Diagnostic accuracy of MRI for detecting cervical invasion in patients with endometrial carcinoma: A meta-analysis

Qiu Bi
First People's Hospital of Yunnan
Guoli Bi
First People's Hospital of Yunnan
Junna Wang
Xi'an No.3 Hospital
Jie Zhang
First People's Hospital of Yunnan
Hongliang Li
First People's Hospital of Yunnan
Xiarong Gong
First People's Hospital of Yunnan
Lixiang Ren
First People's Hospital of Yunnan
Kunhua Wu (khcgz@sina.com)
First People's Hospital of Yunnan https://orcid.org/0000-0003-3029-6140

Research

Keywords: endometrial carcinoma, magnetic resonance imaging, diffusion-weighted imaging, cervical invasion, meta-analysis

Posted Date: April 16th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-22965/v1

Abstract

Background: Clinical management and the prognosis of endometrial cancer is closely related to cervical invasion. The diagnostic performance of MRI for detecting cervical invasion has not been comprehensively assessed. We aim to evaluate the diagnostic accuracy of magnetic resonance imaging (MRI) in the preoperative assessment of cervical invasion and to analyze the influence of different imaging protocols in patients with endometrial carcinoma.

Methods: An extensive search of articles about MRI in assessing cervical invasion in patients with endometrial carcinoma was performed in PubMed, Embase, Web of Science, Cochrane Library, and Clinical Trials from January 2000 to July 2019. Two reviewers independently evaluated the methodological quality of each study by using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2). Diagnostic accuracy results and additional useful information were extracted. Pooled estimation data was obtained by statistical analysis.

Results: A total of 42 eligible studies were included in the meta-analysis. Significant evidence of heterogeneity was found for detecting cervical invasion (I^2 = 74.1%, P = 0.00 for sensitivity and I^2 = 56.2%, P = 0.00 for specificity). And the pooled sensitivity and specificity of MRI were 0.58 and 0.95 respectively. The use of higher field strength (3.0 T) demonstrated higher pooled sensitivity (0.74). Using diffusion-weighted imaging (DWI) alone presented higher pooled sensitivity (0.86) than using other sequences. Studies that used dynamic contrast-enhanced MRI (DCE-MRI) alone showed higher sensitivity (0.80) and specificity (0.96) than that used T2-weighted image (T2WI) alone.

Conclusions: MRI shows high specificity for detecting cervical infiltration in endometrial carcinoma. Using DWI or a 3.0-T device may improve the pooled sensitivity. The use of DCE-MRI demonstrate higher pooled sensitivity and specificity than T2WI.

Background

Endometrial carcinoma is one of the most common gynecological malignancies [1]. Cervical invasion is one of the important prognostic factors, and is associated with higher risk of lymph node metastases [2, 3]. Hysterectomy and bilateral salpingo-oophorectomy are the primary treatment of endometrial carcinoma [4]. However, in patients with cervical infiltration, radical hysterectomy or preoperative radiotherapy with bilateral salpingo-oophorectomy and bilateral pelvic-para-aortic lymphadenectomy may be necessary [4]. Consequently, it is important to evaluate cervical involvement preoperatively in planning treatment.

Magnetic resonance imaging (MRI) is widely used to detect cervical invasion in endometrial carcinoma and is also more accurate than hysteroscopy [5] and endocervical curettage [6]. Compared with computed tomography [7] and transvaginal sonography [8], MRI has no radiation and has high soft-tissue resolution for uterus and cervix. Therefore, MRI is considered to be optimal imaging modality for a preoperative assessment of cervical invasion [9]. With the development of functional imaging of MRI, diffusion weighted imaging (DWI) and dynamic contrast-enhanced MRI (DCE-MRI) are increasingly applied to detecting cervical infiltration in endometrial carcinoma [10–14]. A mass of studies have investigated the accuracy of MRI in detecting cervical invasion [6, 12–31]. These studies are different in MR pulse sequences, magnetic field strength, and number of patients, so that research results are diverse. Which leading to the ongoing dispute about the availability of MRI and the best imaging protocol for evaluating cervical involvement of endometrial carcinoma.

The purpose of the present study was to evaluate the diagnostic accuracy of MRI in detecting cervical invasion and to analyze the influence of different imaging protocols in patients with endometrial carcinoma.

Methods

Literature search

According to the Preferred Reporting Items for Systematic Reviews-Diagnostic Test Accuracy (PRISMA-DTA) guidelines [32], we performed this meta-analysis. A comprehensive literature search of articles about the accuracy of cervical invasion using MRI in endometrial carcinoma was performed by using the following keywords (including subject word and random word): “endometrial neoplasms”, “magnetic resonance imaging”, and “cervical”. Two authors (GB, a radiologist with 20 years of experience and QB, a radiologist with 5 years of experience) independently conducted the searches on the PubMed, Embase, Web of Science, Cochrane Library, and Clinical trials from January 2000 to December 2019 for English language articles on human subjects. To identify possible missing citation, the reference lists of relevant articles were manually searched.

Study selection

The same two authors who performed a literature search independently reviewed all the titles, abstracts, and full texts to identify potentially eligible articles. Studies meeting the following criterias were included if: (a) Accuracy was evaluated for cervical invasion by using MRI as the index test in endometrial carcinoma; (b) Histopathological results after surgery resection was used as the reference standard; (c) Sufficient information were presented to reconstruct the 2 × 2 tables. When data or patient cohort overlapped in included studies, we choose the article with the largest number of patients.

Data extraction and processing

Data on diagnostic accuracy results and additional useful information in original studies were collected by two researchers (QB and JW) who had experience in data extraction for diagnostic studies independently for 5 years. In case of discrepancies, consensus was made after discussion with each other. For each study, the following items were extracted: author name, year of publication, nation, patient age, sample size, number of observers, study design, patient recruitment, blinded to reference, magnetic field, manufacturer, sequences of observing cervical infiltration, depth of cervical invasion,

interval between MRI and pathology, and the true-positive, true-negative, false-positive, and false-negative values of MRI in detecting cervical invasion in patients with endometrial carcinoma. When two or more observers existed, the most experienced observer was selected, if the experience was not reported, the first observer was prioritized. The most contemporary MRI scan was preferred when different MR pulse sequences were reported at the same time (eg, DWI before DCE-MRI). When the accuracy of any cervical invasion and stromal invasion was reported separately, the latter was preferred.

Assessment of data quality

Quality assessment was conducted by the Quality Assessment of Diagnostic Accuracy Studies-2 [33] (QUADAS-2) by two investigators (GB and JZ, a radiologist with 15 years of experience in pelvic imaging) independently. Any disagreements were resolved by discussion with each other. The QUADAS-2 form is composed of four domains: patient selection (assessing methods of patient selection), index test (assessing the index test and how it was conducted and interpreted), reference standard (assessing the reference standard and how it was conducted and interpreted), and flow and timing (assessing any patients who did not recelve the index test and/or reference standard or who were excluded from the 2 × 2 table).

Statistical analysis

Analyses were performed by using Review Manager 5.3 (The Nordic Cochrane Centre, Copenhagen, Denmark), MetaDisc 1.4 (Ramón y Cajal Hospital, Madrid, Spain), and Stata 15.1 (StataCorp, Texas, USA). The threshold effect was assessed by the spearman correlation coefficient between the logit of sensitivity and the logit of (1-specificity) [34]. P values < 0.05 indicated the threshold effect existed [34]. Heterogeneity for sensitivity and specificity was explored by using the inconsistency index (I^2 value) in forest plots [35]. I^2 values ≥ 50.0% are considered to indicate substantial heterogeneity [35]. A fixed-effects model was used to summarize the overall pooled diagnostic results if homogeneity existed. A random-effects model was utilised if heterogeneity existed. Summary receiver-operating characteristics (sROC) curves and the area under the curve were used to elucidate the relationship between sensitivity and specificity. If heterogeneity existed, meta-regression was performed to assess covariates. Several relevant covariates were as follows: patient age (≥ 60 year or < 60 year), magnetic field (1.5 T or 3.0 T), MR pulse sequences, design (prospective or retrospective), blind to reference (yes or unknown), depth of cervical infiltration (stromal invasion or any cervical invasion), and appropriate interval between MRI and pathology (yes or unknown). Sensitivity analyses were performed on the basis of those potential influencing factors of heterogeneity. Publication bias was assessed by using Deeks'funnel plot with P values < 0.05 [36].

