

论 著

¹⁸F-FDG PET/CT对女性盆腔恶性肿瘤转移与复发诊断价值的Meta分析*

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【摘要】目的 系统评价¹⁸F-FDG PET/CT对盆腔恶性肿瘤转移复发的诊断价值。方法 万方数据库检索、科学引文索引、科技会议录索引、知网查询索引、Web of Science、Pubmed及EMBASE中¹⁸F-FDG PET/CT诊断盆腔恶性肿瘤转移复发的随机对照试验(RCT),盆腔恶性肿瘤转移复发,检索有效时间截止至2021年12月31日。通过纳入及排除标准进行文献筛选、资料提取的方法,两位研究者对纳入文献进行质量后采用Meta-disc14.0进行Meta(荟萃)分析。结果 最终纳入15项研究,共834例患者,Meta分析显示:¹⁸F-FDG PET/CT诊断盆腔恶性肿瘤术后复发的敏感度(sensitivity, SEN)为0.94(95%CI: 0.91~0.96, P=0.1168)、特异性(specificity, SPE)为0.86(95%CI: 0.81~0.89, P=0.00001)、阳性似然比(positive likelihood ratio, +LR)为6.17(95%CI: 2.69~14.13, P=0.000001)、阴性似然比(negative likelihood ratio, -LR)为0.11(95%CI: 0.07~0.16, P=0.3536)、诊断比值比(diagnostic odds ratio, DOR)为83.73(95%CI: 29.17~240.31, P=0.0073)和SROC曲线下面积为0.9737。结论 ¹⁸F-FDG PET-CT用于盆腔恶性肿瘤复发具有较高的诊断价值。

【关键词】正电子发射断层显像; ¹⁸F-FDG PET/CT; 盆腔恶性肿瘤复发; 诊断; Meta分析

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Diagnostic Value of ¹⁸F-FDG PET/CT for the Detection of Metastasis and Recurrence of Pelvic Malignancy in women: A Meta-analysis*

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ABSTRACT

Objective To systematically evaluate the diagnostic value of ¹⁸F-FDG PET/CT for metastatic recurrence of pelvic malignant tumor. **Methods** Randomized controlled trials (RCTs) of ¹⁸F-FDG PET/CT in diagnosis of pelvic malignant tumor metastasis and recurrence were conducted in Wanfang database search, Science Citation index, Science and technology Conference Proceedings index, Knowledge network query index, Web of Science, Pubmed and EMBASE. The search will be valid until December 31, 2021. By using inclusion and exclusion criteria for literature screening and data extraction, the two researchers conducted Meta-disc14.0. **Results** A total of 834 patients were included in 15 studies. Meta-analysis showed that the sensitivity (SEN) of ¹⁸F-FDG PET/CT in the diagnosis of postoperative recurrence of pelvic malignant tumor was 0.94 (95%CI: 0.91-0.96, P=0.1168), specificity (SPE) was 0.86 (95%CI: 0.81~0.89, P=0.00001), positive likelihood ratio (+LR) was 6.17 (95%CI: 2.69-14.13, P=0.000001), negative likelihood ratio (-LR) was 0.11 (95%CI: 0.07-0.16, P=0.3536), diagnostic odds ratio (DOR) was 83.73 (95%CI: 29.17-240.31, P=0.0073), and the area under SROC curve was 0.9737. **Conclusion** ¹⁸F-FDG PET-CT has high diagnostic value in pelvic malignant tumor recurrence.

Keywords: Positron Emission Computed Tomography; ¹⁸F-FDG PET/CT; Recurrence of pelvic malignant tumor; Diagnosis Test; Meta-analysis; Supported by: Health Research Foundation of Hubei Province, No. WJ2021M084; Science and technology project of Huanggang City

盆腔恶性肿瘤对女性健康构成重大威胁^[1]。据估计,全世界每六名女性癌症患者中就有一名患有妇科癌症。目前手术切除及淋巴结清扫仍然是主要的治疗手段,然而,女性盆腔恶性肿瘤在完全缓解后较易复发。据估计,其复发率在10%至74%之间^[2],这取决于多种因素,如癌症类型、肿块直径、浸润程度和淋巴结状态等。盆腔恶性肿瘤的复发与不良预后有关,对复发的患者进行再次治疗既困难又复杂^[3]。早期发现复发和准确评估复发状态与选择最佳治疗策略和结果密切相关^[4]。因此,需要高质量的影像学检查,以便早期发现复发,精确评估复发状态,并进行最佳可行的外科干预。

