Original Article

Systematic review and meta-analysis of imaging differential diagnosis of benign and malignant ovarian tumors

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Background: With the increasing incidence of gynecological ovarian tumors, the differential diagnosis of benign and malignant ovarian tumors is of great significance for subsequent treatment. Currently, ovarian examinations commonly use computed tomography (CT) or magnetic resonance imaging (MRI). This study sought to compare the value of CT and MRI in differentiating between benign and malignant ovarian tumors.

Methods: The PubMed, Cochrane Central Register of Controlled Trials, Embase, Web of Science, China National Knowledge Infrastructure, Wanfang, and Weipu databases were searched for published articles using the following terms "CT" or "Computed Tomography" or "MRI" or "Magnetic Resonance imaging" and "ovarian cancer" or "ovarian tumor" or "ovarian neoplasm" or "adnexal mass" or "adnexal lesion". The articles were screened and the data were extracted based on the inclusion and exclusion criteria. The Quality Assessment of Diagnostic Accuracy Studies-2 recommended by the Cochrane Collaboration was used to assess the methodological quality of the included studies, and the network meta-analysis was performed by Stata 15.0.

Results: The results showed that the overall sensitivity and specificity of CT were 0.79 [95% confidence intervals (CI): 0.70–0.87] and 0.87 (95% CI: 0.80–0.92), respectively. The overall sensitivity and specificity of MRI were 0.94 (95% CI: 0.91–0.95) and 0.91 (95% CI: 0.90–0.93), respectively. The area under the curve of the CT and MRI summary receiver operating characteristics were 0.9016 and 0.9764, respectively. The positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio of CT were 5.26 (95% CI: 2.78–9.93), 0.26 (95% CI: 0.13–0.50), and 22.19 (95% CI: 7.54–65.30), respectively. The positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio of MRI were 8.69 (95% CI: 5.06–14.92), 0.07 (95% CI: 0.04–0.13), and 146.19 (95% CI: 68.88–310.24), respectively.

Conclusions: Compared to CT, MRI has a stronger ability to differentiate between benign and malignant ovarian tumors. It's a promising non-radiological imaging technique and a more favorable choice for patients with ovarian tumors. However, in the future, large-sample, multi-center prospective studies need to be conducted to compare the performance of MRI and CT in distinguishing between benign and malignant ovarian tumors.

Keywords: Ovarian tumor; computed tomography (CT); magnetic resonance imaging (MRI); differential diagnosis

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Introduction

The incidence of ovarian cancer is very high, and it is also one of the main causes of female deaths due to tumors in the reproductive system. Current reports show that ovarian cancer is the cause of death of more than 180,000 women worldwide every year (1). High heterogeneity is a characteristic of ovarian cancer, which can be divided into epithelial tumors, germ cell tumors, and sex cord-stromal tumors according to pathology (2). Among them, epithelial ovarian cancer is the most common, accounting for about 90% of all cases (3). Common risk factors for the onset of ovarian cancer include family genetic history, exercise, lifestyle, diet, fertility and breastfeeding, menstruation, body mass index, gynecological related diseases, hormone replacement therapy, and even psychological factors (4-8).

Ovarian cancer is a highly aggressive ovarian tumor. Because ovarian cancer rarely observes specific clinical manifestations or signs in the early stage, it is easy to be overlooked in the early stage and cannot be diagnosed. Studies have shown that only 20–25% of patients can be detected and diagnosed in the early stages of ovarian cancer (9). Additionally, approximately 60% of patients with ovarian cancer are unfortunate, and they are diagnosed at an advanced stage (10). Patients diagnosed at an advanced stage usually have a poor prognosis, and the 5-year survival rate is often <30% (10). Benign tumors often lack typical symptoms, such as occasional bloating and abdominal masses in the lower abdomen. Malignant tumors grow rapidly and have irregular masses. Systemic symptoms, such as fever, weakness, loss of appetite, and weight loss, may appear in a short period. Benign lesions can be treated with surgery to achieve a good prognosis. Malignant lesions can be treated with multiple surgical and chemotherapy programs to control the condition, but the prognosis is usually poor when ovarian cancer is in the middle and late stages.

Clinical symptoms combined with blood tumor marker tests, ultrasound examinations, computed tomography (CT) scans, magnetic resonance imaging (MRI) scans, etc., can often make the diagnosis of ovarian cancer, but the differentiation of benign and malignant requires further judgment. Comparative studies of the sensitivity and specificity of routine examinations are extremely important for the differentiation between benign and malignant ovarian tumors. Clinical consideration needs to be directed to the diagnosis of the disease, and the formulation and implementation of treatment plans. Spiral CT and MRI are 2 commonly used diagnostic methods, which are easy to operate and have strong feasibility. The main purpose of this study was to analyze the value of CT and MRI in the differential diagnosis of benign and malignant ovarian tumors.

