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TOPIC HIGHLIGHT

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Utility of PET/CT in diagnosis, staging, assessment of resectability and metabolic response of pancreatic cancer

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Abstract

Pancreatic cancer is one of the most common gastrointestinal tumors, with its incidence staying at a high level in both the United States and China. However, the overall 5-year survival rate of pancreatic cancer is still extremely low. Surgery remains the only potential chance for long-term survival. Early diagnosis and precise staging are crucial to make proper clinical decision for surgery candidates. Despite advances in diagnostic technology such as computed tomography (CT) and endoscopic ultrasound, diagnosis, staging and monitoring of the metabolic response remain a challenge for this devastating disease. Positron emission tomography/CT (PET/CT), a relatively novel modality, combines metabolic detection with anatomic information. It has been widely used in oncology and achieves good results in breast cancer, lung cancer and lymphoma. Its utilization in pancreatic cancer has also been widely accepted. However, the value of PET/CT in pancreatic disease is still controversial. Will PET/CT change the treatment strategy for potential surgery candidates? What kind of patients benefits most from this exam? In this review, we focus on the utility of PET/CT in diagnosis, staging, and assessment of resectability of pancreatic cancer. In addition, its ability to monitor metabolic response and recurrence after treatment will be emphasis of discussion. We hope to provide answers to the questions above, which clinicians care most about.

Key words: Position emission tomography/computed tomography; Pancreatic cancer; Diagnosis; Staging; Metabolic response

Core tip: Position emission tomography/computed tomography (PET/CT) is a useful modality in the detection of pancreatic cancer, while its use in staging is limited by the lack of enhanced CT scan and a relatively poor sensitivity in detecting metastatic lymph nodes. It has the advantage in monitoring metabolic response, making it optimal in evaluation of different kinds of treatment and also in detecting suspected recurrence. The correlation between Standardized Uptake Value and prognosis remains controversial. Many efforts have been made to improve the diagnostic efficacy of PET/CT.

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INTRODUCTION

Pancreatic cancer, one of the most common gastrointestinal tumors, remains a great threat to public health. In the United States, the estimated incidence of pancreatic cancer in 2013 ranks 10th for men and 9th for women. However, the estimated mortality ranked 4th for both sexes[1]. In China, from 1998 to 2007, the annual incidence for men and women showed an increase in both urban and rural area[2]. In 2009, pancreatic cancer incidence ranked 7th among all malignancies, with reported mortality ranking 6th[3]. The overall 5-year survival rate of pancreatic cancer is still extremely low, lesser than 5%[4,5]. Although surgery is a potential therapeutic method for long-term survival, the 5-year survival rate after radical resection fluctuates around 10%-29%[6-8].

To date, standard diagnostic workup for pancreatic cancer includes conventional imaging such as multi-detector computed tomography (MDCT), magnetic resonance imaging (MRI), endoscopic ultrasound (EUS), as well as invasive procedures such as EUS-guided fine-needle aspiration (EUS-FNA). MDCT remains the most widely used imaging modality for cancer staging. It makes the golden standard for local infiltration. However, missing of small liver metastasis has been reported[9]. Although MRI has been widely used for evaluation of pancreatic lesions, its overall value is controversial[10]. Recently, EUS has been more widely used in detection of clinically suspected pancreatic lesions. With FNA, it has been reported to be the most accurate imaging technique for pancreatic neoplasms[11,12]. However, Doppler ultrasonography including contrast enhancement also has limitations, such as blooming artifacts, poor spatial resolution, and low sensitivity (SE) to slow flow[13-15].

Increased glycolysis is a characteristic metabolic feature of malignant tumors[16]. Although many tracers have been introduced, ^{18}F-fluorodeoxyglucose (^{18}F-FDG), which aims to glucose metabolism, remains the most widely used one. After converted into ^{18}FDG-6-PO4, it does not continue along the glycolytic cycle and accumulates in cancer cells. Based on this principle, positron emotion tomography (PET) was introduced in 1976. However, the lack of precise anatomic information had limited its use. Since the combination of PET and CT in 1999[17], PET/CT had been widely applied in oncology. In this review, we focus on the utility of PET/CT in the diagnosis, staging, and assessment of resectability and metabolic response of pancreatic cancer.

