European Journal of Obstetrics and Gynecology 297 (2024) 233–240

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.journals.elsevier.com/european-journal-of-obstetrics-and-gynecology-and-reproductive-biology

Review article

Transvaginal ultrasound with bowel preparation versus transvaginal ultrasound with bowel preparation and water contrast for diagnosing Recto-Sigmoid endometriosis. A systematic review and Meta-Analysis

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ARTICLE INFO

Keywords:
Endometriosis
Transvaginal ultrasound
Bowel preparation
Water contrast
Rectosigmoid

ABSTRACT

Transvaginal ultrasound is effective in diagnosing endometriosis involving the rectosigmoid bowel. Some authors suggest enhanced detection of rectosigmoid involvement with bowel preparation. Conversely, conflicting views argue that bowel preparation may not improve diagnostic precision, yielding similar results to rectal water contrast. No existing *meta*-analysis compares these approaches. Our study aims to conduct a *meta*-analysis to evaluate the diagnostic performance of transvaginal ultrasound with bowel preparation, with and without rectal water contrast. Studies published between 2000 and 2023 were searched in PubMed, Scopus, Cochrane and Web of Science. From 561 citations, we selected nine studies to include in this *meta*-analysis. The study quality was assessed using QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies-2). The mean prevalence of endometriosis rectosigmoid was 43.6% (range 17,56–76,66%) in the group with bowel preparation and 64,80% (50,0–83,60%) for the group with bowel preparation and rectal water contrast. Pooled sensitivity and specificity were 93% and 94% for bowel preparation and 92% and 95% and for bowel preparation with water contrast. We conclude that, there was no significant difference between performing transvaginal ultrasound with intestinal preparation with and without water contrast. In clinical practice, the absence of a significant difference between these methods should be taken into account when making recommendations.

Introduction

Endometriosis is a chronic and multifocal disease characterized by the presence of endometrium-like epithelium and stroma outside the endometrial and myometrial boundaries [1]. Although it can virtually affect any part of the body, this condition, which impacts up to 10 % of women's reproductive age, is typically confined to the pelvic cavity [2,3]. Clinical manifestations may vary across a broad spectrum depending on the affected structures, ranging from asymptomatic women to those with severe symptoms such as dysmenorrhea, dyspareunia and infertility [4].

Deep pelvic endometriosis affects more often the posterior compartment of the pelvis, particularly the recto-sigmoid bowel. This disease poses a clinical challenge and can be assessed by transvaginal ultrasound. This imaging technique is a highly valuable tool that proved to have a comparable or better accuracy than other imaging tests such as MRI when it comes to determine the presence and dimension of endometriotic lesions [5–10].

Despite its good accuracy, efforts have been made in an attempt to progressively improve the ultrasound technique when patients present with DIE involving the bowel. On one hand, some authors suggested that transvaginal ultrasonography with bowel preparation (BP) can better detect recto-sigmoid involvement, thereby guiding surgical strategy [11]. On the other hand, other authors contend that bowel preparation does not enhance ultrasound performance when it comes to diagnose recto-sigmoid endometriosis, having the same result when it is added to

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https://doi.org/10.1016/j.ejogrb.2024.04.015
Received 3 January 2024; Accepted 11 April 2024
Available online 12 April 2024

rectal water contrast (RWC) in transvaginal ultrasonography [12,13].

To the best of our knowledge, there is no *meta*-analysis comparing TV after BP with and without rectal water contrast. Therefore, the aim of our study is to perform a systematic review and *meta*-analysis of studies using BP with and without RWC in order to assess whether the use or RWC improves or adds to the diagnostic performance of our technique.

Materials and methods

Protocol and registration

We used the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) recommendations to perform this *meta*-analysis a well as the SEDATE (Synthesizing Evidence from Diagnostic Accuracy Tests) guidelines [14,15]. Inclusion and exclusion criteria for primary studies to be included in this *meta*-analysis were defined prior to start research. The *meta*-analysis was registered in PROSPERO (CDR42023485325). There was no need for an ethics committee's approval given the nature and design of this study.

Data sources and searches

A search between January 2000 and October 2023 was performed using four electronic databases (PubMed, Scopus, Cochrane and Web of Science), to identify eligible primary studies addressing the question under review. We did not use methodological filters in database searches in order to avoid possible omission of relevant studies.

To do the research we included the following terms "Endometriosis" AND "Ultrasound" AND "transvaginal" AND "Bowel OR rectal" in the search place.

Study selection and data collection

Once we had compiled the preliminary list of potential studies, all titles were screened independently by four authors (ES, SM, ML and TA) to eliminate any duplications. In the next step, we filtered the titles and subsequently examined abstracts to identify and exclude irrelevant articles. These included those not directly related to the topic under review, as well as non-observational studies, such as reviews, case reports, and letters to the editor.

To ensure we did not exclude any valid study to our research, all the abstracts were evaluated and validated by five authors (ES, SM, ML, TA and JLA). Then, the records were again filtered with a complete reading of the full text of the studies that remained after exclusion.

