

# The diagnostic performance of $^{18}\text{F}$ -FDG PET/CT and MRI in differentiating benign and malignant ovarian tumors: an indirect comparative analysis

**Xianwen Hu**

Affiliated Hospital of Zunyi Medical University; Weng'an Qingzhu Hospital;

**Dandan Li**

Zunyi Hospital of Traditional Chinese Medicine

**Zhigang Liang**

Affiliated Hospital of Zunyi Medical University

**Yan Liao**

Affiliated Hospital of Zunyi Medical University

**Ling Yang**

Affiliated Hospital of Zunyi Medical University

**Rui Wang**

Affiliated Hospital of Zunyi Medical University

**Pan Wang**

Affiliated Hospital of Zunyi Medical University

**Jiong Cai** (✉ [jiong\\_cai@163.com](mailto:jiong_cai@163.com))

Affiliated Hospital of Zunyi Medical University

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## Research Article

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## Abstract

**Objective:** To compare the value of Fluorodeoxyglucose positron emission tomography (FDG-PET)/computed tomography (CT) and magnetic resonance imaging(MRI) in differentiating benign and malignant ovarian tumors.

**Material and Methods:** Retrieved the research on the diagnostic performance of MRI or <sup>18</sup>F-FDG PET/CT in identifying benign and malignant ovarian tumors published in PubMed and Embase from January 2000 to January 2021. Two authors independently extracted the data of the characteristics of each study. If the data of the study report can be used to construct a 2X2 contingency table comparing <sup>18</sup>F-FDG PET/CT and MRI, these studies were selected. The Quality Assessment of Diagnostic Accuracy Studies were used to evaluate the quality of the studies. According to the sensitivity and specificity of <sup>18</sup>F-FDG PET/CT and MRI, forest plots is generated.

**Results:** A total of 27 articles including 11<sup>18</sup>F-FDG PET/CT studies and 17 MRI studies on the differentiation of benign and malignant ovarian or accessory tumors were included for this meta-analysis. The pooled sensitivity and specificity for <sup>18</sup>F-FDG PET/CT in differentiating benign and malignant ovarian tumors were 0.92 (95% CI, 0.86-0.96) and 0.86 (95% CI, 0.79-0.91), respectively, and the pooled sensitivity and specificity for MRI were 0.92 (95% CI: 0.89-0.95) and 0.85 (95% CI: 0.79-0.89), respectively.

**Conclusion:** MRI and <sup>18</sup>F-FDG PET/CT have the same diagnostic performance in the differential diagnosis of ovarian benign and malignant tumors. However, MRI is more worthy of clinical application because of its lack of radiation, shorter scanning time, and lower medical costs.

## Introduction

Ovarian cancer is the disease with the highest mortality rate among malignant tumors of female reproductive tract. According to statistics, more than 180 thousand women die of ovarian cancer every year in the world, which is a serious threat to women's life and health[1]. Ovarian cancer has insidious onset, lack of specific clinical symptoms in early stage, and unsatisfactory clinical early diagnosis effect. More than 70% of ovarian cancer patients are already in the advanced stage of the disease when they visit the doctor, so its prognosis is poor[2, 3]. Therefore, it is of great significance to find a highly sensitive and specific diagnostic method for early diagnosis, clinical staging, guiding treatment and improving prognosis of ovarian cancer.

Screening for ovarian cancer includes serological tumor markers and imaging methods such as ultrasound, CT, MRI, and PET/CT. Serum carbohydrate antigen (CA)125 is the most widely studied biomarker for ovarian cancer [4]. CA125 is increased in more than half of ovarian cancer patients, but its specificity is low. CA125 is also positive in some malignant tumors such as lung cancer, colorectal cancer, endometrial cancer, breast cancer, lymphoma and so on [5]. Secondly, the expression level of CA125 is also increased in common pelvic benign diseases such as adnexal cyst, endometriosis, uterine fibroids and pelvic inflammatory disease [6]. In addition to CA125, carcinoembryonic antigen (CEA), gonadal hormone, CA72-4, CA15-3 and alkaline phosphatase have also been used as serum markers for ovarian cancer, but their specificity and sensitivity are low [7]. Ultrasound is a commonly used imaging method for gynecological diseases because of its simplicity and non-radiation. However, the small size of early ovarian cancer is limited to the ovary and does not cause ovarian morphological changes, which makes it easier to produce false negative results. Moreover, ultrasound is difficult to distinguish ovarian cancer from ovarian cystadenoma, immature teratoma and other diseases [8]. CT and MR can provide the anatomical information of the ovarian and its surrounding tissues, which are of great clinical significance for determining the extent of ovarian cancer and the formulation of auxiliary surgery plans, and MRI is superior to CT in soft tissue resolution, but there are still challenges in detecting ovarian tumors smaller than 5mm[9]. <sup>18</sup>F-FDG PET/CT is a more sensitive method for early detection of tumors. Its main advantage is that it can locate the disease activity before anatomical changes and detect smaller ovarian lesions than conventional imaging. However, the non-specific uptake mechanism of FDG may cause false positive results[10]. Therefore, we conducted a systematic review and meta-analysis on the diagnostic value of MRI and <sup>18</sup>F-FDG PET/CT in ovarian cancer, and indirectly compared the differential diagnosis performance of MRI and <sup>18</sup>F-FDG PET/CT in ovarian benign and malignant tumors.