由于手术治疗改变了解剖结构并可能掩盖小肿瘤复发,传统成像方式如超声、电子计算机断层扫描(CT)和核磁共振检查(MRI)的诊断能力受到限制^[5]。在缺乏软组织对比度的情况下,MRI和CT检查作为一种有效的分期和随访成像技术已被广泛接受,但其缺点是不能为临床提供高分辨率解剖结构信息,有研究表明,PET/CT用于评估疑似盆腔恶性肿瘤复发的患者,能够同时获取CT的形态学信息和PET组件所代表的功能数据,为检测和表征盆腔恶性肿瘤的复发提供了令人满意的诊断价值^[6]。目前已经被应用到临床实践中,用于描绘各种癌症的范围,然而,这些报告中可能存在诊断价值差异很大的现象,仍然缺乏关于¹⁸F-FDG PET/CT在女性盆腔恶性肿瘤转移与复发中的应用诊断性能的充分证据,其在妇科盆腔肿瘤复发疾病检测中的临床应用和诊断价值仍有待进一步探究^[7]。因此,我们进行了这项荟萃分析,以更准确地验证PET/CT在妇科盆腔肿瘤疑似复发患者诊断中的价值。

1 材料与方法

1.1 纳入标准与排除标准

纳入标准:文献类型:关于¹⁸F-FDG PET/CT与金标准比较诊断盆腔恶性肿瘤的诊断性试验,金标准为病理诊断;研究对象:盆腔恶性肿瘤行手术治疗的患者;诊断试验方法,病理诊断检查及PET/CT检查;结局指标:敏感度(sensitivity, SEN)、特异性(specificity, SPE)、真阳性率(positive likelihood ratio, +LR)、真阴性率(negative likelihood ratio, -LR)、诊断优势比(diagnostic odds ratio, DOR)、集成ROC法曲线下面积。排除标准:非妇科盆腔恶性肿瘤患者的研究文献;未行外科手术治疗的研究文献;无四格表资料或从文中无法获取数据的研究文献

1.2 检索策略 中文检索词包括:正电子发射断层显像、电子计算机断层扫描(CT)、计算机断层成像摄影、PET/CT、正电子发射计算机断层摄影成像、计算机断层显像、CT、盆腔恶性肿瘤、宫颈癌、宫颈肿瘤、卵巢癌、卵巢肿瘤、淋巴结、敏感特异性、特

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异度、诊断结果等；英文检索词包括：computed tomography imaging, positron emission tomography, PET/CT, CT, sensivity, specificity, diagnosis, Endometrial Cancer, Endometrial neoplasms, pelvic cavity, malignant tumor检索数据库包括万方数据库、科学引文索引、科技会议录索引、知网查询索引、Web of Science、Pubmed及EMBASE。检索截止日期为2021年12月1日，不限文献的语种。

1.3 文献筛选和资料提取 文献筛选工作由2名评价者独立进行，第一步进行阅读相关文献关键字题及摘要，排除明显不符合的文献，然后逐一仔细阅读全文判断进一步筛选符合标准的文献，如有不同意见确定该文献是否纳入采取通过讨论或提请第三人裁定。如该文献研究符合纳入标准采取统一的数据提取表提取以下信息：作者、国家、年代、PET/CT厂商、肿瘤类型、样本数量、真、假阳性、真、假阴性等。

1.4 质量评价 根据Cochrane协作网推荐的OUADAS—2工具[8]，2位评价员独立对纳入研究进行风险评估。使用Revman5.3对各研究进行质量评价，主要包括如何选择病例、待评价试验、诊断的金标准以、病选取流程及相关进展情况等四方面的内容，对每个种类做出“是”、“否”或“不清楚”的准确判断。