We present the following article in accordance with the PRISMA reporting checklist (https://gs.amegroups.com/article/view/10.21037/gs-21-889/rc).

Methods

Search strategy

We searched for articles that reported on using MRI or CT to distinguish between benign and malignant ovarian tumors, and then included these articles in the study. The following English biomedical databases were searched: PubMed, Cochrane Central Register of Controlled Trials, Embase, and Web of Science. The following major Chinese biomedical databases were searched: China National Knowledge Infrastructure, Wanfang, and Weipu. The following search terms were used: "CT" or "Computed Tomography" or "MRI" or "Magnetic Resonance imaging" and "ovarian cancer" or "ovarian tumor" or "ovarian neoplasm" or "adnexal mass" or "adnexal lesion." The searches were limited to articles published in English or Chinese from January 2000 to September 2021.

Inclusion and exclusion criteria

The included studies should meet the following criteria: (I) be published between January 2000 and September 2021; (II) be a study that evaluated the accuracy of CT or/and MRI in distinguishing between benign and malignant ovarian tumors; (III) include data on the histopathological findings for the diagnosis of benign or malignant ovarian tumors; (IV) include research data on the sensitivity, specificity, and accuracy of CT or/and MRI; and (V) include data that enabled the true positive, false positive, false

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negative, and true negative values to be derived. Studies were excluded from the meta-analysis if they met any of the following exclusion criteria: (I) the sample in the study was <10 patients; (II) the magnetic field strength for MRI research was <1.5 T or not recorded; (III) other radiotracers were used for the CT research; (IV) the article concerned a study on which repeated articles had been published (in which case the latest published article was selected); and/or (V) the article reported on animal experiments.

Paper screening and data extraction

According to the pre-established inclusion criteria, 2 of the authors independently reviewed the titles and abstracts of all the retrieved articles. If the reviewers' opinions differed, a third reviewer participated in the decision. The 2 reviewers independently extracted data from the selected articles after the screening. The extracted data included the first author, the country of the institute, the year of publication, and the CT or MRI diagnosis of the tumor (i.e., benign or malignant). Disagreements in the data extraction process were resolved via discussion until a consensus was reached. If the required information was unclear and the full text was not available, and the review author could not be contacted to obtain the relevant information, the article was excluded.

Quality assessment

The included articles were evaluated for quality, and the scope of the evaluation included patient selection, index testing, reference standards, flow, and time. Each indicator was evaluated based on the risk of bias, and the first 3 indicators were evaluated based on applicability issues. Each methodological quality was rated as "low risk", "high risk", or "unclear". The Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) recommended by the Cochrane Collaboration was used to assess the methodological quality of the research.

Statistical analysis

The main outcome indicators extracted from the enrolled studies were calculated. A hierarchical logistic regression model and a summary receiver operating characteristic (SROC) model with 95% confidence and prediction area were used in this study to calculate the sensitivity and specificity of the included research indicators. The Chi-square test and Higgins I^2 test were used to assess the heterogeneity of the included studies. And a sensitivity analysis was carried out according to the Cochrane systematic review method for included studies. The positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR) were calculated using the bivariate generalized linear mixed model and the random-effects model. All analyses were performed using Stata 15.0 (StataCorp LLC, College Station, TX, USA), and set $P<0.05$ as the difference is statistically significant.

Results

Search results and study characteristics

A total of 537 records were confirmed in all databases, and 57 unusable records were eliminated. After screening, 391 records were used for retrieval, and finally 217 articles were retrieved; 126 articles in English and 91 articles in Chinese. After reading the full text and determining that 207 articles did not meet the research criteria, as the data were incomplete, or the article was a review or case report, 10 available articles remained. The specific process for the study is shown in *Figure 1*. In relation to the 10 remaining articles, the publication times ranged from 2008 to 2020. Basic data, such as the first author, country, publication year, journal, and identification auxiliary inspection method of the article, were extracted. The basic characteristics of the articles are shown in *Table 1*.

Risk of bias and applicability judgments

In relation to the risk of bias assessment, the risk of bias for the patient selection in 2 articles was unclear, and the risk of bias for the patient selection in the other 8 articles was low. In relation to the index test bias, 3 articles had a high risk, 1 article had an unclear risk, and 6 articles had a low risk. The reference standard bias, flow, and time bias risks of all the articles were low. In the applicability bias assessment, the 3 indicators of patient selection bias, index test bias, and reference standard bias were all low risk. The results of the risk of bias assessment are shown in *Figure 2*.