Results

Literature search and data extraction

The detailed flowchart summarizing literature search and selection is given in Fig. 1. A total of 1111 records from January 2000 to December 2019 for English language articles on human subjects were provided. Two additional records identified, after manual reference checking. After duplicates, 678 unique citations remained. Based on screening of titles and abstracts, 599 studies were excluded. The full text of 79 studies was reviewed, then a total of 42 eligible studies comprising 4196 patients were included in this meta-analysis. The details of principal characteristics of every included studies are summarized in Table 1.

Table 1
Description of the included studies.

Study	Year	Country	Age (y)	Sample size	Design	Patient recruitment	Blind to reference	Magnetic field	Manufacturer	Sequences	Depth of cervical invasion
Morimura	2000	Japan	U	47	R	U	U	U	U	T2	Any cervix
Seki	2000	Japan	U	39	P	U	Yes	1.5T	Siemens	DCE	Any cervix
Cunha	2001	Portugal	63.2	40	P	U	Yes	1.0T	Philips	T2 + DCE	Any cervix
Manfredi	2004	Italy	58.8	37	P	C	Yes	1.5T	GE	T2	Any cervix
Akaeda	2005	Japan	56.8	21	P	U	Yes	1.5T	Siemens	CO2-VIBE	Any cervix
Haider	2006	Canada	56	38	R	U	Yes	1.5T	GE	T2	Any cervix
Nagar	2006	UK	65.5	135	R	C	Yes	1.5T	Siemens	T2	Stroma
Rockall	2007	UK	61	84	R	U	Yes	1.5T	GE	DCE	Stroma
Vasconcelos	2007	Portugal	68.5	101	P	U	Yes	1.0T	Philips	T2 + DCE	Any cervix
Cabrita	2008	Portugal	64.6	162	U	U	U	1.5T	U	U	Any cervix
Cicinelli	2008	Italy	67.3	100	U	C	Yes	1.5T	Philips	T2	Any cervix
Sanjuan	2008	Spain	U	72	R	C	U	1.0T	Siemens	T2 + DCE	Any cervix
Savelli	2008	Italy	63	74	P	C	Yes	U	U	T2	Any cervix
Hori	2009	Japan	58.7	30	P	C	Yes	3.0T	GE	T2	Any cervix
Undurraga	2009	Switzerland	69.5	108	R	C	Yes	1.5T	U	T2 + CE	Stroma
Celik	2010	Turkey	58.9	64	P	C	Yes	1.5T	Siemens	U	Any cervix
Emlik	2010	Turkey	U	53	P	C	Yes	1.5T	Siemens	DCE	Any cervix
Duncan	2012	UK	U	748	U	U	U	U	U	U	Stroma
Haldorsen	2012	Norway	66	146	P	U	Yes	1.5T	Siemens	U	Stroma
Tong	2012	China	52	168	R	C	U	1.5T	GE	T2 + DCE	Stroma
Zamani	2012	Iran	53.3	54	U	U	Yes	1.5T	U	U	Stroma
Aly	2013	Egypt	59	40	U	U	Yes	1.5T	GE	DCE	Stroma
Antonsen	2013	Denmark	65	226	P	C	Yes	1.5T	Philips	U	Any cervix
Foti	2013	Italy	62	20	P	C	Yes	1.5T	GE	T2	Any cervix
Hahn	2013	Korea	53.1	131	R	U	Yes	1.5T	Philips	U	Stroma
Hori	2013	Japan	57.6	71	P	C	Yes	3.0T	Philips	T2 + DWI	Stroma
Kitajima	2013	Japan	62.4	30	R	U	Yes	1.5T	GE	U	Stroma

U, unknown; P, prospective; R, retrospective; C, consecutive; CE, contrast-enhanced MRI; DCE, dynamic contrast-enhanced MRI;

DWI, diffusion weighted imaging; CO2-VIBE, CO_2-volumetric interpolated breathhold examination.

Study	Year	Country	Age (y)	Sample size	Design	Patient recruitment	Blind to reference	Magnetic field	Manufacturer	Sequences	Depth of cervical invasion
Gitte	2013	Denmark	U	143	P	U	Yes	1.5T	GE	U	Any cervix
Koplay	2014	Turkey	58	58	P	C	Yes	1.5T	Siemens	DWI	Any cervix
Teng	2015	China	57.9	167	R	U	Yes	1.5T	GE	T2 + DCE	Any cervix
Yin	2015	China	54.6	98	R	U	Yes	3.0T	U	T2 + DCE	Any cervix
Zamani	2015	Iran	U	68	P	U	Yes	U	U	U	Stroma
Angioli	2016	Italy	53	41	P	U	Yes	1.5T	GE	DWI	Any cervix
Chan	2016	China	55.2	90	R	U	Yes	1.5T	Siemens	T2 + DCE	Stroma
Shrivastava	2016	India	52.8	36	R	U	Yes	1.5T	Philips	U	Stroma
Lin	2017	China	56	83	U	C	Yes	3.0T	Siemens	DWI	Stroma
Rahmani	2018	Iran	U	27	P	U	Yes	3.0T	Siemens	U	Any cervix
Xu	2018	China	51.89	88	R	U	U	U	U	U	Any cervix
Yildirim	2018	Turkey	61.1	40	P	U	Yes	1.5T	Philips	U	Any cervix
Ytre-Hauge	2018	Norway	67	178	P	C	Yes	1.5T	Siemens	U	Stroma
Goel	2019	India	60.2	58	P	U	Yes	1.5T	GE	T2 + DCE	Any cervix
Yang	2019	China	54.1	182	R	U	Yes	3.0T	GE	T2	Any cervix

U, unknown; P, prospective; R, retrospective; C, consecutive; CE, contrast-enhanced MRI; DCE, dynamic contrast-enhanced MRI;

DWI, diffusion weighted imaging; CO2-VIBE, CO_2-volumetric interpolated breathhold examination.

Quality assessment and publication bias

Figure 2 is the methodological quality graph of the evaluation of the risk of bias and applicability concerns of the selected studies, according to QUADAS-2. Regarding risk of bias and the domain patient selection, 14 studies explicitly reported that the patients were consecutives [10, 12, 13, 16, 21, 23, 25–28, 31, 37–39], the remaining 28 studies only reported the start and end times of collecting patients [5, 6, 8, 11, 14, 15, 17–20, 22, 24, 29, 30, 40–53]. Concerning the domain index test, 6 studies did not interpret that histopathology was blinded from MRI [5, 22, 23, 27, 40, 45]. Eleven studies did not present the threshold defining cervical invasion [5, 8, 15, 17, 22, 37, 38, 45, 48, 51, 52]. As for the domain reference standard, only 7 studies explicitly stated that pathology results were blinded to MRI findings [18, 20, 24, 26, 31, 38, 41], the rest 35 studies were short of reporting. In relation to the domain flow and timing, twenty four studies reported an appropriate interval between MRI and pathological examination [5, 6, 8, 10, 12–16, 18–21, 23, 24, 26, 30, 31, 38, 39, 41, 44, 45, 50], the remaining 18 studies did not reported it. All studies applied pathological evaluation of the removed uterus except for one study wasn't reported [22].

The slope coefficients for the Deeks'funnel plot for MRI in assessing cervical invasion in endometrial carcinoma are presented in Fig. 3. Publication bias was detected in the diagnosis of cervical invasion in the funnel plots (P = 0.01).

Diagnostic accuracy

The threshold effect did not exist for detecting cervical invasion (spearman correlation coefficient = -0.282, P = 0.070). Figure 4 was the forest plots of sensitivity and specificity of MRI for detecting cervical invasion, which showed significant evidence of heterogeneity (I^2 = 74.1%, P = 0.000 for sensitivity and I^2 = 56.2%, P = 0.000 for specificity). The pooled sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratios for diagnostic accuracy of MRI in detecting cervical invasion were 0.58 (95% confidence interval [CI] 0.55–0.62), 0.95 (95% CI 0.94–0.95), 9.37 (95% CI 7.78–11.28), 0.43 (95% CI 0.36–0.51), and 29.68 (95% CI 21.16–41.63), respectively. On the basis of sROC (Fig. 5), the area under the curve were 0.94. Fagan

nomograms showed that the pre-test probability of cervical invasion was 50%, the corresponding positive post-test probability and negative post-test probability were 93% and 27% respectively (Fig. 6).

