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REVIEW ARTICLE

Gynecology

Transvaginal ultrasound versus magnetic resonance imaging for diagnosing adenomyosis: A systematic review and head-to-head meta-analysis

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Abstract

Background: Transvaginal ultrasound (TVS) and magnetic resonance imaging (MRI) are used for the clinical diagnosis of adenomyosis.

Objectives: To compare the diagnostic accuracy of TVS and MRI for the diagnosis of adenomyosis.

Search Strategy: A search of studies was performed in five databases comparing TVS and MRI for the diagnosis of adenomyosis from January 1990 to May 2022.

Selection Criteria: Studies were eligible if they reported on the use of TVS and MRI in the same set of patients. The reference standard must be pathology (hysterectomy).

Data Collection and Analysis: The quality of studies was assessed using the QUADAS-2 tool. Pooled sensitivity and specificity of both techniques were estimated and compared.

Main Results: Six studies comprising 595 women were included. The risk of bias of patient selection was high in three studies. The risk of bias for index tests and reference test was low. Pooled estimated sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio for TVS were 75%, 81%, 3.9, and 0.31, respectively. These figures for MRI were 69%, 80%, 3.5, and 0.39, respectively. No statistically significant differences were found ($p = 0.7509$). Heterogeneity was high.

Conclusions: MRI and TVS have similar performances for the diagnosis of adenomyosis.

KEYWORDS

adenomyosis, diagnosis, magnetic resonance imaging, transvaginal ultrasound

1 | BACKGROUND

Adenomyosis is an estrogen-dependent disorder, characterized by the existence of endometrial glands and stroma within the thickness of the myometrium, along with hyperplasia and hypertrophy of the smooth muscle fibers.[1] The prevalence of adenomyosis is highly variable, in the range of 5%–70%, depending on the different diagnostic criteria, such as clinical, imaging, or histological.[2] This disease mainly affects multiparous women aged 40–50 years. The clinical presentations of adenomyosis include menorrhagia, metrorrhagia, dysmenorrhea, dyspareunia, chronic pelvic pain, and infertility. However, adenomyosis is asymptomatic in one-third of patients[3]

and its etiology and pathogenic mechanisms that cause adenomyosis are poorly understood.[4]

The definitive diagnosis should be based on the histological study of the hysterectomy specimens.[5] However, accurate preoperative diagnostic tools would be advisable to avoid an unnecessary hysterectomy and, if possible, to investigate non-surgical alternatives. The role of imaging techniques in the evaluation of these patients will make it possible to establish a diagnostic approach, determine the depth and extent of myometrial penetration, and monitor the evolution of patients receiving conservative therapy.[6] Both transvaginal ultrasound (TVS) and magnetic resonance imaging (MRI) are currently considered the best imaging techniques for the non-invasive diagnosis of adenomyosis. Previous meta-analyses assessing the diagnostic performance of TVS and MRI for diagnosing adenomyosis have been reported.[7–9] Even though these meta-analyses concluded that the diagnostic performance of both techniques is similar, the fact is that the reported pooled sensitivity and specificity for TVS and MRI varied significantly. Such variation could be reduced by considering only studies that examine both techniques in a single set of patients. However, it is believed that there is no reported head-to-head meta-analysis comparing the diagnostic performance between TVS and MRI in the diagnosis of adenomyosis.

2 | OBJECTIVES

The aim of the present study was to perform a head-to-head meta-analysis.

3 | SEARCH STRATEGY

The present meta-analysis followed the Synthesizing Evidence from Diagnostic Accuracy Tests (SEDATE) guidelines[10] and PRISMA guidelines.[11] The methodology for the inclusion and exclusion criteria, data collection, and quality assessment was defined in advance. The protocol was not registered. Approval from the institutional review board was waived due the design of the study.

A search using five electronic databases (PubMed/MEDLINE, Web of Science, Cochrane, Scopus, and CINHAL) was conducted in order to identify potentially eligible studies published between January 1990 and May 2022. The terms included in the search were "adenomyosis," "transvaginal ultrasound," and "magnetic resonance imaging." There was no language restriction in the search. The full search strategy in each database is shown in Supplementary Material S1.

4 | SELECTION CRITERIA

Two authors (JV, CU) screened the titles and abstracts obtained during the search in order to exclude clearly irrelevant articles. Full texts of the remaining articles were obtained to determine which were potentially relevant to the study. To do so, the following inclusion criteria were applied: (1) a prospective or retrospective cohort study including patients who underwent both MRI and TVS, as index tests, for the diagnosis of adenomyosis; (2) a histopathological analysis after hysterectomy as the reference standard; and (3) availability of the data required to construct the 2 ×2 table of diagnostic performance (Figure 1).