Meta-analysis results

Overall analyses of CT

The meta-regression analysis showed that the pooled sensitivity of CT in distinguishing between benign and malignant ovarian tumors was 0.79 (95% CI: 0.70–0.87;

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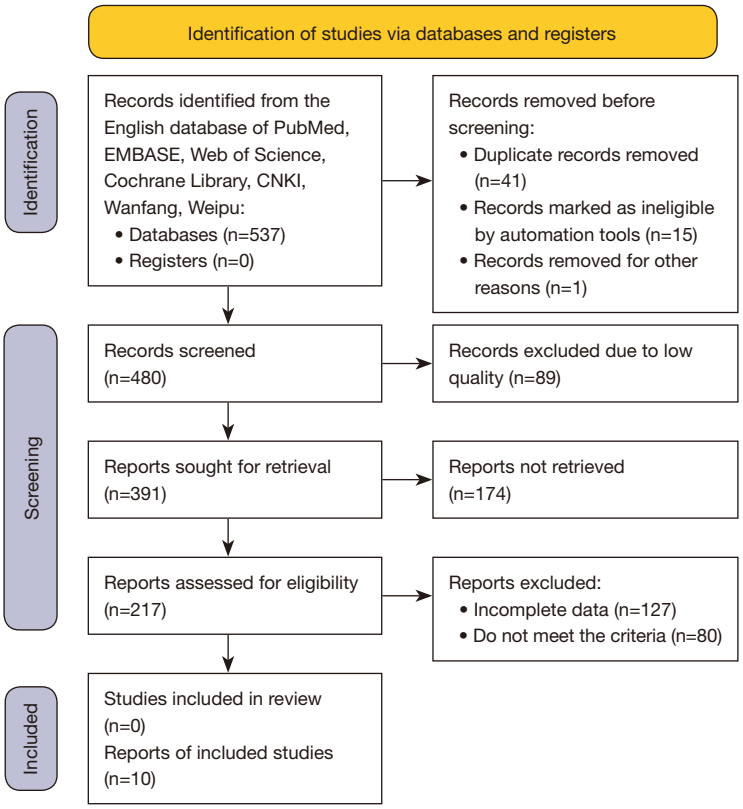

Figure 1 Flow diagram of the search, screening, and inclusion process.

Table 1 Basic characteristics of the study articles

Author	Country	Year	Journal	CT	MRI
Fan *et al.* (11)	China	2018	*Taiwan J Obstet Gynecol*	√	
Guo *et al.* (12)	China	2016	*Chinese Journal of CT and MRI*	√	√
Tsili *et al.* (13)	Greece	2008	*Eur Radiol*	√	
Jiang *et al.* (14)	China	2020	*Hainan Med J*	√	
Gity *et al.* (15)	Iran	2019	*Asian Pac J Cancer Prev*		√
Michielsen *et al.* (16)	Belgium	2017	*Eur J Cancer*		√
Pereira *et al.* (17)	Brazil	2018	*Diagn Interv Radiol*		√
Shimada *et al.* (18)	Japan	2018	*Int J Clin Oncol*		√
Thomassin-Naggara *et al.* (19)	France	2020	*JAMA Netw Open*		√
Zhang *et al.* (20)	China	2019	*Eur Radiol*		√

CT, computed tomography; MRI, magnetic resonance imaging.

Figure 3), and the pooled specificity was 0.87 (95% CI: 0.80–0.92; *Figure 4*). In addition, the sensitivity and specificity I^2 were 58.2% and 57.7%, respectively. The SROC area under the curve (SAUC) showed high accuracy (SAUC =0.9016; *Figure 5*). The closer the AUC of the SROC to 1.0, the more accurate CT was in distinguishing between benign and malignant ovarian tumors.

The positive likelihood ratio is the multiple of the

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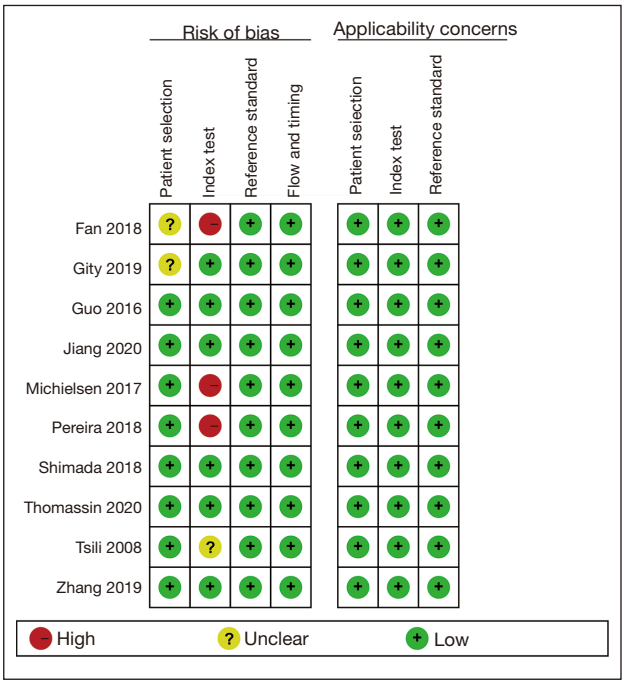