PET/CT IN DIAGNOSIS OF PANCREATIC CANCER

PET has always been reported to be a highly sensitive and accurate method for detecting pancreatic cancer. The reported SE ranges from 78% to 95%, and accuracy from 64% to 91%[18-25]. The combination of PET and CT improves them to 85%-97%, and 85%-95%[26-32]. However, the specificity (SP) is relatively low and varies greatly among different studies, with 50%-87% for PET alone[18-25] and 61%-94% for PET/CT[26-32]. Several studies on utilization of PET/CT in diagnosis of pancreatic cancer are shown in Table 1. A meta-analysis conducted by Tang *et al*[33] showed a pooled SE of 90.1%, with an SP of 80.1%. Another meta-analysis by Wu *et al*[34] revealed similar results with a pooled SE of 87% and an SP of 83%. The possible reason for the relatively low SP may be misdiagnosis of mass forming pancreatitis as tumors on PET imaging.

The differential diagnosis between mass-forming pancreatitis and pancreatic carcinoma has always been a challenge. Long-term chronic inflammation will lead to rich fibrosis of pancreatic parenchyma which makes the lesion appear as a low density mass on CT with a weak or no enhancement[19]. The reported SE and SP of CT for differentiating chronic pancreatitis from cancer were 82%-94% and 83%-90%, respectively[35]. MRI showed similar results as CT, with the SE and SP of 93% and 87%, respectively[36].

^{18}FDG-PET was once thought to be the solution to this problem. Reske *et al*[37] reported that the overexpression of glucose transporter 1 was generally increased in pancreatic cancer but not in chronic pancreatitis, which revealed the possibility of diagnosing pancreatic cancer from mass-forming pancreatitis. Positive results were reached by Imdahl *et al*[38] in 1998 and by van Kouwen *et al*[19] in 2004 through prospective study. Detailed information of PET/CT in differential diagnosis of pancreatic carcinoma and mass-forming pancreatitis is showed in Table 2. However, value of FDG-PET/CT in differential diagnosis of pancreatic cancer from chronic pancreatitis is still controversial, as a consensus has not been reached on whether or when PET/CT should be applied.

FDG uptake caused by increased glycolytic activity has been shown in inflammatory cells such as neutrophils and activated macrophages[39,40]. Accordingly, FDG has been reported to accumulate in various inflammatory processes, including acute pancreatitis[41], auto-immune pancreatitis[42-45], tuberculosis[46,47], and mass-forming chronic pancreatitis. High ^{18}FDG-uptake by mass forming chronic pancreatitis has been also reported by many studies[27,48,49]. A recent study by Kato *et al*[50] indicated that differentiation between metastasis-free pancreatic cancer and mass-forming pancreatitis was difficult by FDG-PET/CT due to considerable overlapping between

Table 1 Position emission tomography/computed tomography in detection of malignant pancreatic tumors

