Ultrasound Obstet Gynecol 2022; **60**: 604–611
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.24967.

Three-dimensional transvaginal ultrasound *vs* magnetic resonance imaging for preoperative staging of deep myometrial and cervical invasion in patients with endometrial cancer: systematic review and meta-analysis

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KEYWORDS: 3D transvaginal ultrasound; cervical invasion; deep myometrial invasion; endometrial cancer; meta-analysis

CONTRIBUTION

What are the novel findings of this work?
Our systematic review and meta-analysis comparing the diagnostic test accuracy (DTA) of three-dimensional transvaginal ultrasound (3D-TVS) and magnetic resonance imaging (MRI) for deep myometrial invasion (DMI) and cervical invasion demonstrated good performance of 3D-TVS, confirming its value for preoperative staging and surgery planning in patients with endometrial cancer.

What are the clinical implications of this work?
This is the first systematic review to compare the DTA of 3D-TVS and MRI in the assessment of DMI and cervical invasion in patients with endometrial cancer. Given the importance of preoperative staging, accurate imaging assessment is essential for adequate surgical planning. The DTA of 3D-TVS was comparable with that of MRI, indicating that both techniques may be used for the evaluation of DMI and cervical invasion.

ABSTRACT

Objectives *To evaluate and compare the diagnostic test accuracy (DTA) of three-dimensional transvaginal ultrasound (3D-TVS) and magnetic resonance imaging (MRI) for deep myometrial infiltration (DMI) and cervical invasion for preoperative staging and surgery planning in patients with endometrial cancer (EC).*

Methods *This systematic review and meta-analysis investigated the DTA of MRI and 3D-TVS for DMI and cervical invasion in patients with EC. A literature search was performed using MEDLINE, Scopus, EMBASE, ScienceDirect, The Cochrane library, ClinicalTrials.gov, Cochrane Central Register of Controlled Trials, EU Clinical Trials Register and World Health Organization International Clinical Trials Registry Platform to identify relevant studies published between January 2000 and December 2021. Study quality was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool.*

Results *Five studies, including a total of 450 patients, were included in the systematic review. All five studies compared the DTA of 3D-TVS* vs *MRI for DMI, and three studies compared the DTA of 3D-TVS* vs *MRI for cervical invasion. Pooled sensitivity, positive likelihood ratio and negative likelihood ratio for detecting DMI using 3D-TVS were 77% (95% CI, 66–85%), 4.57 and 0.31, respectively. The respective values for detecting DMI on MRI were 80% (95% CI, 73–86%), 4.22 and 0.24. Bivariate metaregression indicated a similar DTA of 3D-TVS and MRI (*P = *0.80) for the correct identification of DMI. Pooled ln diagnostic odds ratio for detecting cervical invasion was 3.11 (95% CI, 2.09–4.14) for 3D-TVS and 2.36 (95% CI, 0.90–3.83) for MRI. The risk of bias was low for most of the four domains assessed in QUADAS-2.*

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Accepted: 25 May 2022

Conclusion *3D-TVS demonstrated good diagnostic accuracy in terms of sensitivity and specificity for the evaluation of DMI and cervical invasion, with results comparable with those of MRI. Thus, we confirmed the potential role of 3D-TVS in the preoperative staging and surgery planning in patients with EC.* © *2022 The Authors. Ultrasound in Obstetrics & Gynecology published by John Wiley & Sons Ltd on behalf of International Society of Ultrasound in Obstetrics and Gynecology.*

INTRODUCTION

Endometrial cancer (EC) is the most common gynecological malignancy in Europe, and it represents the sixth most frequent cancer in women worldwide[1–3]. Office hysteroscopy-guided endometrial sampling is the preferred tool for the histological diagnosis of EC[4,5].

According to the European Society of Gynaecological Oncology (ESGO), the European Society for Radiotherapy and Oncology (ESTRO) and the European Society of Pathology (ESP) guidelines[6], total hysterectomy with bilateral salpingo-oophorectomy represents the standard method of surgical staging. With regard to lymph-node status, the guidelines recommend sentinel lymph-node biopsy in patients with low- or intermediate-risk disease and systematic pelvic/para-aortic lymphadenectomy in those with high-risk disease. To determine the correct surgical management, it is fundamental to assess the following risk factors: (1) tumor grade and molecular classification; (2) lymphovascular space invasion; (3) non-endometrioid histology; (4) cervical invasion; (5) deep myometrial invasion (DMI); (6) lymph-node involvement and distant metastasis[6]. The first three risk factors can be identified only on histology. Other factors can be identified using cross-sectional imaging modalities, including computed tomography (CT) or positron emission tomography to assess for lymph node involvement and distant metastasis, magnetic resonance imaging (MRI) to assess for DMI, cervical invasion and lymph node metastasis and transvaginal sonography (TVS) to assess for DMI and cervical invasion[7–11].