Figure 2 Literature quality evaluation details.

correctly diagnosed disease and the wrongly diagnosed disease in the diagnostic auxiliary examination. Thus, in this study, the greater the positive likelihood ratio, the higher the accuracy of CT in distinguishing between benign and malignant ovarian tumors. The analysis results show that the pooled positive likelihood ratio of CT in distinguishing between benign and malignant ovarian tumors was 5.26 (95% CI: 2.78–9.93), indicating that CT did not have a high value in distinguishing between benign and malignant ovarian tumors (*Figure 6*).

The negative likelihood ratio is the multiple of the probability of incorrectly diagnosing a negative disease to the multiple of the negative probability of correctly diagnosing the disease. Thus, in this study, the smaller the negative likelihood ratio, the higher the accuracy of CT as an auxiliary examination in distinguishing and diagnosing benign and malignant ovarian tumors. The negative likelihood ratio summarized in this study was 0.26 (95% CI: 0.13–0.50), indicating that CT is not accurate in distinguishing between benign and malignant ovarian tumors (*Figure 7*).

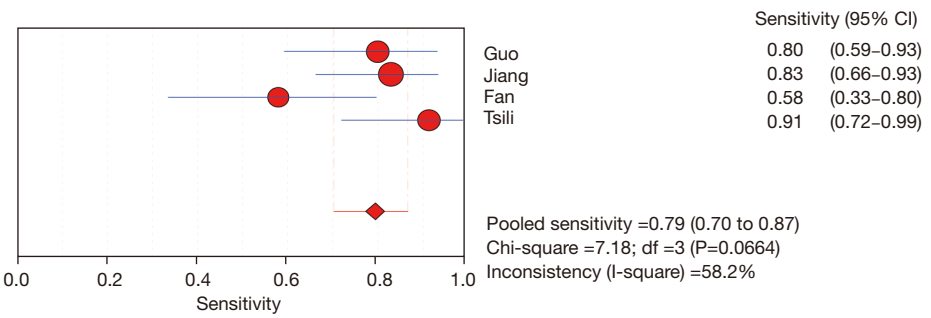

Figure 3 Sensitivity of studies: forest plot of sensitivities of 4 studies. Statistical method: inverse variance of the random-effects model. CI, confidence interval.

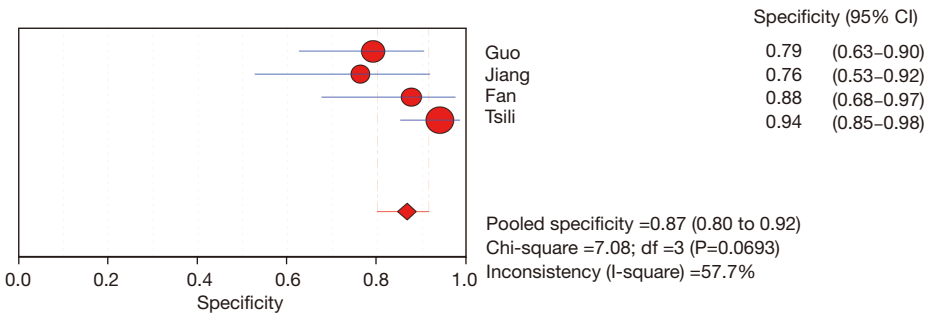

Figure 4 Specificity of studies: forest plot of specificities of 4 studies. Statistical method: inverse variance of the random-effects model. CI, confidence interval.

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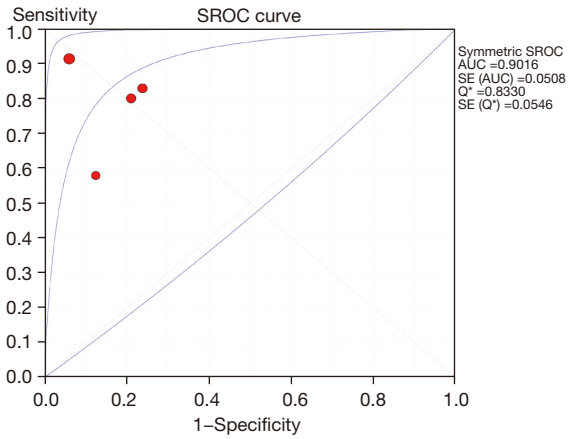

Figure 5 SROC curve for individual studies on the CT differential diagnosis of benign and malignant ovarian tumors. SROC, summary receiving operation characteristic; AUC, area under the curve; SE, standard error; CT: computed tomography.