Ref.	Study design	Maligancy/all (*n*)	SUV (max) of malignant lesions (mean ± SD)	SUV (max) of benign lesions (mean ± SD)	Cutoff value	SE	SP	PPV	NPV	LR(+)	LR(-)	Accuracy
Keogan *et al*[24]	R	25/37	5.4	1.4	-	88.00%	83.33%	91.67%	76.92%	5.28	0.144	86.49%
[1]Rose *et al*[23]	R	52/65	5.0 ± 1.2	0.85 ± 0.1	-	92.30%	84.62%	96.00%	73.33%	6	0.09	90.76%
[1]Delbeke *et al*[22]	R	52/65	5.1 ± 2.6	0.85 ± 1.7	3.0	92.30%	84.62%	96.00%	73.33%	6	0.09	90.76%
[2]Lemke *et al*[20]	R	64/100	-	-	3.5	84.37%	61.11%	79.41%	68.75%	2.17	0.26	76.00%
[1]Lytras *et al*[18]	R	72/112	-	-	-[3]	73.00%	60.00%	80.00%	49.00%	-	-	64.00%
Heinrich *et al*[32]	P	46/59	-	-	-	89.13%	69.23%	91.11%	64.29%	2.89	0.16	84.75%
Nishiyama *et al*[31]	R	55/86	5.75 ± 2.69	3.69 ± 1.58	3.5	89.09%	70.97%	84.48%	78.57%	3.07	0.15	82.56%
Bang *et al*[30]	R	93/102	5.1 ± 2.1	3.2 ± 1.8	-	96.77%	77.78%	97.82%	70.00%	4.35	0.04	95.09%
Kauhanen *et al*[29]	P	19/38	4.85 ± 2.77	2.25 ± 0.75	2.6	85.00%	94.44%	94.44%	85.00%	15.3	0.16	89.47%
Buchs *et al*[28]	R	36/45	6.5 ± 4.5	3.4 ± 3.1	-	72.00%	33.30%	80.00%	25.00%	-	-	64.00%
[4]Buchs *et al*[28]	R	36/45	6.5 ± 4.5	3.4 ± 3.1	-	96.00%	66.60%	92.30%	80.00%	-	-	90.30%
Santhosh *et al*[27]	R	57/87	8.64 ± 5.21	4.86 ± 4.54	2.8	96.36%	78.57%	94.64%	84.61%	4.49	0.05	92.75%
Hu *et al*[26]	R	54/80	6.3 ± 2.4	2.9 ± 2.0	3.5	96.29%	72.72%	89.65%	88.89%	3.53	0.05	89.47%

[1]Fluorodeoxyglucose-position emission tomography (FDG-PET) scan without computed tomography (CT); [2]Voxel-based retrospective registration and fusion of CT and PET were performed with software. PET imaging and CT were not taken at the same time; [3]Lesions measured visually; [4]Data obtained with extra scan of enhanced PET/CT. SE: Sensitivity; SP: Specificity; NPV: Negative predictive value; PPV: Positive predictive value; R: Retrospective study; P: Prospective study.

Table 2 Position emission tomography/computed tomography in differential diagnosis of pancreatic carcinoma and mass-forming pancreatitis

Ref.[1]	Study design	PC/CP	SUV(max) of PC (mean ± SD)	SUV(max) of CP (mean ± SD)	Cutoff value	SE	SP	PPV	NPV	LR(+)	LR(-)	Accuracy
Stollfuss *et al*[25]	R	43/30	3.16 ± 1.22	1.00 ± 0.55	1.53	93.18%	93.10%	95.35%	90.00%	13.51	0.07	93.15%
Mertz *et al*[21]	R	31/4	-	-	2.80	87.09%	50.00%	93.33%	33.33%	1.74	0.25	82.86%
van Kouwen *et al*[19]	R	32/77	-	-	-[2]	90.62%	87.01%	74.35%	95.71%	6.97	0.11	88.07%
Lytras *et al*[18]	R	54/25	-	-	-[3]	78.00%	55.00%	78.00%	55.00%	-	-	64.00%

[1]Fluorodeoxyglucose-position emission tomography (FDG-PET) scan without computed tomography (CT); [2]Results were judged to be abnormal if focal accumulation of the tracer was detected in the area of the pancreas. Faint and/or diffuse FDG uptake in the pancreatic region (*i.e.*, uptake slightly higher than the surrounding background, but clearly lower than the liver) was not considered suspicious for pancreatic cancer; [3]Lesions measured visually. SE: Sensitivity; SP: Specificity; NPV: Negative predictive value; PPV: Positive predictive value; R: Retrospective study; P: Prospective study.

the Standardized Uptake Value (SUVmax) values of these two diseases.