Meta-regression and sensitivity analyses

Meta-regression showed that patient age, magnetic field, MR pulse sequences, design, blind method, depth of cervical infiltration, and interval between MRI and pathology did not explain heterogeneity observed for sensitivity and specificity (Table 2).

Table 2
The results of meta-regression of MRI.

Variable	Coefficient	Standard error	*P* value	Diagnostic odd ratio	95% CI
Age	0.402	0.2274	0.0850	1.49	(0.94–2.37)
Design	-0.082	0.2363	0.7296	0.92	(0.57–1.49)
Blind to reference	0.444	0.4159	0.2926	1.56	(0.67–3.61)
Magnetic feld	0.383	0.2181	0.0865	1.47	(0.94–2.28)
Sequences	0.109	0.0660	0.1080	1.11	(0.98–1.27)
Depth of cervical invasion	-0.043	0.3423	0.8996	0.96	(0.48–1.91)
Interval between MRI and pathology	-0.309	0.3274	0.3518	0.73	(0.38–1.42)
CI, confidence interval					

Table 3 presents the results of sensitivity analyses performed for different subgroups. Overall, several differences were observed for sensitivity and specificity estimates in sensitivity analyses, and the forest plots of sensitivity and specificity are presented in Fig. 7–8. Studies with higher field strength (3.0 T) had higher pooled sensitivity (0.74; 95% CI: 0.60–0.84) than studies with a 1.5-T device (0.60; 95% CI: 0.56–0.65) or 1.0-T device (0.51; 95% CI: 0.37–0.65). And the higher the field strength, the higher the pooled sensitivity. But the pooled specificity was lower by using a 3.0-T device (0.96; 95% CI: 0.93–0.97) than 1.0-T device (0.99; 95% CI: 0.96-1.00). In regard to the MR pulse sequences of observing cervical invasion, three studies [10, 16, 17] that used DWI alone had higher sensitivity (0.86; 95% CI: 0.71–0.95) compared with studies that used DCE-MRI (0.80; 95% CI: 0.65–0.91) or T2-weighted image (T2WI) (0.73; 95% CI: 0.64–0.80) alone. Four studies [11, 13, 14, 43] that used DCE-MRI alone presented higher sensitivity (0.80; 95% CI: 0.65–0.91) and specificity (0.96; 95% CI: 0.92–0.98) than that used T2WI alone. T2WI combined with DCE-MRI could not improve diagnostic performance in comparison with DCE-MRI alone. As for the depth of cervical invasion, the pooled sensitivity and specificity of MRI were 0.55 (95% CI 0.50–0.61) and 0.95 (95% CI 0.94–0.96) respectively for assessing stromal invasion in endometrial carcinoma.

Table 3
Sensitivity analyses performed for subgroups of studies.

Analysis	Number of studies	Sensitivity	Specificity	PLR	NLR	DOR
Overall	42	0.58 (0.55–0.62)	0.95 (0.94–0.95)	**9.37 (7.78–11.28)**	0.43 (0.36–0.51)	**29.68 (21.16–41.63)**
Age(y) ≥ 60 < 60	15 19	0.51 (0.45–0.56) 0.72 (0.66–0.78)	0.93 (0.92–0.95) 0.94 (0.93–0.96)	**6.73 (5.18–8.74)** **10.95 (8.61–13.94)**	0.54 (0.44–0.67) 0.27 (0.18–0.42)	**15.54 (9.49–25.45)** **58.71 (37.51–91.89)**
Design Prospective Retrospective	21 15	0.58 (0.52–0.64) 0.64 (0.58–0.70)	0.94 (0.92–0.95) 0.94 (0.93–0.95)	**7.96 (5.93–10.68)** **9.62 (7.53–12.30)**	0.43 (0.33–0.56) 0.38 (0.26–0.54)	**26.78 (15.43–46.50)** **35.25 (23.09–53.81)**
Blind to reference Yes Unknown	36 6	0.61 (0.57–0.65) 0.51 (0.44–0.59)	0.94 (0.93–0.95) 0.95 (0.93–0.96)	**9.81 (7.82–12.30)** **8.76 (6.21–12.35)**	0.39 (0.32–0.49) 0.53 (0.39–0.72)	**34.44 (23.00–51.57)** **19.45 (11.01–34.34)**
Magnetic feld 3.0T 1.5T 1.0T	6 28 3	**0.74 (0.60–0.84)** 0.60 (0.56–0.65) **0.51 (0.37–0.65)**	0.96 (0.93–0.97) **0.93 (0.92–0.94)** **0.99 (0.96–1.00)**	**16.22 (8.69–30.25)** **8.15 (6.61–10.04)** **19.99 (5.73–69.76)**	**0.33 (0.19–0.58)** 0.40 (0.31–0.51) **0.54 (0.39–0.76)**	**68.56 (28.18–166.78)** **27.08 (17.60–41.66)** **39.81 (9.15–173.19)**
MR pulse sequences DWI DCE T2 T2 + DCE	3 4 9 9	**0.86 (0.71–0.95)** **0.80 (0.65–0.91)** **0.73 (0.64–0.80)** 0.60 (0.52–0.67)	**0.92 (0.87–0.96)** **0.96 (0.92–0.98)** **0.92 (0.89–0.94)** 0.96 (0.94–0.97)	**10.18 (4.97–20.86)** **17.65(8.10–38.48)** **8.34 (6.14–11.33)** **14.35 (7.78–26.46)**	**0.16 (0.07–0.37)** 0.21 (0.07–0.61) 0.33 (0.21–0.51) 0.45 (0.30–0.67)	**61.42 (19.65–191.93)** **78.46 (24.60–250.18)** **34.57 (19.48–61.35)** **42.38 (20.56–87.35)**
Depth of cervical invasion Stromal invasion Any cervical invasion	16 26	0.55 (0.50–0.61) 0.61 (0.56–0.66)	0.95 (0.94–0.96) 0.94 (0.93–0.95)	**9.29 (7.01–12.30)** **9.53 (7.38–12.32)**	0.46 (0.36–0.59) 0.39 (0.30–0.50)	**25.98 (16.52–40.85)** **33.69 (20.43–55.56)**
Interval between MRI and pathology Appropriate Unknown	24 18	0.59 (0.54–0.63) 0.58 (0.53–0.64)	0.94 (0.93–0.95) 0.95 (0.94–0.96)	**9.10 (7.00–11.83)** **9.86 (7.68–12.65)**	0.42 (0.32–0.54) 0.43 (0.34–0.54)	**30.02 (17.73–50.80)** **28.66 (20.11–40.86)**

PLR, positive likelihood ratio; NLR, negative likelihood ratio; DOR, diagnostic odds ratios; DWI, diffusion weighted imaging; DCE, dynamic contrast-enhanced MRI.

Data in parentheses are 95% confidence interval.

Bold fonts, indicating I^2 values < 50.0%.

Discussion

This meta-analysis demonstrated high pooled specificity of MRI for detecting any cervical infiltration and stromal invasion in patients with endometrial carcinoma. Sensitivity analyses revealed that magnetic field and MR pulse sequences were helpful to explain heterogeneity observed for sensitivity and specificity of MRI for detecting cervical invasion.

Clinical management and the prognosis of endometrial carcinoma are closely related to cervical invasion [4]. Using a preoperative technique to detect cervical invasion of endometrial carcinoma may be helpful to reduce the scope of operation, minimize costs, and offer fertility-preserving treatment options for young women without cervical invasion [54]. MRI is considered as the best non-invasive method for preoperative staging of endometrial carcinoma [9]. In this meta-analysis, MRI shows low sensitivity (0.58) and high specificity (0.95) for detecting cervical invasion. It is similar to a previous meta-analysis [55]. More than that, further sensitivity analyses of magnetic field strength were performed in our meta-analysis. We found that studies with higher field strength (3.0 T) had higher sensitivity (0.74) than studies with a 1.5-T device (0.60) or 1.0-T device (0.51). Hori et al [25] discovered that 3.0-T imaging improved tumor signal-to-noise ratio by around 12% compared with 1.5 T imaging. The main reason is the signal-to-noise ratio is influenced by magnetic field strength, with higher fields having a better signal-to-noise ratio. Hence, using a 3.0-T device can provide a better quality of MRI and demonstrate higher pooled sensitivity (0.74) for detecting cervical invasion in endometrial carcinoma. At the same time, there are some problems associated with 3.0 T imaging particularly for the pelvis, such as larger susceptibility effect, larger chemical shift, and so on [25]. These factors may affect diagnostic accuracy for detecting cervical infiltration in endometrial carcinoma. As a consequence, the pooled specificity was not the highest by using a 3.0-T device (0.96).