The inclusion criteria used were as follows: Primary studies including prospective or retrospective diagnostic studies including women previously diagnosed with endometriosis or with clinical suspicion of deep infiltrating endometriosis who underwent transvaginal ultrasonography with prior bowel preparation with or without water contrast, the collected data allow the construction of a 2×2 table to estimate true positive, true negative, false positive, and false negative cases for the index test assessed, and the reference test used was surgical findings and /or histological confirmation.

The exclusion criteria were the following: studies not related to the topic, secondary studies (other *meta*-analysis or systematic reviews) or those where enough data was not provided, articles that did not report specific data regarding the use of bowel preparation or water contrast during patient's examination, studies where other imaging studies such as MRI or CT were considered, studies where surgical findings and/or histology was not the gold standard or was not available.

If the dates of two cohort studies published by the same authors overlapped, we excluded the first one in order to avoid the inclusion of duplicate cohorts. We used the snowball strategy to identify potential interesting papers by reading the reference lists of the papers selected for full text reading.

Four authors (ES, SM, ML, TA and JLA) independently retrieved the following data from each study: first author, year of publication, country, study design, number of centers participating, patients' inclusion criteria, patients' exclusion criteria, patients' age, number of patients, number of patients with endometriosis, index test used, definition of recto-sigmoid nodule, number of examiners and if they were experts or not, whether the examiner was blinded or not to the reference standard, the reference standard used, and also if surgeons and/or pathologist were blinded or not, the diagnostic accuracy results, and the time elapsed from the index test to the reference standard test. Disagreements arising during the process of study selection and data extraction were solved by consensus and discussion with a fifth collaborator (JLA).

Risk of bias in individual studies

The quality assessment of the studies included in the *meta*-analysis was conducted using the tool provided by the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) [16]. The QUADAS-2 format includes four domains: patient selection, index test, reference standard, and timing. For each domain, the risk of bias and concerns about applicability (not applying to the domain of flow and timing) were analyzed and rated as low, high, or unclear risk. Four authors (ES, SM, ML and TA) independently evaluated the methodological quality. Disagreements were solved by discussion with a fifth collaborator (JLA).

The assessment of the quality was based on whether the article described the study's design, inclusion, and exclusion criteria, if the operators were blinded, whether the study reported on how the index test was performed and interpreted, which was the reference standard used, and a description of the time elapsed from the index test assessment to the reference standard result. Unclear risk was stated when the corresponding information for each domain was not reported in the study.

When evaluating risk of bias in patient selection, those patients with previous surgeries due to endometriosis were considered high risk. For the flow-and-timing domain, we considered a high risk of bias when time from the index test assessment to the reference standard was over three months. The fact that examiners were not blinded to ultrasound findings was considered to pose a high risk of bias. Surgery and/or histological study was defined as the reference standard.

Statistical analysis

A random-effects model was employed to calculate the overall pooled sensitivity, specificity, positive likelihood ratio (LR +), and negative likelihood ratio (LR-). Likelihood ratios were utilized to describe the clinical utility of the tests and ascertain the post-test probability of disease.

Forest plots of the sensitivity and specificity of all studies were plotted. Heterogeneity for sensitivity and specificity was assessed using Cochran's Q statistic and the I2 index. A p-value < 0.1 indicates heterogeneity. I^2 values of 25 %, 50 %, and 75 % would be considered to indicate low, moderate, and high heterogeneity, respectively [17].

Meta-regression was used if heterogeneity existed to assess covariates that could explain this heterogeneity. The co-variates analyzed for *meta*-regression were year of publication, sample size (n) and prevalence.

The comparison between pool sensitivity and specificity was obtained by using bi-variate method.

Summary receiver operating characteristic (sROC) curves were plotted to illustrate the relationship between sensitivity and specificity, and the area under the curve (AUC) was calculated.

Mean prevalence of rectosigmoid involvement in each subset was used, together with the LRs extracted for each assessed technique, in order to calculate post-test probabilities and plot Fagan nomograms.

Publication bias was assessed using Deek's method [18].

Statistical analysis was performed using STATA version 12.0 for Windows (Stata Corporation, College Station, TX, USA). A p-value $<$

0.05 was considered statistically significant.

Results

Search results

The electronic search provided 561 citations. We excluded 240 duplicate records, and 28 reviews. After that, 293 citations remained. After reading titles and abstracts, 181 citations were excluded (papers not related to the topic (n = 128), assessing biomarkers (n = 5) and other diagnostic methods used (n = 48)). One hundred and twelve papers remained for full-text reading. We could not get full text of two studies and they were also excluded. After reading the full text of the remaining one hundred and ten paper, 101 articles were excluded, (no data about bowel preparation (n = 40), descriptive reports (n = 55) and not providing statistical data (n = 6)). Therefore, nine studies were ultimately included in this *meta*-analysis for qualitative and quantitative synthesis. A flowchart summarizing the literature search is shown in Fig. 1.

Out of the nine studies included in this *meta*-analysis, five studies assessed TV ultrasound with bowel preparation [19–22] and five studies assessed TV ultrasound with bowel preparation and rectal water contrast [13,24–26]. One of the included studies was classified in both groups as its sample included evaluation of both diagnostic methods [23]. These papers were published between 2001 and 2020 and reported the data of 969 women with ages ranging from 18 to 54 years old in the final analysis. The mean prevalence of endometriosis recto-sigmoid was 43.6 % (range 17,6–76,7%) in the group with bowel preparation and 64.8 % (50,0–83,6%) for the group with bowel preparation and rectal water contrast.