MRI has demonstrated high specificity for the preoperative assessment of DMI, cervical invasion and lymph-node metastasis owing to its good performance in soft tissue evaluation[8,9]. The diagnostic test accuracy (DTA) of TVS for detecting DMI is similar to that of MRI[6]. Preoperative TVS assessment for DMI and cervical invasion is best performed by an expert sonographer, because the assessment of these medical professionals shows greater agreement with the results of histopathology and better interobserver reproducibility than does that of gynecologists[6].

In recent years, the potential of three-dimensional TVS (3D-TVS) to replace MRI has been studied. Studies comparing 3D-TVS and MRI have shown similar DTA in assessing DMI and cervical invasion[12–15]. A meta-analysis comparing two-dimensional TVS (2D-TVS) and MRI for the preoperative detection of myometrial infiltration has been published[11], but no meta-analysis has compared the DTA of MRI with that of 3D-TVS in preoperative staging. Furthermore, ESGO/ESTRO/ESP guidelines do not recommend the use of intraoperative frozen section for DMI because of its poor reproducibility and interference with adequate pathological processing[6]. Therefore, although the correct assessment of DMI and cervical invasion is a fundamental step for preoperative staging and surgical planning, there is no consensus regarding the best diagnostic approach.

In this systematic review and meta-analysis, we compared the DTA of 3D-TVS and MRI in the assessment for DMI and cervical invasion for preoperative staging and surgery planning in patients with EC.

METHODS

Study design and eligibility criteria

This systematic review and meta-analysis investigated the DTA of MRI and 3D-TVS for DMI and cervical invasion in patients with EC, using final histological assessment of hysterectomy specimens as the reference standard. The report was written in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses and the Synthesizing Evidence from Diagnostic Accuracy Tests guidelines[16]. The protocol did not require registration.

Observational prospective or retrospective studies comparing the DTA of 3D-TVS and MRI for DMI and cervical invasion in patients with EC were included. Narrative or systematic reviews, case reports, case series and conference abstracts were excluded from the analysis. Only studies in which all included patients underwent surgery were considered eligible. Eligibility criteria for studies were as follows: study population comprising patients with a diagnosis of EC; 3D-TVS and MRI used as index tests; histological examination after surgery used as the reference standard; evaluation of DTA of TVS *vs* MRI for DMI and cervical invasion; study conducted at a tertiary center hospital; and sufficient information available to produce a 2×2 table for the calculation of sensitivity and specificity. No language restrictions were applied. DMI was diagnosed if myometrial invasion was $\geq 50\%$[17]. Cervical invasion was defined as positive when the tumor invaded cervical stroma but did not extend beyond the uterus[17].

Study selection and data extraction

A literature search of relevant studies published between January 2000 and December 2021 was conducted using the following electronic databases: MEDLINE, Scopus, EMBASE, ScienceDirect, The Cochrane library, ClinicalTrials.gov, Cochrane Central Register of Controlled Trials, EU Clinical Trials Register and World Health Organization International Clinical

Trials Registry Platform. The strategy for electronic search was as follows: Endometrial cancer [MeSH] OR uterine cancer [MeSH] OR myometrial invasion OR cervical invasion AND three-dimensional transvaginal sonography OR 3D transvaginal sonography OR transvaginal sonography OR magnetic resonance imaging.

Two authors (G.S. and M.N.) independently screened the records for inclusion in this review and extracted all relevant data. A manual search of references of the included studies was also performed to ensure that relevant studies were not missed. Any disagreement was resolved by consensus. Data collection included general information about each study and relevant outcome measures, including the number of true-positive, false-positive, true-negative and false-negative cases.

Quality assessment

As recommended by The Cochrane Collaboration[18], quality assessment was conducted using the Quality Assessment of Diagnostic Accuracy Studies-2 tool[19], which includes four domains: (1) patient selection, (2) index test, (3) reference standard and (4) flow and timing. Each domain was assessed in terms of risk of bias, and the first three domains were assessed in terms of concerns regarding applicability. Each item was rated as having low, high or unclear risk. Three authors (A.V., M.N. and F.C.) independently evaluated the methodological quality using a standard form with quality assessment criteria and a flow diagram. Any disagreement was resolved by consensus.

Statistical analysis

Statistical analysis was performed using the mada[20] package in R version 4.1 (R Foundation for Statistical Computing, Vienna, Austria)[21]; $P < 0.05$ was considered to indicate statistical significance. Given that the sensitivity and specificity of a diagnostic test are interrelated, the bivariate approach was favored over the univariate approach in the meta-analysis of DTA[22,23]. The bivariate approach estimates a bivariate normal model for the logit-transformed pairs of sensitivity and false-positive rate (FPR), using a linear mixed model with random effects[23,24]. DTA was compared between the two imaging methods using hierarchical summary receiver-operating-characteristics (HSROC) curves and metaregression. Post-test probabilities were calculated and plotted on Fagan nomograms, which were constructed using positive (LR+) and negative (LR−) likelihood ratios. LR+ and LR− were used to characterize the clinical utility of a test and estimate the post-test probability of disease.