## Material And Methods

### Study search strategy

This systematic review and meta-analysis was performed in accordance with PRISMA 2009 guidelines [11]. The Pubmed and Embase databases searched for MRI or <sup>18</sup>F-FDG PET/CT in English literature on the detection performance of ovarian cancer were included in the analysis of this study. The following search terms were used: ("PET/CT" OR "PET-CT" OR "positron emission tomography/computed tomography" OR "positron emission tomography-computed tomography" OR "MR" OR "Magnetic Resonance") AND ("ovarian cancer" OR "ovarian tumor" OR "ovarian neoplasms" OR "adnexal mass" OR "adnexal lesions", the publication time of the literature is limited to January 2000 to January 2020. Two independent reviewers examined all potentially qualified articles in which PET/CT and/or MR imaging for ovarian tumor evaluation after reading the abstract. When the results of two independent reviewers are inconsistent, a group discussion will be held until a consensus is reached.

### Study selection

### The study should meet all of the following inclusion criteria: (i) published

between January 2000 and January 2020;(ii) all patients are at risk of ovarian cancer during the attachment mass screening; (iii) patients accepted <sup>18</sup>F-FDG PET/CT and/or MRI to diagnose ovarian cancer; (iv) reference standard should at least include histopathological examination results and (v) research data must include or be able to derive true positive, false positive, false negative, and true negative values based on the sensitivity, specificity, accuracy, etc. provided in the article to construct a 2x2 contingency table. The exclusion criteria are as follows: (i) the sample in the study is less than 10 patients with

ovarian tumors; (ii) for MRI research, the magnetic field strength is less than 1.5T or the magnetic field strength information is not recorded; (iii) for PET/CT studies, the tracer is not  $^{18}\text{F}$ -FDG and (iv) studies in which data or data subsets were published more than once were excluded.

## Data extraction and quality assessment

This meta-analysis extracted the first author, publication time, country, sample size, average age, study design type, patient selection (consecutive or nonconsecutive), interpretation of test results (blind or not), true-positive (TP), false-positive (FP), false-negative (FN), true-negative (TN) results from the included studies, CT technology for PET/CT, magnetic field strength for MRI and other data. The Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) was used for quality assessment of enrolled studies [12]. Data extraction and critical evaluation are carried out independently by two authors, and disputes are resolved by consensus reached by a third reviewer.

## Statistical analyses

Stata software version 14.0 (Stata Corporation, College Station, TX, USA) was used for the statistical processing of this meta-analysis, and  $P < 0.05$  was considered statistically significant. The sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR) and the area under the receiver operating characteristic (ROC) curves (AUC) with their 95% confidence intervals (CIs) for each individual study were calculated, according to the TP, FP, FN and TN values extracted from the enrolled study. The hierarchical Logistic regression model was used to calculate general estimates of the sensitivity and specificity of the enrolled study, including the hierarchical summary receiver operating Characteristics (HSROC) model and concomitant variables. HSROC curves with 95% confidence and prediction regions were used to map the results for their sensitivity and specificity. PLR, NLR and DOR are calculated by bivariate generalized linear mixed model and random effects model. Cochran's Q test and Higgins  $I^2$  test were used to examine their heterogeneity [13]. In Cochran's Q test,  $p < 0.05$  was the test standard, indicating the existence of heterogeneity. Higgins  $I^2$  test was used to evaluate the degree of heterogeneity using the following criteria: inconsistency index ( $I^2$ )  $< 50\%$  was considered as heterogeneity may not be important;  $I^2 = 50\text{--}80\%$  was deemed as the possibility of moderate heterogeneity;  $I^2 > 80\%$  suggested the possibility of significant heterogeneity. The subgroup analysis of MRI and  $^{18}\text{F}$ -FDG PET/CT is carried out according to the sample size of the study, average age, study design type, patient selection, etc. The funnel plots and Deeks' asymmetry tests are used as the assessment of publication bias for MRI and  $^{18}\text{F}$ -FDG PET/CT [14].

## Results

### *Literature search*

The literature search through related subject terms initially produced 1894 articles, consisting of 1413 articles in PubMed and 481 articles in Embase. After gradually deleting overlapping, irrelevant, comments, case reports, conferences and other articles, a total of 1,791 articles were excluded, and the remaining 103 potentially eligible original texts were further evaluated. Since the full text is not completely published in English ( $n = 5$ ), it is impossible to extract sufficient data to construct a 2x2 quadrilingual table ( $n = 14$ ), and further exclude papers in areas of non-interest ( $n = 57$ ). Finally, 27 papers on the differentiation of benign and malignant ovarian or accessory tumors were included for meta-analysis [15–41]. The detailed process of document retrieval is shown in Fig. 1.

## Study characteristics

The included 27 articles included 3730 patients with 3842 tumors, consisting of 10 PET/CT, 16 MRI, and 1 article that included both PET/CT and MRI to differentiate benign and malignant ovarian tumors. Among them, 17 studies were prospectively designed, 9 were retrospective studies, and 1 was unspecified. The sample size of the enrolled studies ranged from 30 to 1130 patients, and the average age of the patients ranged from 39.9 to 64.0 years old. For PET/CT, 7 of the 12 studies recorded the cutoff value of the maximum standard uptake value (SUVmax) between benign and malignant to study its diagnostic performance. As for MRI, 5 of the 17 studies used the cutoff value of the apparent diffusion coefficient (ADC) value to distinguish benign and malignant ovarian tumors. In all the enrolled studies, histopathological examination was used as the reference standard, and 4 of them also included the follow-up time of at least half a year into the reference standard. The detailed characteristics of the enrolled studies and patients are summarized in Table 1, and the characteristics of PET/CT are shown in **Table S1**, and the characteristics of MRI are shown in **Table S2**.