The diagnostic odds ratio reflects the closeness of the relationship between the diagnostic test results and the corresponding disease. The greater the diagnosis rate, the greater the ability to represent whether the disease is diagnosed by the diagnostic test or auxiliary examination. The results of this study showed that the combined diagnostic odds ratio of CT in distinguishing between benign and malignant ovarian tumors was 22.19 (95% CI: 7.54–65.30). Thus, the accuracy of CT in distinguishing between benign and malignant ovarian tumors cannot be considered sufficiently strong (*Figure 8*).

Overall analyses of MRI

The meta-regression analysis showed that the pooled sensitivity of MRI in distinguishing between benign and malignant ovarian tumors was 0.94 (95% CI: 0.91–0.95) (*Figure 9*), and the pooled specificity was 0.91 (95% CI:

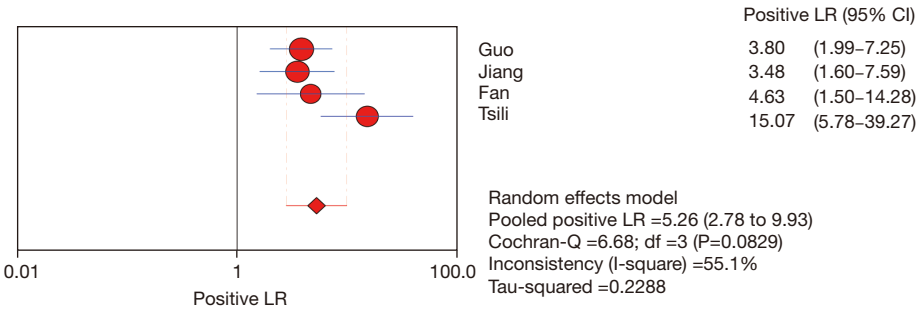

Figure 6 Forest plot of positive LR. Comparison of positive LR between the benign group and the malignant group. Statistical method: inverse variance of the random-effects model. LR, Likelihood ratio; CI, confidence interval.

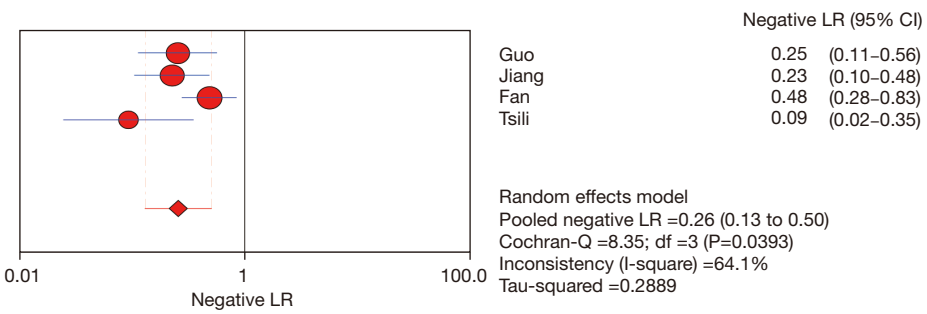

Figure 7 Forest plot of negative LR. Comparison of negative LR between the benign group and the malignant group. Statistical method: inverse variance of the random-effects model. LR, Likelihood ratio; CI, confidence interval.

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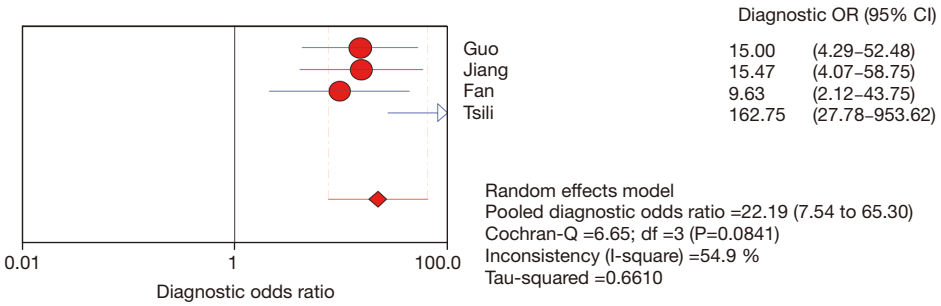

Figure 8 Forest plot of diagnostic odds ratio. Comparison of diagnostic odds ratio between the benign group and the malignant group. Statistical method: inverse variance of the random-effects model. OR, odds ratio; CI, confidence interval.

