

FDG-PET in diagnosis, staging and prognosis of pancreatic carcinoma: A meta-analysis

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Supported by Grant from The Natural Science Foundation of Guangxi Zhuang Autonomous Region of China, No. 0832113 and 2012GXNSFDA239001; and the Research Project of Guangxi Education Department, No. 201012MS062

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Received: March 6, 2013 Revised: May 2, 2013

Accepted: May 16, 2013

Published online: August 7, 2013

Abstract

AIM: To investigate the potential role of positron emission tomography (PET) in the diagnosis, staging and prognosis predicting of pancreatic carcinoma (PC).

METHODS: A systematic review of relevant literatures in PubMed, Embase and Cochrane Library was performed. The sensitivity and specificity of diagnostic and staging studies, and HRs for prognosis predicting studies were pooled. The bivariate model was used for diagnostic studies and the random-effect model for prognostic studies. Heterogeneity between included studies was tested using χ^2 test, and subgroup analysis was performed to explain the heterogeneities. All of the calculations were performed using Stata version 11.0.

RESULTS: A total of 39 studies were included. The pooled sensitivity of PET in diagnosing PC (30 studies, 1582 patients), evaluating N staging (4 studies, 101 patients) and liver metastasis (7 studies, 316 patients) were 0.91 (95%CI: 0.88-0.93), 0.64 (95%CI: 0.50-0.76), and 0.67 (95%CI: 0.52-0.79), respectively; and the corresponding specificity was 0.81 (95%CI: 0.75-0.85), 0.81 (95%CI: 0.25-0.85), and 0.96 (95%CI: 0.89-0.98), respectively. In prognosis analysis (6 studies, 198 patients), significant difference of overall survival was observed between high and low standardized uptake value groups (HR = 2.39, 95%CI: 1.57-3.63). Subgroup analysis showed that PET/CT was more sensitive than PET alone in evaluating liver metastasis of PC, 0.82 (95%CI: 0.48-0.98) and 0.67 (95%CI: 0.52-0.79), respectively.

CONCLUSION: PET can be used as a valuable diagnostic and predictive tool for PC, but its effect in the staging of PC remains indeterminate.

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Key words: Pancreatic carcinoma; Positron emission tomography; Diagnosis; Staging; Prognosis; Meta-analysis

Core tip: Positron emission tomography (PET) is an important tool for the diagnosis, staging and prognosis predicting of tumors. However, no consensus has been reached with regard to the role of PET in pancreatic carcinoma (PC) diagnosis. We performed meta-analysis of 39 included studies. The pooled results showed that PET can be used as a valuable diagnostic and predictive tool for PC, but its effect in the staging remains indeterminate. New tracers and PET scanning technology, as well as other parameters besides of standardized uptake value should be noticed in order to improve the diagnostic and predictive accuracy of PET in PC.

Wang Z, Chen JQ, Liu JL, Qin XG, Huang Y. FDG-PET in diagnosis, staging and prognosis of pancreatic carcinoma: A meta-analysis. *World J Gastroenterol* 2013; 19(29): 4808-4817 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v19/i29/4808.htm> DOI: <http://dx.doi.org/10.3748/wjg.v19.i29.4808>

INTRODUCTION

Pancreatic carcinoma (PC) is one of the leading causes of cancer death worldwide and is steadily increasing in incidence in most countries^[1]. In industrialized countries, the incidence of PC ranks second after colorectal cancer among all gastrointestinal malignancies^[1]. Despite recent significant advances in cancer diagnosis and treatment, the prognosis of PC remains extremely unfavorable with a reported 5-year survival rate of only 1%-10%^[2,3]. For PC, surgery remains the only curative treatment, and the success depends on the stage of disease at diagnosis, but not the histological type^[4]. Unfortunately, only 10%-15% of cancers are found to be resectable at the time of diagnosis for the late onset of the symptoms^[5]. Therefore, to choose the most appropriate treatment and to avoid unnecessary surgical risk, timely diagnosis and staging is essential in the evaluation of patients with PC.

Although significant advances have been achieved in diagnostic technologies such as computed tomography (CT), endoscopic ultrasonography (EUS) and magnetic resonance imaging (MRI), the preoperative diagnosis and staging of PC remains suboptimal, which restricts the treatment planning of this disease^[5]. The discrimination between inflammatory processes and PC, and the assessment of local resectability and distant metastases of the PC are still challenging with different imaging modalities^[6]. Over the years, positron emission tomography (PET) has played an important role in oncology, especially for diagnosis, staging, and for evaluating the response to treatment and the prognosis of tumors^[7]. However, there has been no consensus with regard to the role of PET in PC now. Some researchers held that PET could be used as a valuable measure in the diagnosis, staging and prognosis predicting of PC^[8]; but others did not find enough evidences to justify the use of PET in PC^[9]. Therefore, a systemic review aimed to evaluate the effect of PET in the diagnosis, staging and prognosis predicting of PC is urgently needed.

