahl RL. Does FDG uptake measure proliferative activity of human cancer cells? In vitro comparison with DNA flow cytometry and tritiated thymidine uptake. J Nucl Med 1993;34:414-419.

36. Mataki Y1, Shinchi H, Kurahara H et al. Clinical usefulness of FDG-PET for pancreatic cancer. Gan To Kagaku Ryoho 2009;36:2516-2520.
37. Xu HX, Chen T, Wang WQ et al. Metabolic tumor burden assessed by 18F-FDG PET/CT associated with serum CA19-9 predicts pancreatic cancer outcome after resection. Eur J Nucl Med Mol Imag 2014;41:1093-1102.
38. Lee SM, Kim TS, Lee JW et al. Improved prognostic value of standardized uptake value corrected for blood glucose level in pancreatic cancer using F-18 FDG PET. Clin Nucl Med 2011;36:331-336.
39. Liu L, Xu HX, Wang WQ et al. Cavin-1 is essential for the tumor-promoting effect of caveolin-1 and enhances its prognostic potency in pancreatic cancer. Oncogene 2013;22:2728-2736.
40. Boellaard R, Krak NC, Hoekstra OS et al. Effects of noise, image resolution, and ROI definition on the accuracy of standard uptake values: a simulation study. J Nucl Med 2004;45:1519-1527.
41. Westerterp M, Pruim J, Oyen W et al. Quantification of FDG PET studies using standardised uptake values in multi-centre trials: effects of image reconstruction, resolution and ROI definition parameters. Eur J Nucl Med Mol Imag 2007;34:392-404.
42. Heinrich S, Goerres GW, Schäfer M et al. Positron emission tomography/computed tomography influences on the management of resectable pancreatic cancer and its cost-effectiveness. Ann Surg 2005;242:235-243.