Table 1  
The principal characteristics of eligible studies

Study /Year /Country	No. of patients	Mean age	Study design	Consecutive	Scanner	Cutoff value		Reference standard	Interval between index tests and HP	TP	FP
						SUVmax	ADC( $10^{-3}\text{mm}^2/\text{s}$ )				
Castellucci P /2007 /Italy(15)	50	64	P	Yes	PET/CT (Non-CE)	3.0		HP;follow-up	≤ 2W	28	0
Kitajima K/2011 /Japan(16)	108(111tumor)	55.4	NR	NR	PET/CT (Non-CE + CE)	2.55		HP	NR	70	6
Zytoon AA/2012 /Egypt(17)	98	57.7	P	yes	PET/CT (Non-CE)	4.3		HP;follow-up	≤ 4W	87	0
Risum S/2007 /Denmark(18)	97	60	P	yes	PET/CT (Non-CE + CE)	NR		HP	≤ 2W	57	3
Tanizaki Y/2014 /Japan(19)	160	NR	R	NR	PET/CT (Non-CE)	2.9		HP	NR	54	5
Dauwen H/2013 /Belgium(20)	69	60	P	Yes	PET/CT (Non-CE + CE)	NR		HP	≤ 17d	52	3
Yamamoto Y/ 2008/Japan(21)	30	47.7	P	Yes	PET/CT (Non-CE)	3.0		HP	NR	10	3
Takagi H/2018 /Japan(22)	76	59	R	NR	PET/CT (Non-CE)	3.97		HP	NR	39	5
Michielsen K/2013 /Belgium(23)	32	61.9	P	Yes	PET/CT (Non-CE)	NR		HP	NR	29	2
Lee JW/2015/ Korea(24)	72	51	R	NR	PET/CT (Non-CE + CE)	2.5		HP	≤ 7W	45	3
Nam EJ/2009 /Korea(25)	133	51	P	NR	PET/CT (Non-CE + CE)	NR		HP	≤ 4W	93	10
Nam EJ/2009 /Korea(25)	133	51	P	NR	MRI (1.5T)		NR	HP	≤ 4W	69	7
Kawahara K/ 2004/Japan(26)	38	55.3	P	yes	MRI (1.5T)		NR	HP	≤ 2W	21	2
Kierans AS/2013 /USA(27)	37	54	R	Yes	MRI(1.5/3T)		NR	HP	≤ 137D	6	3
Türkoğlu S/ 2020/Turkey(28)	43	51.26	R	Yes	MRI (1.5T)		0.93	HP	≤ 1W	15	5
Michielsen K/ 2017/Belgium(29)	161	NR	P	Yes	MRI (3T)		NR	HP	NR	122	8
Uehara T/2012 /Japan(30)	50	51	R	Yes	MRI(3T)		NR	HP	NR	18	3
Booth SJ/ 2008/UK(31)	191	56	R	NR	MRI(3T)		NR	HP	NR	90	22
Shimada K/2017 /Japan(32)	265	NR	P	Yes	MRI(1.5T)		NR	HP	≤ 4M	52	18

B = Benign ,M = malignant;HP = histopathology; P = Prospective; R = Retrospective; NR: not report; W = week; M = month; D = day.

Study /Year /Country	No. of patients	Mean age	Study design	Consecutive	Scanner	Cutoff value		Reference standard	Interval between index tests and HP	TP	FP
						SUVmax	ADC( $10^{-3}\text{mm}^2/\text{s}$ )				
Zhang H/2019 /China(33)	85	52.7	R	Yes	MRI(1.5T)		1.162	HP	NR	51	3
Zhang P/2012/ China(34)	191(202tumor)	56.5	R	Yes	MRI(1.5T)		1.20	HP	NR	85	43
Li W/2011/ China(35)	127(131tumor)	B = 46.2,M = 59.9	R	Yes	MRI(1.5T)		1.25	HP	NR	77	5
Fan X/2015/ China(36)	64	46.7	R	NR	MRI(3T)		0.878	HP	NR	54	5
Sohaib SA/2003/ UK(37)	104(155tumor)	50	P	Yes	MRI(1.5T)		NR	HP	NR	61	11
Gity M/2019/ Iran(38)	43(49tumor)	39.9	P	Yes	MRI(3T)		NR	HP	NR	21	9
Pereira PN/2018/Brazil(39)	200(237tumor)	B = 47.1;M = 57.8	P	Yes	MRI(1.5T)		NR	HP + follow-up	NR	75	4
Van TP/2007/ UK(40)	76	B = 46;M = 57	P	Yes	MRI(1.5T)		NR	HP	NR	23	7
Thomassin NI/ 2020/France(41)	1130	49	P	Yes	MRI(1.5/3T)		NR	HP + follow-up	NR	189	79

B = Benign ,M = malignant;HP = histopathology; P = Prospective; R = Retrospective; NR = not report; W = week; M = month; D = day.

## Quality Assessment

The quality of all studies is considered satisfactory because it meets at least 5 of the 7 reference standards. Regarding the risk of bias for reference standards, all studies include at least histopathological examinations, which are considered low-risk. Since most studies do not report the time interval between the index test and the reference standard test, the risk of bias in flow and time cannot be assessed. Also, in two studies, the long time interval between the index test and the reference standard test (within 4 months and 137 days, respectively) is considered to be a higher risk [27, 32]. In terms of patient selection, all patients included in this study were suspected of being ovarian tumors by ultrasound or serum tumor markers, and the risk of publication bias and application concerns was considered low. The results of the QUADAS-2 assessment are shown in **Table S3**.

