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• 临床诊断 •

# FDG-PET/CT在胰腺癌诊断、分期及预后中作用的Meta分析

崔钢, 颜彬, 陶永光

**Effect of FDG-PET/CT in Diagnosis, Staging and Prognosis of Pancreatic Cancer: A Meta-analysis**

CUI Gang, YAN Bin, TAO Yongguang

Cancer Research Institute, Central South University, Changsha 410078, China

Corresponding Author: TAO Yongguang, E-mail: taoyong@csu.edu.cn



**Abstract: Objective** To assess the potential role of deoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) in the diagnosis, staging and prognosis of pancreatic cancer using Meta-analysis. **Methods** Computer-based retrieval was conducted on PubMed, Ovid, Cochrane Library, CNKI and VIP to search reports about diagnosis, staging and prognosis of pancreatic cancer, collected data and evaluated the quality based QUASAD. All calculations were performed by Meta-Disc software and Stata software. **Results** Studies related to diagnosis, staging and prognosis: 42 articles in total were finally included after deducting repeats. The pooled sensitivity of FDG-PET/CT in diagnosis pancreatic cancer, evaluating lymph node metastasis and distant metastasis were 0.93 (95%CI: 0.92-0.94), 0.65 (95%CI: 0.56-0.74) and 0.82 (95%CI: 0.71-0.90), respectively; and the corresponding specificity was 0.73 (95%CI: 0.70-0.76), 0.86 (95%CI: 0.79-0.91) and 0.95 (95%CI: 0.91-0.98), respectively. In prognosis analysis, significant difference of overall survival ( $HR_{pooled}=1.96$ , 95%CI: 1.52-2.52) and progress free survival ( $HR_{pooled}=2.26$ , 95%CI: 1.33-3.83) were both observed between high and low standardized uptake value groups. **Conclusion** FDG-PET/CT can be used as a valuable tool for diagnosis and prediction of overall survival for pancreatic cancer; however, the effect in the staging of pancreatic cancer was still indeterminate and to be further researched.

**Key words:** FDG-PET/CT; Pancreatic Cancer; Diagnosis; Staging; Prognosis; Meta-analysis

**摘要: 目的** 系统评价FDG-PET/CT在胰腺癌诊断、分期及预后预测中的作用。**方法** 对数据库PubMed、Ovid、Cochrane Library、CNKI和VIP进行计算机检索, 筛选相关文献后提取数据、根据QUADAS进行质量评估并采用Meta-Disc和Stata进行数据分析。**结果** 胰腺癌诊断、分期和预后相关文献共42篇纳入研究。Meta分析结果显示, FDG-PET/CT对胰腺癌的诊断、淋巴结转移和远期转移诊断敏感度<sub>合并</sub>和特异性<sub>合并</sub>分别为0.93 (95%CI: 0.92~0.94)、0.65 (95%CI: 0.56~0.74)和0.82 (95%CI: 0.71~0.90), 其对应的特异性<sub>合并</sub>分别为0.73 (95%CI: 0.70~0.76)、0.86 (95%CI: 0.79~0.91)和0.95 (95%CI: 0.91~0.98)。预后分析结果显示, 总生存期 ( $HR_{合并}=1.96$ , 95%CI: 1.52~2.52) 和无进展生存期 ( $HR_{合并}=2.26$ , 95%CI: 1.33~3.83) 在高低SUV<sub>max</sub>组间差异有统计学意义。**结论** FDG-PET/CT可作为胰腺癌诊断和总生存期预测分析的重要影像学工具, 但其在胰腺癌分期中的作用仍待进一步研究。

**关键词:** FDG-PET/CT; 胰腺癌; 诊断; 分期; 预后; Meta分析

中图分类号: R735.9 文献标识码: A

## 0 引言

胰腺癌作为世界五大恶性肿瘤之一<sup>[1]</sup>, 5年生存率不足10%, 手术作为目前唯一有效治疗方法可明显提高胰腺癌患者的5年生存率, 但这依赖于胰腺癌诊断和分期。不幸的是, 80%的胰腺癌患者