Dual-phase ^{18}FDG imaging has been supposed to improve diagnostic efficacy. Mean value of SUVdelayed was significantly higher than that of SUVearly ($P < 0.01$) in pancreatic cancer. In benign pancreatic disease, there was a tendency of decreased SUVdelayed compared to SUVearly, but there was no significant difference in the mean values. Retention index [RI = (SUVdelayed-SUVearly) × 100/SUVearly] had a diagnostic accuracy of 88% and an SE of 93% for suspected pancreatic cancer[31]. Recent studies[50] revealed that the ranges of SUV(max) for pancreatic cancer and mass forming pancreatitis were mostly overlapped.

^{18}FDG with enhanced CT was another attempt to improve diagnostic efficacy. In the study by Buchs *et al*[28], the statistical parameters of enhanced PET/CT surpassed those of unenhanced one, although none of them was of statistical significance (SE: 96% *vs* 72%, $P = 0.076$; SP: 66.6% *vs* 33.3%, $P = 0.52$; accuracy 90.3% *vs* 64%, $P = 0.085$).

PET/CT IN STAGING AND ASSESSMENT OF RESECTABILITY OF PANCREATIC CANCER

Precise pre-operative staging is crucial to make appropriate treatment decisions. Generally, resectability of pancreatic cancer concerns two problems: local tumor invasion of major vascular structures and distant metastasis. The ultimate goal is to save patient from unnecessary surgical exploration.

In most medical centers, an enhanced CT scan is not included in the routine PET scan. The plain CT is used for location only, thus limiting PET/CT's value in T staging. Wakabayashi *et al*[51] reported that FDG-PET without enhancement only detected 22.2% (2/9) of cases of invasion into the major arteries while CT found all 9 cases (100%). Strobel *et al*[52] reported using contrast-enhanced ^{18}F-FDG PET/CT to detect all five arterial infiltrations (100%/100%). However, PET and unenhanced PET/CT failed to detect arterial infiltration in all 5 cases

Table 3 ^{18}F-fluorodeoxyglucose-position emission tomography/computed tomography in N-staging and detection of liver metastasis of pancreatic cancer

Ref.	Study design	SE (%) (true positive/total positive)		
		PET/CT	CT	*P* value
N-staging				
Heinrich *et al*[32]	P	21.42 (3/14)	-	-
Maemura *et al*[59]	R	50.00 (3/6)	66.67 (4/6)	0.56
[1]Wakabayashi *et al*[51]	P	57.10 (8/14)	78.6 (11/14)	0.42
Kauhanen *et al*[29]	P	38	-	-
[1]Imai *et al*[60]	R	0 (0/6)	0 (0/6)	
Detection of liver metastasis				
Fröhlich *et al*[63]	R	68 (15/22)		
Mertz *et al*[21]	R	78 (7/9)	33.33 (3/9)	0.06
Lytras *et al*[18]	R	22	20	0.81
Heinrich *et al*[32]	P	81 (13/16)	56 (9/16)	0.22
Maemura *et al*[59]	R	37.5 (3/8)	87.5 (7/8)	0.04
Wakabayashi *et al*[51]	P	52.6 (10/19)	73.7 (14/19)	0.18
Farma *et al*[62]	R	61	57	
Strobel *et al*[52]	R	46 (5/11)		
Kauhanen *et al*[29]	P	88(6/7)	42.86 (3/7)	0.09

[1]^{18}F-fluorodeoxyglucose-position emission tomography (FDG-PET) scan without computed tomography (CT). SE: Sensitivity; SP: Specificity; NPV: Negative predictive value; PPV: Positive predictive value; R: Retrospective study; P: Prospective study.

(0%/100%).