In this study, we assessed the pertinent literatures and conducted a meta-analysis to further investigate the potential role of PET in PC.

MATERIALS AND METHODS

Literature search

A systematic literature search was performed to identify studies assessing the effect of PET in the diagnosis, staging and prognosis predicting of PC. The PubMed, Embase and Cochrane Library databases were searched

with the MeSH headings ("pancreatic neoplasms" and "tomography emission computed") and keywords ("pancreas or pancreatic neoplasms" or "pancreatic tumor/tumour" or "pancreatic cancer" or "PC" or "cancer of the pancreas") and (PET or "diffusion" or "weighted imaging"). The upper limit of search date was not limited, and the lower limit was December 2012. The language was not limited. In addition, reference lists from the included studies were hand searched.

Inclusion and exclusion criteria

Inclusion criteria for this meta-analysis were: (1) Studies assessing the effect of PET in the diagnosis, staging and prognosis predicting of PC. The participants were clinically suspected of PC, and diagnosed with PC by histology or follow-up exceeding 6 mo; (2) For diagnosis and staging, the results were judged with histopathology or clinical follow-up exceeding 6 mo; (3) For diagnosis and staging, true-positive (TP), false-positive (FP), true-negative (TN), and false-negative (FN) results of imaging methods could be calculated for per-patient; for prognosis, HRs and their 95%CIs for overall survival (OS) data were available or able to be calculated from original articles; (4) For eligible studies with data published more than once, we only included the articles with the largest sample size of patients; and (5) PET was performed with intravenous administration of ¹⁸F-FDG.

Exclusion criteria for this meta-analysis were: (1) studies included patients with non-primary PC in staging or prognosis analysis (*e.g.*, metastatic cancer); (2) primary data were confounding and not able to be analyzed; (3) for staging, studies included patients who received radiotherapy or chemotherapy preoperatively, which may cause downstaging because neo-adjuvant protocols can lead to tumor downstaging and affect the diagnostic accuracy of imaging; (4) vitro studies and animal experiments; (5) Studies with a sample size less than 10; and (6) papers were not original research in type (*e.g.*, review articles).

Data extraction and quality assessment

Two authors extracted data using pre-defined tables, which included the following items: authors and publication time, country, study design, participants, sample size, quality score, and outcomes (TP, FP, TN and FN for diagnosis and staging analysis; HRs and their 95%CIs of OS for prognosis analysis). Follow-up period was recorded for prognosis analysis.

For diagnosis and staging, nine items of QUADAS closely related to this study were used to assess the methodological quality of eligible studies (the other five items of QUADAS were not related to this test)^[10]. For prognosis, four items (closely related to this study) from previous literatures were selected as the quality standard^[11]. Each item was described as Yes (high quality), Unclear, or No (low quality).

Statistical analysis

For diagnosis and staging analysis, the calculation was

based on max standardized uptake value (SUV), and pooled estimates of sensitivity and specificity of PET (with corresponding 95% CIs) were analyzed using the bivariate model^[12], which was considered as a more valid statistical model for diagnostic meta-analysis^[13,14]. The bivariate model uses a random effect approach for both sensitivity and specificity, which allows for heterogeneity beyond chance as a result of clinical and methodological differences between studies. To graphically present the results, we plotted the hierarchical summary receiver operating characteristic (HSROC) curves^[13]. As a concern for meta-analysis of diagnostic trials, publication bias was tested using the funnel plot and Deeks test^[15], which was conducted by a regression of diagnostic log OR against $1/\sqrt{\text{effective sample size}}$, weighting by effective sample size, with $P < 0.1$ for the slope coefficient indicating significant asymmetry.

For prognosis analysis, HRs and their CIs for OS were retrieved from each primary study. In case they were not directly reported in primary literatures, we derived them from the survival curves using published method^[16,17]. Kaplan-Meier curves of included studies were read by Engauge Digitizer version 2.11 (free software downloaded from <http://sourceforge.net>). HR calculation spreadsheet was freely downloaded from <http://www.trialsjournal.com/content/supplementary/1745-6215-8-16-s1.xls>. HRs for OS were pooled using a random-effect model.

Heterogeneity between included studies was tested using χ^2 test ($P < 0.1$ was considered significant). If heterogeneities were present, subgroup analysis was attempted to explain them.

All of the calculations were performed using Stata version 11.0. All P values were two-sided and all CIs had a two-sided probability coverage of 95%.