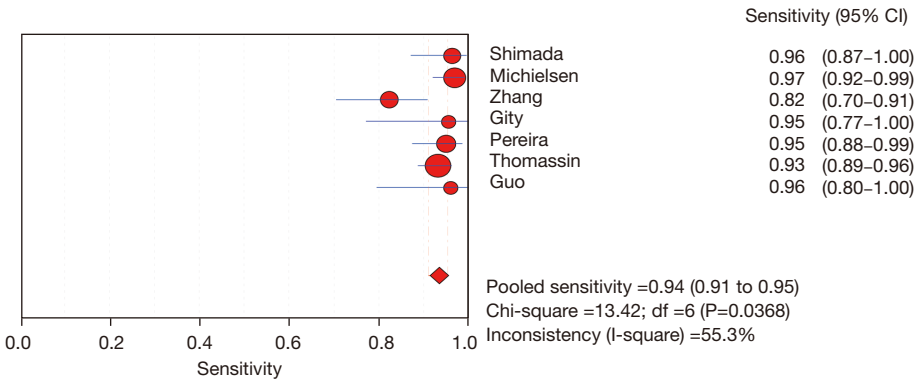

Figure 9 Sensitivity of studies: forest plot of sensitivities of 7 studies. Statistical method: inverse variance of the random-effects model. CI, confidence interval.

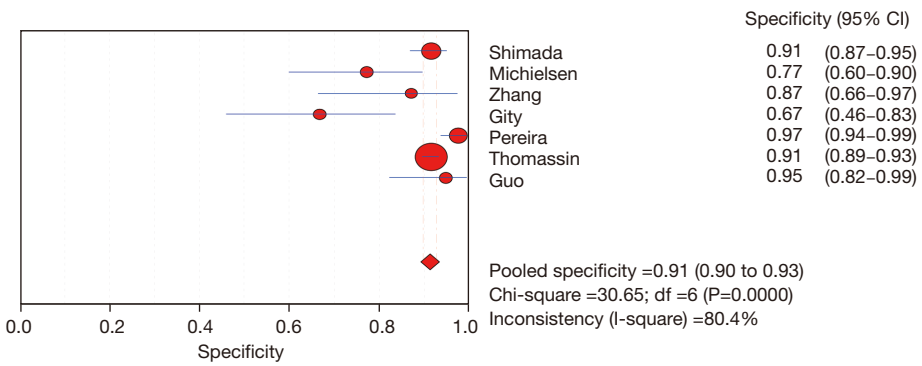

Figure 10 Specificity of studies: forest plot of specificities of 7 studies. Statistical method: inverse variance of the random-effects model. CI, confidence interval.

0.90–0.93) (*Figure 10*). In addition, the sensitivity and specificity I^2 were 55.3% and 80.4%, respectively. The SROC of MRI showed higher accuracy (SAUC =0.9764) than CT (*Figure 11*). The closer the AUC value of the SROC to 1.0, the more accurate MRI was in distinguishing between benign and malignant ovarian tumors.

The positive likelihood ratio is the multiple of the correctly diagnosed disease and the wrongly diagnosed disease in the diagnostic auxiliary examination. Thus, in this study, the greater the positive likelihood ratio, the

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higher the accuracy of MRI in distinguishing between benign and malignant ovarian tumors. The analysis results showed that the pooled positive likelihood ratio of MRI in the differential diagnosis of benign and malignant ovarian tumors was 8.69 (95% CI: 5.06–14.92), indicating that MRI has a higher value for distinguishing between benign and malignant ovarian tumors (*Figure 12*).

The negative likelihood ratio is the multiple of the probability of incorrectly diagnosing a negative disease, as the multiple of the negative probability of correctly diagnosing the disease. Thus, in this study, the smaller the negative likelihood ratio, the higher the accuracy of MRI as an auxiliary examination in distinguishing and diagnosing benign and malignant ovarian tumors. The negative likelihood ratio in this study was 0.07 (95% CI: 0.04–0.13), indicating that MRI is more accurate than CT in distinguishing between benign and malignant ovarian tumors (*Figure 13*).

The diagnostic odds ratio reflects the closeness of the relationship between the diagnostic test results and the corresponding disease. The greater the diagnosis rate, the greater the ability to represent whether the disease is diagnosed by the diagnostic test or auxiliary examination. The results of this study showed that the combined diagnostic odds ratio of MRI for distinguishing between benign and malignant ovarian tumors was 146.19 (95% CI: 68.88–310.24). Thus, MRI is more accurate in distinguishing between benign and malignant ovarian tumors (*Figure 14*).