T2WI is a conventional MR pulse sequence and one of the best MRI protocols for staging in patients with endometrial carcinoma according to the Updated Guidelines of the European Society of Urogenital Radiology [56]. On T2WI, cervical invasion was defined as a mass within the endocervical canal and/or disruption of the normal cervical stroma [25]. The normal cervical stroma appears hypointense on T2WI on account of containing rich fibrous tissue, and endometrial carcinoma appears hyperintense, leading to high contrast resolution [31]. In consequence, MRI shows high specificity for detecting cervical invasion. However, microscopic cervical infiltration may not be observed by using MRI, only macroscopic cervical invasion could be found, result in low sensitivity for detecting cervical invasion in patients with endometrial carcinoma [55].

According to a recent meta-analysis, DCE-MRI can help improve sensitivity and specificity for detecting myometrial invasion [55]. Because DCE-MRI provides the observer with obvious contrast resolution between the markedly enhanced normal myometrium and the moderately enhanced tumor. On DCE-MRI, cervical invasion was defined as interruption of the enhancement of the normal cervical epithelium [16]. Moreover, delayed DCE-MRI (4–5 min after the injection) are optimal for the detection of cervical invasion [56]. Previous research reported that DCE-MRI improved the detection of cervical infiltration by endometrial carcinoma [11]. Our meta-analysis also found that using DCE-MRI could improve sensitivity (0.80) and specificity (0.96) than using T2WI. DCE-MRI is accepted as the state-of-the-art standard for tumour delineation and is accepted as one of the best approach for local staging of endometrial carcinoma [56]. However, it is commonly difficult to assess cervical invasion when endometrial carcinoma enter the endocervical canal and give rise to obliterating the interface between the tumor and the cervix [57]. Other MRI functional imaging techniques are needed for accurate preoperative evaluation of cervical infiltration.

DWI is a functional technique of MRI to reflect the diffusivity of water molecules in tumors. DWI offers potential advantages over DCE-MRI owing to it does not need to use a contrast administration and entails a shorter imaging time. Recent evidence suggests that DWI improves the evaluation of myometrial invasion of endometrial carcinoma on account of DWI is able to determine malignant lesions as a hyperintense area with excellent tissue contrast [10]. To avoid the influence of T2 shine-through effect, cervical invasion was defined as the appearance of higher signal intensity on high-b-value DWI and low signal intensity on apparent diffusion coefficient (ADC) maps, compared with the surrounding normal cervical parenchyma [16, 56]. This meta-analysis found studies that used DWI alone had higher sensitivity (0.86) compared with studies that used DCE-MRI (0.80) or T2WI (0.73) alone. Significant improvement in sensitivity was also found in DWI compared with DCE-MRI and T2WI for detecting cervical invasion in a previous original study [16]. False positive rate may increase when cervical mucus presents, because it shows a high signal on DWI and low signal on ADC maps. Which will lead to a decrease in specificity. Furthermore, DWI also has other disadvantages, such as limited spatial resolution and image distortions because of susceptibility artefacts. Thus referring to other MR pulse sequences for an anatomical landmark is warranted. As a result, DWI is now routinely used as an adjunct to T2WI and DCE-MRI [56].

There are some limitations in this meta-analysis. Firstly, due to the lack of support of enough literature, sensitivity analyses of other technicals such as CO_2-volumetric interpolated breathhold examination was not performed. Secondly, some studies did not afford sequences of observing cervical infiltration. In addition, the number of included studies is limited. It remains to be determined whether combined DWI and T2WI is superior to DCE-MRI, whether a 3.0-T device combined with DWI or DCE-MRI had the higher sensitivity and specificity, and so on. Thirdly, publication bias was existed. One possible reason was that we excluded relevant studies published in other languages. Another possible reason was that the sensitivity for detecting cervical invasion was low. Perhaps some articles of negative results were not published.

In conclusion, this meta-analysis shows low pooled sensitivity and high specificity of MRI for detecting any cervical infiltration and stromal invasion in endometrial carcinoma. Studies with 3.0-T device demonstrate the higher pooled sensitivity than any other study. And the higher the field strength, the higher the pooled sensitivity. Using DWI alone demonstrated higher pooled sensitivity compared with using DCE-MRI or T2WI only. Studies that used DCE-MRI alone showed higher sensitivity and specificity than that used T2WI alone.

Abbreviations

MRI: magnetic resonance imaging; DWI: diffusion-weighted imaging; DCE-MRI: dynamic contrast-enhanced MRI; T2WI: T2-weighted image; ADC: apparent diffusion coefficient; sROC: summary receiver-operating characteristics; CI: confidence interval; PRISMA-DTA: Preferred Reporting Items for Systematic Reviews-Diagnostic Test Accuracy; QUADAS-2: Quality Assessment of Diagnostic Accuracy Studies-2

Declarations

Ethics approval and consent to participate: Not applicable.

Consent for publication: Not applicable.

Availability of data and materials: All data generated or analysed during this study are included in this published article.

Competing interests: The authors declare that they have no competing interests.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions: QB and GB: literature search, study selection, and writing and preparation of manuscript. QB and JW: data extraction and processing. GB and JZ: assessment of data quality. HL, XG, and LR: statistical analysis. KW: study design, manuscript editing.