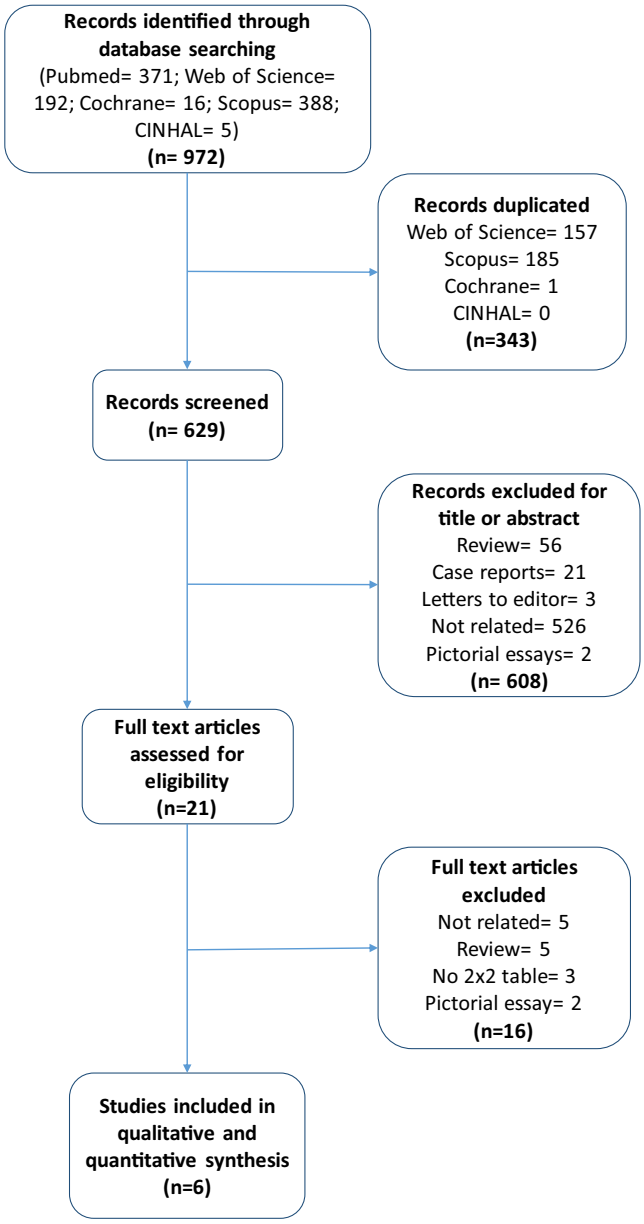

FIGURE 1 Flow chart showing the study selection process.

5 | DATA COLLECTION AND ANALYSIS

A description of the included studies was created using the Patients, Interventions, Comparator, Outcomes, and Study design (PICOS) criteria. Three of the authors (JV, CU, JLA) retrieved diagnostic accuracy results (true positive, true negative, false positive, and false negative cases for TVS and MRI) and additional useful information

about patients and procedures from selected primary studies independently. The following data were retrieved: first author's name; year of publication; country; study design; number of patients recruited; consecutive or non-consecutive recruitment; number of patients excluded; reasons for patient exclusion; number of patients with disease according to the reference standard; technical specifications of the ultrasound machine used (mainly frequency of the ultrasound probe used); ultrasound criteria for diagnosing adenomyosis; number of TVS examiners; blinding of TVS examiners; technical specifications of the magnetic field used in the MRI examination; use of contrast enhancement in MRI examinations; MRI criteria for diagnosing adenomyosis; number of MRI readers; blinding of MRI readers; reference standard used (hysterectomy or other); and blinding of the pathologist. Disagreements emerging during the selection process and data collection were resolved by consensus among these three authors. In case of missing data, the corresponding author of the primary study was contacted.

In order to assess the quality of the studies included in the meta-analysis, the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool was adapted.[12] This format includes four domains: (1) patient selection; (2) index test; (3) reference standard; and (4) flow and timing. For each domain, the risk of bias and concern about applicability (the latter one not referring to the flow and timing domain) were examined and rated as low, high, or unclear risk. The results of these analyses were used to establish the overall quality of the included studies and to assess potential sources of heterogeneity.

Three authors (JV, CU, JLA) independently evaluated the methodological quality using specific criteria. Any arising disagreement was solved by discussion between these three authors. The methodological quality criteria were based on the description of inclusion and exclusion criteria for patient selection domain, detailed explanation of how the index tests were performed and interpreted for the index test domain, histopathological study as the gold standard for the reference standard domain, and, finally, specification of the time elapsed between the implementation of the index test and reference standard result.

A random-effects model was used to determine the overall pooled sensitivity, specificity, positive likelihood ratio (LR+), and negative likelihood ratio (LR-). Likelihood ratios were used to characterize the clinical utility of the tests and to determine the post-test probability of disease. The mean prevalence of adenomyosis (pre-test probabilities) in each subset was used, together with the likelihood ratios extracted for each assessed technique, in order to calculate post-test probabilities and plot Fagan nomograms. The heterogeneity for sensitivity and specificity was assessed with Cochran's Q statistic and the I^2 index, setting the p value at <0.1 to determine heterogeneity. The I^2 values indicating the different degrees of heterogeneity were established at 25%, 50%, and 75% for low, moderate, and high heterogeneity, respectively.[13] Forest plots were drawn of the sensitivity and specificity, including all studies. In the cases in which heterogeneity existed, a meta-regression was used to assess the covariates that could explain it. The covariates analyzed were the year in which the study took place, study design (prospective or retrospective), sample size, prevalence of adenomyosis, and number