确诊时已失去手术价值<sup>[2]</sup>。因此, 为胰腺癌患者提供一个准确、敏感的诊断和分期工具至关重要。目前, 超声、CT和MRI是胰腺癌诊断和分期的主要影像学工具, 但其敏感度无法达到临床要求。FDG-PET/CT通过肿瘤高葡萄糖摄取率实现功能代谢和解剖结构同机融合, 被认为是一种具有高敏感度和特异性的影像学诊断方法。近年来关于FDG-PET/CT对胰腺癌的诊断研究较多, 结果不一致且样本量较少; 对于胰腺癌的分期和预后也无相关文献对其进行系统阐述。为此, 本文拟在已

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作者单位: 410078 长沙, 中南大学肿瘤研究所

通信作者: 陶永光, E-mail: taoyong@csu.edu.cn

作者简介: 崔钢 (1982-), 男, 硕士, 主治医师, 主要从事肿瘤影像学的研究

发表研究的基础上对FDG-PET/CT在胰腺癌诊断、分期和预后预测的作用进行Meta分析，为胰腺癌的临床诊治提供依据。

## 1 资料和方法

### 1.1 文献检索

通过计算机对数据库PubMed、Ovid、Cochrane Library、中国知网(CNKI)和维普中文科技期刊数据库(VIP)进行检索，并联合手工检索及参考文献追查。英文检索词为(“positron emission tomography/computed tomography” OR “PET/CT”) AND (“pancreatic cancer” OR “pancreatic neoplasms” OR “pancreatic tumor” OR “pancreatic carcinoma”)，中文检索词为正电子发射计算机断层显像、PET/CT、胰腺癌、胰腺肿瘤。检索年限为2000年1月至2016年1月。

### 1.2 文献选择标准

纳入标准：(1)文献为研究FDG-PET/CT对胰腺癌的诊断、分期和预后；(2)对于诊断和分期研究，根据组织学类型或临床随访进行诊断；(3)可直接获得或间接计算出研究指标。剔除标准：(1)病例报道、会议论文、动物实验或综述；(2)数据重复发表；(3)胰腺癌诊断中研究对象为非原发性胰腺癌，胰腺癌预后分析非首次确诊；(4)胰腺癌诊断研究样本量<20例。

### 1.3 资料提取和文献质量评价

在线检索的文献通过NoteExpress进行管理，由2名研究者独立阅读文献题目、摘要和全文，并根据纳入和排除标准进行文献筛选，对于不确定删除的文献通过2人甚至3人作最后商定。对纳入的文献根据预先制定的表格收集第一作者、发表年限、样本量、设计类型、诊断标准、最大SUV值(SUV<sub>max</sub>)等信息，并提取数据：真阳性(TP)、假阳性(FP)、假阴性(FN)和真阴性(TN)用于诊断和分期研究；风险率(HR)及95%置信区间(95%CI)用于预后分析。

根据QUADAS 14条标准就FDG-PET/CT对胰腺癌诊断和分期的文献进行质量评价；预后分析则根据第2、8、12和14条4条标准进行评价，并定义全“是”为“A”，出现一条及以上“不清楚”为“B”，出现一条及以上“否”为“C”。

### 1.4 统计学方法

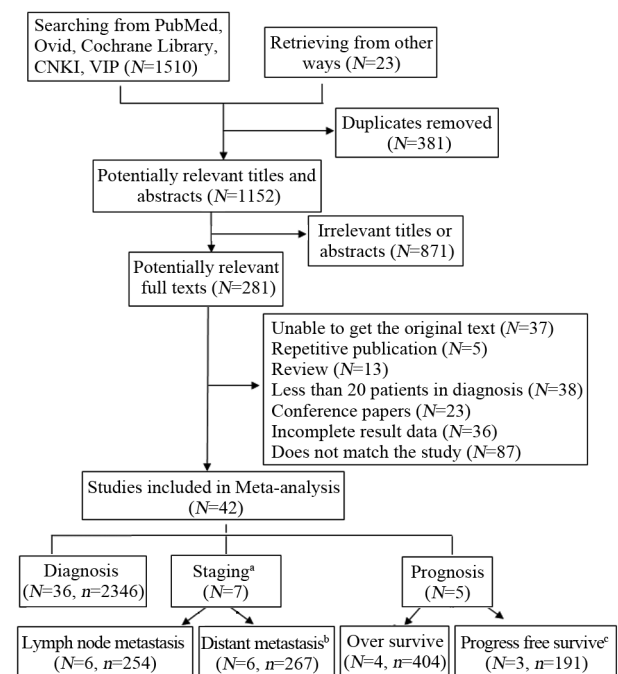
FDG-PET/CT对胰腺癌诊断和分期研究是根据文献中提取的TP、FP、FN和TN并采用Meta-Disc1.4软件对敏感度<sub>合并</sub>、特异性<sub>合并</sub>及其95%CI进