RESULTS

Study selection and description

According to the search strategy, a total of 629 papers were selected: 362 in PubMed, 216 in EMBASE, 37 in Cochrane Library and 14 by hand search. After browsing the titles and abstracts, we found that many studies were irrelevant and some were identified in more than one database; and 103 articles remained for potential inclusion and full texts were obtained. After screening the full text, 64 articles were excluded. The main reasons for exclusion were: nonclinical trials (such as review articles), repetitive publication, incomplete data, and inappropriate reference standard. At last, 39 studies were eligible for inclusion^[18-56]. The number of studies evaluating primary tumor diagnosis, N staging, liver metastasis and prognosis was 30^[18-21,25,32-56], 4^[18-21], 7^[19-25] and 6^[26-31], respectively. The study selection process is summarized in Figure 1. The characteristics of included studies are listed in Tables 1-4. And the quality of included studies is shown in Figure 2.

Meta-analysis

In the diagnosis of primary tumors, 30 studies (1582 patients) were eligible for meta-analysis^[18-21,25,32-56]. The

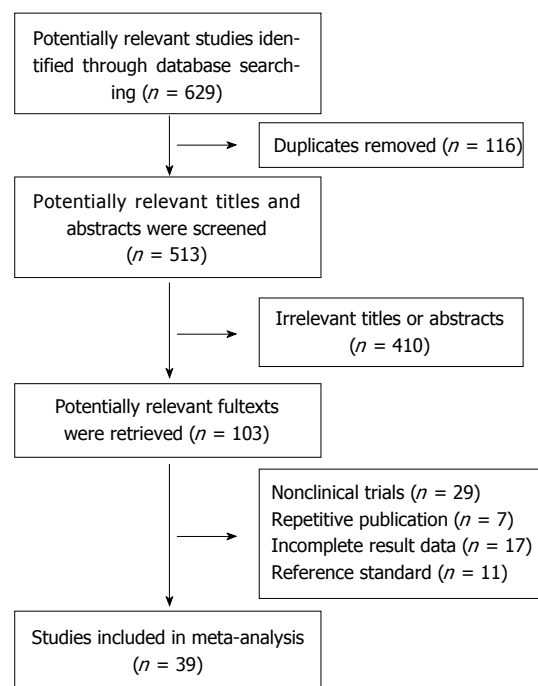


Figure 1 QUORUM flow chart for studies.

pooled sensitivity and specificity of PET in the diagnosis of PC were 0.91 (95%CI: 0.88-0.93) and 0.81 (95%CI: 0.75-0.85), respectively.

For lymph node metastasis, 4 studies (101 patients) were eligible for meta-analysis^[18-21]. The pooled sensitivity, specificity and negative predictive value of PET in the diagnosis of N staging were 0.64 (95%CI: 0.50-0.76), 0.81 (95%CI: 0.25-0.85), and 0.65 (95%CI: 0.28-0.90), respectively.

For liver metastasis, 7 studies (316 patients) were eligible for meta-analysis^[19-25]. The pooled sensitivity and specificity of PET in the diagnosis of liver metastasis were 0.67 (95%CI: 0.52-0.79) and 0.96 (95%CI: 0.89-0.98), respectively.

For predicting the prognosis, 6 studies (198 patients) were eligible for meta-analysis^[26-31]. In the study by Nakata *et al.*^[29], the data about resectable and unresectable tumors were reported separately. The pooled HR for OS was 2.39 (95%CI: 1.57-3.63), which suggested that patients in low SUV group had a significant longer OS than patients in high SUV group (Figure 3).

Subgroup analysis

The P values of heterogeneity test for the meta-analysis were all less than 0.1. Considering that the results might be influenced by the study design and imaging method, we performed subgroup analysis according to the design and imaging method of included studies. The results of subgroup analysis are listed in Table 5.

HSROC curves

We plotted HSROC curves to graphically present the results of diagnosis and staging (Figure 4). In HSROC curves, the index test's sensitivity (TP rate) was plotted on the y axis against 1-specificity (FN rate) on the x axis.