TABLE 1 Main characteristics of the studies included in the present meta-analysis

Author	Year	Country	Study design	No.	Consecutive recruitment	Patients excluded	No. of cases with adenomyosis	TVS MHz	No. of TVS observers	TVS blinded	MRI magnetic field (T)	MRI contrast used	No. of MRI observers	MRI blinded	Reference standard	Pathologist blinded
Ascher	1994	USA	NA	20	NA	0	17	5	3	Yes	1.0 1.5	Yes	3	Yes	Histology after hysterectomy	NA
Reinhold	1996	USA	Prospective	147	Yes	28	28	5	2	Yes	1.5	NA	1	Yes	Histology after hysterectomy	Yes
Duelhom	2001	Denmark	Prospective	178	Yes	72	22	5–8	1	Yes	1.5	NA	1	Yes	Histology after hysterectomy	NA
Bazot	2001	France	Prospective	167	NA	47	50	5–9	NA	NA	1.5	Yes	NA	NA	Histology after hysterectomy	Yes
Alborzi	2021	Iran	Retrospective	154	NA	NA	58	7.5	1	NA	NA	NA	1	NA	Histology after hysterectomy	NA
Tariq	2022	Pakistan	Prospective	162	Yes	0	105	5–8	1	Yes	1.5	NA	1	Yes	Histology after hysterectomy	Yes

Abbreviations: MRI, magnetic resonance imaging; NA, not available; T, tesla; TVS, transvaginal ultrasound.

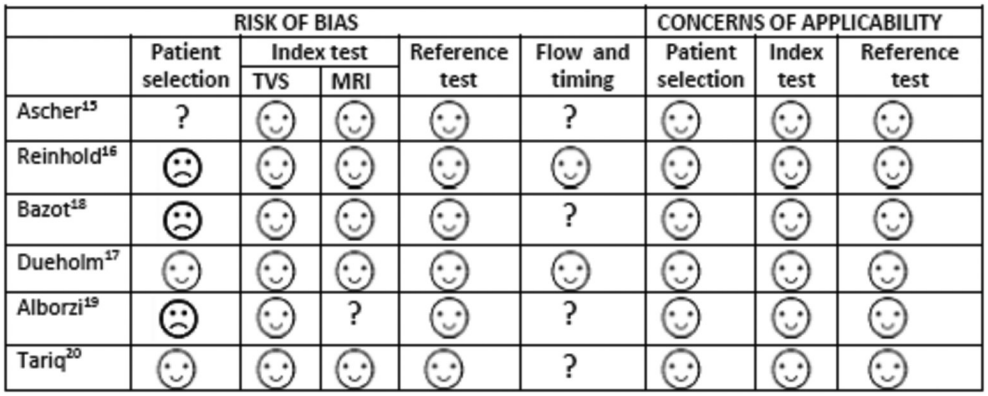

FIGURE 2 Quality assessment (risk of bias and concerns about applicability) for all studies included in the meta-analysis. MRI, magnetic resonance imaging; TVS, transvaginal ultrasound.

TABLE 2 Diagnostic criteria for adenomyosis using TVS and MRI in the studies included in the meta-analysis

Author	Year	TVS criteria	MRI criteria
Ascher	1994	(a) Thickening and asymmetry of the anterior and posterior myometrial walls (b) Increased echotexture of the myometrium (c) Heterogeneous, indistinctly marginated areas in the myometrium	(a) A myometrial mass with indistinct margins of primarily low signal intensity with all sequences (b) Diffuse or focal widening (>0.5 cm) of the junctional zone on T2-weighted images, fast T2-weighted SE images, and contrast material-enhanced T1-weighted images
Reinhold	1996	(a) Presence of a poorly defined area of abnormal echotexture within the myometrium (b) Abnormal myometrial echotexture, defined as the area(s) of the myometrium demonstrating heterogeneity, decreased or increased echogenicity (c) Presence of myometrial cysts	(a) Subjective impression of localized or diffuse thickening of the uterine JZ (with or without the presence of small foci of increased signal intensity within the JZ) (b) Presence of a low-signal-intensity myometrial mass with ill-defined borders
Dueholm	2001	(a) Presence of focal areas with not well-defined borders or abnormal echo texture (b) Myometrial heterogeneity (c) Increased or decreased areas of echogenicity (d) Presence of myometrial cysts	(a) JZ maximum thickness >15 mm (b) For a JZ thickness of 12–15 mm, adenomyosis was thought to be present when one of the criteria was met, such as a non-uniform, thickened JZ or focal not well-demarcated high or low intensity areas in the myometrium
Bazot	2001	(a) Myometrial cysts (b) Distorted and heterogeneous myometrial echotexture (c) Poorly defined focus of abnormal myometrial echotexture (d) Globular and/or asymmetric uterus	(a) Large asymmetric uterus without leiomyomas (b) JZ maximum thickness ≥ 12 mm and/or an ill-defined, low-signal-intensity myometrial area distinguished from well-circumscribed lesions related to myoma (c) JZ ratio > 40% (d) Punctate high-intensity myometrial foci (e) Small hypointense spots within myometrium on contrast-enhanced (gadolinium) T1-weighted images
Alborzi	2021	Three or more of the following: (a) Globally enlarged uterus (enlarged fundus) (b) Asymmetrically enlarged uterus (c) Round cystic area (2–9 mm) within the myometrium (d) Heterogeneous myometrial echotexture (e) Hyperechogenic islands (f) Myometrial hypoechoic linear striations (fan-shaped shadowing) (g) Indistinct and fuzzy transitional zone (h) Diffuse minimal vascularity (i) Question mark sign	(a) Increased thickness (>12 mm) of JZ (b) Formation of an ill-defined area of low signal intensity on T2-weighted image (c) Cystic dilatation of gland (d) Hemorrhagic foci (e) Uterus enlarged with asymmetric outline
Tariq	2022	(a) Myometrial heterogeneity (b) Increased or decreased areas of echogenicity (c) Presence of myometrial cysts	(a) JZ maximum thickness >15 mm (b) For a JZ thickness of 12–15 mm, adenomyosis was thought to be present when one of the criteria was met, such as a non-uniform, thickened JZ or focal not well-demarcated high or low intensity areas in the myometrium