行计算。FDG-PET/CT对胰腺癌预后分析则根据文献提取的HR和95%CI采用Stata12.0对总生存期和无进展生存期HR<sub>合并</sub>进行计算。采用 $\chi^2$ 检验进行异质性检验，异质性指数( $I^2$ ) $\leq 50\%$ 时，认为异质性在可接受范围内。采用Stata12.0通过不对称性检验对纳入文献进行发表偏倚检验。

## 2 结果

### 2.1 文献检索结果

对五大数据库初步检索及通过其他来源补充检索后共获得1533篇文献；根据纳入和剔除标准最终纳入诊断研究36篇、分期研究7篇(其中6篇与诊断性研究重叠)、预后分析5篇，共计42篇。具体文献筛选流程见图1。



a: 6 articles overlap with diagnosis; b: 5 articles overlap with lymph node metastasis; c: 2 articles overlap with prediction of overall survival  
图1 筛选FDG-PET/CT对胰腺癌诊断、分期和预后的文献流程

Figure1 Flow chart for FDG-PET/CT in diagnosis, staging and prognosis of pancreatic cancer filtering

### 2.2 纳入研究的特征分析及数据提取

最终纳入的诊断研究36篇共2 346个研究样本中：出自中国的20篇，前瞻性研究8篇，依赖组织学检查进行确诊的18篇。根据QUADAS评价标准，文献质量评价A4篇、B11篇、C21篇。纳入分析的文献特征及数据提取结果见表1。

共纳入7篇FDG-PET/CT对胰腺癌分期的文献，其中淋巴结转移和远期转移各6篇，且两者均

表1 36篇被纳入的FDG-PET/CT对胰腺癌诊断性研究的文献特征

Table1 Characteristics of 36 included studies for FDG-PET/CT in diagnostic pancreatic cancer

First author	Year	Study design	Diagnostic criteria	Quality	Sample	TP	FP	FN	TN
Lemke <sup>[3]</sup>	2004	P	H	A	100	57	13	7	23
Heinrich <sup>[4]</sup>	2005	P	H	A	59	41	4	5	9
Maemura <sup>[5]</sup>	2006	R	H	B	33	26	1	4	2
Wang <sup>[6]</sup>	2006	R	H or F	C	32	24	2	2	4
Wang <sup>[7]</sup>	2007	R	H or F	C	40	26	3	1	10
Farma <sup>[8]</sup>	2008	R	H	C	82	58	2	7	15
Schick <sup>[9]</sup>	2008	P	H	B	46	24	5	3	14
Strobel <sup>[10]</sup>	2008	R	H	B	50	23	12	0	15
Kauhanen <sup>[11]</sup>	2009	P	H or F	A	38	17	1	3	17
Wei <sup>[12]</sup>	2009	R	H or F	C	46	23	3	3	17
Chi <sup>[13]</sup>	2010	R	H or F	C	61	48	3	0	10
Wang <sup>[14]</sup>	2010	R	H	B	67	49	6	4	8
Buchs <sup>[15]</sup>	2011	P	H	B	45	32	4	4	5
Guan <sup>[16]</sup>	2011	R	H or F	C	73	44	6	3	20
Xiao <sup>[17]</sup>	2011	R	H	B	87	72	4	2	9
Beliao <sup>[18]</sup>	2012	R	H	C	24	11	4	4	5
Gu <sup>[19]</sup>	2012	R	H or F	B	60	38	8	2	12
Herrmann <sup>[20]</sup>	2012	R	H or F	C	41	30	4	3	4
Yao <sup>[21]</sup>	2012	R	H or F	A	37	31	1	2	3
Zhang <sup>[22]</sup>	2012	R	H or F	C	94	66	11	2	15
Fang <sup>[23]</sup>	2013	R	H or F	C	41	24	5	2	10
Hu <sup>[24]</sup>	2013	P	H	C	80	50	6	4	20
Nagamachi <sup>[25]</sup>	2013	R	H or F	C	119	93	13	3	10
Pan <sup>[26]</sup>	2013	R	H	B	47	39	2	2	4
Santhosh <sup>[27]</sup>	2013	P	H	C	87	53	3	4	27
Yu <sup>[28]</sup>	2013	R	H	C	65	44	2	4	15
Ergul <sup>[29]</sup>	2014	R	H or F	C	52	33	2	0	17
Hamidian <sup>[30]</sup>	2014	R	H	C	161	73	9	10	69
Liu <sup>[31]</sup>	2014	R	H or F	C	112	66	14	8	24
Wang <sup>[32]</sup>	2014	R	H	C	92	76	4	6	6
Bian <sup>[33]</sup>	2015	R	H or F	C	70	34	4	1	31
Cheng <sup>[34]</sup>	2015	R	H or F	B	118	65	19	2	32
Kauhanen <sup>[35]</sup>	2015	P	H	B	31	6	4	0	21
Su <sup>[36]</sup>	2015	R	H or F	C	51	38	4	1	8
Tang <sup>[37]</sup>	2015	R	H or F	C	35	20	2	1	12
Zhang <sup>[38]</sup>	2015	R	H	B	70	46	7	4	13