Table 1 Characteristics of included studies for diagnosis

Ref.	Study design	Imaging	Population	n (M/F)	Results			
					TP	FP	FN	TN
Stollfuss <i>et al</i> ^[32]	NR	PET	Suspected PC or CP	73 (54/19)	41	3	2	27
Wang <i>et al</i> ^[33]	NR	PET	Pancreatic mass	40 (27/13)	26	3	1	10
Rose <i>et al</i> ^[34]	R	PET	Suspected PC	65 (NR)	48	2	4	11
Kauhanen <i>et al</i> ^[18]	P	PET	Suspected PC	38 (19/19)	17	3	1	17
Herrmann <i>et al</i> ^[35]	P	PET	Suspected PC or CP	41 (27/14)	30	4	3	4
		PET/CT		31 (NR)	24	5	1	1
Nakamoto <i>et al</i> ^[36]	P	PET	Suspected PC	47 (31/16)	22	3	5	17
Friess <i>et al</i> ^[37]	P	PET	Suspected PC or CP	74 (57/17)	41	4	1	28
Keogan <i>et al</i> ^[38]	P	PET	Suspected PC	37 (22/15)	22	2	3	10
Koyama <i>et al</i> ^[39]	NR	PET	Suspected PC	86 (50/36)	53	4	12	17
Nishiyama <i>et al</i> ^[19]	NR	PET	Suspected PC	86 (64/22)	49	11	6	20
Inokuma <i>et al</i> ^[40]	P	PET	Suspected PC	46 (25/21)	33	2	2	9
Bares <i>et al</i> ^[20]	P	PET	Suspected PC	40 (25/15)	25	2	2	11
Van <i>et al</i> ^[41]	NR	PET	Suspected PC or CP	109 (65/44)	29	10	3	67
Zimny <i>et al</i> ^[42]	P	PET	Suspected PC	106 (NR)	63	5	11	27
Kato <i>et al</i> ^[43]	NR	PET	Patients with PC or CP	24 (20/4)	14	2	1	7
Ruf <i>et al</i> ^[21]	R	PET	Suspected PC	32 (20/12)	14	10	1	7
Rasmussen <i>et al</i> ^[44]	P	PET	Suspected PC	20 (12/8)	9	1	3	7
Delbeke <i>et al</i> ^[45]	R	PET	Suspected PC	65 (33/32)	52	3	0	10
Farma <i>et al</i> ^[46]	R	PET/CT	Suspected PC	82 (43/39)	58	2	7	15
Borbath ^[25]	R	PET	Suspected PC	59 (29/30)	42	5	6	6
Sendler <i>et al</i> ^[47]	P	PET	Suspected PC	42 (21/21)	22	4	9	7
Bang <i>et al</i> ^[48]	NR	PET	Suspected PC	102 (76/26)	90	2	3	7
Papós <i>et al</i> ^[49]	NR	PET	Suspected PC	22 (13/9)	6	2	0	14
Rajput <i>et al</i> ^[50]	R	PET	Suspected PC	11 (NR)	8	0	1	2
Ho <i>et al</i> ^[51]	NR	PET	Suspected PC	14 (7/7)	8	2	0	4
Mertz <i>et al</i> ^[52]	P	PET	Suspected PC	35 (NR)	27	2	4	2
Takanami <i>et al</i> ^[53]	R	PET/CT	Suspected PC	16 (13/3)	7	0	2	7
Sperti <i>et al</i> ^[54]	P	PET	Suspected PC	64 (33/31)	24	1	2	37
Tann <i>et al</i> ^[55]	R	PET	Suspected PC	30 (16/14)	4	8	3	15
		PET/CT		30 (16/14)	6	2	1	21
Bares <i>et al</i> ^[56]	NR	PET	Suspected PC	15 (11/4)	12	0	1	2

M: Male; F: Female; NR: Not report; R: Retrospective study; P: Prospective; PC: Pancreatic carcinoma; CP: Chronic pancreatitis; TP: True-positive; FP: False-positive; FN: False-negative; TN: True-negative; PET: Positron emission tomography; CT: Computed tomography.

Table 2 Characteristics of included studies for N staging

Ref.	Study design	Imaging method	Population	n (M/F)	Results			
					TP	FP	FN	TN
Kauhanen <i>et al</i> ^[18]	P	PET	Histologically proved PC	8 (NR)	2	0	5	1
Nishiyama <i>et al</i> ^[19]	NR	PET	PC diagnosed by histology or follow-up	55 (NR)	14	1	6	34
Bares <i>et al</i> ^[20]	P	PET	Histologically proved PC	23 (NR)	10	2	3	8
Ruf <i>et al</i> ^[21]	R	PET	PC diagnosed by histology or follow-up	15 (9/6)	8	2	5	0

M: Male; F: Female; NR: Not report; R: Retrospective study; P: Prospective; PC: Pancreatic carcinoma; TP: True-positive; FP: False-positive; FN: False-negative; TN: True-negative; PET: Positron emission tomography.

Additionally, the 95%CI and a 95% prediction region around the pooled estimates were plotted to illustrate the precision with which the pooled values were estimated (confidence ellipse of a mean) and to show the between-study variation (prediction ellipse; the likely range of values for a new study)^[13].

Publication bias

Because the included studies for staging and prognosis were too few (less than 10), we explored publication bias

using the data of PET/CT in the diagnosis of primary tumors, which included 30 studies. As a result, the funnel plot seemed symmetrical with a *P* value of 0.11, which suggested a low risk of publication bias (Figure 5).