## Diagnostic accuracy

The sensitivity of 11 studies containing  $^{18}\text{F}$ -FDG PET/CT methods to differentiate benign and malignant ovarian tumors ranged from 0.71 (95% CI, 0.42–0.92) to 1.0 (95% CI, 0.94–1.00), and the specificity was 0.33 (95% CI, 0.94–1.00) to 1.0 (95%CI, 0.40–1.00). The pooled sensitivity and specificity of  $^{18}\text{F}$ -FDG PET/CT in differentiating benign and malignant ovarian tumors were 0.92 (95% CI, 0.86–0.96) and 0.86 (95% CI, 0.79–0.91), respectively, as shown in Fig. 2A. Both Cochran's Q test and Higgins  $I^2$  test showed significant heterogeneity in sensitivity ( $Q = 42.89, P \leq 0.01; I^2 = 74.35$ ) and specificity ( $Q = 27.54, P \leq 0.01; I^2 = 60.06$ ). A total of 17 studies included the diagnostic performance of MRI in detecting ovarian cancer, with sensitivity and specificity ranging from 0.65 (95% CI: 0.43–0.84) to 0.97 (95% CI: 0.92–0.99), and 0.46 (95% CI: 0.19–0.75) to 0.97 (95% CI: 0.94–0.99), the combined sensitivity and specificity were 0.92 (95% CI: 0.89–0.95) and 0.85 (95% CI: 0.79–0.89), respectively, as shown in Fig. 2B. Also, Cochran's Q test and Higgins  $I^2$  test showed heterogeneity between studies in sensitivity and specificity. The pooled PLR and NLR of  $^{18}\text{F}$ -FDG PET/CT, with effect estimates of 6.88 (95% CI: 4.56–10.36) and 0.10 (95% CI: 0.06–0.17), respectively. As for MRI, the combined effect estimates of PLR and NLR are 6.06 (95% CI: 4.24–8.66) and 0.09 (95% CI: 0.06–0.13), respectively. The combined DOR value of ovarian tumors diagnosed by  $^{18}\text{F}$ -FDG PET/CT was 77 (95% CI: 36–163), and the combined DOR value for MRI was 67 (95% CI: 38–118), respectively, as shown in Table 2. There was no statistical difference between the diagnostic odds ratio of MRI compared with that of PET/CT ( $P = 0.79$ ). The area under the SROC curve of  $^{18}\text{F}$ -FDG PET/CT is 0.94, with a 0.92–0.96 of 95%CI. The difference between the 95% confidence contour and the prediction contour is significant, which also indicates the heterogeneity among studies. As for MRI, the area under the SROC curve is 0.95 (95%CI: 0.93–0.97), as shown in Fig. 3.

Table 2  
Summary of the diagnostic performance characteristics of PET/CT and MRI in distinguishing benign and malignant ovarian tumors

Parameter	<sup>18</sup> F-FDG PET/CT		MRI	
	Estimate	95% CI	Estimate	95% CI
Sensitivity	0.92	0.86, 0.96	0.92	0.89, 0.95
Specificity	0.86	0.79, 0.91	0.85	0.79, 0.89
Positive Likelihood Ratio	6.7	4.3, 10.5	6.1	4.2, 8.7
Negative Likelihood Ratio	0.09	0.05, 0.16	0.09	0.06, 0.13
Diagnostic Odds Ratio	77	36, 163	67	38, 118
AUC	0.95	0.92, 0.96	0.95	0.92, 0.96

Notes:<sup>18</sup>F-FDG = Fluorine-18 labeled deoxyglucose; PET = Positron emission computer; CT = Computed tomography; MRI = Magnetic resonance imaging; DWI = Diffusion weighted imaging; CI = confidence interval; AUC = area under curve.

## Publication bias

Deeks et al.'s funnel plot for publication bias for MRI and <sup>18</sup>F-FDG PET/CT are shown in Fig. 4. It can be seen from the figure that the P values of the slope coefficients are all greater than 0.05 (for PET/CT,  $P=0.43$ , for MRI,  $P=0.08$ ), indicating that the possibility of publication bias between studies is low.

## Exploration of heterogeneity

The results of meta regression analysis are summarized in Table 3. Both <sup>18</sup>F-FDG PET/CT and MRI studies in the differentiation of benign and malignant ovarian tumors, the results of meta-regression analysis show that the type of study design (prospective vs. retrospective) is a factor affecting heterogeneity ( $P<0.01$ ). Specifically, for PET/CT, the sensitivity of prospective research design is higher than retrospective research (0.95[95%CI:0.91–0.98] versus 0.88 [95%CI:0.78–0.98]), but the specificity is lower than retrospective research (0.86 [95%CI:0.77–0.94] versus 0.90 [95%CI:0.83–0.98]). As for MRI, the sensitivity and specificity of studies designed for prospective studies are higher than those of retrospective studies, which are 0.95 (95%CI:[0.93–0.97]) versus 0.88 (95%CI:[0.85–0.92]), 0.86(95%CI: [0.80–0.93]) versus 0.83 (95%CI:[0.75–0.91]), respectively. In addition to the study design, the average age of patients between studies using PET/CT to differentiate benign and malignant ovarian tumors also showed heterogeneity. The sensitivity and specificity of the study with the average age of the enrolled patients greater than 60 years old are higher than those of the group with the average age of enrolled patients less than or equal to 60 years old, which are 0.96(95%CI: [0.92-1.00]) versus 0.91(95%CI: [0.84–0.97]) and 0.89(95%CI: [0.82–0.97]) versus 0.81 (95%CI:[0.74–0.88]), respectively. Otherwise, the sample size is not a factor that affects the heterogeneity between PET/CT studies. Also, for MRI, the magnetic field strength (1.5T or 3.0T), whether the diffusion weighted sequence is used, and the sample size included in the study are not factors that affect the heterogeneity between studies.