1.5 统计分析 首先对纳入研究的诊断四格表数据进行提取，使用Meta-Disc14.0软件计算¹⁸F-FDG PET/CT诊断盆腔恶性肿瘤术后复发的敏感度(sensitivity, SEN)、特异性(specificity, SPE)、真阳性率(positive likelihood ratio, +LR)、真阴性率(negative

likelihood ratio, -LR)、诊断优势比(diagnostic odds ratio, DOR)、集成ROC法曲线下面积。采用 χ^2 检验和I²检验的方法对各纳入研究结果间的异质性进行分析。采用随机效应模型进行Meta(荟萃)分析。纳入研究的发表偏倚采用漏斗图分析的方法。

2 结 果

2.1 纳入文献的基本特征和质量评价 1225篇文献通过初检得到，首先剔除相关重复文献，阅读文题及摘要后排除非盆腔肿瘤，剔除无关文献，收集到RCT 研究24篇，进一步阅读全文，其中不符合纳入标准的研究 9篇被排除，最终纳入 15 项英文文献研究^[9-23]，共834例患者，文献筛选流程(图1)，纳入文献的基本特征见表1，纳入文献的质量根据QUADAS-2量表14条标准评价。以上纳入诊断试验方法学质量均较好，评价结果见图2。

2.2 Meta 分析结果 ¹⁸F-FDG PET/CT诊断盆腔恶性肿瘤术后复发的敏感度(sensitivity, SEN)为0.94(P=0.1168,95%CI: 0.91~0.96)、特异度(specificity, SPE)为0.86(P=0.00001,95%CI: 0.81~0.89)、真阳性率(positive likelihood ratio, +LR)为6.17(P=0.000001,95%CI: 2.69~14.13)、阴性似然比(negative likelihood ratio, -LR)为0.11(P=0.3536,95%CI: 0.07~0.16)、诊断优势比(diagnostic odds ratio, DOR)为83.73(P=0.0073,95%CI: 29.17~240.31)和SROC曲线下面积为0.9737。(图3~图9)。

表1 纳入研究的基本特征

纳入研究	国家	机型	研究类型	肿瘤类型	例数	TP	FP	FN	TN	
Carolyn B.Hebela 2014 ^[9]	荷兰	Philips Gemini TF 16	RCT	卵巢癌	48	37	1	1	9	37
Johannes Grueneisena 2015 ^[10]	德国	Siemens, Healthcare Sector, Germany	RCT	盆腔恶性肿瘤复发	24	20	1	0	3	20
Daniela Rusu 2015 ^[11]	法国	Siemens,Knoxville,TN,USA	RCT	卵巢癌	53	47	0	4	2	47
Evis Sala 2010 ^[12]	英国	Discovery LS, GE	RCT	卵巢癌	35	33	0	2	0	33
Hyun Hoon Chung 2008 ^[13]	韩国	Philips, Gemini	RCT	子宫内膜癌	31	12	1	0	18	12
J.-Y. PARK 2008 ^[14]	韩国	Siemens/CTI	RCT	子宫内膜癌	24	22	1	0	1	22
Julian Kirchner 2017 ^[15]	德国	Siemens, Healthcare GmbH, Erlangen	RCT	复发性盆腔恶性肿瘤	43	36	2	2	3	36
Kazuhiro Kitajima 2008 ^[16]	日本	Biograph, Sensation 16, Siemens Systems, Erlangen, Germany	RCT	子宫内膜癌	30	14	1	1	14	14
Melissa M. Thrall 2007 ^[17]	美国	Siemens, Knoxville, TN	RCT	卵巢癌	51	33	0	4	14	33
P. Ozcan Karaa 2011 ^[18]	土耳其	Biograph, Siemens	RCT	子宫内膜癌	35	12	1	0	22	12
Punit Sharma 2012 ^[19]	印度	Biograph 2, Siemens, Erlangen, Germany	RCT	子宫内膜癌	101	48	3	6	44	48
Sandro Sironi 2006 ^[20]	意大利	Discovery LS; GE Medical Systems, Milwaukee, WI	RCT	子宫癌	25	13	0	1	11	13
Sang-Young Ryu 2010 ^[21]	韩国	Siemens, Knoxville, TN, USA; General Electric, Waukesha, WI, USA	RCT	子宫内膜癌	127	19	13	0	95	19
Satoshi Takeuchi 2014 ^[22]	美国	Discovery ST, STe, or RX; GE Healthcare	RCT	卵巢癌	48	24	15	4	5	24
Tsuneo SAGA 2003 ^[23]	日本	Advance, General Electric Medical Systems, Milwaukee, WI	RCT	子宫内膜癌	32	13	4	0	15	13