Pancreatic carcinoma tends to transfer to lymph nodes at an early stage. In a study by the Japanese Pancreas Society (JPS), 306 of 822 TS1 (tumors < 2 cm in diameter) pancreatic cancer (37.2%) already had lymph node metastasis[53]. Kat'uchová *et al*[54] also reported that out of 319 histopathologically negative lymph nodes (34 patients), 134 lymph nodes were classified as immunohistochemically positive (21 patients). The detection of metastatic lymph nodes has always been a challenge. CT can only detect lymphadenopathy which may also be caused by inflammation. Lymph node size is not a reliable parameter for the evaluation of metastatic involvement[55]. FDG-PET/CT has reached good results in the N staging of non-small cell lung cancer, periorbital malignancies and nasopharyngeal carcinoma[56-58]. However, its utilization in pancreatic cancer is limited. The reported SE of FDG-PET/CT for detecting metastatic lymph nodes ranges from 21%-38%[20,29,32]. Maemura *et al*[59] reported an SE of 50% for para-aortic lymph node, while Imai *et al*[60] reported an SE of 0%. Detailed information is showed in Table 3. Lesions that smaller than 5 mm in diameter are hard to detect even for FDG-PET/CT. The low metabolic state and partial volume effect may be the reasons. Thus, it is improper to decide the necessity and range of lymphadenectomy based on FDG-PET/CT pre-operative N-staging results.

As a whole body exam, PET/CT possesses the unparalleled advantage in M staging. The reported SP is as high as 91%-100%. Strobel *et al*[52] reported an SE of 100% for detecting lung and bone metastases. Kitajima *et al*[61] reported three pancreatic cancer patients with ovarian metastases detected only by FDG-PET/CT. In the study by Strobel *et al*[52], unenhanced and enhanced PET/CT had accuracies of 60% and 80% for detecting peritoneal implantation. Farma *et al*[62] also reported two peritoneal metastases found by PET/CT alone. The particular SE for detecting liver metastasis, however, dropped to 22% to 88%[18,21,29,32,51,59,62,63]. The detailed information of studies focused on the detection of liver metastasis by FDG-PET/CT is showed in Table 3. One of the possible reasons may be that the detection of small liver metastatic lesions is limited by partial volume effects[64]. The high metabolic background of the liver may be another reason[56].

The overall influence of ^{18}F-FDG PET/CT on the management of pancreatic cancer has been widely studied. In early years, FDG-PET without CT did not perform well. Wakabayashi *et al*[51] reported that FDG-PET only surpassed CT in the detection of bone metastasis and concluded that PET did not perform precisely enough in staging of the disease. Since then, many studies revealed the capability of FDG-PET/CT to evaluate pre-operative staging by providing extra information. In the study conducted by Farma *et al*[62], 11% (7/82) of patients with invasive cancer had a change in their management, as PET/CT detected metastatic lesions that were not identified by the standard staging protocol in these patients. Bang *et al*[30] reported that ^{18}FDG-PET/CT changed the pretreatment stage in 26.9% (25/93) of patients with pancreatic ductal adenocarcinoma. More importantly, ^{18}FDG-PET/CT scanning resulted in a change in resectability status in 20 cases (21.5%). Although some investigators hold a negative opinion[29], PET/CT plays a critical role in changes in the management of pancreatic cancer[21,59,65,66].

PET/CT IN TUMOR RECURRENCE DETECTION AND METABOLIC RESPONSE MONITORING

Early detection of tumor recurrence and accurate postoperative staging are crucial for prescribing optimal individualized treatment[67,68]. Elevation of serum level of CA19-9 has been shown to be a sensitive indicator of recurrent pancreatic cancer but did not provide information about location of recurrence[69]. For patients who underwent surgery, PET/CT is able to detect recurrence early during the follow-up. Ruf *et al*[70] conducted a study including 31 patients with suspected recurrence after surgery. Among the 23 patients with local recurrence, the detection rate of FDG-PET was 96%, while that of CT/MRI was 39%. Among 12 liver metastases, the detection rate of FDG-PET was 42%, while that of CT/MRI was 92%. Other malignant abdominal lesions were detected by FDG-PET only. Similar results were reported by Sperti *et al*[71]. In their study, tumors recurred in 63 of 72 (87.5%) patients. Tumor relapse was detected by CT in 35 patients, while by FDG-PET in 61. FDG-PET influenced treatment strategies in 32 of 72 patients

(44.4%). The confirmation of recurrent pancreatic cancer in the remnant pancreas has also been reported by other researchers[72,73].