Notes: P: prospective study; R: retrospective study; H: histology; F: follow up; TP: true positive; FP: false positive; FN: false negative; TN: true negative

分别有2篇前瞻性研究和3篇出自中国。关于淋巴结转移诊断文献质量：A2篇、B1篇、C3篇；关于远期转移诊断：A、B、C各2篇。纳入分期诊断研究的文献特征和数据提取结果见表2。

在FDG-PET/CT显像中根据SUV<sub>max</sub>对胰腺癌患者总生存期HR和无进展生存期HR进行预测的Meta分析共纳入文献5篇，其中总生存期HR4篇，无进展生存期HR3篇，两类研究中均有1篇前瞻性设计、2篇研究来自中国、2篇文献质量为B。被纳入预后预测研究的相关文献特征及数据提取见表3。

2.3 数据分析结果

表2 7篇被纳入的FDG-PET/CT对胰腺癌淋巴结和远期转移研究的文献特征

Table2 Characteristics of 5 included studies for FDG-PET/CT in lymph node metastasis and distant metastasis of pancreatic cancer

First author	Year	Study design	Diagnostic criteria	Quality	Sample	TP	FP	FN	TN
Lymph node metastasis									
Heinrich <sup>[4]</sup>	2005	P	H	A	25	3	0	11	11
Kauhanen <sup>[11]</sup>	2009	P	H or F	A	8	2	0	5	1
Imai <sup>[39]</sup>	2010	R	H	C	69	0	1	6	62
Pan <sup>[26]</sup>	2013	R	H	B	41	18	10	6	7
Yu <sup>[28]</sup>	2013	R	H	C	29	13	2	4	10
Wang <sup>[32]</sup>	2014	R	H	C	82	40	6	9	27
Distant metastasis									
Heinrich <sup>[4]</sup>	2005	P	H	A	32	13	7	3	9
Strobel <sup>[10]</sup>	2008	R	H or F	B	50	9	1	2	38
Kauhanen <sup>[11]</sup>	2009	P	H or F	A	14	6	0	1	7
Pan <sup>[26]</sup>	2013	R	H	B	41	4	0	1	36
Yu <sup>[28]</sup>	2013	R	H	C	48	15	1	2	30
Wang <sup>[32]</sup>	2014	R	H	C	82	8	1	3	70

Notes: P: prospective study; R: retrospective study; H: histology; F: follow up; TP: true positive; FP: false positive; FN: false negative; TN: true negative

表3 5篇被纳入FDG-PET/CT对胰腺癌预后预测研究的文献特征

Table3 Characteristic of 5 included studies for FDG-PET/CT in prognosis of pancreatic cancer