In the meta-analysis of DTA, heterogeneity is anticipated, but univariate measures of heterogeneity, such as the I^2 statistic, may not be appropriate. Hence, the observed heterogeneity was evaluated graphically by the scatter of points and from the prediction ellipse[18].

The DTAs of MRI and TVS were investigated for both DMI and cervical invasion. If the number of studies assessing each specific outcome was ≥ 5, it was considered adequate for the application of the bivariate approach, which has been recommended over the univariate approach for the meta-analysis of DTA, where appropriate[18]. The bivariate approach allows the estimation of summary measures of sensitivity and specificity, which are more informative for the reader. If the analysis included fewer than five studies, the univariate approach to the meta-analysis of DTA was adopted. Since pooled sensitivity or specificity can be misleading, the diagnostic odds ratio (DOR) was pooled for descriptive purposes[18].

Of note, the limited number of included studies did not allow meaningful investigation of the publication bias or the performance of sensitivity analysis, subgroup analysis and metaregression with stratifying factors[18,25].

RESULTS

Study selection and characteristics

The electronic search yielded a total of 220 citations. After the removal of 111 duplicate records, 109 references remained. Of these, 99 records were excluded following title/abstract screening, as they were not relevant to the review. The full text of the 10 remaining manuscripts was examined, and five of these were excluded because they did not meet the inclusion criteria (four studies used only 3D-TVS and one study did not provide sufficient data to obtain a 2×2 table). Thus, five studies were included in the systematic review and meta-analysis[26–30]; a flowchart summarizing study identification and selection is shown in Figure S1.

The included studies were published between 2012 and 2019 and included a total of 450 patients[26–30]. Two studies were prospective[26,27] and three were retrospective[28–30]. All five studies compared 3D-TVS with MRI for DMI, while only three studies compared the DTA of 3D-TVS and MRI for cervical invasion[27–29] (Table 1). All studies evaluated the histological grade of the tumor and reported its histological type (endometrioid *vs* non-endometrioid). On definitive histology, 138 (30.7%) women in our population had DMI (myometrial invasion $\geq 50\%$) and 40 (12.0%) had cervical invasion.

Three studies specified the experience of the examiners for both techniques[26–28], while two studies specified the examiner's experience only for one of the techniques[29,30]. In the study by Saarelainen *et al.*[26], 3D-TVS was performed by examiners with 2 years' experience in 3D ultrasound, and MRI assessment was performed by two radiologists experienced in oncological MRI. In the study by Christensen *et al.*[28], 3D-TVS examination was performed by senior doctors, and the radiologist had more than 5 years' experience in pelvic MRI for the evaluation of myometrial involvement. Similarly, in the study by Yildirim *et al.*[27], 3D-TVS investigators had more than

Table 1 Characteristics of studies comparing three-dimensional transvaginal ultrasound (3D-TVS) with magnetic resonance imaging for detection of deep myometrial invasion (DMI) and cervical invasion (CI) in patients with endometrial cancer (EC) included in systematic review and meta-analysis

Study	*Study period*	*Study design*	n	*Patients' age (years) (mean (range))*	*Inclusion/exclusion criteria*	*DMI (≥ 50%) (n)*	*CI (n)*	*Pathologist blinded*
Saarelainen (2012)[26]	2008–2009	Prosp	20	68.0 (59–81)	Included all cases with EC diagnosis	12	NE	Yes
Christensen (2016)[28]	2008–2011	Retro	110	65.5 (32–85)	Included cases with endometrial hyperplasia with atypia and EC; excluded cases with Stage 3–4, serous, clear-cell or Grade 3 carcinomas	34	9	Yes
Rodríguez-Trujillo (2016)[30]	2012–2015	Retro	98	NS	Excluded cases with advanced EC	34	NE	Yes
Yildirim (2018)[27]	2013–2016	Prosp	40	61.1 (41–80)	Excluded cases with advanced EC	17	7	NS
Yang (2019)[29]	2016–2017	Retro	182	54.1 (32–78)	Included all patients with EC diagnosis	33	9	Yes

Only first author of each study is given. The reference standard was definitive histology for all studies. NE, not evaluated; NS, not specified; Prosp, prospective; Retro, retrospective.

4 years of experience, and the radiologist was experienced in abdominal radiology. In the study by Yang *et al.*[29], all radiological diagnoses were made by three senior radiologist doctors, while the experience of the examiners performing 3D-TVS was not specified. In the study by Rodríguez-Trujillo *et al.*[30], 3D-TVS was performed by a single gynecologist experienced in gynecological ultrasound, but the authors did not specify the experience of the radiologist.

