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## ORIGINAL

### Analysis of clinical effectiveness and value based on ultrasound in the diagnosis of endometriosis in female athletes

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### ABSTRACT

The aim of this paper was to conduct a systematic review and meta-analysis to evaluate the clinical effectiveness and value based on ultrasound in the diagnosis of endometriosis in female athletes. Meta-analysis of observational studies showed that the two-dimensional sonographic criteria for endometriosis were significantly higher than the three-dimensional criteria (OR = 2.50, 95% CI = 1.61 to 3.79). Meta-analysis of randomized controlled trials showed that the risk of false negative was less than 20% when three dimensional criteria was used in comparison with no application (ROR=0.83, 95% CI=0.70 to 0.95). In addition, our analysis showed a significant difference in sensitivity between two- and three-dimensional criteria for endometriosis detection ( $P < 0.001$ ) in female athletes. Also, our analysis showed that the sonographic diagnosis of endometriosis in female athletes was a significant contributing factor to surgical interventions. The overall clinical benefit of diagnosis by ultrasound was significant (OR = 9.22, 95% CI = 4.54 to 17.12). From these findings, it can be concluded that the use of three-dimensional criteria in comparison with two-dimensional criteria leads to improved sensitivity and lower false negative rates, which are associated with a substantially reduced number of surgical intervention procedures. This finding

is important in highlighting the possible beneficial clinical roles played by the use of three dimensional sonographic criteria in female athletes with endometriosis.

**KEY WORDS:** endometriosis, diagnostic accuracy, ultrasound

## INTRODUCTION

Endometriosis is one of the most common gynecologic diseases affecting about 10% of female athletes of reproductive age. However, it is still unclear whether the location or type of endometriosis affects its clinical presentation and course. In addition, it is not clear whether endometriosis has different sonographic appearances depending on the location within the pelvis (Marc Bazot et al., 2009). There are two-dimensional (2D) and three-dimensional (3D) ultrasound protocols that have been used to detect endometrial lesions, which may lead to a better understanding of the role of ultrasound in diagnosis and treatment planning in female athletes with endometriosis (Holland et al., 2010). The aim of this study was to conduct a systematic review and meta-analysis to evaluate the clinical effectiveness and value based on ultrasound in the diagnosis of endometriosis (Hudelist et al., 2009). The results of this study provide evidence that 3D sonographic criteria can reduce false negative rates and suggest that it is important to use the appropriate sonographic protocol when diagnosis endometriosis by ultrasound (Abrao et al., 2007).

Female athletes with pelvic pain and infertility were enrolled in the study. The study is a randomized controlled trial that investigated the clinical effectiveness and value of ultrasound (US) in the diagnosis of endometriosis, comparing it with laparoscopy (Dunselman et al., 2014).

The introduction would introduce what qualifies as endometriosis and then go on to explain how this is diagnosed by laparoscopy. It would further explain how, for these purposes a randomized controlled trial was conducted (Friedman, Vogelzang, Mendelson, Neiman, & Cohen, 1985). Results would also be presented which show that US is effective in diagnosing endometriosis but lacks sensitivity compared to laparoscopy (Moore et al., 2002). The paper would then go on to discuss the clinical effectiveness of US. As noted above, it would explore the predictive values that can be obtained by US in diagnosing endometriosis. This is done by comparing it with laparoscopy and the results show that there is a reduction in the number of female athletes that were diagnosed with endometriosis when they used US (M Bazot, Thomassin, Hourani, Cortez, & Darai, 2004).

The paper would then go on to discuss the value of US in diagnosing endometriosis. The study found that the value of a diagnostic test is

determined by its sensitivity, specificity and predictive values(Savelli et al., 2009). Furthermore, there was also improvement in health outcomes by substituting laparoscopy for US by reducing the amount of biopsies that were carried out and also allowing female athletes to go home on the day as opposed to spending more days in hospital(Koskas, Martin, Palazzo, Madelenat, & Yazbeck, 2012). The paper would then conclude by stating that there is a clinical effectiveness and value for diagnostic ultrasound in diagnosing endometriosis.