Table 3  
The results of meta-regression analysis of PET/CT and MRI to differentiate benign and malignant ovarian tumors.

Covariates	Subgroup	No. of studies	Sensitivity(95%CI)	Specitivity(95%CI)	P
<sup>18</sup> F-FDG PET/CT					
Study design	Prospective	7	0.95 [0.91–0.98]	0.86 [0.77–0.94]	0.01
	Retrospective	3	0.88 [0.78–0.98]	0.90 [0.83–0.98]	
CT technique	Without enhanced CT	5	0.94 [0.88–0.99]	0.82 [0.74–0.91]	0.39
	With enhanced CT	6	0.91 [0.84–0.98]	0.90 [0.84–0.96]	
Sample size	>50	8	0.93 [0.88–0.98]	0.87 [0.80–0.93]	0.91
	≤ 50	3	0.91 [0.80–1.00]	0.85 [0.69–1.00]	
Mean age	≥ 60	4	0.96 [0.92–1.00]	0.89 [0.82–0.97]	0.01
	<60	6	0.91 [0.84–0.97]	0.81 [0.74–0.88]	
MRI*					
Study design	Prospective	9	0.95 [0.93–0.97]	0.86 [0.80–0.93]	0.01
	Retrospective	8	0.88 [0.85–0.92]	0.83 [0.75–0.91]	
Magnetic field strength	With 1.5T	12	0.91 [0.88–0.94]	0.86 [0.81–0.92]	0.22
	Only 3.0T	5	0.95 [0.91–0.98]	0.80 [0.68–0.92]	
Scan sequence	With DWI	11	0.91 [0.88–0.95]	0.87 [0.82–0.93]	0.16
	Without DWI	6	0.94 [0.91–0.98]	0.78 [0.67–0.90]	
Sample size	>50	12	0.93 [0.91–0.96]	0.85 [0.79–0.91]	0.09
	≤ 50	5	0.85 [0.76–0.94]	0.83 [0.72–0.95]	
No. of imaging planes	3	7	0.92 [0.92–0.92]	0.83 [0.83–0.83]	1.00
	2	9	0.93 [0.93–0.93]	0.85 [0.85–0.85]	
Notes: <sup>18</sup> F-FDG = Fluorine-18 labeled deoxyglucose; PET = Positron emission computer; CT = Computed tomography; MRI = Magnetic resonance imaging; DWI = Diffusion weighted imaging; CI = confidence interval; *As for MRI, the mean age of all patients with ovarian tumors enrolled in the study was less than 60 years old, so they were not included in the subgroup analysis.					

## Discussion

Based on the published diagnostic differences between MRI and <sup>18</sup>F-FDG PET/CT in identifying benign and malignant ovarian tumors, we conducted a meta-analysis that indirectly compared the diagnostic value of the two. The results show that the pooled sensitivity and specificity of MRI and PET/CT in the diagnosis of ovarian cancer are similar, which were 0.92 (95% CI: 0.86–0.96) vs 0.92 (95% CI: 0.89–0.95) and 0.86 (95% CI: 0.79–0.91) vs 0.85 (95% CI: 0.79–0.89). Also, our results show that the correct diagnosis rate of MRI for ovarian tumors is equivalent to that of <sup>18</sup>F-FDG PET/CT, and the AUC values are both 0.95 (95%CI: 0.92 ~ 0.96), both of which show good diagnostic results.

The published studies of <sup>18</sup>F-FDG PET/CT and MRI in the diagnosis of ovarian tumors show significant heterogeneity in the pooled sensitivity and specificity results. According to the results of meta-regression analysis, the statistically significant factors that cause the heterogeneity between PET/CT studies may be attributed to the type of study design and the average age of the enrolled patients. Specifically, retrospective studies have lower sensitivity and higher specificity than prospective studies, which may be related to the small number of retrospective studies [19, 22, 24]. Moreover, the sensitivity and specificity of studies with an average patient age greater than 60 years are higher than those with an average age of 60 years or less, but the reason is not clear. As for MRI, the same reason is that the type of research design shows heterogeneity, and the sensitivity and specificity of prospective design research are higher than retrospective research. We analyzed the possible reason that when performing retrospective studies, compared with the prospective design, imaging diagnostic doctors cannot obtain enough clinical data for some patients, resulting in lower sensitivity and specificity. It is worth noting that in both PET/CT and MRI studies, only two studies included follow-up as the reference standard. Therefore, studies using only pathological biopsy and combined pathological biopsy and follow-up time as reference standards were not included for meta-regression analysis.