Index test evaluation

3D-TVS

In three studies, 3D-TVS examiners compared the most suspicious area for myometrial invasion with the endometrial–myometrial junction in the adjacent and opposite sides of the uterus[27,29,30]. Marked asymmetry was considered indicative of DMI (≥ 50% infiltration); if myometrial thickness of the two myometrial walls was similar, infiltration was considered to be superficial (< 50%). Saarelainen *et al.*[26] assessed the myometrium in sagittal, transverse and coronal planes on 3D-TVS, and the maximum depth of myometrial invasion was estimated in all planes based on the subjective impression of the examiner. Christensen *et al.*[28] used a formula to categorize myometrial invasion as deep (≥ 50%) or superficial (< 50%).

For cervical invasion on 3D-TVS, diagnosis was based on the subjective identification of tumor invasion by the examiner in the study by Yildirim *et al.*[27]. In the study by Yang *et al.*[29], cervical invasion was diagnosed on 3D-TVS if the cervix was destroyed by the tumor or the cervical canal was enlarged owing to growth of tumor tissue. A vaginal probe was also used to apply pressure onto the cervix, and a lack of movement was considered to indicate cervical involvement. Finally, in the study by Christensen *et al.*[28], cervical involvement was diagnosed on 3D-TVS when the borders of the tumor extended to the uterine cervix or there was disruption of normal echogenicity of the cervical stroma.

MRI

In four studies, the diagnostic criteria for DMI on MRI were based on the evaluation of the junctional zone[26–29]. If the low signal intensity, circular endometrial–myometrial junction was irregular or incomplete, the myometrium was considered to be infiltrated; if signal intensity of the tumor on T2-weighted imaging was greater than half compared with the maximum thickness of the myometrium, it was considered indicative of DMI. In the study by Rodríguez-Trujillo *et al.*[30], the extent of myometrial infiltration on MRI was estimated subjectively by the examiner according to their impression of depth of invasion (≥ 50% or < 50%) during virtual navigation using the same method as for 3D-TVS examination.

Yildirim *et al.*[27] defined cervical invasion as positive if the examiner suspected tumor invasion on subjective assessment. In the study by Christensen *et al.*[28], cervical involvement was defined as present when the tumor borders extended to the uterine cervix or there was disruption of the normal low-signal cervical stroma. Yang *et al.*[29] did not provide a clear definition of cervical invasion.

Diagnostic performance of 3D-TVS *vs* MRI

All five studies evaluated the DTA of 3D-TVS and MRI for the identification of DMI[26–30]. Pooled sensitivity was 77% (95% CI, 66–85%) for 3D-TVS and 80% (95% CI, 73–86%) for MRI. Pooled FPR was 18% (95% CI, 11–29%) for 3D-TVS and 19% (95% CI, 11–30%) for MRI. HSROC curves for 3D-TVS and MRI are shown in Figure 1. Bivariate metaregression indicated a similar DTA of 3D-TVS and MRI ($P = 0.80$) for the correct

identification of myometrial invasion. Heterogeneity is presented graphically by the prediction ellipses in Figure 1.

Pooled ln DOR was 2.84 (95% CI, 1.88–3.81) for 3D-TVS and 3.07 (95% CI, 2.37–3.78) for MRI. LR+ and LR– for the detection of DMI using 3D-TVS were 4.57 and 0.31, respectively. LR+ and LR– for the detection of DMI using MRI were 4.22 and 0.24, respectively. Fagan nomograms suggested that a positive test on 3D-TVS and MRI increased the pretest probability of DMI from 40%[15] to 74% and 74%, respectively, while a negative test on 3D-TVS and MRI decreased the pretest probability from 40% to 16% and 14%, respectively (Figure 2).

Three studies[25–27] evaluated the DTA of 3D-TVS and MRI for the identification of cervical invasion. Using the univariate approach, we found a pooled ln DOR of 3.11 (95% CI, 2.09–4.14) for 3D-TVS and 2.36 (95% CI, 0.90–3.83) for MRI.

Quality assessment

Risk of bias

For the patient selection domain, the overall quality of the studies was high, and all studies provided a specific description of the inclusion strategy. The inclusion of patients with hyperplasia with atypia was considered to increase the risk of overestimating the accuracy