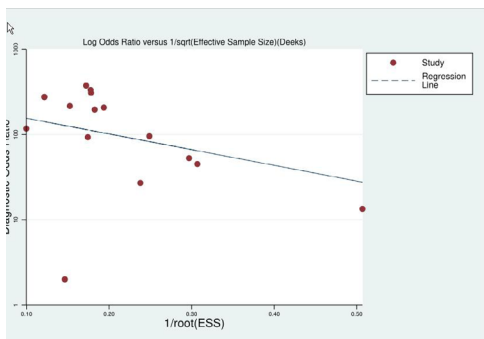
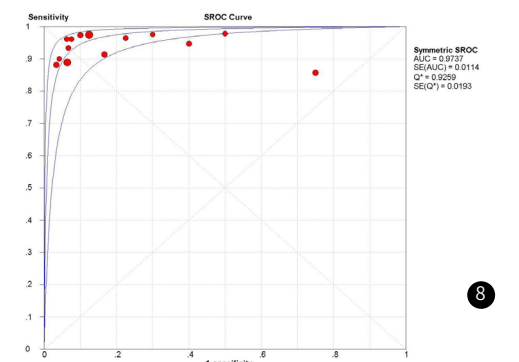
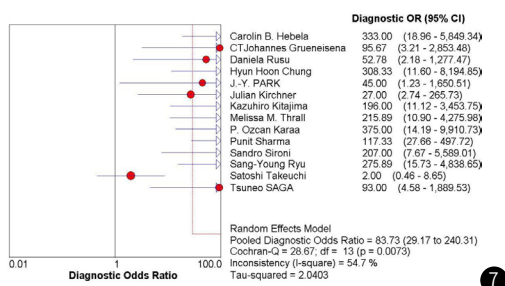
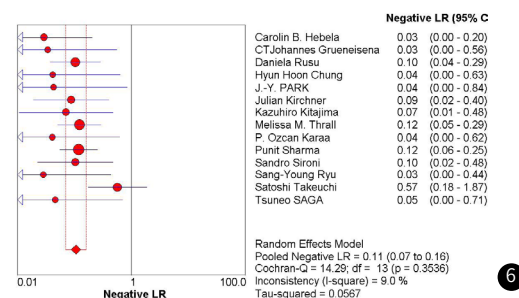
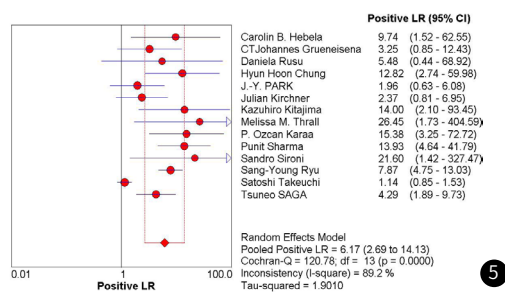
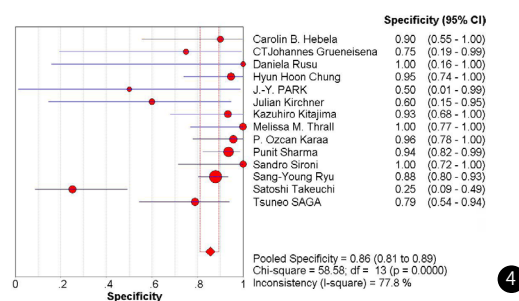
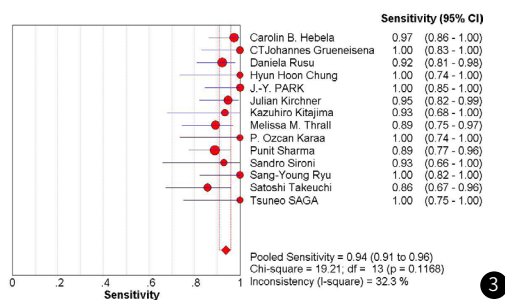
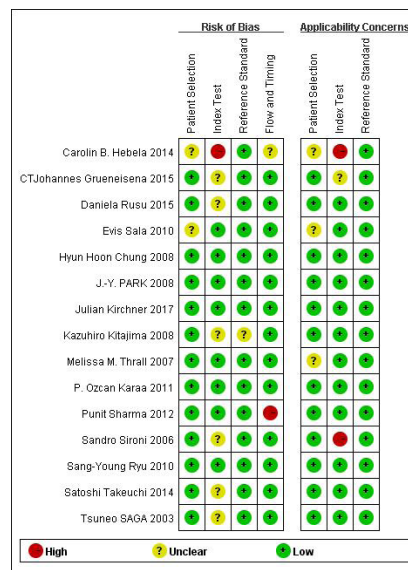
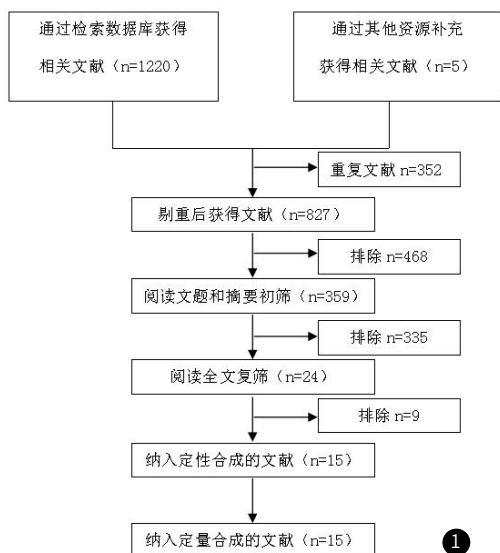