PET/CT showed good diagnostic performance in ovarian cancer lymph node metastasis and assessment of prognosis, which was confirmed by previous meta-analysis studies [44–46]. Moreover, a meta-analysis compared the diagnostic performance of PET/CT and MRI in ovarian cancer lymph node metastasis, and the results showed that PET/CT is superior to MRI [47]. Our meta-analysis includes 11 PET/CT studies to identify benign and malignant ovarian tumors, and shows good diagnostic performance [15–25]. And meta-regression analysis showed that the use of enhanced CT technology and only low-dose CT did not show a statistical difference ( $P=0.39$ ). Therefore, from the perspective of patients receiving radiation dose, whether enhanced CT technology is necessary in future research needs to be reconsidered.

A previous meta-analysis showed that MRI is slightly better than ultrasound and CT in identifying benign and malignant ovarian tumors, but because a small number of MRI studies were included in the group, the results were slightly different from the results of our meta-analysis, and the meta-analysis did not include the PET/CT study in the comparative analysis [48]. Our meta-analysis included 17 MRI studies, which also showed the same diagnostic performance as PET/CT. Further research may be needed to truly determine the added value of DWI sequences in identifying benign and malignant ovarian tumors, because meta-regression analysis shows that there is no statistical difference between using DWI sequences and not using DWI sequences. In addition, in terms of the magnetic field strength of MRI, the sensitivity of using 3.0T is higher than 1.5T (0.95 [95%CI:0.91–0.98] vs 0.91 [95%CI:0.88–0.94]), but the specificity is lower (0.80 [95%CI:0.68–0.92] vs 0.86 [95%CI:0.81–0.92]). In general, the use of magnetic field strength of 1.5T or 3.0T is not a factor that affects its diagnostic performance ( $P = 0.22$ ). Also, the number of imaging planes (2 or 3) is not a factor that affects the accuracy of MRI diagnosis ( $P = 1.0$ ).

There is no difference in the diagnostic performance of PET/CT and MRI in the diagnosis of ovarian cancer, so both methods seem to be worthy of clinical promotion. However, compared with PET/CT, MRI can shorten the examination time, and the medical cost is lower and benefit the patient more [42]. Also, MRI can avoid ionizing radiation, which will benefit female patients with organs such as breasts and ovaries that are sensitive to radiation [43]. Of course, in addition to PET/CT showing good diagnostic performance in distinguishing benign and malignant ovarian tumors, PET/CT also detects ovarian cancer metastases at the same time, and it is an important method for ovarian cancer staging and treatment evaluation. Therefore, a prospective study of comparing whole-body MRI and PET/CT in the staging of ovarian cancer is needed in future work. Because the current research only discusses the diagnostic value of differentiating benign and malignant ovarian tumors, based on the above advantages of MRI, we have reason to recommend MRI as the first choice of auxiliary examination method.

The main limitation of the present study is that it is an analysis indirectly comparing the diagnostic accuracy of PET/CT and MRI, and different methods were used between studies and different characteristics of patients were included, resulting in great heterogeneity in the estimation of diagnostic accuracy, which limits the quality of this meta-analysis. Secondly, both PET/CT and MRI studies, inconsistent interpretation of the results is also a major drawback. For instance, some studies classify borderline ovarian tumors as benign tumors [17, 18], but some studies classify them as malignant tumors [16, 19, 21, 25, 32, 38, 40]. Moreover, most of the studies included in the group did not describe the characteristics of ovarian tumors, such as the average size of benign and malignant tumors, the SUVmax value for the PET/CT study, the ADC value for the MRI study, which limits further subgroup analysis research. Even so, the study with a large sample size indirectly compared MRI with  $^{18}\text{F}$ -FDG PET/CT still provides a relatively good tool for the differential diagnosis of benign and malignant ovarian tumors.

## Conclusion

MRI and  $^{18}\text{F}$ -FDG PET/CT have the same diagnostic performance in the differential diagnosis of benign and malignant ovarian tumors. However, in contrast to PET/CT, which has certain characteristics of radiation, longer scanning time, and relatively expensive costs, MRI may benefit more patients with ovarian tumors and is worthy of promotion in clinical applications. Prospective studies that directly compare the diagnostic performance of MRI and  $^{18}\text{F}$ -FDG PET/CT in the differentiation of benign and malignant ovarian tumors are needed in the future.

## Declarations

### *Ethics approval and consent to participate*

This study did not involve any patients and had no ethical implications.

### *Consent for Publication*

All the authors read the article and agreed to publish it.

### *Availability of data and material*

The datasets used and materials during the current study are available from the corresponding author on reasonable request.

### *Ethical approval*

This is a meta-analysis, does not involve human research, and does not require the approval of the ethics committee.

### *Competing interests*

All authors state that there are no conflicts of interest.

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### *Authors' contributions*

Xianwen Hu performed investigation, methodology, visualization, and writing-first draft; Jiong Cai did investigation and research, methodology, writing-review and editing; Dandan Li did formal analysis and software operations; Yan Liao and Zhigang Liang did research methods and essay writing; Ling Yang and Rui

Wang did data curation; Pan Wang participated in the review and revision of the paper; All authors reviewed the manuscript.