Abbreviations: JZ, junctional zone; MRI, magnetic resonance imaging; TVS, transvaginal ultrasound.

of observers for the index test (single or multiple). Summary receiver operating characteristics (sROC) curves were plotted to visually describe the relationship between sensitivity and specificity. The area under the curve (AUC) was estimated. The diagnostic performance of TVS and MRI for detecting adenomyosis was compared using the bivariate method. Publication bias was assessed using Deeks' method.[14] A sensitivity analysis was not performed.

All analyses were performed using Meta-analytical Integration of Diagnostic Accuracy Studies (MIDAS) and METANDI commands in STATA version 12.0 for Windows (Stata Corp.). $p < 0.05$ was considered statistically significant.

6 | MAIN RESULTS

The electronic search provided 972 citations. After removing 343 duplicate records, 629 papers remained. Of these, 608 were excluded because they were not relevant to the review (reviews, case reports, papers not assessing diagnostic performance or not related to the topic). The full texts of the remaining 21 studies were examined. Finally, a further 16 articles were excluded because they did not meet any of the inclusion criteria. Thus, the remaining six studies were ultimately included in the meta-analysis[15–20] (Figure 1).

Six studies published between 1990 and 2022 reporting data on 595 patients (age range 20–88 years) were included in the final analyses. In 270 patients, adenomyosis was identified in the surgical specimen. The mean prevalence of adenomyosis was 52% (range 21%–85%). The PICOS features of the included studies are given in Table 1.

All data sought were available for all studies and there was no need to contact the corresponding author of any study included in the meta-analysis. The study design was clearly stated as prospective in three studies and as retrospective in one, while the data collection in the other two studies was not described as prospective or retrospective. The QUADAS-2 method used for the assessment of the risk of bias and concerns regarding the applicability of the selected studies is shown in Figure 2.

With regard to the risk of bias in the patient selection domain, one study was unclear about its inclusion and exclusion criteria[15] and three studies were considered high risk due to inappropriate exclusion (e.g. excluding patients with poor quality TVS or MRI scans).[16,18,19] Two studies had a low risk of bias.[17,20] Regarding the index test domain, focusing on TVS, all the studies comprehensively described the method as well as how it was performed and interpreted. Regarding MRI, most of the studies adequately outlined how the index test was performed and interpreted. Only one study was