Characteristics of included studies

The PICOS features of the included studies are given in Table 1.

Methodological quality of included studies

Regarding the studies incorporated into this *meta*-analysis, eight were prospective [13,19–21,23–26], while one was retrospective [22], with all comprising a cohort population. In all studies, the individuals conducting ultrasonography were proficient experts, maintaining blinding to the results of the index tests in all cases, except for two studies, and not provided in one of them.

The diagnostic criteria for an endometriotic nodule with intestinal involvement were not exactly the same in all studies, but generally, it was defined as hypoechoic masses adjacent or close to the rectal wall. It was specified that infiltration into the muscularis propria was required in three of the studies [13,22,26].

The risk of biased evaluation and concerns regarding the applicability of the selected studies can be seen in Table 2.

Six studies were deemed high-risk in the "patient selection" domain due to exclusion criteria [13,22–24,26], which excluded patients with a previous surgical or radiological diagnosis of bowel endometriosis. All inclusion criteria were consistent across all studies (clinical suspicion of deep infiltrating endometriosis and the possibility of undergoing transvaginal sonography).

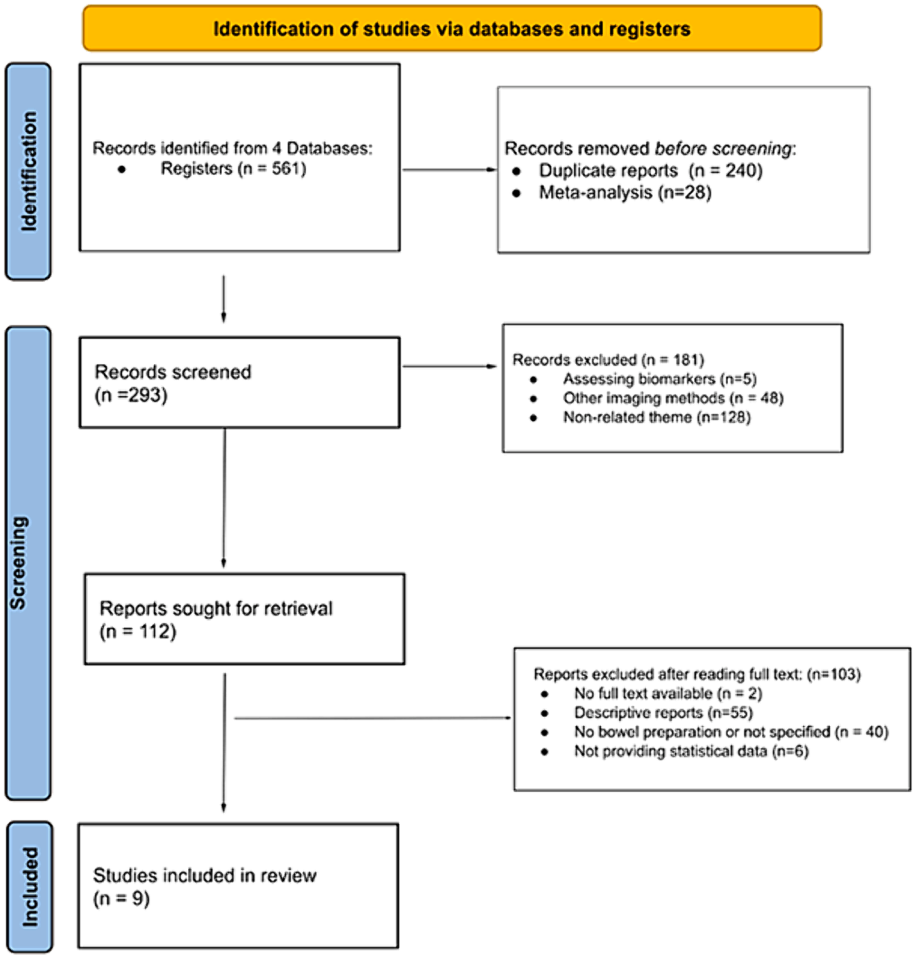

Fig. 1. Flowchart showing the study selection process, indicating the titles found in each database, and the final number of articles included in the meta-analysis.

Table 1
Main characteristics of the studies included in the *meta*-analysis.

Author	Year	Country	Study design	N patients	N recto-sigmoid affected	Age	Bowel preparation with or without water contrast	Reference standard	Examiner blinded	Time until surgery (Days ±SD)
Menada [23]	2008	Italy	Prospective	90	69	Median: 32.0 (18– 42)	TVS+BP+RWC TVS+BP	Surgery and AP	Yes	ND
Bergamini [25]	2010	Italy	Prospective	61	51	Median: 33.1 (28–37)	TVS+BP+RWC	Surgery and AP	Yes	ND
Ferrero [26]	2011	Italy	Prospective	96	48	ND	TVS+BP+RWC	AP	Yes	1
León [19]	2014	Chile	Prospective	51	13	Mean: 32.9 (23–43)	TVS+BP	Surgery and AP	ND	ND
Piessens [20]	2014	Brazil	Prospective	205	36	(18–48)	TVS+BP	Surgery and AP	No	ND
Ros [21]	2017	Spain	Prospective	40	18	Mean ± SD 36.8±5	TVS+BP	Surgery and AP	Yes	3.6 ± 1.5
Young [22]	2017	USA	Retrospective	113	60	Median: 35.0 (19–54)	TVS+BP	Surgery and AP	No	12
Ferrero [13]	2019	Italy	Prospective	155	92	Mean ± SD 32.5 ± 4.2 32.6 ± 4.7	TVS+BP+RWC	Surgery and AP	Yes	ND
Barra [24]	2020	Italy	Prospective	68	37	Mean ± SD 35.4 ± 6.0	TVS+BP+RWC	Surgery and AP	Yes	6