Acknowledgements: The authors are grateful to Professor Ying Zhao at the Department of MRI, the First People's Hospital of Yunnan Province, the Affiliated Hospital of Kunming University of Science and Technology, for their consistent support of the study.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics. 2019. CA Cancer J Clin. 2019;69(1):7–34.
2. Solmaz U, Mat E, Dereli ML, et al. Lymphovascular space invasion and positive pelvic lymph nodes are independent risk factors for para-aortic nodal metastasis in endometrioid endometrial cancer. Eur J Obstet Gynecol Reprod Biol. 2015;186:63–7.
3. Taskin S, Ortac F, Kahraman K, Goc G, Oztuna D, Gungor M. Cervical stromal involvement can predict survival in advanced endometrial carcinoma: a review of 67 patients. Int J Clin Oncol. 2013;18(1):105–9.
4. Colombo N, Preti E, Landoni F, et al. Endometrial cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24(Suppl 6):i33-8.
5. Xu G, Wang D, Ling X, et al. Diagnostic value of assessment of cervical involvement in early-stage endometrial adenocarcinoma: comparison of magnetic resonance imaging (MRI) versus hysteroscopy. Med Sci Monitor. 2018;24:7952–7.
6. Haldorsen IS, Berg A, Werner HM, et al. Magnetic resonance imaging performs better than endocervical curettage for preoperative prediction of cervical stromal invasion in endometrial carcinomas. Gynecol Oncol. 2012;126(3):413–8.
7. Kinkel K, Kaji Y, Yu KK, et al. Radiologic staging in patients with endometrial cancer: a meta-analysis. Radiology. 1999;212(3):711–8.
8. Yildirim N, Saatli B, Kose S, et al. Predictability of myometrial, lower uterine segment and cervical invasion with 3D transvaginal ultrasonography and magnetic resonance imaging in endometrial cancer patients: a prospective cohort study. Med Ultrason. 2018;20(3):348–54.
9. Haldorsen IS, Salvesen HB. Staging of endometrial carcinomas with MRI using traditional and novel MRI techniques. Clin Radiol. 2012;67(1):2–12.
10. Koplay M, Dogan NU, Erdogan H, et al. Diagnostic efficacy of diffusion-weighted MRI for pre-operative assessment of myometrial and cervical invasion and pelvic lymph node metastasis in endometrial carcinoma. J Med Imaging Radiat Oncol. 2014;58(5):538 – 46, 648.
11. Aly AM, Moustafa YI, Shaaban HM, Abbas A. Can dynamic contrast enhanced magnetic resonance imaging change treatment planning in endometrial carcinoma? Egypt J Radiol Nucl Med. 2013;44(2):367–73.
12. Hori M, Kim T, Onishi H, et al. Endometrial cancer: preoperative staging using three-dimensional T2-weighted turbo spin-echo and diffusion-weighted MR imaging at 3.0 T: a prospective comparative study. Eur Radiol. 2013;23(8):2296–305.
13. Emlik D, Kiresi D, Ozdemir S, Celik C, Karakose S. Preoperative assessment of myometrial and cervical invasion in endometrial carcinoma: comparison of multi-section dynamic MR imaging using a three dimensional FLASH technique and T2-weighted MR imaging. J Med Imaging Radiat Oncol. 2010;54(3):202–10.
14. Seki H, Takano T, Sakai K. Value of dynamic MR imaging in assessing endometrial carcinoma involvement of the cervix. Am J Roentgenol. 2000;175(1):171–6.
15. Ytre-Hauge S, Dybvik JA, Lundervold A, et al. Preoperative tumor texture analysis on MRI predicts high-risk disease and reduced survival in endometrial cancer. J Magn Reson Imaging. 2018;48(6):1637–47.
16. Lin G, Huang Y, Chao A, et al. Endometrial cancer with cervical stromal invasion: diagnostic accuracy of diffusion-weighted and dynamic contrast enhanced MR imaging at 3T. Eur Radiol. 2017;27(5):1867–76.
17. Angioli R, Plotti F, Capriglione S, et al. Preoperative local staging of endometrial cancer: the challenge of imaging techniques and serum biomarkers. Arch Gynecol Obstet. 2016;294(6):1291–8.
18. Teng F, Zhang YF, Wang YM, et al. Contrast-enhanced MRI in preoperative assessment of myometrial and cervical invasion, and lymph node metastasis: diagnostic value and error analysis in endometrial carcinoma. Acta Obstet Gyn Scan. 2015;94(3):266–73.
19. Kitajima K, Suenaga Y, Ueno Y, et al. Value of fusion of PET and MRI for staging of endometrial cancer: Comparison with 18F-FDG contrast-enhanced PET/CT and dynamic contrast-enhanced pelvic MRI. Eur J Radiol. 2013;82(10):1672–6.
20. Ørtoft G, Dueholm M, Mathiesen O, et al. Preoperative staging of endometrial cancer using TVS, MRI, and hysteroscopy. Acta Obstet Gyn Scan. 2013;92(5):536–45.
21. Antonsen SL, Jensen LN, Loft A, et al. MRI, PET/CT and ultrasound in the preoperative staging of endometrial cancer—A multicenter prospective comparative study. Gynecol Oncol. 2013;128(2):300–8.
22. Duncan KA, Drinkwater KJ, Frost C, Remedios D, Barter S. Staging cancer of the uterus: a national audit of MRI accuracy. Clin Radiol. 2012;67(6):523–30.
23. Tong T, Yajia G, Huaying W, Weijun P. Application of 1.5 T magnetic resonance imaging in endometrial cancer. Arch Gynecol Obstet. 2012;285(4):1113–8.
24. Zamani F, Goodarzi S, Hallaji F, et al. Diagnostic value of pelvic MRI for assessment of the depth of myometrial invasion and cervical involvement in endometrial cancer: comparison of new versus old FIGO staging. Iran J Radiol. 2012;9(4):202–8.
25. Hori M, Kim T, Murakami T, et al. MR imaging of endometrial carcinoma for preoperative staging at 3.0 T: Comparison with imaging at 1.5 T. J Magn Reson Imaging. 2009;30(3):621–30.
26. Cicinelli E, Marinaccio M, Barba B, et al. Reliability of diagnostic fluid hysteroscopy in the assessment of cervical invasion by endometrial carcinoma: a comparative study with transvaginal sonography and MRI. Gynecol Oncol. 2008;111(1):55–61.

27. Sanjuán A, Escaramís G, Ayuso JR, et al. Role of magnetic resonance imaging and cause of pitfalls in detecting myometrial invasion and cervical involvement in endometrial cancer. Arch Gynecol Obstet. 2008;278(6):535–9.
28. Savelli L, Ceccarini M, Ludovisi M, et al. Preoperative local staging of endometrial cancer: transvaginal sonography vs. magnetic resonance imaging. Ultrasound Obstet Gynecol. 2008;31(5):560–6.
29. Nagar H, Dobbs S, McClelland HR, Price J, McCluggage WG, Grey A. The diagnostic accuracy of magnetic resonance imaging in detecting cervical involvement in endometrial cancer. Gynecol Oncol. 2006;103(2):431–4.
30. Akaeda T, Isaka K, Takayama M, Kakizaki D, Abe K. Myometrial invasion and cervical invasion by endometrial carcinoma: Evaluation by CO2-volumetric interpolated breathhold examination (VIBE). J Magn Reson Imaging. 2005;21(2):166–71.
31. Manfredi R, Mirk P, Maresca G, et al. Local-regional staging of endometrial carcinoma: role of MR imaging in surgical planning. Radiology. 2004;231(2):372–8.
32. Frank RA, Bossuyt PM, McInnes M. Systematic reviews and meta-analyses of diagnostic test accuracy: the PRISMA-DTA statement. Radiology. 2018;289(2):313–4.
33. Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011;155(8):529–36.
34. Zamora J, Abraira V, Muriel A, Khan K, Coomarasamy A. Meta-DiSc: a software for meta-analysis of test accuracy data. Bmc Med Res Methodol. 2006;6:31.
35. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557–60.
36. Deeks JJ, Macaskill P, Irwig L. The performance of tests of publication bias and other sample size effects in systematic reviews of diagnostic test accuracy was assessed. J Clin Epidemiol. 2005;58(9):882–93.
37. Undurraga M, Petignat P, Pelte M, Jacob S, Dubuisson J, Loubeyre P. Magnetic resonance imaging to identify risk of lymph node metastasis in patients with endometrial cancer. Int J Gynecol Obstet. 2009;104(3):233–5.
38. Celik C, Ozdemir S, Kiresi D, Emlik D, Tazegul A, Esen H. Evaluation of cervical involvement in endometrial cancer by transvaginal sonography, magnetic resonance imaging and frozen section. J Obstet Gynaecol. 2010;30(3):302–7.
39. Foti PV, Farina R, Coronella M, et al. Endometrial carcinoma: MR staging and causes of error. La radiologia medica. 2013;118(3):487–503.
40. Morimura Y, Soeda S, Hashimoto T, et al. The value of pre-operative diagnostic procedures for cervical involvement in uterine corpus carcinoma. Fukushima J Med Sci. 2000;46(1–2):1–11.
41. Cunha TM, Felix A, Cabral I. Preoperative assessment of deep myometrial and cervical invasion in endometrial carcinoma: comparison of magnetic resonance imaging and gross visual inspection. Int J Gynecol Cancer. 2001;11(2):130–6.
42. Haider MA, Patlas M, Jhaveri K, Chapman W, Fyles A, Rosen B. Adenocarcinoma involving the uterine cervix: magnetic resonance imaging findings in tumours of endometrial, compared with cervical, origin. Can Assoc. Radiol J. 2006;57(1):43–8.
43. Rockall AG, Meroni R, Sohaib SA, et al. Evaluation of endometrial carcinoma on magnetic resonance imaging. Int J Gynecol Cancer. 2007;17(1):188–96.
44. Vasconcelos C, Felix A, Cunha TM. Preoperative assessment of deep myometrial and cervical invasion in endometrial carcinoma: comparison of magnetic resonance imaging and histopathologic evaluation. J Obstet Gynaecol. 2007;27(1):65–70.
45. Cabrita S, Rodrigues H, Abreu R, et al. Magnetic resonance imaging in the preoperative staging of endometrial carcinoma. Eur J Gynaecol Oncol. 2008;29(2):135–7.
46. Hahn H, Song H, Lee I, et al. Magnetic resonance imaging and intraoperative frozen sectioning for the evaluation of risk factors associated with lymph node metastasis in endometrial cancer. Int J Gynecol Cancer. 2013;23(8):1411–6.
47. Yin X, Jia H, Shi M, Wu H, Li Y. Magnetic resonance imaging for detection of depth of myometrial invasion and cervical invasion in patients with endometrial carcinoma. Int J Clin Exp Med. 2015;8(10):19501–5.
48. Zamani N, Modares GM, Zamani F, Zamani MH. Utility of pelvic MRI and tumor markers HE4 and CA125 to predict depth of myometrial invasion and cervical involvement in endometrial cancer. J Family Reprod Health. 2015;9(4):177–83.
49. Shrivastava S, Barmon D, Kataki AC, et al. Magnetic resonance imaging in pre-operative staging of endometrial cancer. Indian J Cancer. 2016;53(1):181–5.
50. Chan C, Shek S, Kwok S, et al. Diagnostic accuracy of preoperative magnetic resonance imaging in staging endometrial cancer: a five-year experience. Hong Kong J Radiol. 2017;19(4):249–55.
51. Rahmani M, Heydari S, Mousavi A, Ahmadinejad N, Azhdeh S, Shakiba M. Accuracy of imaging in preoperative local staging of endometrial cancer: could imaging predict low risk patients? Int J Women's Health Reprod Sci. 2018;6(3):363–8.
52. Goel G, Rajanbabu A, Sandhya CJ, Nair IR. A prospective observational study evaluating the accuracy of MRI in predicting the extent of disease in endometrial cancer. Indian J Surg Oncol. 2019;10(1):220–4.
53. Yang T, Tian S, Li Y, et al. Magnetic resonance imaging (MRI) and three-dimensional transvaginal ultrasonography scanning for preoperative assessment of high risk in women with endometrial cancer. Med Sci Monitor. 2019;25:2024–31.
54. Eskander RN, Randall LM, Berman ML, Tewari KS, Disaia PJ, Bristow RE. Fertility preserving options in patients with gynecologic malignancies. Am J Obstet Gynecol. 2011;205(2):103–10.