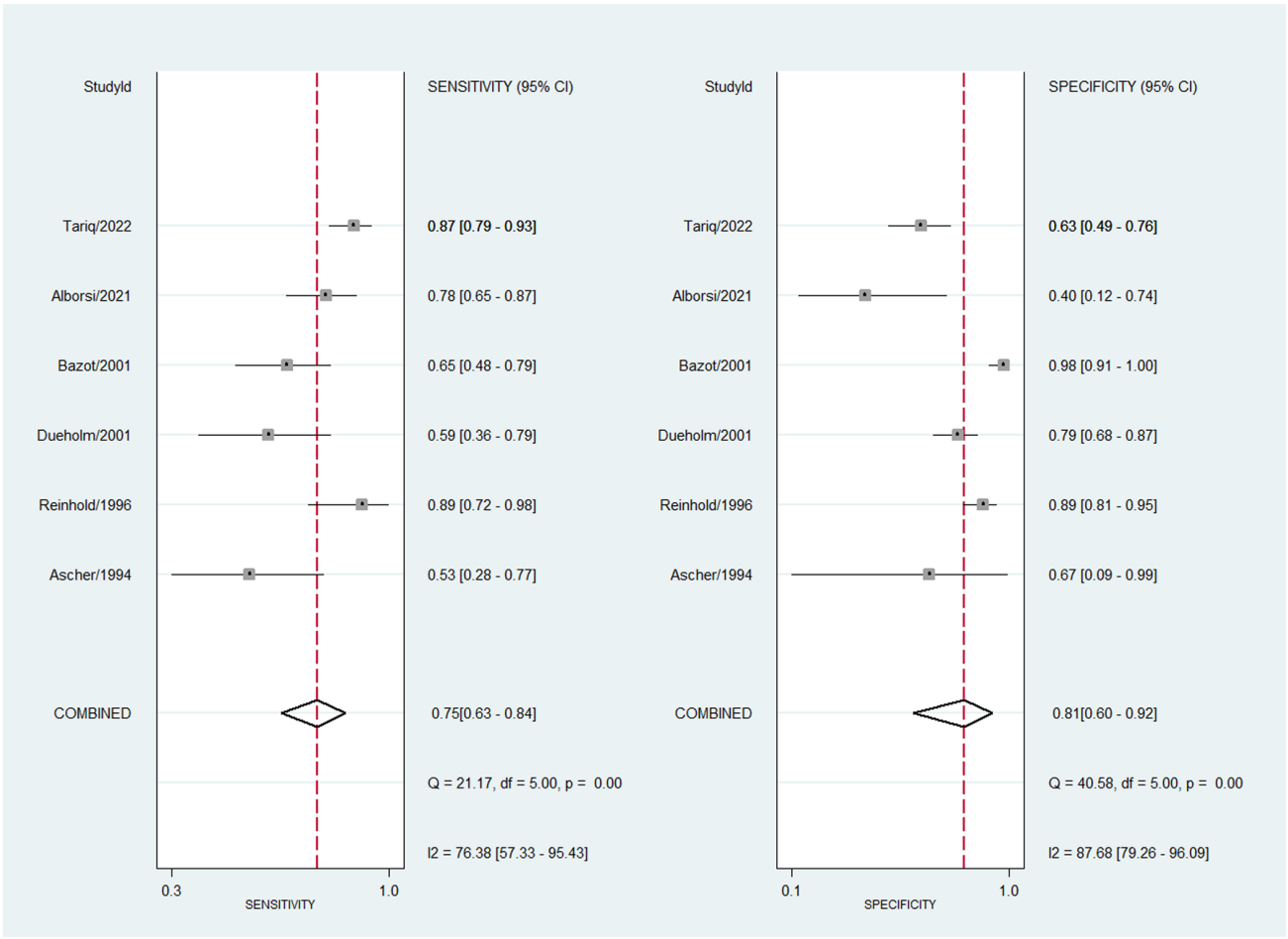

FIGURE 3 Forest plot for sensitivity and specificity for each study and pooled sensitivity and specificity for (a) transvaginal ultrasound and (b) magnetic resonance imaging.