First author	Year	Study design	Quality	Sample	HR	95%CI		SUV <sub>max</sub>
						LL	UL	
Overall survival								
Hwang <sup>[40]</sup>	2012	R	B	165	2.13	1.38	3.31	4.1
Xu <sup>[41]</sup>	2014	R	A	122	1.60	0.98	2.61	6.2
Li <sup>[42]</sup>	2015	P	B	48	2.25	1.33	3.91	5.9
Wang <sup>[43]</sup>	2015	R	A	69	1.89	1.01	3.52	5.5
Progress free survival								
Moon <sup>[44]</sup>	2013	R	B	21	5.19	1.03	26.22	6.8
Xu <sup>[41]</sup>	2014	R	A	122	1.53	0.97	2.40	6.2
Li <sup>[42]</sup>	2015	P	B	48	2.73	2.02	4.24	5.9

Notes: P: prospective study; R: retrospective study; HR: hazard rate; LL: lower limit; UL: upper limit; SUV<sub>max</sub>: maximum standardized uptake value

FDG-PET/CT对胰腺癌诊断研究的数据加权定量合并结果为：敏感度<sub>合并</sub>=0.93（95%CI: 0.92~0.94, I<sup>2</sup>=27.7%），特异性<sub>合并</sub>=0.73（95%CI: 0.70~0.76, I<sup>2</sup>=51.1%）；对胰腺癌淋巴结转移诊断的敏感度<sub>合并</sub>为0.65（95%CI: 0.56~0.74, I<sup>2</sup>=86.2%），特异性<sub>合并</sub>为0.86（95%CI: 0.79~0.91, I<sup>2</sup>=85.7%）；而对远期转移诊断的敏感度<sub>合并</sub>（0.82, 95%CI: 0.71~0.90, I<sup>2</sup>=0.0%）和特异性<sub>合并</sub>（0.95, 95%CI: 0.91~0.98, I<sup>2</sup>=82.7%）均高于淋巴

结转移诊断，但其特异性<sub>合并</sub>异质性较高。FDG-PET/CT对胰腺癌诊断、淋巴结转移诊断和远期转移诊断的数据加权定量分析结果见表4。

FDG-PET/CT对胰腺癌预后预测Meta分析结果显示，总生存期的 $HR_{合并}=1.96$  (95%CI: 1.52~2.52,  $I^2=0.0\%$ )；无进展生存期 $HR_{合并}=2.26$  (95%CI: 1.33~3.83,  $I^2=58.9\%$ )，见图2。

FDG-PET/CT对胰腺癌诊断、分期（淋巴结转移和远期转移）诊断及预后预测分析均采用随机效应模型进行加权定量合并。

#### 2.4 异质性检验

FDG-PET/CT对胰腺癌诊断、淋巴结转移诊断及远期转移诊断的SROC曲线见图3。以上三个研究中，SROC曲线均非典型的“肩臂形”外观，Spearman相关性分析也都提示不存在阈值效应 ( $P>0.05$ )。FDG-PET/CT对胰腺癌诊断敏感度<sub>合并</sub>的 $I^2$ 为27.7%，与远期转移诊断敏感度<sub>合并</sub>、总生存期 $HR_{合并}$ 的异质性均在可接受范围，但淋巴结转移诊断敏感度<sub>合并</sub>、特异性<sub>合并</sub>和远期转移的特异性<sub>合并</sub>