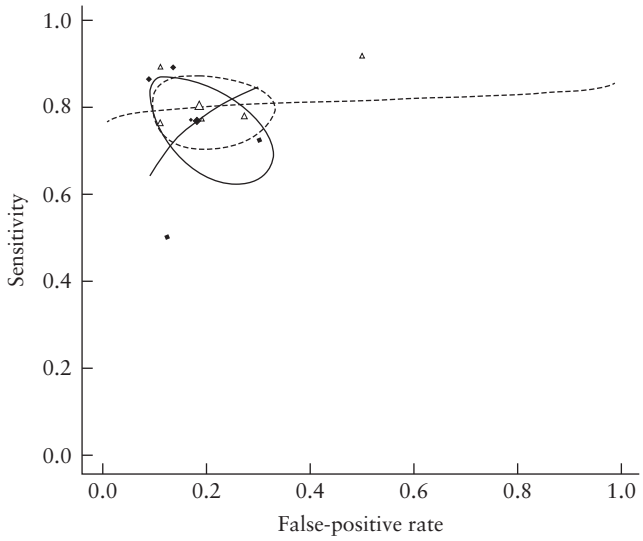

Figure 1 Summary receiver-operating-characteristics curves showing diagnostic test accuracy of transvaginal ultrasound (–◆–) and magnetic resonance imaging (--△--) for deep myometrial invasion. Confidence region of summary estimate for each approach is represented by circle.

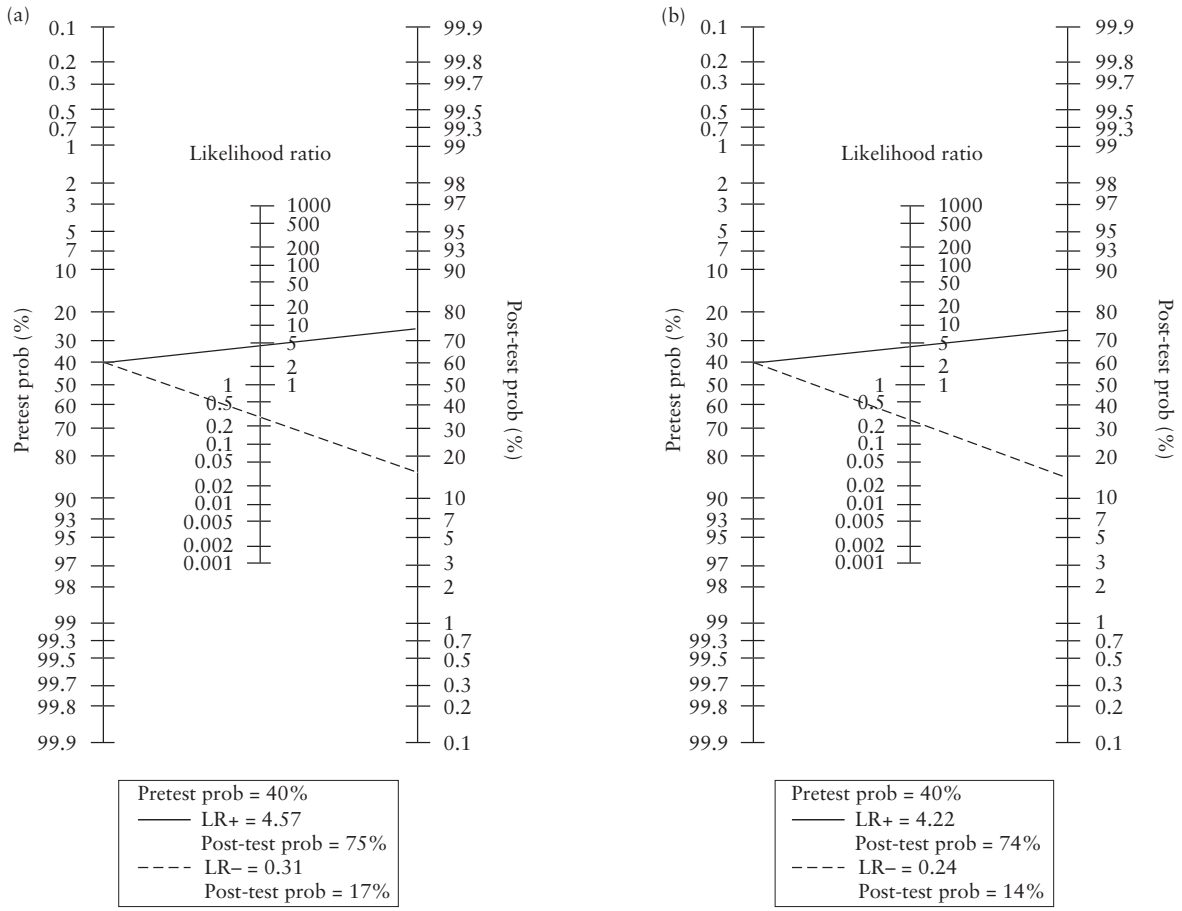

Figure 2 Fagan plots demonstrating post-test probability (prob) of deep myometrial invasion in patients with endometrial cancer following a positive (——) or negative (-----) result on three-dimensional transvaginal ultrasound (a) or magnetic resonance imaging (b). LR+, positive likelihood ratio; LR–, negative likelihood ratio.

of MRI and 3D-TVS for myometrial invasion ≥ 50%, considering the premalignant definition of this diagnosis. Three studies did not include patients with advanced EC[27,28,30]. Christensen *et al.*[28] included patients with endometrial hyperplasia with atypia on preoperative histology and excluded women with known Stage 3–4, serous, clear-cell or Grade 3 carcinomas based on endometrial samples; the study was considered to have a high risk of bias in patient selection. Rodríguez-Trujillo *et al.*[30] included patients diagnosed with early-stage endometrial cancer, with the tumor confined to the corpus uteri, and Yildirim *et al.*[27] excluded patients who had clinically advanced EC. Both studies were considered to have a low risk of bias. The studies by Saarelainen *et al.* and Yang *et al.* included all patients with a diagnosis of EC[26,29], and were considered to have an unclear risk of bias.