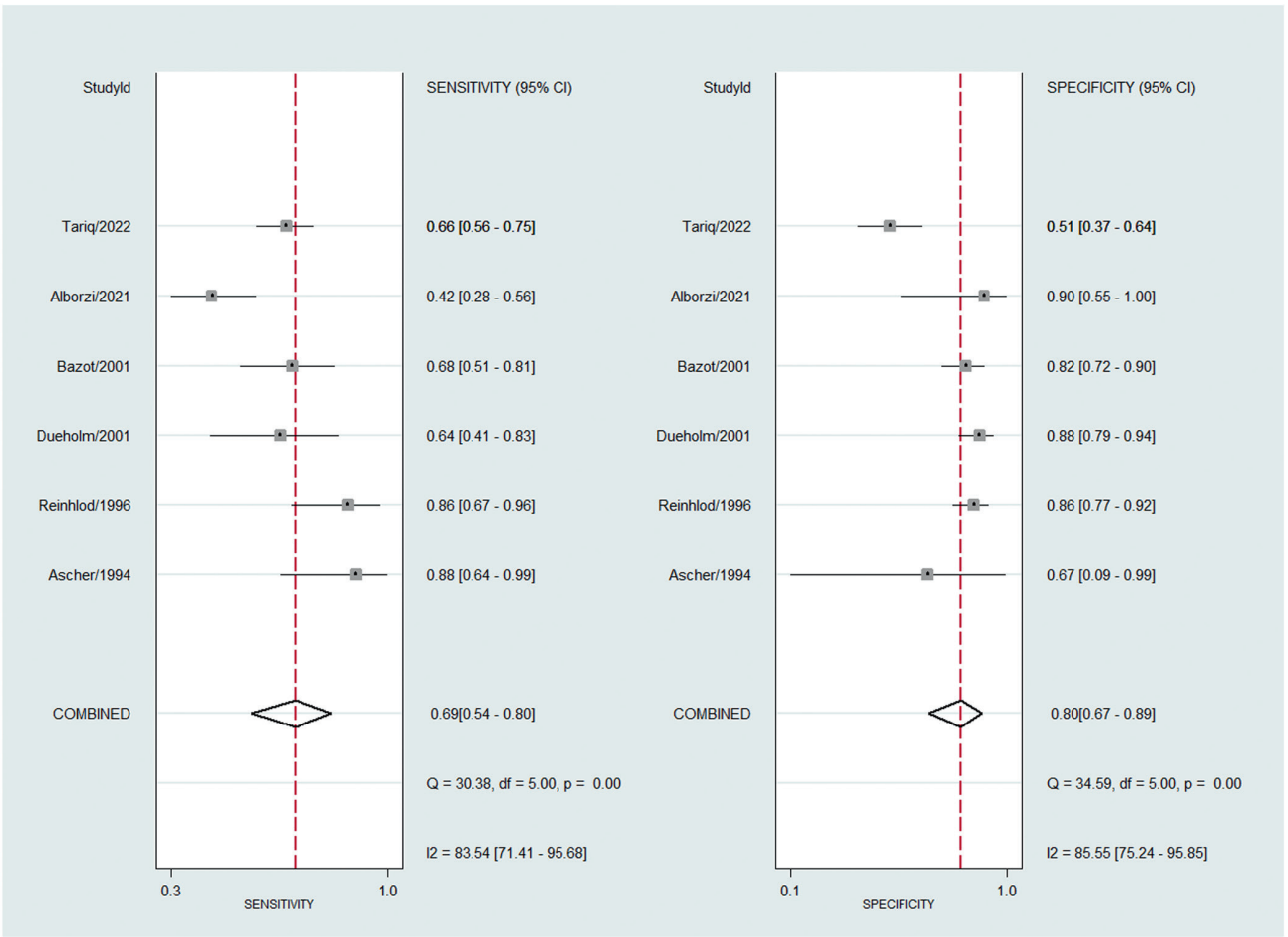

FIGURE 3 (Continued)

classified as unclear as the diagnosis criteria were described but not the MRI method.[19] The diagnostic criteria for TVS used in each study are shown in Table 2.

Every study compared the imaging findings to the histopathology of the surgical specimen. Therefore, all of them can be considered to have a low risk of bias concerning the reference standard domain, although only four studies specifically stated that the pathologists were blinded to the imaging results. Regarding the flow and timing domain, the time lapse between the index tests and the reference standard was low risk in two studies, because less than 2 weeks passed between the index tests and histopathological confirmation of the findings.[16,17] In the remaining four studies, the flow timing was unclear.

With regard to applicability, for the patient selection domain, index test domains and reference test, it was low risk in all the studies included.

Overall, the pooled sensitivity, specificity, LR+, and LR- of TVS for detecting adenomyosis were 75% (95% confidence interval [CI] 63–84), 81% (95% CI 60–92), 3.9 (95% CI 1.7–9), and 0.31 (95% CI 0.21–0.47), respectively. High heterogeneity was found for both specificity (I^2 87.78%; Cochran Q 40.58; p <0.001) and for sensitivity (I^2 76.38%; Cochran Q 21.17; p <0.001). A univariate meta-regression analysis was carried out, but none of the variables assessed were found to explain the heterogeneity.

On the other hand, the pooled sensitivity, specificity, LR+, and LR- of MRI to adenomyosis involvement were 69% (95% CI 54–80), 80% (95% CI 67–89), 3.5 (95% CI 1.9–6.2), and 0.39 (95% CI 0.25–0.6), respectively. High heterogeneity was found for both sensitivity (I^2 83.54%; Cochran Q 30.38; p <0.001) and specificity (I^2 85.55%; Cochran Q 34.59; p <0.001). A univariate meta-regression analysis was performed but none of the variables assessed were found to explain the heterogeneity. Figure 3 shows the forest plots for both methods. When comparing both methods, no statistical differences were found (p = 0.751).

Figure 4 shows the sROC curves for TVS (Figure 4a) and MRI (Figure 4b). Both techniques had almost identical AUCs, with very similar 95% prediction contours. The AUC for TVS was 0.83 (95% CI 0.79–0.86) and for MRI the AUC was 0.81 (95% CI 0.54–0.80).

The Fagan nomograms showed that a positive test for TVS and MRI significantly increases the pre-test probability for adenomyosis, from 52% to 81% in the case of TVS and from 52% to 79% in the case of MRI. On the other hand, a negative test result significantly decreases the pre-test probability for adenomyosis from 52% to 25% in the case of TVS (Figure 5a) and from 52% to 30% in the case of