图1 文献筛选流程图。图2 QUADAS-2质量评价结果。图3 盆腔恶性肿瘤术后复发敏感度PET/CT诊断meta(荟萃)分析。图4 盆腔恶性肿瘤术后复发PET/CT诊断特异度的meta(荟萃)分析。图5 盆腔恶性肿瘤术后复发PET/CT诊断阳性似然比的meta(荟萃)分析。图6 盆腔恶性肿瘤术后复发PET/CT诊断阴性似然比的meta(荟萃)分析。图7 盆腔恶性肿瘤术后复发PET/CT诊断比值比的meta(荟萃)分析。图8 盆腔恶性肿瘤术后复发PET/CT诊断ROC曲线的meta(荟萃)分析。图9 盆腔恶性肿瘤术后复发PET/CT诊断发表偏倚漏斗图。

3 讨论

本研究通过特定的设计和适当的统计进行meta分析,同时结合各种不同的独立调查数据,客观真实地阐述已存在的结果和定量并对一个特定的问题做出结论。因此,本研究发现通过meta分析,评估¹⁸F-FDG PET/CT在女性盆腔恶性肿瘤转移与复发中的应用并为其进一步相关的成本效益提供了重要依据。

meta分析研究结果表明,¹⁸F-FDG PET/CT是一种进行评估盆腔恶性肿瘤转移复发的高精度成像方式,具有灵敏度高,特异性强的特点。与传统的诊断方法CT扫描和磁共振成像(MRI)形成鲜明对比,PET/CT在葡萄糖摄取增加的基础上呈现图像,具有更高的诊断准确性。研究结果表明,盆腔恶性肿瘤术后复发的敏感度、特异度、真阳性率、真阴性率、诊断比值比以及曲线下面积通过¹⁸F-FDG PET/CT诊断均具有显著优势,这与陈小莉^[24],张家华^[25]等研究报道关于肝转移瘤、宫颈癌腹主动脉淋巴结转移通过¹⁸F-FDG PET/CT高诊断价值的研究结论一致。本研究表明女性盆腔恶性肿瘤转移与复发诊断中¹⁸F-FDG PET/CT具有较高的诊断价值,因此,它的引入可以让大多数病人避免不适当的探查手术。通过提高术后随访及筛查,诊断肿瘤是否复发,可以避免增加不必要的再次手术,从而减轻患者心理及生理伤害刺激,提高患者生活质量、生存质量、生命时间,均具有重要意义^[26]。随着医疗技术发展,¹⁸F-FDG PET/CT提供了超过了传统的放射学诊断方法许多优势,不仅为初步诊断提供必要信息,而且可用于治疗、随访和潜在并发症的检测^[27-28]。