异质性均较大 ( $I^2>80\%$ )。

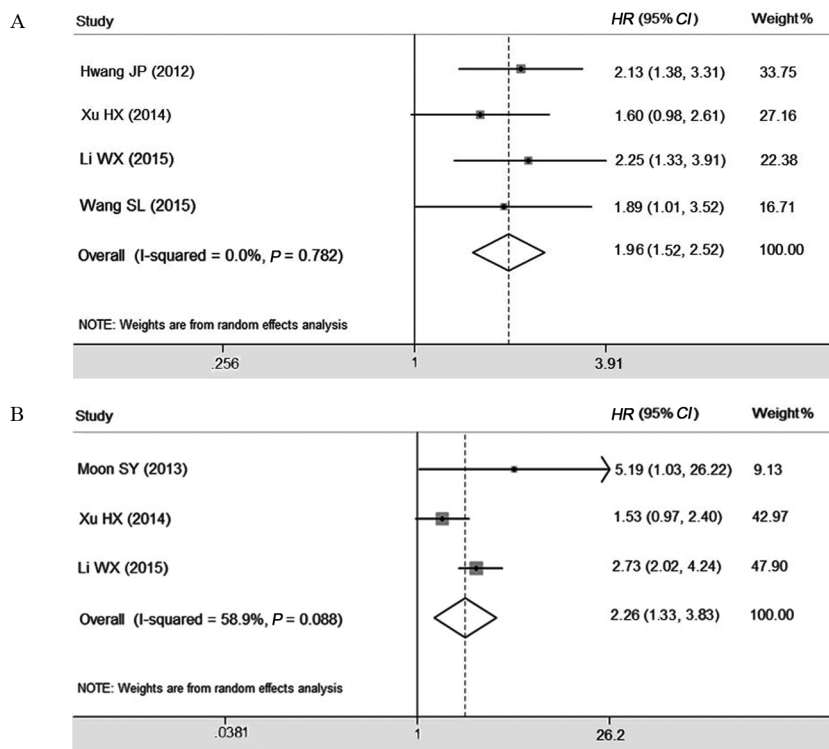
FDG-PET/CT对胰腺癌诊断的分层分析和回归分析显示，研究样本量、发表语言、研究设计类型、诊断标准、研究对象年龄、 $SUV_{max}$ 值界定等因素均非造成特异性异质性较大的因素（数据未给出）。而FDG-PET/CT对胰腺癌分期和预后预测分析等研究因纳入的研究及样本量有限，未进一步进行分层或回归分析。

#### 2.5 发表偏倚

由于本Meta分析中纳入的FDG-PET/CT对胰腺癌分期诊断和预后的文献较少 (<10)，本研究仅对FDG-PET/CT对胰腺癌诊断相关文献进行了不对称性检验，从漏斗图上看并无明显的不对称性，提示纳入分析的文献存在发表偏倚的可能性很小，见图4。

### 3 讨论

近年来，FDG-PET/CT被广泛用于胰腺癌诊断、分期及预后预测，但结论不一。本研究通过



A: forest plot for overall survival, B: forest plot for progress free survival

图2 FDG-PET/CT对胰腺癌预后分析的Meta分析森林图

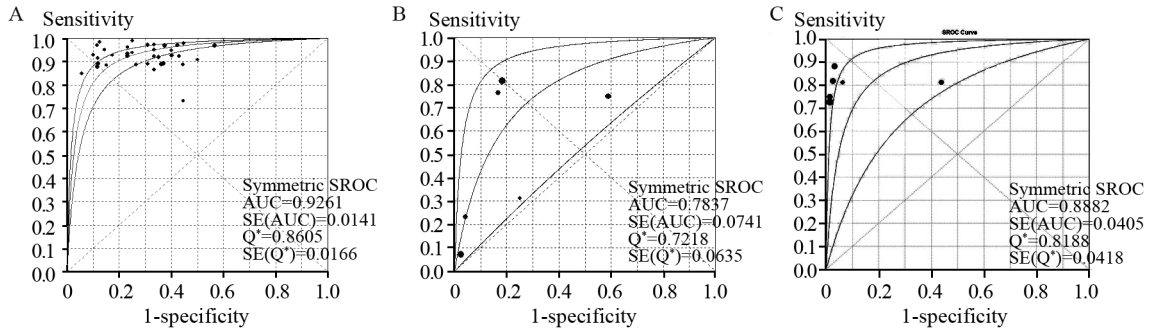
Figure2 Forest plot of FDG-PET in prognosis of pancreatic cancer

表4 FDG-PET/CT对胰腺癌诊断及分期的Meta分析

Table4 Meta-analysis of FDG-PET/CT in diagnosis and staging of pancreatic cancer

Objectives	N	Sen pooled (95%CI)	Spe pooled (95%CI)	+LR pooled (95%CI)	-LR pooled (95%CI)	DOR pooled (95%CI)	AUC	Q*
Diagnosis	36	0.93(0.92-0.94)	0.73(0.70-0.76)	3.10(2.63-3.66)	0.12(0.10-0.14)	32.42(24.22-43.40)	0.93	0.86
Staging	7							
Lymph node metastasis	6	0.65(0.56-0.74)	0.86(0.79-0.91)	2.71(1.15-6.37)	0.56(0.29-1.08)	6.78(2.39-19.22)	0.78	0.72
Distant metastasis <sup>a</sup>	6	0.82(0.71-0.90)	0.95(0.91-0.98)	17.79(2.92-108.41)	0.23(0.14-0.37)	75.80(15.94-360.52)	0.89	0.82