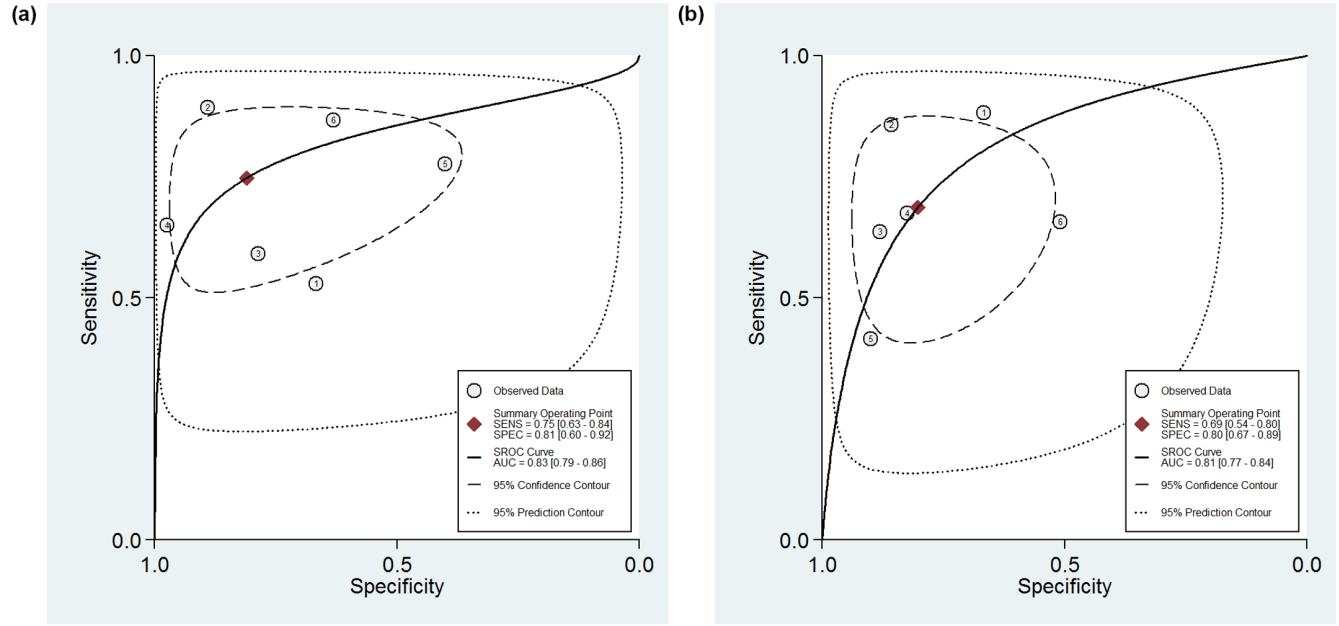

FIGURE 4 Summary ROC curve for (a) transvaginal ultrasound and (b) magnetic resonance imaging. AUC, area under the curve; SENS, sensitivity; SPEC, specificity; SROC, summary receiver operating characteristic.