本研究也存在一定的局限性,首先,病例构成和随访时间的差异可能会受到影响评价的效率。如果患者最初呈阴性结果经¹⁸F-FDG PET/CT检查发现盆腔恶性肿瘤后一段时间的随访,检查的阴性结果实际上是假阴性,表明¹⁸F-FDG PET/CT在检查复发或转移病变时FDG-PET灵敏度降低。当然,同时存在¹⁸F-FDG PET/CT检查最初的阴性结果后出现复发或转移。同样的,在某些情况下,¹⁸F-FDG PET/CT的特异性可能被高估了。例如部分¹⁸F-FDG PET/CT检查后确定为真阳性病例实际上不可能把所有的病变都显示出来,通过病理检查,提示遗漏、假阳性病变。其次,纳入研究仅包含英文文献,由于语种局限性而产生的偏倚,发表偏倚倾向于发表阳性结果的文章作者、资助机构或者出版机构。

综上所述,对于女性盆腔恶性肿瘤术后转移复发,¹⁸F-FDG PET/CT具有较高的准确率,可作为女性盆腔恶性肿瘤术后随访和筛查的重要方法之一。

参考文献

- [1] 张家华,葛龙,田金徽,等. PET/CT和CT诊断宫颈腺癌淋巴结转移间接比较的Meta分析[J]. 兰州大学学报(医学版), 2015, 41(1): 34-42.
- [2] Peiretti M, Zapardiel I, Zanagnolo V, et al. Maggioni A. Management of recurrent cervical cancer: a review of the literature[J]. Surg Oncol 2012; 21: e59-e66.
- [3] Javadi S, Ganeshan DM, Qayyum A, et al. Bhosale P (2016) ovarian cancer, the revised FIGO staging system, and the Role of imaging. AJR American journal of roentgenology, 2016 Jun, 206(6): 1351-1360.
- [4] Zang RY, Harter P, Chi DS, et al. Predictors of survival in patients with recurrent ovarian cancer undergoing secondary cytoreductive surgery based on the pooled analysis of an international collaborative cohort[J]. Br J Cancer, 2011, 105: 890-896.
- [5] Sironi S, Picchio M, Landoni C, et al. Post-therapy surveillance of patients with uterine cancers: value of integrated FDG PET/CT in the detection of recurrence[J]. Eur J Nucl Med Mol Imaging, 2007, 34: 472-479.
- [6] Chen YM, Chen T, Zee CS, et al. Is there an impact of ¹⁸F-FDG PET/CT on the surveillance and clinical management of recurrent ovarian cancer? Research based on a large sample in a single PET/CT center[J]. Nucl Med Commun, 2014, 35: 347-352.
- [7] Nie J, Zhang J, Gao J, et al. Diagnostic role of ¹⁸F-FDG PET/MRI in patients with gynecological malignancies of the pelvis: a systematic review and meta-analysis[J]. PLoS One 2017, 12: e0175401