55. Bi Q, Chen Y, Wu K, et al. The diagnostic value of MRI for preoperative staging in patients with endometrial cancer: a meta-analysis. Acad Radiol. 2019.
56. Nougaret S, Horta M, Sala E, et al. Endometrial cancer MRI staging: Updated Guidelines of the European Society of Urogenital Radiology. Eur Radiol. 2019;29(2):792–805.
57. Freeman SJ, Aly AM, Kataoka MY, Addley HC, Reinhold C, Sala E. The revised FIGO staging system for uterine malignancies: implications for MR imaging. Radiographics. 2012;32(6):1805–27.

Figures

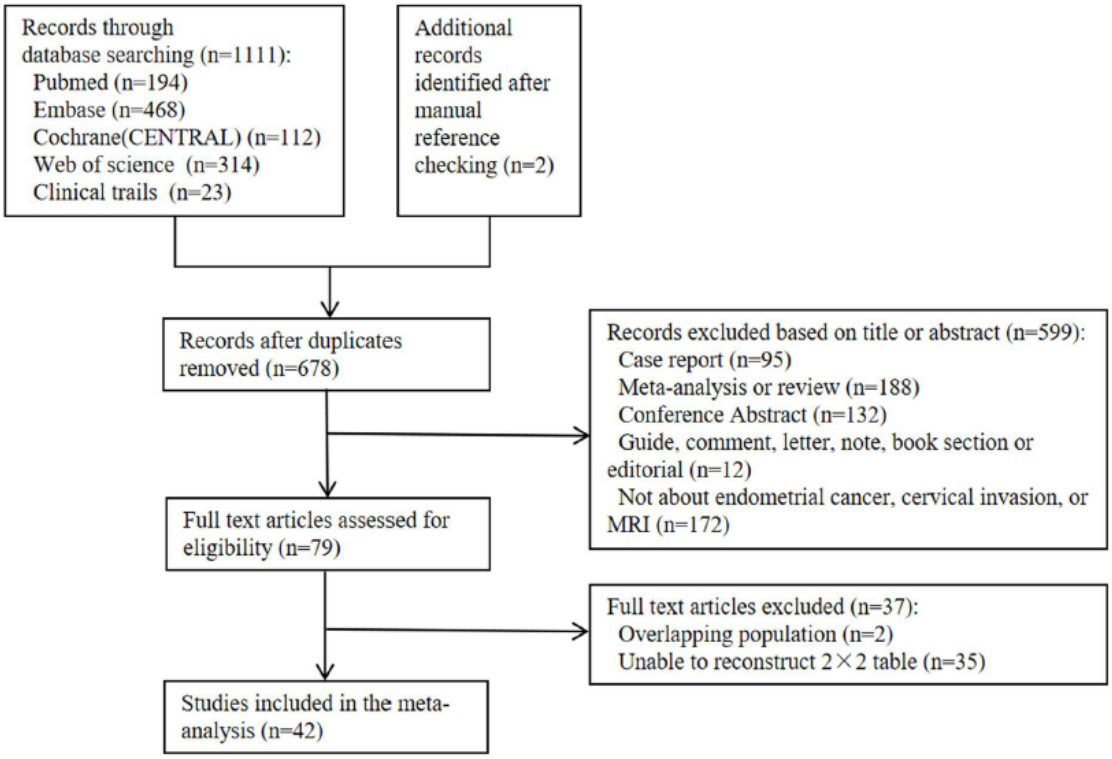

Figure 1

Flowchart of the study selection process.

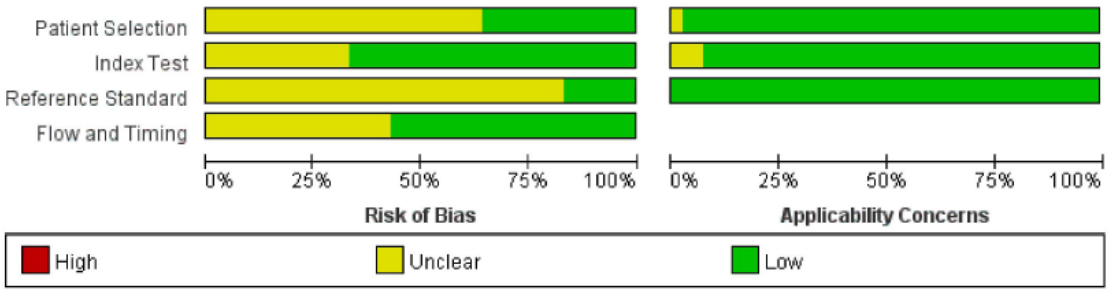

Figure 3

Histogram plot of the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) scores of methodological study quality.

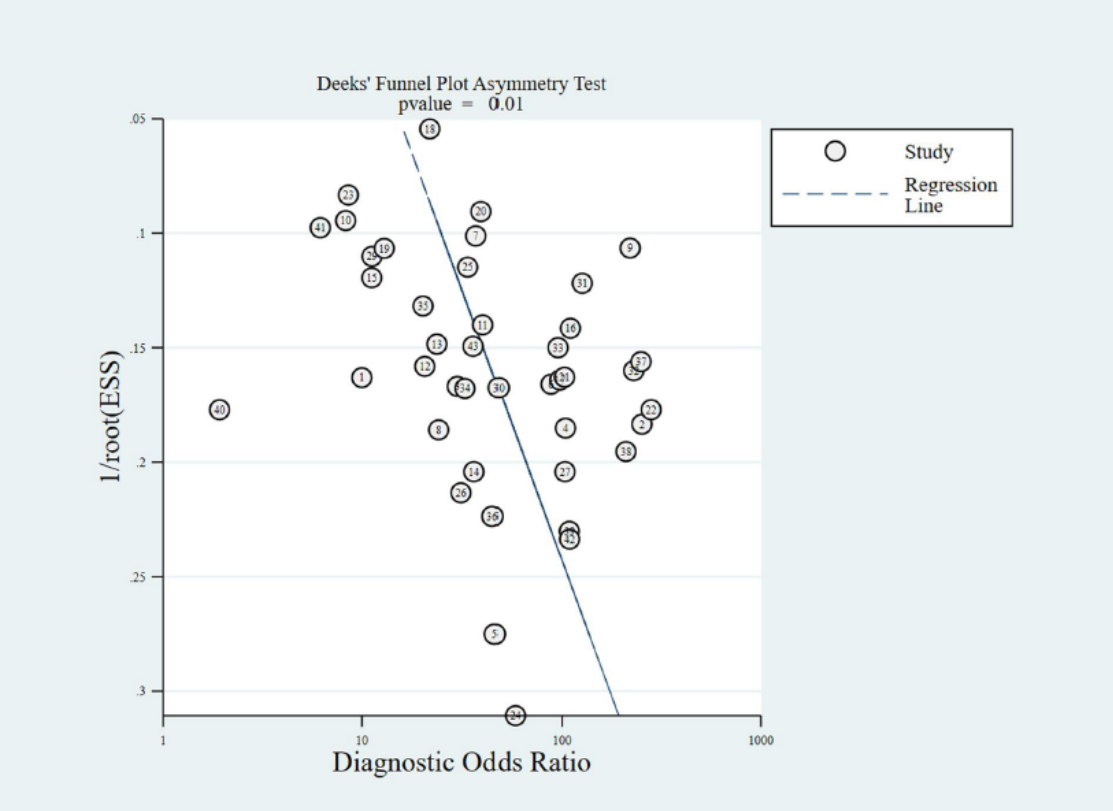

Figure 6

Deeks'funnel plot for evaluating cervical invasion in endometrial carcinoma. A value of P<0.05 was considered to indicate significant publication bias. Numbers in circles represent study number. ESS, effective sample size.