DISCUSSION

In recent years, PET imaging has been increasingly used to identify and stage PC, and also utilized as a prognostic indicator. However, the value of PET in the management

Table 3 Characteristics of included studies for liver metastasis

Ref.	Study design	Imaging	Population	n (M/F)	Results			
					TP	FP	FN	TN
Strobel <i>et al</i> ^[22]	R	PET	Histologically proved PC	50 (25/25)	5	0	6	39
		PET/CT		50 (25/25)	9	1	2	38
Nakamoto <i>et al</i> ^[23]	NR	PET	Histologically proved PC	34 (22/12)	11	2	1	20
Nishiyama <i>et al</i> ^[24]	NR	PET	Histologically proved PC	42 (26/16)	10	3	3	26
Nishiyama <i>et al</i> ^[19]	NR	PET	PC diagnosed by histology or follow-up	55 (NR)	11	0	7	37
Bares <i>et al</i> ^[20]	P	PET	Histologically proved PC	23 (NR)	4	1	3	15
Ruf <i>et al</i> ^[21]	R	PET	PC diagnosed by histology or follow-up	15 (9/6)	3	2	5	5
Borbath <i>et al</i> ^[25]	R	PET	PC diagnosed by histology or follow-up	47 (NR)	10	1	2	34

M: Male; F: Female; NR: Not report; R: Retrospective study; P: Prospective; PC: Pancreatic carcinoma; TP: True-positive; FP: False-positive; FN: False-negative; TN: True-negative; PET: Positron emission tomography.

Table 4 Characteristics of included studies for prognosis

Ref.	Study design	Imaging method	Population	n (M/F)	Follow-up period	HR (95%CI)
Sperti <i>et al</i> ^[26]	R	PET	Histologically proved PC	60 (34/26)	NR	3.96 (1.92-8.17)
Maisey <i>et al</i> ^[27]	P	PET	Histologically proved PC	11 (7/4)	NR	3.4 (2.01-5.73)
Zimny <i>et al</i> ^[28]	NR	PET	Histologically proved PC	52 (33/19)	NR	2.27 (1.69-3.05)
Nakata <i>et al</i> ^[29]	NR	PET	Histologically proved PC	37 (21/16)	NR	0.93 (0.70, 1.25) ¹
Maemura <i>et al</i> ^[30]	NR	PET	PC diagnosed by histology or follow-up	24 (NR)	NR	4.9 (1.19-20.2) ²
Nakata <i>et al</i> ^[31]	NR	PET	Histologically proved PC	14 (NR)	6-17 mo	2.1 (1.5-2.92)

¹Patients received operation; ²Patients did not receive operation. M: Male; F: Female; NR: Not report; R: Retrospective study; P: Prospective; PC: Pancreatic carcinoma; PET: Positron emission tomography.

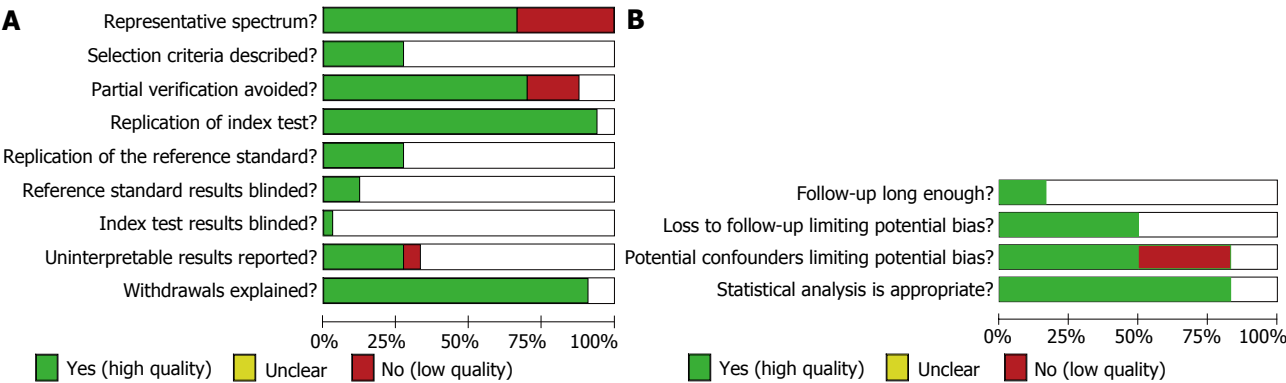


Figure 2 Methodological quality graph. A: Diagnosis and staging studies; B: Prognosis studies. Authors' judgments about each methodological quality item presented as percentages across all included studies.

of PC remains indeterminate. In our study, we collected existing data to assess the value of PET in the diagnosis, staging and prognosis predicting of PC. We found that PET could be used as a valuable diagnostic and predictive tool for PC; but for staging, PET has a moderate sensitivity and a relatively high specificity (Table 5).