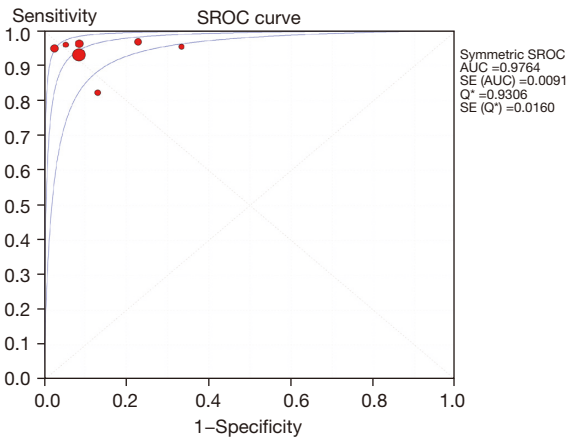

Figure 11 SROC curve for individual studies on MRI differential diagnosis of benign and malignant ovarian tumors. SROC, summary receiving operation characteristic; AUC, area under the curve; SE, standard error.

Risk of bias

The quality assessment found that in relation to the patient selection bias, 8 articles had a low risk (12-14,16-20) and 2 articles had an unclear risk (11,15). In the research index test bias, 3 articles had a high risk (11,16,17), 6 articles had a low risk (12,14,15,18-20), and 1 article had an unclear risk (13). In relation to the standard bias, flow and time bias, all the articles were low risk. In relation to the risk of applicability bias, the patient selection bias, index test bias, and reference standard bias all of the articles were low risk (*Figure 15*).

Discussion

The appearance of ovarian tumors is closely related to body factors and genetic factors, and is divided into benign tumors and malignant tumors. The former has a good

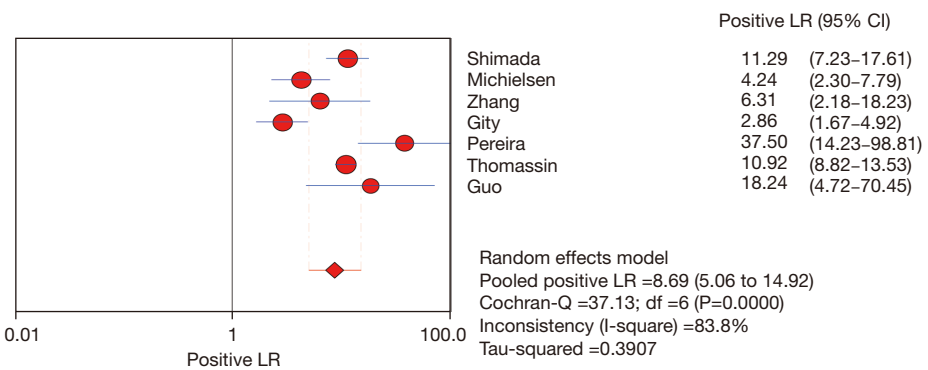

Figure 12 Forest plot of positive LR. Comparison of positive LR between the benign group and the malignant group. Statistical method: inverse variance of the random-effects model. LR, Likelihood ratio; CI, confidence interval.

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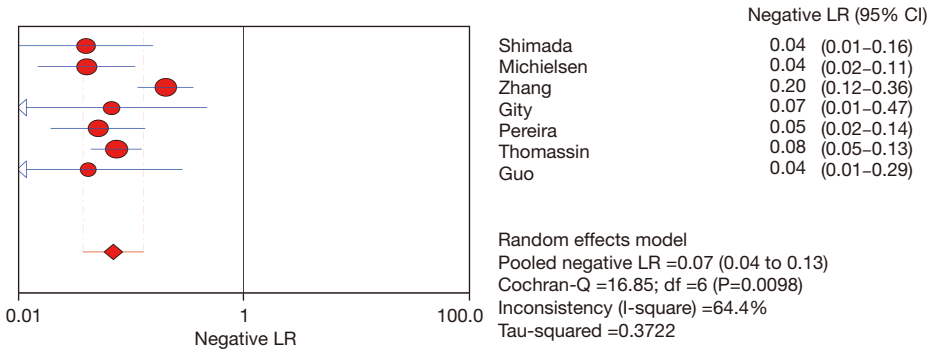

Figure 13 Forest plot of negative LR. Comparison of negative LR between the benign group and the malignant group. Statistical method: inverse variance of the random-effects model. LR, Likelihood ratio; CI, confidence interval.

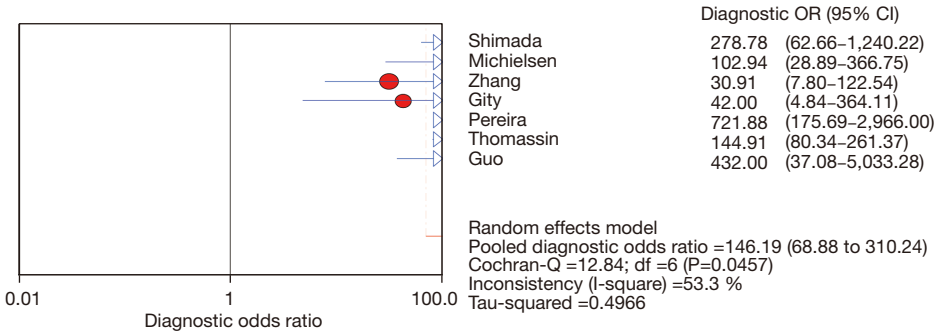

Figure 14 Forest plot of diagnostic odds ratio. Comparison of diagnostic odds ratio between the benign group and the malignant group. Statistical method: inverse variance of the random-effects model. OR, odds ratio; CI, confidence interval.