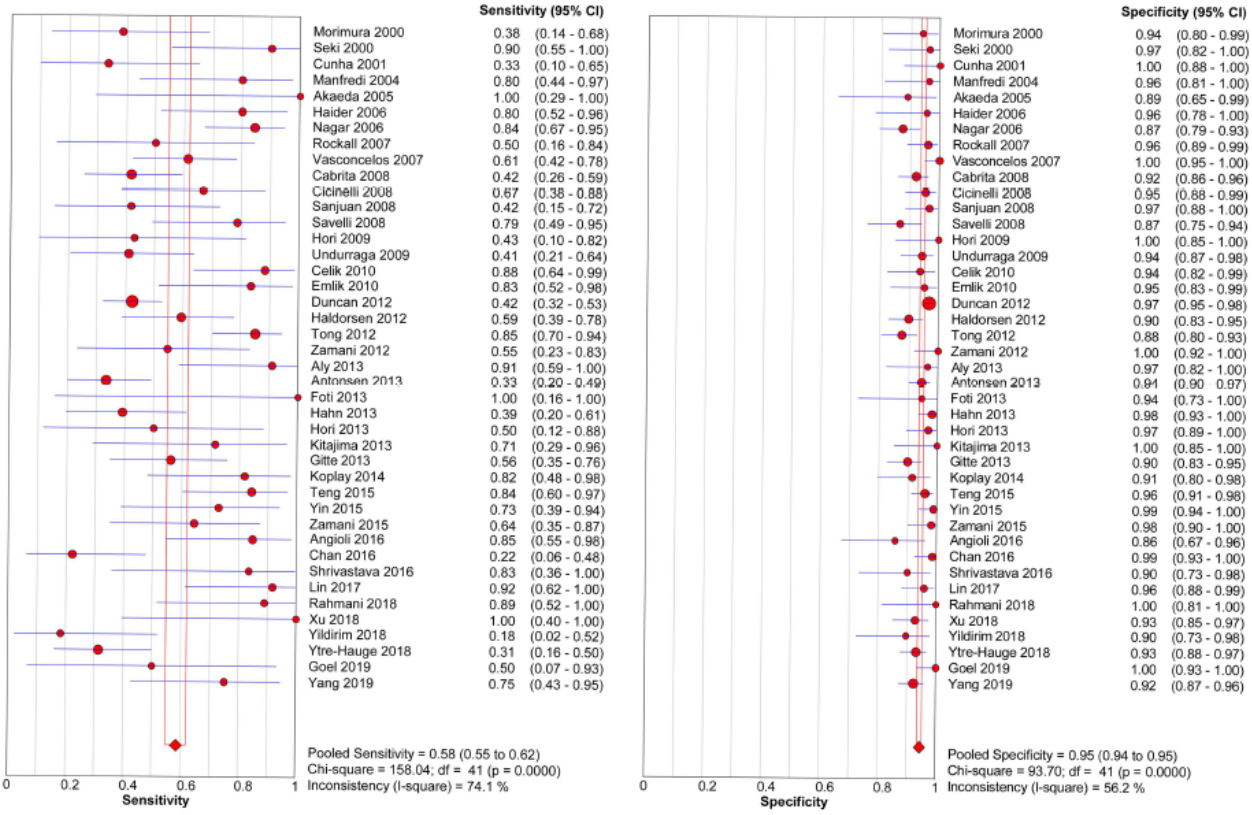

Figure 7

Forest plots show the pooled sensitivity and specificity of MRI for detecting cervical invasion in endometrial carcinoma. I2 values ≥ 50.0% are considered to indicate substantial heterogeneity in each study. CI, confidence interval.

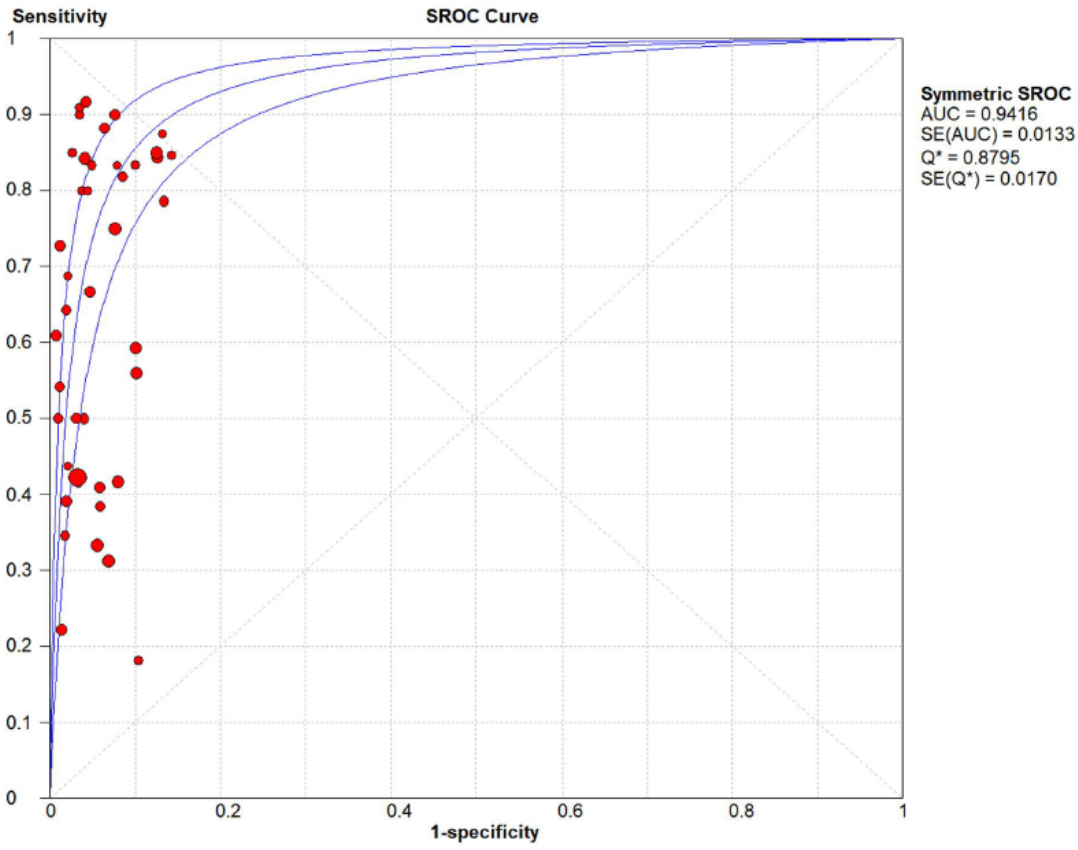

Figure 9

Summary receiver-operating characteristics (sROC) curves of MRI for detecting cervical invasion in endometrial carcinoma. AUC, area under the curve.

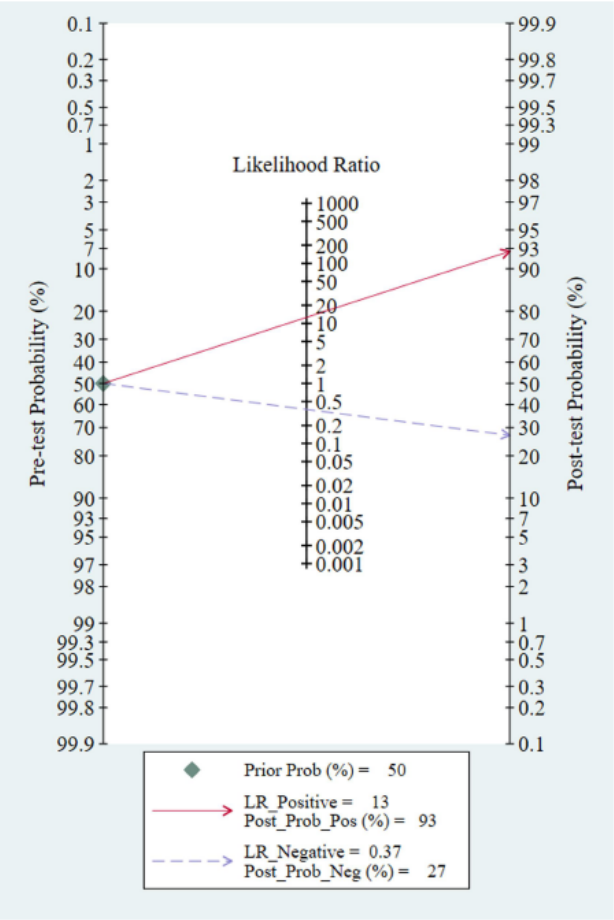

Figure 11

Fagan nomogram shows pre-test probability, positive post-test probability, and negative post-test probability of MRI for assessing cervical involvement in endometrial carcinoma. LR, likelihood ratio; Prob, probability.