For the index test domain, the studies by Yang *et al.*[29] and Rodríguez-Trujillo *et al.*[30] were judged to have an unclear risk of bias because they did not report clearly whether examiners were blinded to histological results and did not detail their experience in abdominal radiology or gynecological 3D-TVS. Moreover, Yang *et al.*[29] did not explain clearly the method adopted to assess cervical involvement on MRI. In the other three studies, the index test was performed by an examiner who was blinded to the pathology report[26–28]. These studies provided an adequate description of procedures to define DMI (≥ 50% of myometrial thickness in any of the three spatial orthogonal planes) and cervical invasion[26–28]. In all three studies, the examiners had significant experience in gynecological ultrasound and radiological imaging. Thus, these studies were considered to have a low risk of bias.

For the reference standard domain, all studies used the final histopathological diagnosis of myometrial and cervical invasion on hysterectomy specimens as the reference standard. Yildirim *et al.*[27] did not report whether the pathologist was blinded to 3D-TVS or MRI findings, making the risk of bias unclear. In the other four studies, the pathologist was blinded, thus we consider these studies to have a low risk of bias[26,28–30]. In all the studies, histological samples were reviewed by a pathologist specializing in gynecological pathology.

Finally, for the flow and timing domain, two studies did not report the time interval between the index and reference tests and were considered to have an unclear risk of bias[29,30]. In other studies, the authors specified the time interval between the index and reference tests. In the study by Yildirim *et al.*[27], patients underwent surgery within 2 months after biopsy and underwent MRI and 3D-TVS within 15 days before surgery. In the study by Christensen *et al.*[28], all women underwent surgery within 21 days after ultrasound and MRI examination. In the study by Saarelainen *et al.*[26], MRI examination was performed 1–17 days and ultrasound examination 24 h prior to the operation. These three studies were considered to have a low risk of bias. Table S1 summarizes the risk of bias of the included studies.

Applicability concerns

For the patient selection domain, the quality of included studies was high, and all were considered to have low applicability concerns[26–30]. For the index test domain, four studies were judged to be of good quality (low concerns regarding applicability) because they described adequately the methodology of the index test[26–28,30]. In contrast, Yang *et al.*[29] did not describe clearly the methods adopted to evaluate cervical invasion on MRI. Finally, for the reference standard domain, all studies used histology as the reference test; therefore, all studies were considered to be of good quality (low concerns regarding applicability). Table S1 summarizes the applicability of the included studies.

DISCUSSION

Synthesis of results and comparison with existing literature

To our knowledge, this is the first meta-analysis to compare 3D-TVS with MRI for the diagnosis of DMI and cervical invasion in patients with EC. We found that 3D-TVS and MRI had comparable DTA for the diagnosis of DMI with low between-study heterogeneity. Using the univariate approach, we found comparable DOR for 3D-TVS and MRI for cervical invasion (CIs overlapping). These results confirmed the potential value of 3D-TVS for staging EC in terms of DMI and cervical invasion. In addition, compared with MRI, 3D-TVS is a less expensive technology, widely available in most settings and without contraindications for its application. It could be performed during the first oncological visit, reducing costs, time of preoperative diagnostic work-up and patients' anxiety[11,31–34].

The prognosis for patients with EC is improved when the diagnosis is made at an early stage (survival rates: from 95% in Stage I to 17% in Stage IV)[6]. Therefore, an accurate presurgical staging method is fundamental to prognosis and surgery planning[6]. MRI and 2D-TVS are the most commonly used techniques for the preoperative assessment of cervical invasion and DMI[6,8,9,11,35,36]. In large meta-analyses, MRI showed a pooled sensitivity of up to 90% and a pooled specificity of up to 89% for detecting DMI[36,37]. No difference was found between contrast-enhanced MRI and diffusion-weighted MRI[30,36–38]. For cervical invasion, all studies reported low sensitivity (up to 55%) and high specificity (up to 95%) of MRI[39–41].