* Age of the patients is expressed as in the source articles in years as "Mean" or "Median".
Range in parentheses. SD: standard deviation. ND: no data. TVS: transvaginal ultrasound. BP: bowel preparation. RWC: rectal water contrast

Table 2
Quality assessment (risk of bias and concerns of applicability) for all studies included in the *meta*-analysis.

Author	Year	Patient selection	Index test	Reference Standard	Flow and timing
Bergamini [25]	2001	Low risk	Low risk	Low risk	Unclear
Menada [23]	2008	High risk	Low risk	Low risk	Unclear
Ferrero [26]	2011	High risk	Low risk	Low risk	Low risk
León [19]	2014	Low risk	Low risk	Low risk	Unclear
Piessens [20]	2014	Low risk	Low risk	Low risk	Unclear
Ros [21]	2017	Low risk	Low risk	Low risk	High risk
Young [22]	2017	High risk	Low risk	Low risk	High risk
Ferrero [13]	2019	High risk	Low risk	Low risk	Unclear
Barra [24]	2020	High risk	Low risk	Low risk	High risk

Concerning the domain "index test," all studies were considered to have a low risk of bias because diagnostic test results were considered as objective and potentially reproducible, leading to lower bias in the evaluation of the test's performance.

The standard reference employed was reliable and widely accepted for determining the true status of the condition (surgical procedure and histological confirmation), allowing for accurate comparisons with the diagnostic test results, therefore, all the studies were considered low-risk for the domain "reference standard".

Regarding the domain "flow and timing," five articles were considered to have an unclear risk of bias because the time elapsed between the ultrasound and laparoscopy with histological confirmation was not described [13,19,20,23,25]. In the remaining four studies, it was considered low risk in one of them as the time lapse was one only one month [26], and high in three of them as more than three months occurred between both interventions [21,22,24].

Diagnostic performance of transvaginal ultrasound with bowel preparation and transvaginal ultrasound with bowel preparation and water contrast for rectosigmoid endometriosis diagnosis

Considering transvaginal ultrasound with bowel preparation performance for the diagnosis of endometriosis recto-sigmoid nodules the pooled sensitivity was 93 % (95 % CI 89–96 %) with no heterogeneity (I^2 = 0.00 %; 95 % CI% 0–100 %; Cochran Q = 3.4, p = 0.49). The estimated pooled specificity was 94 % (95 % CI 91–96 %) with low heterogeneity (I^2 = 9.8 %; 95 % CI 0–100 %; Cochran Q = 4.4, p = 0.35). The forest plot is shown in Fig. 2A.

When considering transvaginal ultrasound with bowel preparation and rectal water contrast the pooled sensitivity was 92 % (95 % CI 83–97 %) with a high heterogeneity (I^2 = 86.9 %; 95 % CI% 75.1–96.9 %; Cochran Q = 28.7, p < 0.001). The estimated pooled specificity was 95 % (95 % CI 88–98 %) with moderate heterogeneity (I^2 = 56.1 %; 95 % CI 12.5–99.7 %; Cochran Q = 9.1, p = 0.06). The forest plot is shown in Fig. 2B. The conducted *meta*-regression did not reveal any differences among the analyzed covariables.

When comparing the pooled sensitivity and specificity between both methods, no statistical differences were observed (p = 0.9801).

The ROC curves for the diagnostic performance of the transvaginal ultrasound with bowel preparation only and bowel preparation with rectal water contrast to detect recto-sigmoid endometriosis, are shown in Figs. 3A and 3B, respectively. The area under the curve regarding TV