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## Figures

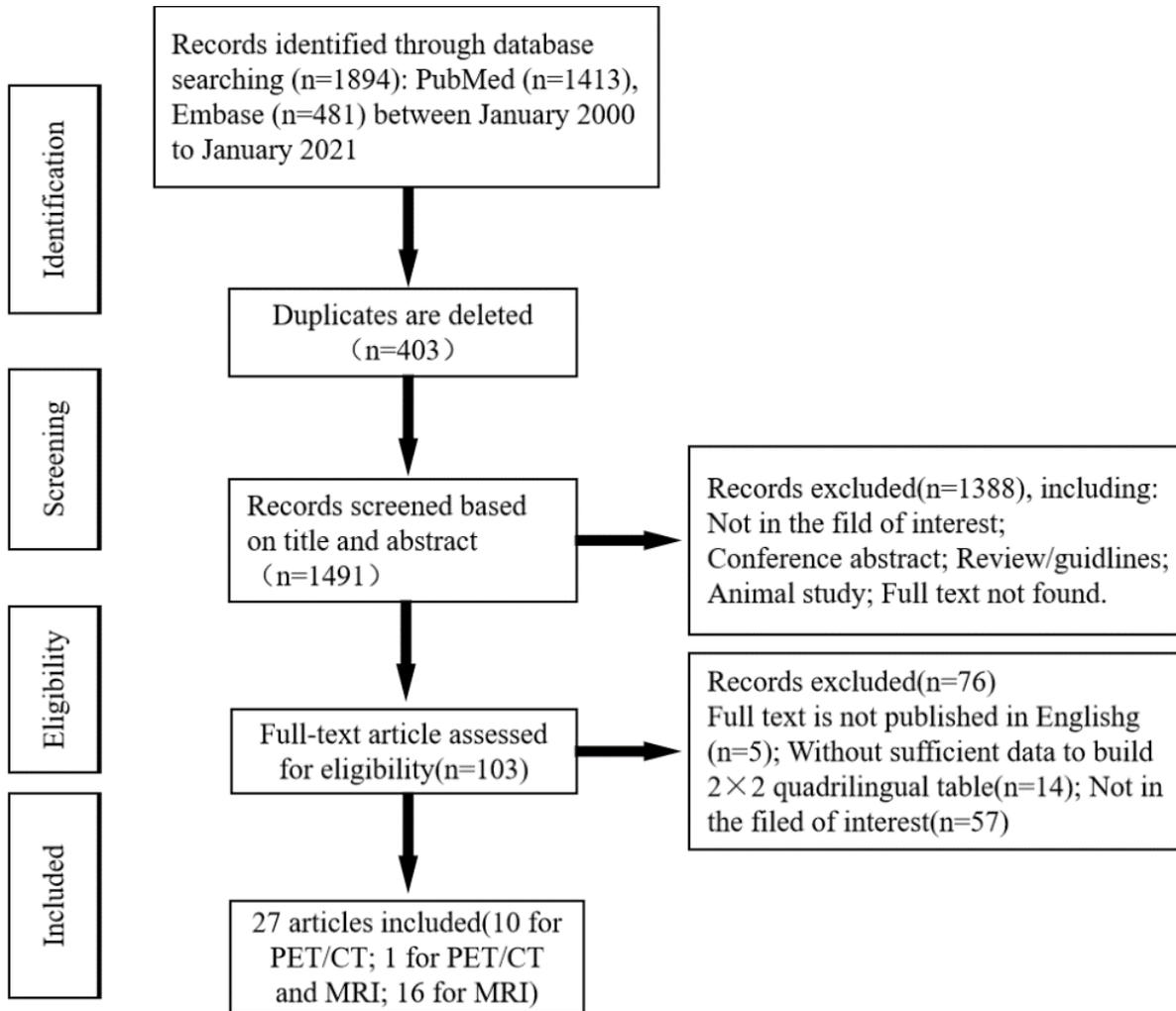


Figure 1

Flow chart of the research selection process.

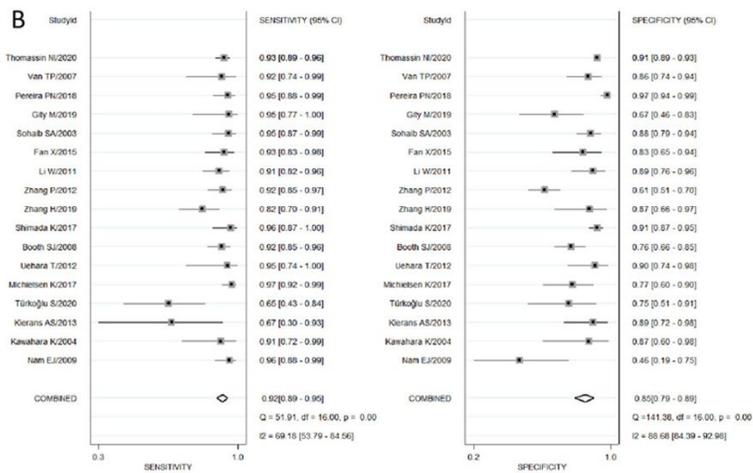
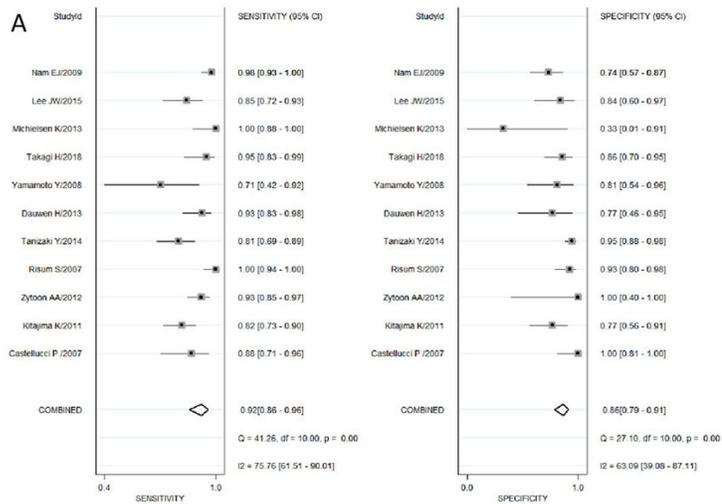


Figure 2

Forest plot of sensitivity and specificity of PET/CT(A) and MRI(B) in the diagnosis of ovarian cancer.