A meta-analysis including 2773 patients evaluated the diagnostic performance of 2D-TVS for the preoperative assessment of DMI and found a pooled sensitivity of 82% and a pooled specificity of 81%[42], which are lower than values reported for MRI. In that study, subjective impression and objective measurements resulted in comparable DTA. Unfortunately, the authors did not distinguish between advanced and early-stage EC, possibly overestimating the DTA[42]. Indeed, the most

recent study including only low-grade and preoperative early-stage EC found a lower sensitivity of 69% and specificity of 87% for 2D-TVS and respective values of 51% and 91% for MRI[43].

Alcázar *et al.*[11] performed a meta-analysis comparing 2D-TVS and MRI (560 patients included). The authors showed that MRI had a higher sensitivity and similar specificity (83% and 82%, respectively) compared with 2D-TVS (75% and 82%, respectively) for detecting DMI. However, the observed difference was not statistically significant, and the authors concluded that 2D-TVS may be used in clinical settings with limited resources.

In recent years, clinicians have proposed 3D-TVS as a new ultrasound technique for the preoperative assessment of patients with EC. This method introduces several advantages because three different axes and the coronal view may add valuable information about DMI in the uterine cornua. Moreover, 3D rendering techniques may increase the contrast between tissues, resulting in enhancement of tissue demarcation[12]. One of the first prospective studies on the use of 3D-TVS demonstrated that subjective impression of DMI had an overall sensitivity of 92.6% and a specificity of 82.3%[12]. Subsequently, Ergenoglu *et al.*[13] reported that 3D-TVS had a sensitivity of 100% and a specificity of 88% for the diagnosis of DMI.

Furthermore, two objective methods for the diagnosis of DMI using 3D-TVS have been proposed. Alcázar *et al.*[12] proposed virtual navigation to measure the shortest myometrial tumor-free distance to the serosa, while Mascilini *et al.*[44] proposed to evaluate the tumor /uterine volume ratio. However, the literature on this topic is limited, and the same studies demonstrated that subjective and objective assessments of DMI were comparable[12,44].

A recent meta-analysis, including patients that underwent 3D-TVS without head-to-head comparison with MRI, indicated a sensitivity and specificity of about 84% and 81%, respectively, considering subjective impression as the reference technique. Despite the different methodological limitations, such as the use of the univariate approach and the small numbers of patients and studies included, these data support the potential value of 3D-TVS in the detection of DMI[15].

As mentioned, the literature on the use of 3D-TVS for detecting cervical invasion is limited. The few studies that compared the sensitivity and specificity of MRI and 3D-TVS for detecting cervical invasion showed no significant differences. However, the positive predictive value of 3D-TVS has been reported to be significantly higher than that of MRI. In all studies, we found that the sensitivity of MRI and 3D-TVS for cervical invasion was inferior to that for DMI. On account of high specificity (> 90%), these techniques are superior for excluding non-invasive cervical cancer[27–29,32].

Strengths and limitations

The main limitation of this meta-analysis is the small number of studies and patients included. The bivariate approach, which is the recommended procedure for DTA meta-analysis, was applicable only for DMI (five or more studies included). The bivariate approach was not appropriate for the meta-analysis of studies evaluating cervical invasion (only three studies included), for which only the univariate approach with DOR was used.

Nevertheless, we must emphasize that this is the first meta-analysis to compare the DTA between 3D-TVS and MRI for the preoperative staging of EC focusing specifically on DMI and cervical invasion. Rigorous methodology, application of the bivariate approach for the evaluation of DMI and low between-study heterogeneity represent the strengths of our study. Finally, we found an overall moderate-to-good quality of the studies when considering the definition of the index test and reference standard.

Conclusions

In conclusion, our findings demonstrate good DTA of 3D-TVS for DMI in patients with EC, showing this technique to be comparable with MRI in terms of sensitivity and specificity. For cervical invasion, although 3D-TVS appeared to perform better than MRI, we cannot give specific recommendations because the literature on this topic is limited. Certainly, there are some topics that need to be investigated further, including the introduction of an objective method for the evaluation of DMI by 3D-TVS and a learning curve that would maximize the test performance. In our opinion, the application of 3D-TVS for the preoperative assessment of DMI in patients with EC has high clinical potential that should be investigated further and validated in large prospective clinical trials.

ACKNOWLEDGMENTS

We thank all members of the research team of the gynecology and obstetrics unit of the University of Padua. Open Access Funding was provided by Universita degli Studi di Padova within the CRUI-CARE Agreement.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Figure S1 Flowchart summarizing inclusion in systematic review and meta-analysis of studies comparing diagnostic test accuracy of three-dimensional transvaginal ultrasound *vs* magnetic resonance imaging for deep myometrial and cervical invasion in patients with endometrial cancer.

Table S1 Quality assessment (risk of bias and concerns about applicability) for all studies included in the meta-analysis according to Quality Assessment of Diagnostic Accuracy Studies criteria

Ultrasound Obstet Gynecol 2022; **60**: 604–611
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.24967.