Notes: a: 5 articles overlap with lymph node metastasis; Sen: sensitivity; Spe: specificity; +LR: positive likelihood ratio; -LR: negative likelihood ratio; DOR: diagnostic odds ratio; AUC: area under curve



A: SROC curve for diagnosis; B: SROC curve for lymph node metastasis; C: SROC curve for distant metastasis

图3 FDG-PET/CT对胰腺癌诊断及分期诊断Meta分析的SROC曲线

Figure3 SROC curves of FDG-PET in diagnosis and staging of pancreatic cancer

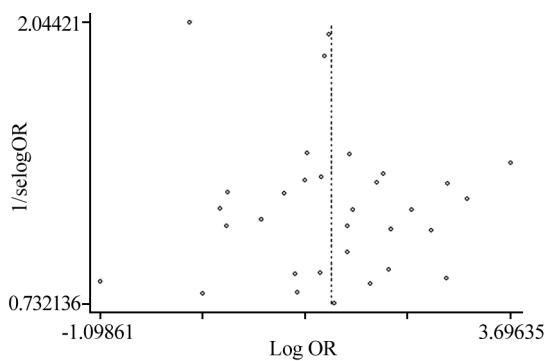


图4 FDG-PET/CT对胰腺癌诊断Meta分析的漏斗图

Figure4 Funnel plot based on the data of FDG-PET/CT for the diagnosis of pancreatic cancer

对已发表的文献进行检索及再分析，综合评定FDG-PET/CT对胰腺癌诊断、分期及预后预测的作用。结果提示，FDG-PET/CT可作为胰腺癌诊断和总生存期预测的重要影像学工具，且对胰腺癌远期转移诊断敏感度尚可（0.82）。与既往研究<sup>[45-46]</sup>相比，我们同时就PET/CT对胰腺癌诊断、分期及预后预测进行分析，涵盖角度更广、纳入文献更全面、样本量更大；对胰腺癌的诊断效能更高且置信区间更窄。

胰腺癌作为起病隐匿、生长迅速、手术清除率低、预后差、五年生存率低的恶性肿瘤，临床上主要依靠腹部彩超、CT和MRI作为其常规检查及诊断方法，但它们的诊断敏感度相对较低（分别为0.81、0.80和0.88）<sup>[29,46-47]</sup>、对早期小病灶不易发现均限制了胰腺癌早期根治手术的开展，明显降低患者的预后及生存率。FDG-PET/CT作为新兴的诊断方法，被认为具有较高的胰腺癌诊断价值，本研究结果也证实其对胰腺癌诊断的敏感度（0.93）远高于超声、CT和MRI，进一步满足了胰腺癌诊断的临床期望。

FDG-PET/CT对胰腺癌分期诊断和无进展生存

期预测Meta分析相关指标异质性较大，且部分临床价值有限，但在相关报道不集中、样本量较小且各研究结果不一致的情况下，本文作为一个阶段性总结为后期相关研究的开展奠定了基础。而其异质性较大的原因可能有纳入文献较少、样本量较小、阈值设定和诊断标准不同等，提示了开展更多的、大样本的相关研究分析的必要性。同时，由于FDG-PET/CT对胰腺癌分期和预后Meta分析中纳入的文献较少和（或）未明确阈值和诊断标准等信息，我们无法进一步进行亚组分析或拟合并回归模型，也无法进行发表偏倚检测。另外，本文仅纳入了中文和英文文献，这可能存在语言偏倚。

总之，FDG-PET/CT作为影像学检查方法之一，在胰腺癌诊断和总生存期预测上具有重要价值，但基于现有文献分析，其对胰腺癌分期诊断和无进展生存期预测的临床价值有限。

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