Clinically, the diagnostic pathway for detection and staging of PC usually starts with abdominal ultrasound (US) followed by CT or MRI of the upper abdomen. However, even combined diagnostic approaches are limited by a low sensitivity for the detection of small lesions (a diameter of less than 2 cm) and for differentia-

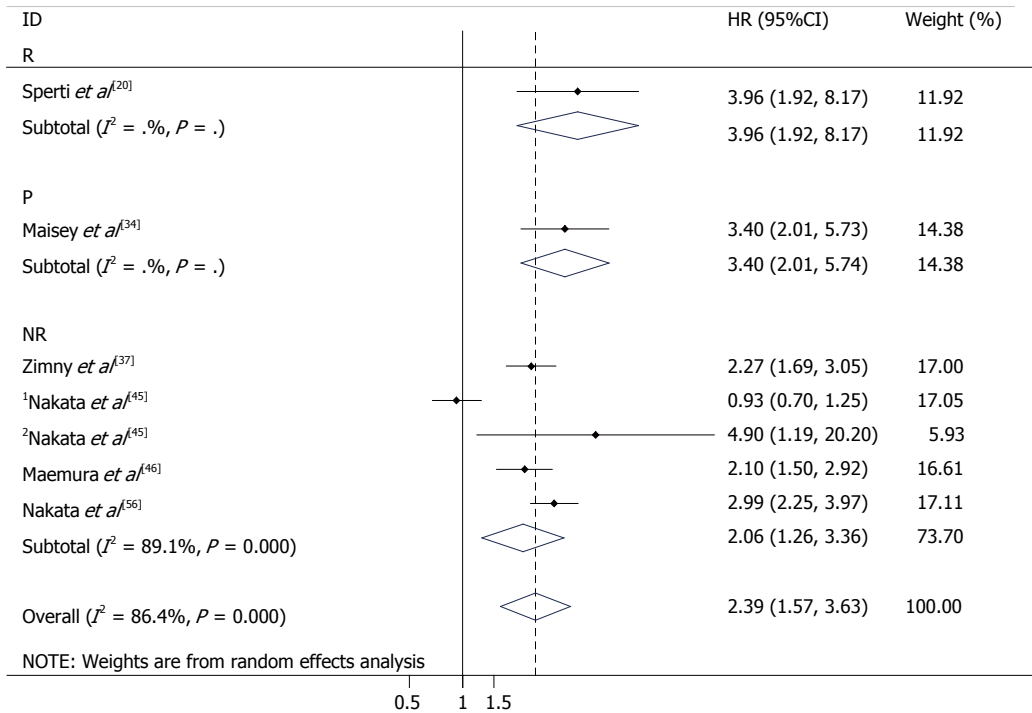


Figure 3 Forrest plot for the prognosis of pancreatic carcinoma. ¹Patients received operation; ²Patients did not receive operation.

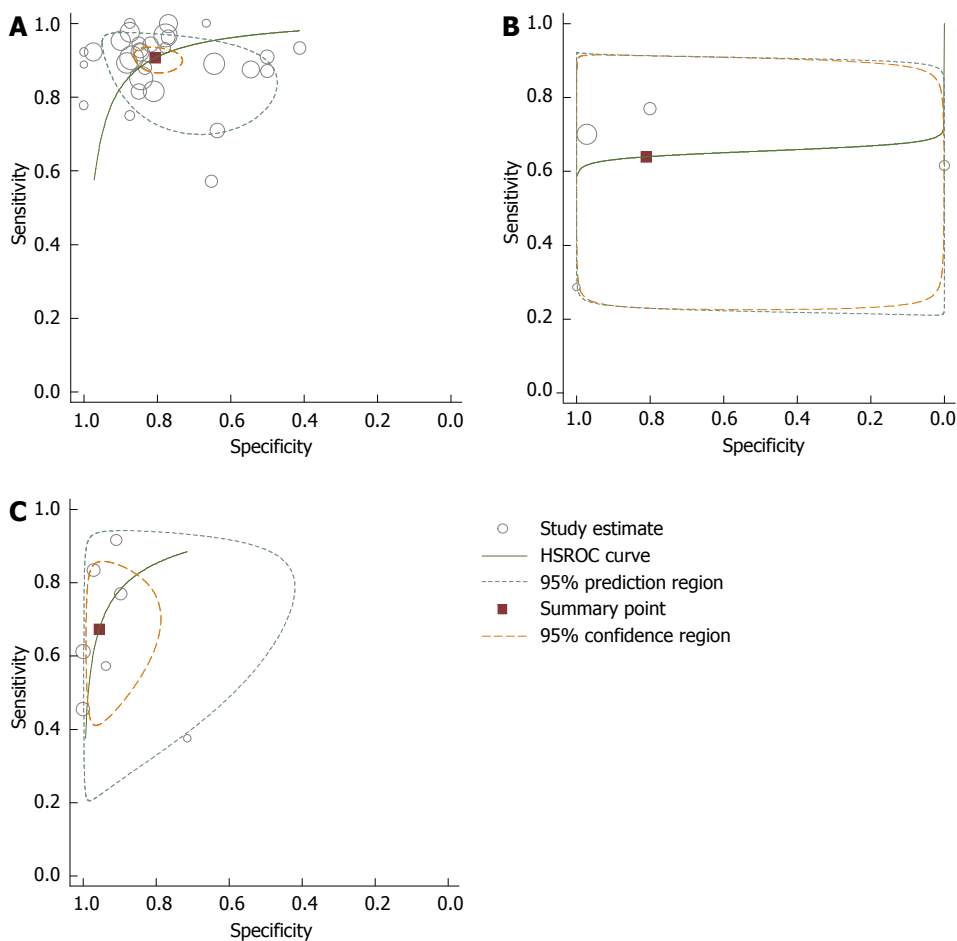


Figure 4 Hierarchical summary receiver operating characteristic curve. A: For the diagnosis of pancreatic carcinoma; B: For N staging of pancreatic carcinoma; C: For liver metastasis of pancreatic carcinoma. HSROC: Hierarchical summary receiver operating characteristic.