Ecografía transvaginal tridimensional frente a imagen por resonancia magnética para la estadificación preoperatoria de la invasión profunda del miometrio y del cuello uterino en pacientes con cáncer de endometrio: revisión sistemática y metaanálisis

RESUMEN

Objetivo. Evaluar y comparar la precisión de la prueba diagnóstica (PPD) de la ecografía transvaginal tridimensional (ETV-3D) y la imagen por resonancia magnética (IRM) para la infiltración miometrial profunda (IMP) y la invasión cervical para la estadificación preoperatoria y la planificación de la cirugía en pacientes con cáncer de endometrio (CE).

Métodos. Esta revisión sistemática y metaanálisis investigó la PPD de la IRM y la ETV-3D para la IMP y la invasión cervical en pacientes con CE. Se realizó una búsqueda bibliográfica en MEDLINE, Scopus, EMBASE, ScienceDirect, The Cochrane Library, ClinicalTrials.gov, el Registro Central Cochrane de Ensayos Controlados, el Registro de Ensayos Clínicos de la UE y la Plataforma del Registro Internacional de Ensayos Clínicos de la Organización Mundial de la Salud para identificar los estudios pertinentes publicados entre enero de 2000 y diciembre de 2021. La calidad de los estudios se evaluó mediante la herramienta de Evaluación de Calidad de los Estudios de Precisión Diagnóstica-2 (QUADAS-2, por sus siglas en inglés).

Resultados. En la revisión sistemática se incluyeron cinco estudios con un total de 450 pacientes. Los cinco estudios compararon la PPD de la ETV-3D frente a la IRM para la IMP, y tres estudios compararon la PPD de la ETV-3D frente a la IRM para la invasión cervical. La sensibilidad combinada, el cociente de verosimilitud positivo y el cociente de verosimilitud negativo para detectar la IMP mediante la ETV-3D fueron del 77% (IC 95%, 66–85%), 4,57 y 0,31, respectivamente. Los valores respectivos para detectar la IMP en la IRM fueron del 80% (IC 95%, 73–86%), 4,22 y 0,24. La metaregresión bivariante indicó una PPD similar de la ETV-3D y la IRM (P=0,80) para la identificación correcta de la IMD. La razón de momios diagnóstica combinada para detectar la invasión cervical fue de 3,11 (IC 95%, 2,09–4,14) para la ETV-3D y de 2,36 (IC 95%, 0,90–3,83) para la IRM. El riesgo de sesgo fue bajo para la mayoría de los cuatro dominios evaluados en QUADAS-2.

Conclusiones. La ETV-3D demostró una buena precisión diagnóstica en términos de sensibilidad y especificidad para la evaluación de la IMD y la invasión cervical, con resultados comparables a los de la IRM. Por tanto, se confirmó el papel potencial de la ETV-3D en la estadificación preoperatoria y la planificación de la cirugía en pacientes con CE.

子宫内膜癌患者深肌层浸润和宫颈浸润术前分期的三维经阴道超声与磁共振成像：系统回顾和荟萃分析

摘要

目的 评价和比较用于子宫内膜癌（EC）患者术前分期和手术计划的三维经阴道超声（3D-TVS）和磁共振成像（MRI）对子宫深肌层浸润（DMI）和宫颈浸润的诊断测试准确性（DTA）。

方法 本系统回顾和荟萃分析研究了MRI和3D-TVS对EC患者DMI和宫颈浸润的诊断测试准确性。使用MEDLINE、Scopus、EMBASE、ScienceDirect、The Cochrane library、ClinicalTrials.gov、Cochrane Central Register of Controlled Trials、EU Clinical Trials Register和世界卫生组织国际临床试验注册平台进行了文献检索，以确定2000年1月至2021年12月期间发表的相关研究。研究质量采用诊断准确性研究质量评价工具-2（QUADAS-2）进行了评估。

结果 五项研究被纳入系统回顾，共计450名患者。所有五项研究都比较了3D-TVS与MRI对DMI的诊断测试准确性，三项研究比较了3D-TVS与MRI对宫颈浸润的诊断测试准确性。使用3D-TVS检测DMI的集合敏感性、阳性似然比和阴性似然比分别为77%（95%CI，66-85%）、4.57和0.31。通过MRI检测DMI的相应数值分别为80%（95%CI，73-86%）、4.22和0.24。双变量元回归显示3D-TVS和MRI对正确发现DMI的诊断测试准确性相似（P=0.80）。3D-TVS检测宫颈浸润的集合诊断优势比为3.11（95%CI，2.09-4.14），MRI为2.36（95%CI，0.90-3.83）。通过QUADAS-2评估的四个领域中，大多数的偏倚风险都很低。

结论 3D-TVS在评估DMI和宫颈浸润的敏感性和特异性方面表现出良好的诊断准确性，其结果与MRI的结果相当。因此，我们证实了3D-TVS在EC患者的术前分期和手术计划中的潜在作用。