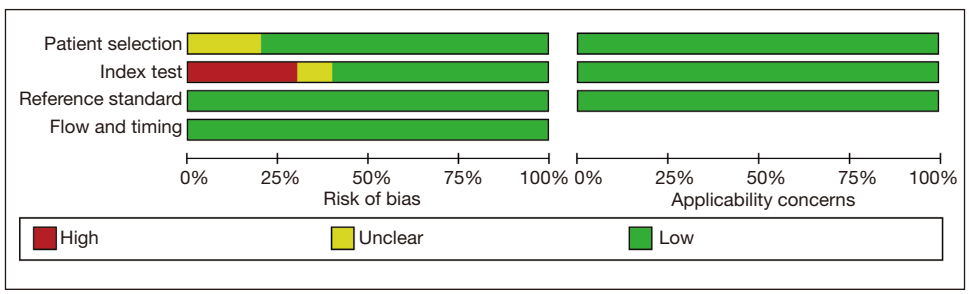

Figure 15 The intensity and distribution of the quality risk of the articles included in the study.

prognosis after treatment. Malignant ovarian tumors are the third most gynecologically malignant tumor after cervical cancer and endometrial cancer. In the early stage of onset, patients lack typical symptoms, growth is fast, and there is a high rate of misdiagnosis and missed diagnosis. By the time of the pathological diagnosis, the tumor has often developed to the middle and late stages, which increases the complexity of the disease and the difficulty of treatment. Further, as the optimal treatment time has been missed, the life of the patient is even endangered. Thus, the diagnosis of the disease must be emphasized to improve the accuracy of the diagnosis results and provide a reference for the formulation and operation of disease treatment plans.

In recent years, due to rapid developments in imaging

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technology, the 64-slice spiral CT enhanced examination has come to be widely used in disease diagnosis. Due to its high efficiency, accuracy, and 3-dimensional advantages, it is used in the diagnosis of diseases in the circulatory system, respiratory system, digestive system, and various parts of the human body. The 64-slice spiral CT enables clinicians to obtain rich details, and also has a reduced radiation dose, and reduced layer thickness. It not only diagnoses disease morphology, but also analyzes benign and malignant tumors (21,22). MRI has many parameters and rich image information. It can scan different sections to display the anatomical structure and condition of the body under examination, which is conducive to the early detection of lesions. In addition, MRI has high soft tissue resolution and high qualitative diagnostic value (23,24). Thus, MRI plays an important role in the diagnosis and differential diagnosis of ovarian tumors.

According to the imaging characteristics, benign tumors usually have complete capsules and relatively regular shapes, while malignant tumors show aggressive growth, irregular shapes and incomplete capsules. Our analysis results show that both MRI and CT have good diagnostic value for ovarian tumors, but MRI has better sensitivity and specificity than CT, and a higher AUC value. Thus, MRI is better than CT in distinguishing between benign and malignant ovarian tumors. As CT scans only show the defect of the cross-sectional image, it is difficult to distinguish between endometriotic cysts, the uterine serosal layer or ovarian tumors (25,26). Conversely, MRI uses multi-directional and multi-level imaging, obtains a larger amount of information, a higher resolution of soft tissues, and clearly defines the range of edema, inflammation, tumors, etc., and thus provides certain biochemical and pathological information (21,24,26).

The current meta-analysis has some inherent limitations, including patient selection bias, research heterogeneity, and population differences. First, the number of articles included in the study was relatively small. Second, the articles included prospective and retrospective studies, which resulted in inconsistent data. Finally, only articles published in Chinese and English were included. Multi-center and large-sample studies need to be conducted to further clarify the sensitivity and predictive value of CT and MRI in the differential diagnosis of ovarian tumors.

Conclusions

For the differential diagnosis of benign and malignant ovarian tumors, MRI and CT have high diagnostic value. However, MRI had stronger differential diagnosis capabilities than CT and is a promising non-radioimaging technology, and thus may be a more advantageous choice for patients with ovarian tumors. In the future, large-sample, multi-center prospective studies are needed to weigh the value of MRI and CT in the diagnosis of ovarian tumors.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-21-889/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-21-889/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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