Table 5 Results of meta-analysis

Groups	Diagnosis		N staging			Liver metastasis		Prognosis HR (95%CI)
	Sen (95%CI)	Spe (95%CI)	Sen (95%CI)	Spe (95%CI)	Pv- (95%CI)	Sen (95%CI)	Spe (95%CI)	
Overall	0.91 (0.88-0.93)	0.81 (0.75-0.85)	0.64 (0.50-0.76)	0.81 (0.25-0.85)	0.65 (0.28-0.90)	0.67 (0.52-0.79)	0.96 (0.89-0.98)	
P subgroup	0.89 (0.84-0.92)	0.84 (0.76-0.89)	0.56 (0.15-0.90)	0.79 (0.48-0.94)	-	0.57 (0.21-0.88)	0.94 (0.68-0.99)	2.39 (1.57-3.63)
R subgroup	0.90 (0.83-0.95)	0.75 (0.58-0.87)	0.61 (0.32-0.85)	0.17 (0.04-0.81)	-	0.56 (0.28-0.81)	0.94 (0.65-0.99)	3.40 (2.01-5.74)
NR subgroup	0.93 (0.88-0.96)	0.82 (0.74-0.87)	0.70 (0.46-0.87)	0.97 (0.84-0.99)	-	0.74 (0.52-0.88)	0.92 (0.83-0.96)	3.96 (1.92-8.17)
PET subgroup	0.91 (0.88-0.93)	0.80 (0.74-0.85)	-	-	-	0.67 (0.52-0.79)	0.96 (0.89-0.98)	2.06 (1.26-3.36)
PET/CT subgroup	0.90 (0.79-0.95)	0.85 (0.38-0.98)	-	-	-	0.82 (0.48-0.98)	0.97 (0.87-1.00)	-

N: Lymph node; P: Prospective; R: Retrospective; NR: Not reporting; Sen: Sensitivity; Spe: Specificity; Pv-: Negative predictive value; PET: Positron emission tomography; CT: Computed tomography.

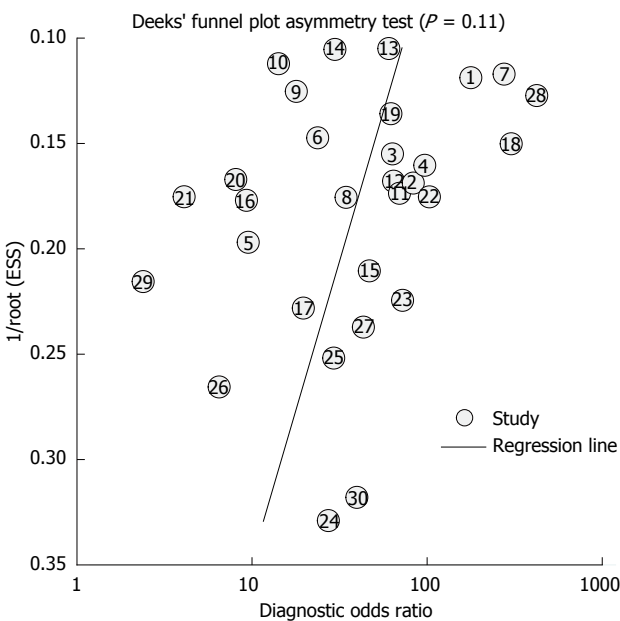


Figure 5 Funnel plot based on the data of positron emission tomography/computed tomography for the diagnosis of pancreatic carcinoma.

tion between malignant and benign lesions^[57]. Recently, promising results in the diagnostic value of PET as a diagnostic and staging tool in PC have been reported^[19-21]. In our review, we found PET had an acceptable sensitivity and specificity [sensitivity: 0.91 (95%CI: 0.88-0.93); specificity: 0.81 (95%CI: 0.75-0.85)] in the diagnosis of PC, which demonstrated that PET was valuable in the diagnosis of PC. This result was consistent with previous reports^[18,22,32,33]. Considering that diagnostic accuracy might be influenced by study design and the usage of CT, we conducted subgroup analysis. However, the other confounding factors (such as tumor diameter, serum glucose and C-reactive protein levels) were not considered because of incomplete data in included studies. This reduced the reliability of our results to some extent, although the impact of these factors on diagnostic accuracy is indeterminate^[19,34].