FDG-PET/CT's ability to detect the metabolic change before morphological changes has been proven by *in vivo* studies[74,75]. It has been successfully utilized in monitoring the metabolic changes during chemotherapy and/or radiation therapy. Chang *et al*[76] reported that PET-CT was a more effective method for evaluating tumor response than conventional CT after radiotherapy for unresectable pancreatic cancer. In another study[77], CT and FDG-PET were done before and after arterial infusion chemotherapy combined with external radiation therapy (ERT) for unresectable patients. CT could not reveal the actual location of the tumor before treatment in two cases. PET image showed high uptake in the pancreatic head before treatment and the significant decrease of SUV after treatment. In addition, FDG-PET image showed therapeutic effects 2 mo before changes appeared on CT images in another two cases. Heinrich *et al*[78] reported a significant SUV decrease (mean SUV from 4.4 to 3.0) that occurred during chemotherapy (P = 0.031) for locally advanced pancreatic cancer (LAPC). Their results were confirmed by many other studies[30,79-82]. With a wide approval in monitoring metabolic response, PET/CT now engages in clinical trials on novel drugs such as nab-paclitaxel[83].

PET/CT IN PREDICTION OF PROGNOSIS

Proliferation index is important for malignant potential in pancreatic cancer and neuroendocrine tumors (NETs). Buck *et al*[84] found that Ki-67 immunoreactivity enabled reliable differentiation between benign and malignant pancreatic tumors. The mean percentage of Ki-67 positive cells was approximately ten-fold higher in pancreatic cancer than in pancreatitis, indicating that proliferative activity is elevated strongly in the former but only slightly in the latter. However, no significant correlation was found between Ki-67 immunoreactivity and FDG uptake (P = 0.65). Their results accorded with *in vitro* results, which indicated no correlation between proliferative activity and FDG uptake in human cancer cells[85].

Whether ^{18}FDG PET is a prognostic factor for patients with pancreatic cancer is debatable. In a study by Sperti *et al*[86], SUV value of ^{18}FDG was calculated in 60 of the patients and divided into high (> 4) and low (≤ 4) groups. The median survival for patients with SUVs > 4.0 (n = 29) was 265 d *vs* 178 d for those with SUVs ≤ 4.0 (n = 31) (P = 0.005). Multivariate analysis showed that only stage (P = 0.001) and SUV (P = 0.0002) were independent predictors of survival. Similar results were obtained by Zimny *et al*[87] using a cutoff value of 6.1. Epelbaum *et al*[88] confirmed that global 18F-FDG influx (^{18}F-FDG INF) was the only significant variable for overall survival (OS) in patients with localized disease, independent of resectability.

Correlation between metabolic response on FDG-PET and prognosis is still controversial. Results varied greatly among various studies. Topkan *et al*[89] conducted a study including 32 unresectable LAPC patients treated with concurrent chemoradiotherapy. Median OS, progression-free survival (PFS), and local-regional PFS for those with greater (n = 16) *vs* lesser (n = 16) SUV (max) change were 17.0 mo *vs* 9.8 mo (P = 0.001), 8.4 mo *vs* 3.8 mo (P = 0.005), and 12.3 mo *vs* 6.9 mo (P = 0.02), respectively. On multivariate analysis, SUV (max) difference was predictive of OS, PFS, and LRPFS, independent of existing covariates. The great SUV decrease indicating better prognosis was also confirmed by several other studies[60,78,88]. On the contrary, Heinrich *et al*[78] revealed that significant SUV decrease occurred during chemotherapy was correlated with Ki-67 expression (P = 0.016), and histologic response (P = 0.01), while the metabolic response was not predictive of the median disease-free survival (P = 0.49) or OS (P = 0.43).