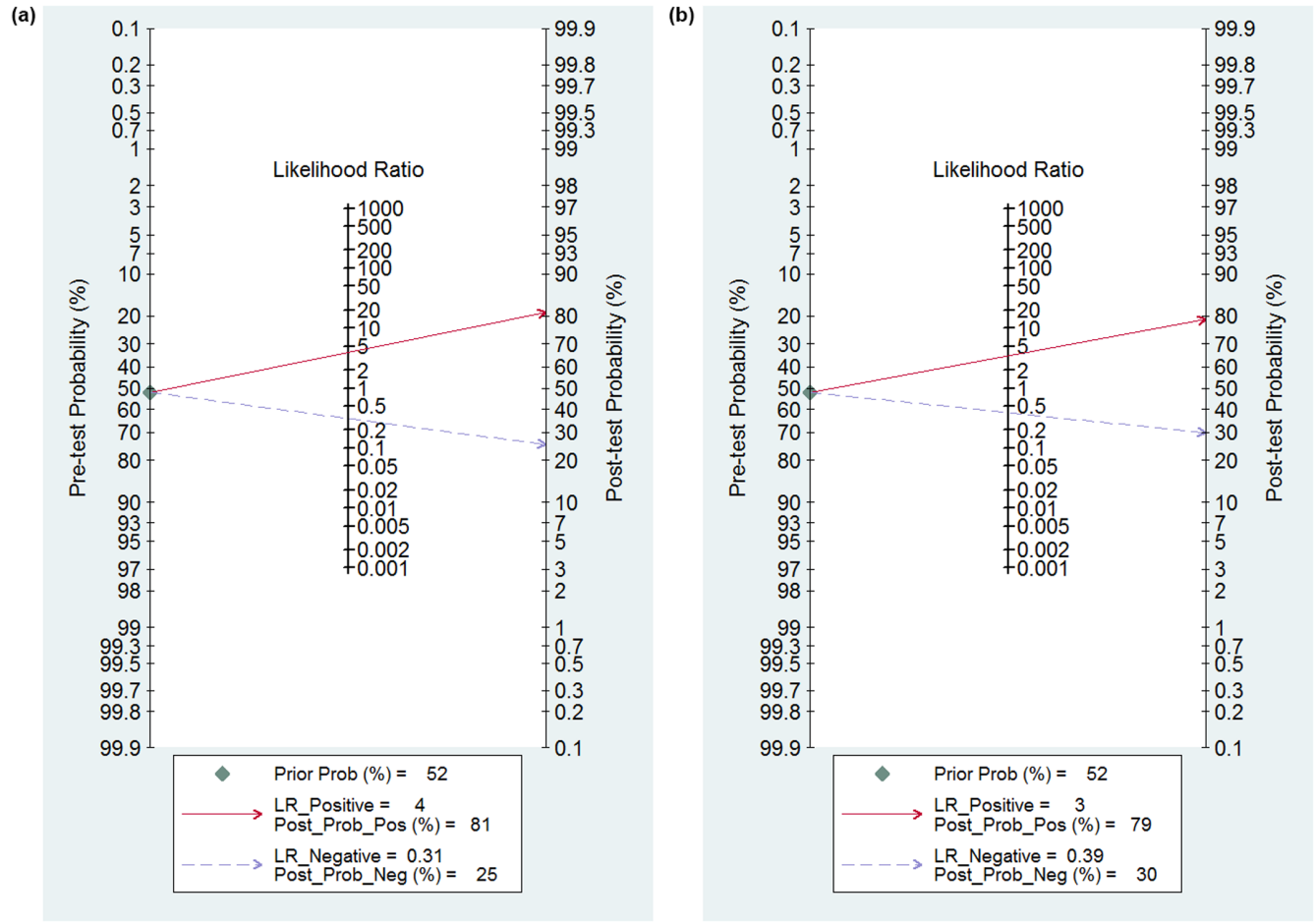

FIGURE 5 Fagan nomograms showing how pre-test probability changes after the test is performed (post-test probability) depending on a positive or negative result for (a) transvaginal ultrasound and (b) magnetic resonance imaging. LR, likelihood ratio.

TABLE 3 Summary of the results of the meta-analyses reported comparing TVS and MRI for diagnosing adenomyosis

Author	Year	No. of TVS studies	No. of MRI studies	Pooled sensitivity: TVS (%)	Pooled sensitivity: MRI (%)	Pooled specificity: TVS (%)	Pooled specificity: MRI (%)
Champaneria[7]	2010	6	3	72	77	81	89
Tellum[8]	2020	8	3	78	78	78	88
Liu[9]	2021	25	6	79	71	86	91
Present study	2022	6	6	75	69	81	80

Abbreviations: MRI, magnetic resonance imaging; TVS, transvaginal ultrasound.

MRI (Figure 5b). There was no risk of bias for either TVS ($p = 0.380$) or MRI ($p = 0.510$).

7 | CONCLUSIONS

There are few studies comparing the diagnostic performance of TVS and MRI for detecting uterine adenomyosis in the same set of patients. In the present meta-analysis, it was discovered that TVS and MRI have a similar performance for diagnosing adenomyosis. The quality of studies assessed was good, except in the case of patient selection as a high risk of bias was observed for half of the studies evaluated.

Our data indicate that both techniques show a high specificity and moderate sensitivity for the diagnosis of adenomyosis. No statistically significant differences were found between one method and the other for the diagnosis of adenomyosis However, a significant heterogeneity was observed. This implies that the results of the present study should be interpreted with caution.

According to the study results, both methods could be used interchangeably. However, on clinical grounds, the use of ultrasound would imply lower costs and this technique is more widely available. Therefore, it should be considered the first choice. This is clinically relevant since MRI is much less available in terms of facilities and cost in low-income countries.

It is believed that the main strength of the present study is that the meta-analysis is the first head-to-head comparison study addressing this issue. There are previously reported meta-analyses comparing TVS and MRI for the diagnosis of adenomyosis.[7–9] These meta-analyses found similar results to those of the present study (Table 3), which confirm the concept that TVS and MRI have a similar diagnostic performance for this entity. The main difference between those studies and the present one is that a formal statistical comparison was carried out in the present study and not in the others.

Despite this, the present study also has some limitations. The main limitation is thought to be the few studies currently available comparing TVS and MRI in the diagnosis of adenomyosis. In fact, is interesting to note that only six studies with a direct comparison of both techniques have been reported in 28 years. In addition, more interesting is observing the fact that no apparent improvement on diagnostic performance is observed during these years, in spite of significant improvements in technical quality imaging for TVS and MRI. Furthermore, the role of three-dimensional ultrasound (3D-TVS) was not assessed. This technique has been advocated as potentially useful for diagnosing uterine adenomyosis, especially for evaluating the so-called junctional zone.[21] In fact, the non-head-to-head meta-analysis reported by Tellum et al.[8] concluded that 3D-TVS was slightly superior to MRI and conventional TVVS.

These facts, combined with the observed high heterogeneity, make it seem necessary that there is a need for more studies assessing this issue.

As mentioned above, more prospective studies with better selection criteria are needed. It is probably that prospective comparative studies using Morphological Uterus Sonographic Assessment criteria would be advisable.[21]

On the other hand, there is a need to establish good and global criteria for the diagnosis of adenomyosis. Moreover, the need to train sonographers for a better diagnosis is also a point to consider.

In conclusion, no statistically significant differences were found between MRI and TVS in the diagnosis of adenomyosis.

AUTHOR CONTRIBUTIONS

Study concept: JLA, SG, and MAP. Study design: JLA and SG. Search and data acquisition: JV, CU, and JLA. Data analysis: JLA. Data interpretation: JLA, SG, MAP, JV, CU, and SA. Draft writing: JLA. Draft reviewing and approval: all authors.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data are available upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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