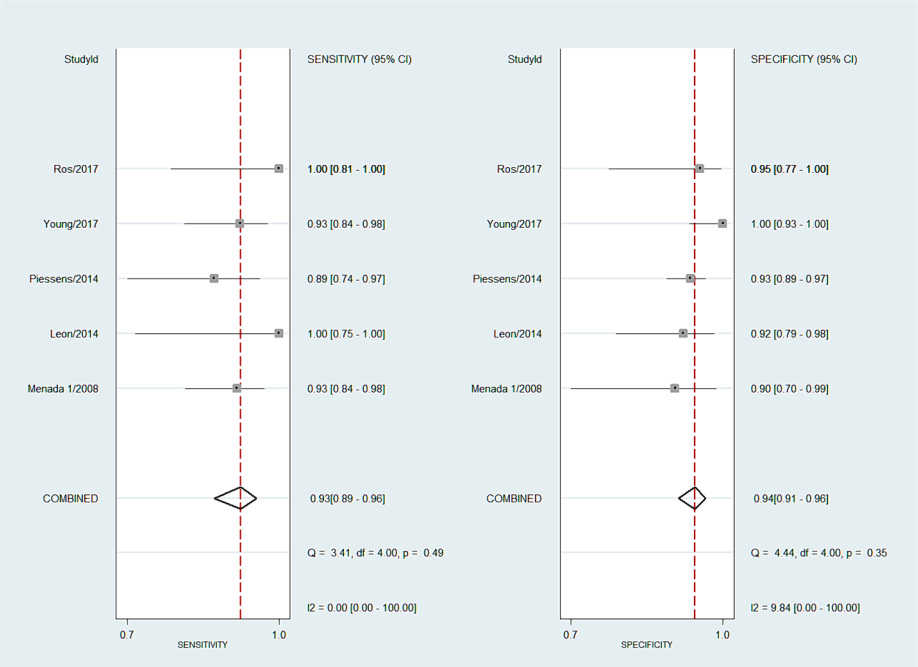

Fig. 2A. Forest plot for sensitivity and specificity for all studies concerning the diagnostic performance of transvaginal ultrasound with bowel preparation.

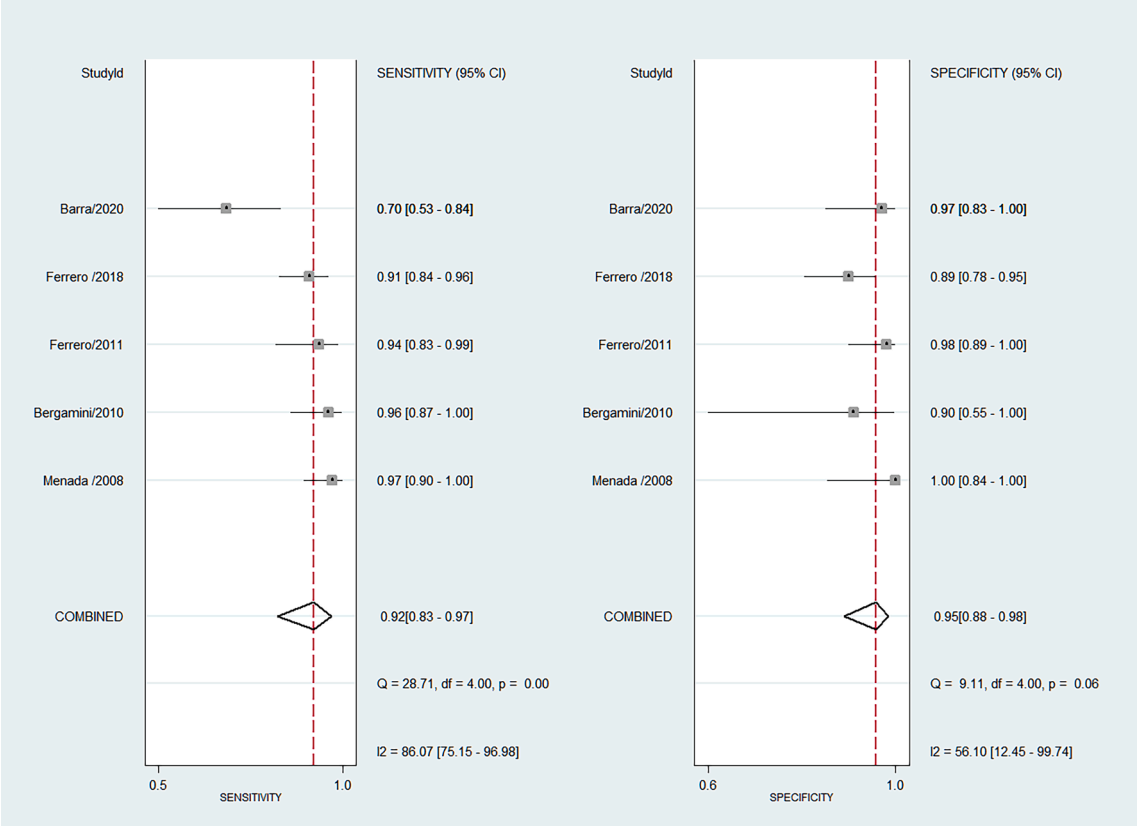

Fig. 2B. Forest plot for sensitivity and specificity for all studies concerning the diagnostic performance of transvaginal ultrasound with bowel preparation and water contrast.

ultrasound with bowel preparation only was 0.98 (95 % CI 0.96–0.99). For TV ultrasound with bowel preparation and water contrast, the area under the curve was 0.98 (95 % CI 0.96–0.99).