NEW DEVELOPMENTS AND PROSPECTS

The fusion of PET and MRI has shown more accurate localization of the FDG uptake in relation to the pancreatic ductal system[89,90]. Tatsumi *et al*[91] showed that the diagnostic accuracy was higher on PET/T1-w or PET/T2-w MRI (93.0 and 90.7%, respectively) than PET/CT (88.4%), although no statistical significance was obtained. Nagamachi *et al*[92] showed that FDG-PET/MRI fusion image, which provided more anatomic information, significantly improved accuracy compared with PET/CT (96.6% *vs* 86.6%). Dilatation of main pancreatic ducts was noted in 65.9 % of solid types and in 22.6% of cystic types on PET/MRI-T2 fusion images. Especially in cystic types, intra-tumor structures such as mural nodules (35.4%) and intra-cystic septum (74.2%) were also detected.

With regard that pancreas is located at a relatively greater distance from the diaphragm, respiratory gating procedure does not ameliorate the diagnostic assessment of primary tumors. Furthermore it could be useful to improve staging both in the liver and lung. In default of respiratory gating equipment, Kasuya *et al*[93] suggested that deep-inspiration breath-hold PET/CT technique seems feasible for accurate localization and improves the quantification of SUV. Further investigation is needed about the real application of these new procedures and protocols.

The finding of more tumor specific tracers is another major endeavor. The most widely reported ^{18}F-FET assesses proportion of cells undergoing active proliferation. von Forstner *et al*[94] demonstrated FLT uptake in Panc-TuI and BxPC-3 pancreatic cancer cell lines. However, the outcomes of clinical studies were controversial[95,96]. The hypoxia agent ^{18}F-FMISO, aimed at the hypoxic environment of pancreatic cancer, was compared with FDG by Segard *et al*[97]. In their study, only 2 pancreatic cancer patients demonstrated increased FMISO activity, while all ten patients showed FDG uptake. Mean FDG SUV (max) was 6 (range: 3.8-9.5) compared to 2.3 for

FMISO (range: 1-3.4). Other reported tracers included choline analogues (^{11}C-CHO, ^{18}F-dOC)[98] and ^{11}C-harmine[99]. The most recent pilot study used antibody like anti-CD147 monoclonal antibody[100] as a probe or even targeted mutant KRAS2 mRNA with ^{111}In-DOTAn-Poly(diamidopropanoyl)m-KRAS2 PNA-D(Cys-Ser-Lys-Cys) nanoparticles[101]. However, none of them is able to replace FDG at the time being. Further study in this field is still needed. Another kind of novel tracers worth noticing is somatostatin receptor (SSTR) tracers, like Yttrium-labelled peptides[102], which are used for imaging and peptide receptor-mediated radiotherapy for pancreatic NETs. Around 80% of enteropancreatic NETs express SSTRs, with some differences in different tumor types and even within the same tumor[103]. Recently, Putzer *et al*[104] reported ^{68}Ga-DOTA-TOC PET imaging to be an established imaging procedure for accurate staging for NET patients. ^{68}Ga-DOTA-TOC revealed more tumor sites than ^{68}Ga-DOTA-LAN. The tumor to background ratios for tumor and liver calculated from SUV(max) measurements were significantly higher for ^{68}Ga-DOTA-TOC than ^{68}Ga-DOTA-LAN ($P < 0.02$).

In conclusion, FDG-PET/CT is a useful modality for detection of pancreatic cancer. Its false positive findings in mass forming pancreatitis may lower its specificity. Its use in tumor staging is limited by the lack of enhanced CT scan and a relatively poor SE in detecting metastatic lymph nodes. However, for most of the time extra information about distant metastasis is vital enough to change clinical management. FDG-PET/CT has the advantage in monitoring metabolic response, making it optimal in evaluation of different kinds of treatments. It is also a valuable tool to detect suspected recurrence. The correlation between SUV and prognosis remains controversial. Many efforts have been made to improve diagnostic efficacy of PET/CT. Though the outcome is not sufficient today, more possibility may lay in the future.

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