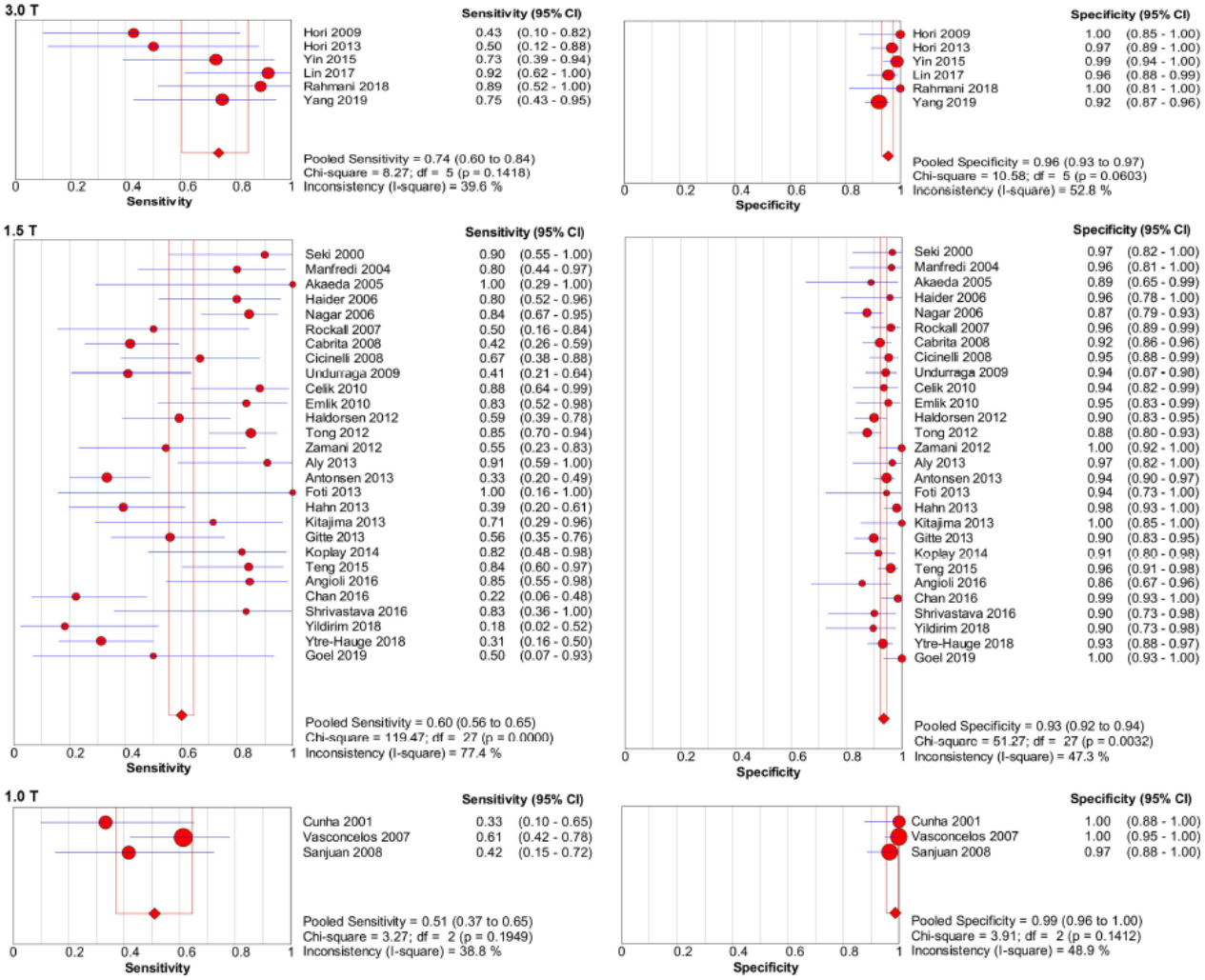

Figure 13

Forest plots of pooled sensitivity and specificity of using a 3.0-T device, 1.5-T device, and 1.0-T device for assessing cervical involvement in endometrial carcinoma. CI, confidence interval.

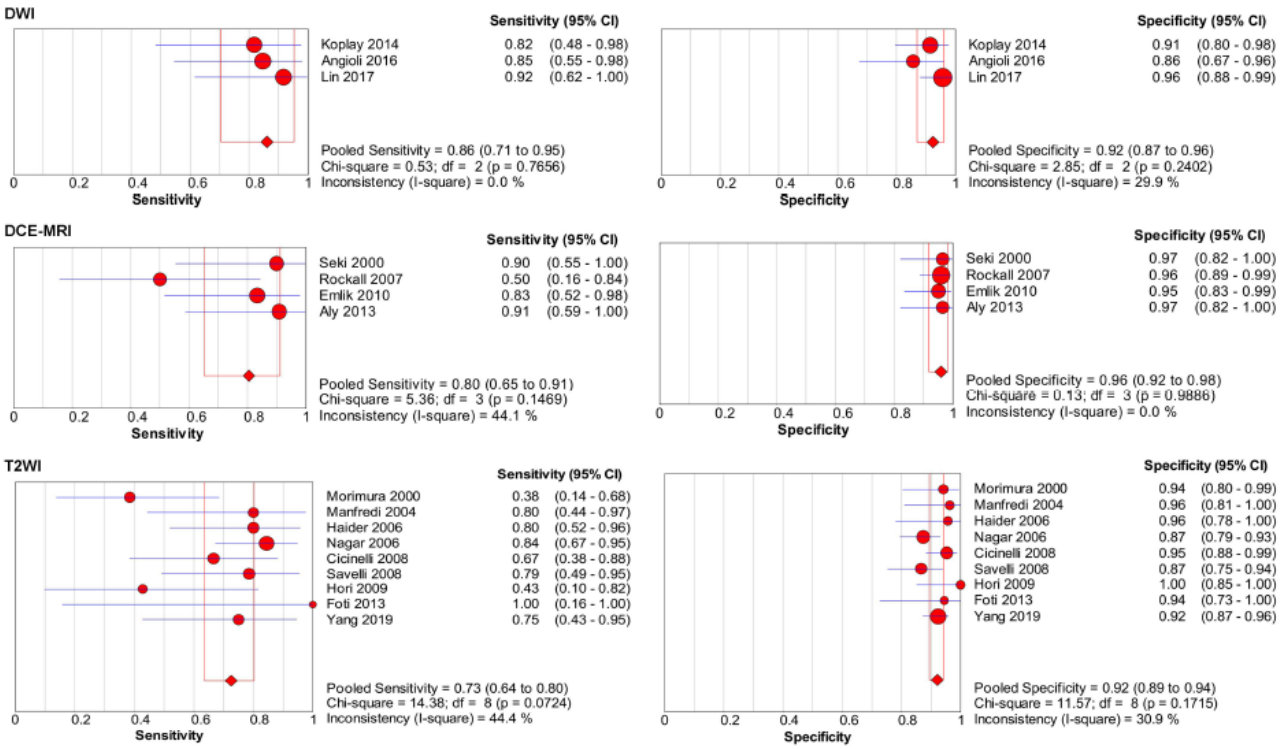

Figure 15

Forest plots of pooled sensitivity and specificity of diffusion weighted imaging (DWI), dynamic contrast-enhanced MRI (DCE-MRI), and T2-weighted image (T2WI) for assessing cervical involvement in endometrial carcinoma. CI, confidence interval.