Fagan's monogram showed that transvaginal ultrasound with bowel preparation increased the pre-test probability of recto-sigmoid endometriosis from 44 % to 93 % and decreased to 5 %, with an LR + and LR − of 17 and 0.07, respectively (Fig. 4A). On the other hand, a positive transvaginal ultrasound with bowel preparation and water contrast

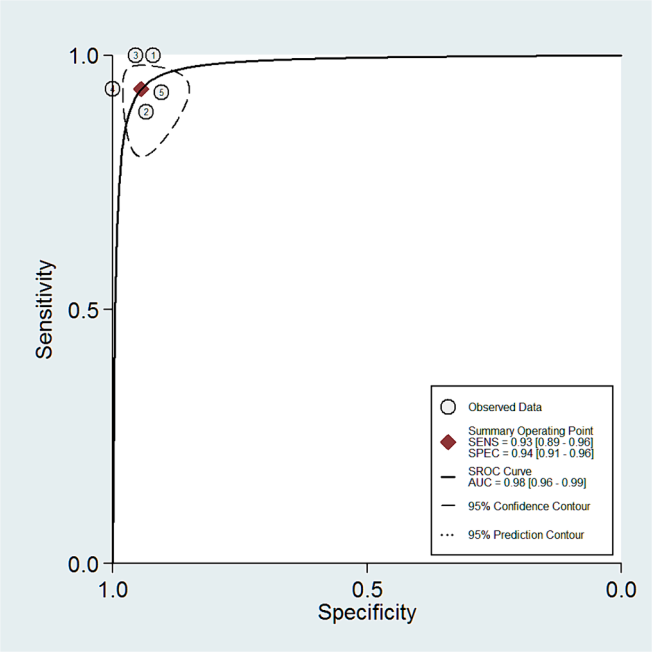

Fig. 3A. Summary ROC curve for the diagnostic performance of transvaginal ultrasound with bowel preparation to detect recto-sigmoid endometriosis, showing the sensitivity and specificity for each study and pooled estimation. The dashed line around the summary point estimate (red diamond) represents the 95% confidence region. The dotted line showing the 95% prediction contour corresponds to the predicted performance taking into account all individual studies. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

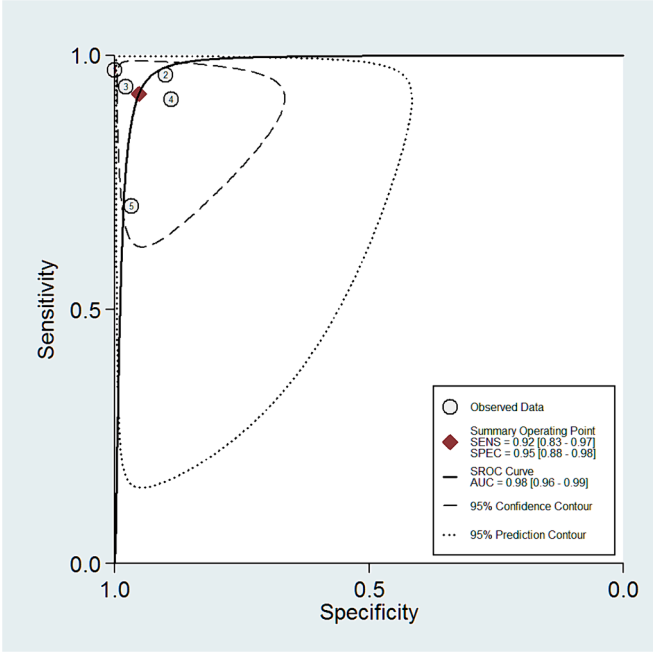

Fig. 3B. Summary ROC curve for the diagnostic performance of transvaginal ultrasound with bowel preparation and rectal water contrast to detect recto-sigmoid endometriosis, showing the sensitivity and specificity for each study and pooled estimation. The dashed line around the summary point estimate (red diamond) represents the 95% confidence region. The dotted line showing the 95% prediction contour corresponds to the predicted performance taking into account all individual studies. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

increased the pre-test probability of recto-sigmoid endometriosis from 65 % to 97 % and if negative, decreased this probability from 65 % to 13 %, with an LR + and LR − of 20 and 0.08, respectively (Fig. 4B).

We did not find publication bias referring to transvaginal ultrasound with bowel preparation (p = 0.62) and TV ultrasound with bowel preparation and water contrast (p = 0.91) (Fig. 5B. and Fig. 5B., respectively).

Discussion

Summary of evidence

In the present study, we conducted a systematic review and *meta*-analysis that included 9 studies. For the assessment of rectosigmoid involvement, ultrasound examinations were performed with transvaginal probe, involving bowel preparation with and without water contrast. Images were then compared with gold standard findings, including laparoscopic and/or histological outcomes.

The nine studies included in the analysis comprised 969 patients with available data. Among them, 493 endometriosis nodules were identified.

In our *meta*-analysis, the pooled sensitivity, specificity positive and negative likelihood ratio were 93 %, 94 %, 16.6 and 0.07, respectively, of transvaginal ultrasound with bowel preparation only; and 92 %, 95 %, 19.6 and 0.08, respectively, of transvaginal ultrasound bowel preparation with water contrast.

Regarding overall quality of the included studies, we observed that a significant proportion of studies had high risk of bias concerning patient selection domain.

Limitations and strengths

The main strength of our study is that this *meta*-analysis is the first to address this issue. Furthermore, endometriosis is a high-prevalence condition with an important impact on the patient's quality of life. Fortunately, its treatment is notably effective, so optimizing its diagnosis is particularly valuable. Ultrasound is a truly cost-effective tool, which avoids other invasive and expensive tests such as MRIs or diagnostic laparoscopies, and therefore optimizing its use is a profitable investment.