Because the only curative treatment for PC is surgery, accurate staging is necessary to properly select patients (surgical resection benefits only those patients with localized disease). Previous studies reported that both PET and CT were poor for N staging, although the diagnostic

accuracy of PET was a little higher than CT^[58]. This is consistent with our study (Table 5). As for liver metastasis, the value of PET is still controversial^[7]. In our study, we found a sensitivity of 0.67 (95%CI: 0.52-0.79) for PET in detecting liver metastasis of PC. This suggests that the value of PET in assessing liver metastasis of PC remains indeterminate, although it has a relatively high specificity [0.96 (95%CI: 0.89-0.98)]. Recently, studies found that combined PET/CT could improve detection rates in the staging of PC^[3]. In our study, we found that combined PET/CT was more sensitive than PET alone in assessing liver metastasis (82% *vs* 67%, Table 5), this confirmed the previous findings. Efforts have been made to improve the diagnostic accuracy of PET in PC. It has been found that delayed PET scanning helped differentiate malignant lesions from benign ones, and new tracers such as ¹⁸F fluorothymidine (FLT) could improve the diagnostic accuracy^[19,59]. However, these findings need to be further validated.

Patients with PC usually have extremely poor prognosis among gastrointestinal malignancies. With conventional imaging modalities, it is often difficult to predict the prognosis of patients with PC preoperatively. Recently, studies found that the metabolic activity of the pancreas tumor, measured by PET usually through SUV, seemed to be useful in evaluating the prognosis of PC^[29]. This result was consistent with ours, which suggested that patients with a higher SUV were associated with worse prognosis (HR = 2.39, 95%CI: 1.57-3.63). Additionally, the result did not change in the subgroup analysis (Table 5). This demonstrated that what we found was reliable. However, some researchers considered that the usage of SUV for prognostic assessment had some serious limitations (besides tumor characteristics, absolute value of SUV can also be influenced by several institution-dependent factors)^[60]. And they found that SUVmax difference (between pre- and post-treatment scans) or the usage of relative values (such as the retention index) allowed more accurate prognostic evaluation^[60,61]. Of course, more studies are needed to confirm these findings in the future.

In this study, we designed a systematic search strategy, selected studies according to the strict inclusion criteria, assessed the methodological quality using uniform criteria, and performed subgroup analysis in the presence of heterogeneity. Thirty-nine studies were included. These increased the reliability of the results to some extent.

However, several concerns must also be addressed when interpreting the pooled results. First, clinical follow-up was used as the reference standard in most of the included studies. Although the follow-up period was long enough, it might not correctly classify the target condition in some cases, which would affect the accuracy of the results. Second, some parameters (such as tumor diameter, glucose and C-reactive protein levels) which would affect the accuracy of the results were not considered in our study because of incomplete data, we failed to perform subgroup analysis or meta-regression, which might find out other possible causes of heterogeneity. Finally, publication bias was not tested because the few number of included studies in evaluating the staging and prognosis of PC may induce potential bias.

In conclusion, PET can be used as a valuable diagnostic and predictive tool for PC, but its effect in the staging of PC remains unclear. New tracers and PET scanning technology, as well as other parameters of PET besides SUV, should be noticed in order to improve the diagnostic and predictive accuracy of PET in PC.

COMMENTS

Background

Pancreatic carcinoma (PC) is one of the leading causes of cancer death worldwide and is steadily increasing in incidence in most countries. In industrialized countries, the incidence of PC ranks second after colorectal cancer among all gastrointestinal malignancies. Although significant advances have been achieved in diagnostic technologies, the preoperative diagnosis and staging of PC remains suboptimal.

Research frontiers

Over the years, positron emission tomography (PET) has played an important role in oncology, especially in the diagnosis, staging and prognosis prediction of tumors. However, there is no consensus with regard to the role of PET in PC now.

Innovations and breakthroughs

PET had an acceptable sensitivity and specificity [sensitivity: 0.91 (95%CI: 0.88-0.93); specificity: 0.81 (95%CI: 0.75-0.85)] in the diagnosis of PC. And higher standard uptake value measured by PET was associated with worse prognosis of PC patients (HR = 2.39, 95%CI: 1.57-3.63). However, the accuracy of PET in evaluating N staging and liver metastasis of PC was unsatisfied. This article gives them a comprehensive update based on previous studies.

Applications

PET can be used as a valuable diagnostic and predictive tool for PC, but its effect in the staging of PC remains indeterminate.

Peer review

Based on previous studies, this study evaluated the comprehensive role of PET in PC, including the diagnosis, staging and prognosis prediction. The authors found that PET can be used as a valuable diagnostic and predictive tool for PC, but its effect in the staging of PC remains indeterminate. The study is well designed, methodologically correct, elaborately prepared and full of significance in the field.

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ISSN 1007-9327