- [8] Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies[J]. Ann Intern Med, 2011, 155(8): 529-536.
- [9] Carolin B. Hebel, Florian F. Behrendt, Alexander Heinzl, et al. Negative ¹⁸F-2-fluorodeoxyglucose PET/CT predicts good cancer specific survival in patients with a suspicion of recurrent ovarian cancer[J]. European Journal of Radiology, 83, (2014), 463-467.
- [10] Johannes Grueneisen, Benedikt Michael Schaarschmidt, et al. Implementation of FAST-PET/MRI for whole-body staging of female patients with recurrent pelvic malignancies: A comparison to PET/CT[J]. European Journal of Radiology, 2015.
- [11] Daniela Rusul, Thomas Carlier, Mathilde Colombié, et al. Clinical and survival impact of FDG PET in patients with suspicion of recurrent ovarian cancer: a 6-year follow-up[J]. Original Research In Medicine, 2015.
- [12] Evis Sala, MD, PhD, et al. Recurrent ovarian cancer: use of Contrast-enhanced CT and PET/CT to accurately localize tumor recurrence and to predict patients' Survival[J]. Genitourinary imaging, 2010.
- [13] Hyun Hoon Chung, Won Jun Kang, et al. The clinical impact of ¹⁸F-FDG PET/CT for the management of recurrent endometrial cancer: correlation with clinical and histological findings[J]. Eur J Nucl Med Mol Imaging, (2008) 35: 1081-1088.
- [14] J.-Y. PARK, E. N. KIM, D. -Y. KIM, et al. Clinical impact of positron emission tomography or positron emission tomography/computed tomography in the posttherapy surveillance of endometrial carcinoma: evaluation of 88 patients[J]. Int J Gynecol Cancer 2008, 18, 1332-1338.
- [15] Kirchner J, Sawicki L M, Suntharalingam, et al. Whole-body staging of female patients with recurrent pelvic malignancies: Ultra-fast ¹⁸F-FDG PET/MRI compared to ¹⁸F-FDG PET/CT and CT[J]. PLoS ONE 2017 12(2): e0172553.
- [16] Kazuhiro Kitajima, Koji Murakami, et al. Performance of FDG-PET/CT in the diagnosis of recurrent endometrial cancer[J]. Ann Nucl Med (2008) 22: 103-109.
- [17] Melissa M. Thrall, Julie A. DeLoia, et al. Clinical use of combined positron emission tomography and computed tomography (FDG-PET/CT) in recurrent ovarian cancer[J]. Gynecologic Oncology 105 (2007) 17-22.
- [18] P. Ozcan Kara, T. Kara, B. Kaya, et al. The value of FDG-PET/CT in the post-treatment evaluation of endometrial carcinoma: A comparison of PET/CT findings with conventional imaging and CA125 as a tumour marker[J]. Rev Esp Med Nucl Imagen Mol. 2012; 31(5): 257-260.
- [19] Punit Sharma, MD, Rakesh Kumar, et al. Carcinoma endometrium role of ¹⁸-FDG PET/CT for detection of suspected recurrence[J]. Clinical Nuclear Medicine, Volume 37, Number 7, July, 2012.
- [20] Sandro Sironi, Maria Picchio, Claudio Landoni, et al. Post-therapy surveillance of patients with uterine cancers: value of integrated FDG PET/CT in the detection of recurrence[J]. Eur J Nucl Med Mol Imaging (2007), 34: 472-479.
- [21] G-Young Ryu, Kidong Kim, Younha Kim, et al. Detection of recurrence by ¹⁸F-FDG PET in patients with endometrial cancer showing no evidence of disease[J]. J Korean Med Sci 2010; 25: 1029-1033.
- [22] Oshi Takeuchi, Martin Lucchini, Kathleen M. Schmeler, et al. Utility of ¹⁸F-FDG PET/CT in follow-up of patients with low-grade serous carcinoma of the ovary[J]. Gynecologic Oncology 133 (2014) 100-104.
- [23] Neo SAGA, Tatsuya HIGASHI, Takayoshi ISHIMORI, et al. Clinical value of FDG-PET in the follow up of post-operative patients with endometrial cancer[J]. Annals of Nuclear Medicine, 2003, Vol. 17, No. 3, 197-203.
- [24] 刘海峰, 黎金葵, 等. ¹⁸F-FDG PET/CT对肝转移瘤诊断价值的Meta分析[J]. 中国CT和MRI杂志, 2019, 17(1): 87-91.
- [25] 葛龙, 田金徽, 等. PET/CT和CT诊断宫颈腺癌淋巴结转移间接比较的Meta分析[J]. 兰州大学学报(医学版), 2015, 41(1): 34-42.
- [26] Munk Jensen M, Erichsen KD, Bjorkling F, Madsen J, et al. Imaging of treatment response to the combination of carboplatin and paclitaxel in human ovarian cancer xenograft tumors in mice using FDG and FLT PET[J]. PLoS One. 2013; 8: e85126.
- [27] Jung TY, Jung S, Ryu HS, et al. Kwon SY (2019) The Application of Magnetic Resonance Imaging-Deformed ¹¹C-Methionine-Positron Emission Tomography Images in Stereotactic Radiosurgery[J]. Stereotactic and functional neurosurgery 97 (4): 217-224.
- [28] 吴丽霞, 鄧艳波, 崔向华, 等. MRI技术及其联合CT在盆腔肿瘤诊断中的应用[J]. 中国CT和MRI杂志, 2019, 17(9): 125-127.

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