In terms of methods, we believe that the methodology used in this study is correct. Our *meta*-analysis is robustly supported by the inclusion of studies involving a final substantial number of patients (N = 969), establishing a strong foundation for our analysis. These studies consistently demonstrated a commendable level of technical detail in describing ultrasound examinations, thereby bolstering the reliability of our findings. The criteria for identifying rectosigmoid endometriosis remained clear and well defined across studies, utilizing laparoscopic and/or histological assessments for precision. The overall quality of our *meta*-analysis is enhanced by the low risk of bias observed in the included studies, ensuring increased reliability and validity of the results. Additionally, the low heterogeneity observed among the studies underscores internal consistency, highlighting a cohesive and harmonized approach in evaluating rectosigmoid endometriosis. These factors enhance the strength and reliability of our *meta*-analysis, making it easier to draw meaningful conclusions.

As limitations of our *meta*-analysis, we consider that the number of studies was low, as well as the quality of some papers; therefore, the results should be taken with caution. Moreover, the presented outcomes regarding sensibility and specificity may be overestimated due to the prevalence of endometriosis diagnosis in the included sample. Lastly, there is no standardized definition for rectosigmoid endometriosis so each group has defined its own diagnostic criteria, even though it was well defined.

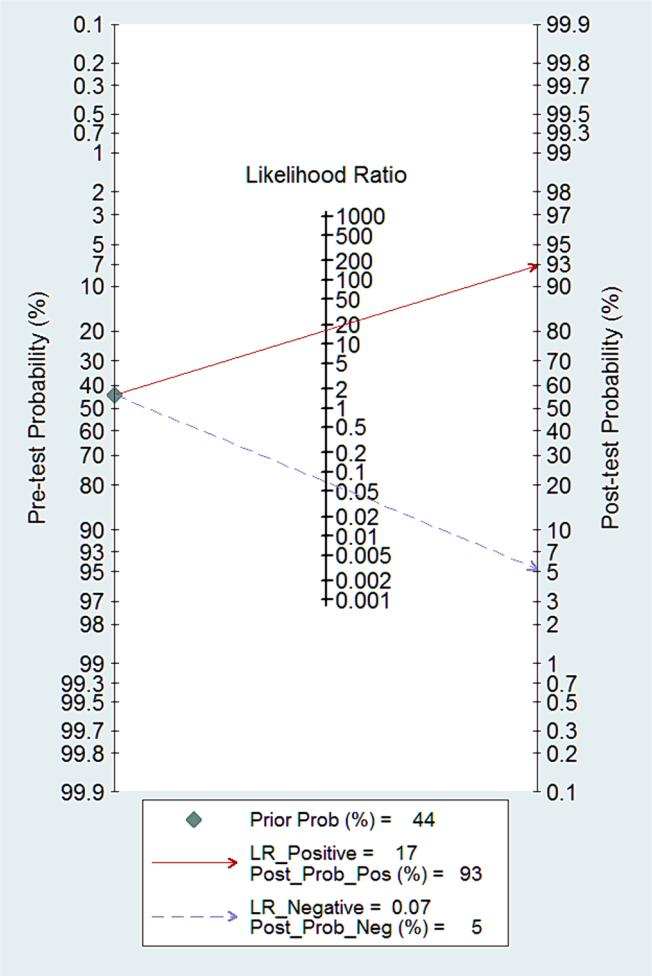

Fig. 4A. Fagan nomogram for transvaginal ultrasonography with bowel preparation only. It can be observed how the test changes the pre-test probability depending on a positive or negative result.

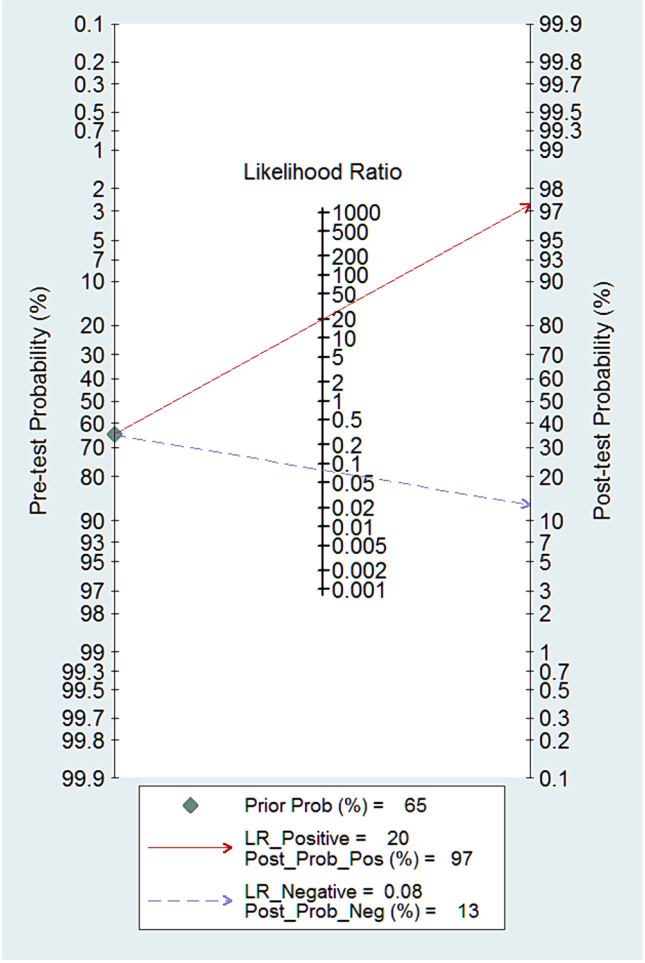

Fig. 4B. Fagan nomogram for transvaginal ultrasonography with bowel preparation aqnd rectal water contrast. It can be observed how the test changes the pre-test probability depending on a positive or negative result.