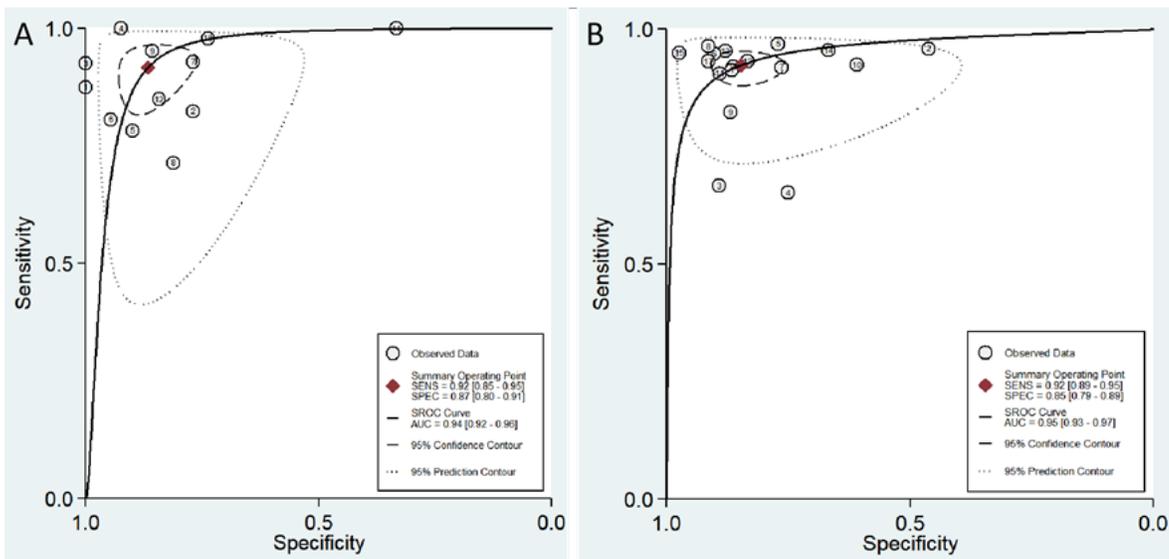


Figure 3

SROC curve of the diagnostic performance of FDG PET/CT(A) and (B) for ovarian cancer. AUC = area under the curve; SENS = sensitivity; SPEC = specificity; SROC = summary receiver operating characteristic.

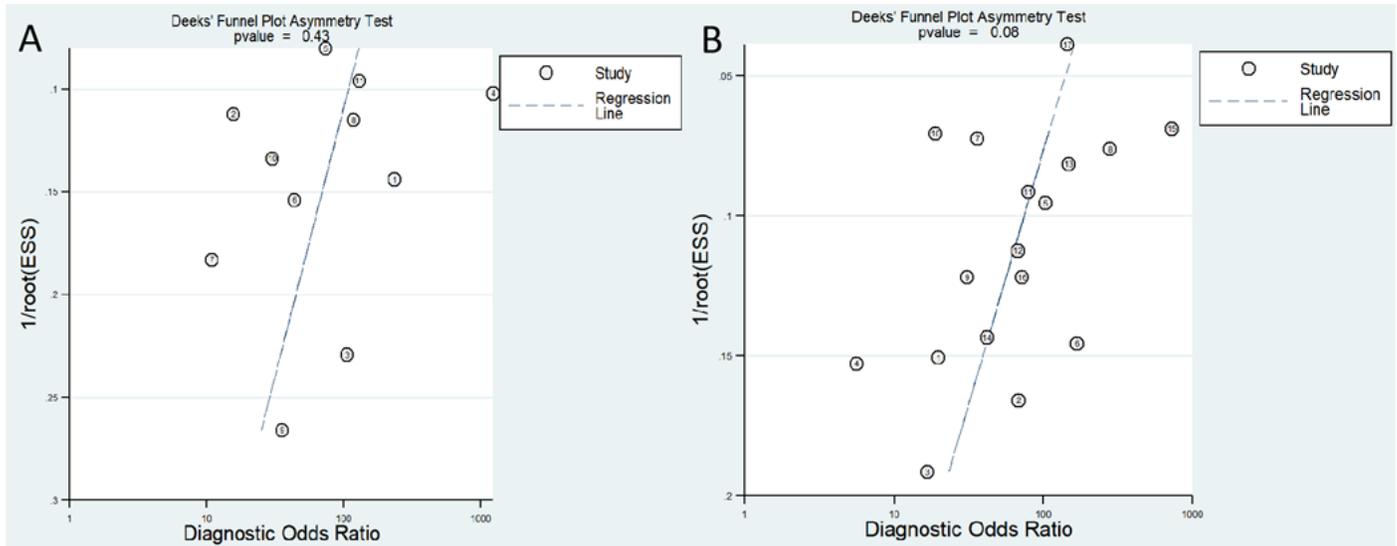


Figure 4

Deeks et al.'s funnel plot for publication bias for 18F-FDG PET/CT(A) and MRI(B).

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