Interpretation of results

Following the completion of our *meta*-analysis, culminating in the conclusion that transvaginal ultrasound after bowel preparation with water contrast provides no benefit compared to ultrasound performed without water contrast, there arises a pertinent question regarding its clinical recommendation.

The comprehensive review of scientific literature has shed light on potential drawbacks associated with transvaginal ultrasound using rectal water contrast, including prolonged examination times, patient discomfort, and financial implications. Considering these factors alongside the outcome of our *meta*-analysis, it becomes evident that the additional step of utilizing water contrast may not yield significant clinical benefits if used as first line diagnostic approach. However, it could be considered as second line approach for better assessment of the extent of the disease and the degree of rectal stenosis, if present. However, it should be borne in mind that, in our *meta*-analysis, all studies used RWC as first line technique.

Certainly, tolerability of RWC was acceptable, according to all reported studies. No study compared tolerability of transvaginal ultrasound with bowel preparation alone and RWC.

Future research agenda

There is a need for better quality studies that use uniform definition criteria in a larger series of patients to valid our preliminary results.

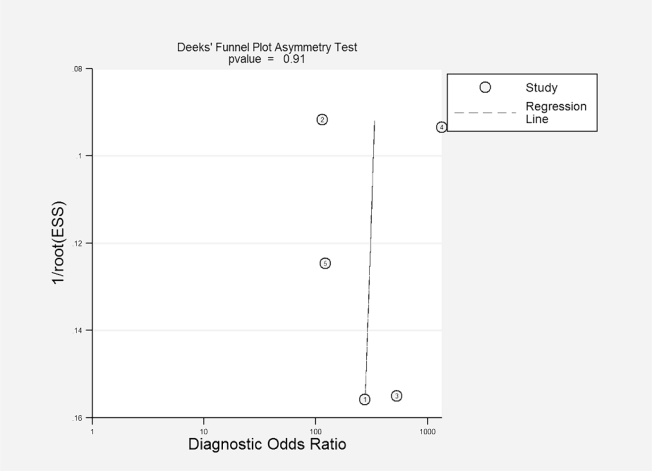

Fig. 5A. Publication bias regarding transvaginal ultrasonography with bowel preparation only

Conclusions

Regarding these results and because the transvaginal ultrasound with bowel preparation and water contrast is an invasive method, we can conclude that transvaginal ultrasound with bowel preparation

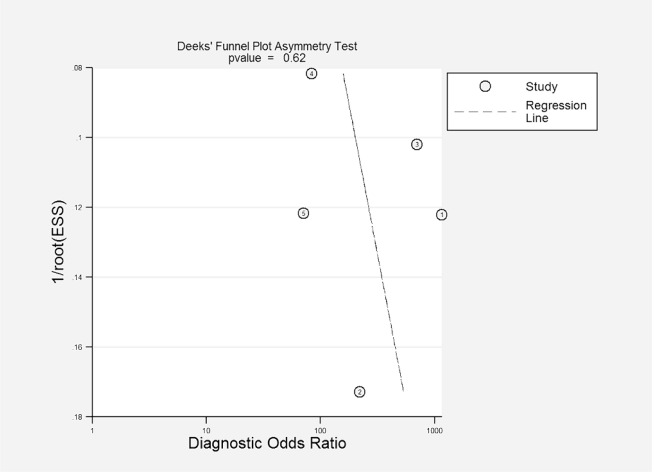

Fig. 5B. Publication bias regarding transvaginal ultrasonography with bowel preparation and rectal water contrast.

without water contrast is the best method for the diagnosis of endometriosis rectosigmoid.

Funding

This research received no external funding.

Author Contributions: Conceptualization, JLA; methodology, JLA, SM, ES, TA, ML, and BN.; software, JLA.; validation, JLA, SM, ES, TA, ML, and BN; formal analysis, JLA, SM, ES, TA, ML, and BN.; investigation, JLA, SM, ES, TA, ML, and BN.; data curation, JLA.; writing—original draft preparation, JLA, SM, ES, TA and ML;—review and editing JLA and SG. All authors have read and agreed to the published version of the manuscript.

The study protocol is available upon reasonable request.

CRediT authorship contribution statement

Sara Madaruelo: Investigation, Methodology, Validation, Writing – original draft. **Elena Satorres:** Formal analysis, Investigation, Methodology, Writing – original draft. **Teresa Arruffat:** Formal analysis, Investigation, Methodology, Writing – original draft. **Mariana Lourenço:** Formal analysis, Investigation, Methodology, Writing – original draft. **Blanca Novillo-Del Álamo:** Formal analysis, Investigation, Validation. **Stefano Guerriero:** Writing – review & editing. **Juan Luis Alcazar:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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