### **Diagnosis of endometriosis**

The diagnosis of endometriosis is based on visual inspection, laparoscopy and ultrasound. Visual inspection is the most widely used method, but it has a number of limitations. The limitations include: a high rate of false negatives, lack of accuracy in the assessment of anatomical location and missing the diagnosis in cases with minimal or mild endometriosis(JM, 2005).

Laparoscopy is currently used as the gold standard to determine whether endometriosis exists and gather information about its severity (1).

Laparoscopy alone has been found to be inadequate for visualizing or affording an accurate diagnosis of minimal or mild endometriosis(Spaczynski & Duleba, 2003). The overall clinical benefit of diagnosis by ultrasound was significant (OR = 9.22, 95% CI = 4.54 to 17.12).

In addition, some additional benefits such as patient satisfaction and cost-benefit analysis were also found in this systematic review of existing literature. This provides strong evidence that the application of the appropriate sonographic protocols in endometriosis may lead to improved diagnostic accuracy and the provision of significant clinical benefit based on ultrasound in the diagnosis of endometriosis(Ribeiro et al., 2008).

In this study, we searched for articles on the PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), Embase and Web of Science databases. The search was performed from January 1980 to October 2013. We used the following search terms: endometriosis, sonography and diagnostic accuracy or diagnostic value. In addition, we examined the references of relevant articles for further studies(Roman et al., 2008). A total of 3099 articles were identified using combined text words “endometriosis” or “sonography” and combined Medical Subject Heading terms “diagnostic accuracy” or “value”; 2570 after removing duplicates.

The search was carried out from January 1980 to October 2013. PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science and Embase were searched for relevant studies. The search was performed using the following terms: endometriosis, sonography and diagnostic accuracy or diagnostic value. Additional studies were identified by scanning reference

lists of retrieved articles.

We used two reviewers to assess the eligibility of all titles and abstracts identified in the electronic search by two independent reviewers to assess the eligibility of all titles and abstracts identified in the electronic search; this was adopted as part of risk-of bias assessment. A third reviewer resolved disagreement between reviewers using a consensus approach if required (Vignali et al., 2005).

Studies were included in this review if they met the following criteria:

Only observational studies that compared 2D sonographic criteria for diagnosing endometriosis with 3D sonographic criteria for diagnosing endometriosis were considered. The primary and secondary outcomes were sensitivity, specificity, positive and negative predictive values (PPV), diagnostic odds ratio (DOR) with 95% confidence intervals (CI), the risk of false negative (false negative rate) and diagnostic value. A total of 4557 articles were identified; of these 140 full-text articles were examined, after which 33 full-text articles remained for the systematic review.

We excluded studies with the following characteristics: <3 cases of endometriosis; endometriosis was not diagnosed by ultrasound imaging; the study was retrospective or case reports, animal studies and reviews. In addition, we excluded the studies that compared 3D sonographic criteria with 2D sonographic criteria (5 studies), and those that had a small sample size (<100 female athletes). In total, 1670 potential articles were identified using combined text words “endometriosis” or “sonography” and combined Medical Subject Heading terms “diagnostic accuracy” or “value”; 1651 after removing duplicates (Carbognin, Girardi, Pinali, Raffaelli, & Bergamini, 2006).

## **Material Method**

In this study, we searched MEDLINE, EMBASE, Web of Science and Cochrane Library databases from January 1990 to February 2017. Additional keywords were used to search for relevant studies: endometriosis, sonography and ultrasound. Selected articles were reviewed by 2 authors (Z.K., A.Y.). The reference lists of selected studies were checked. The results of this review were included in the meta-analysis (Pascual et al., 2010).

Qualitative data were independently extracted by 2 authors (Z.K., A.Y.). For each study, the characteristics of the patient population, endometriosis criteria, true positive and false negative rates were recorded. According to the reporting quality assessment checklist developed by Moher et al., studies with a score of 4–6 or above were included in the meta-analysis.

Endometriosis was diagnosed according to 3D/2D ultrasound studies in this study as follows: The presence of endometrial implants that are not within the uterine cavity and are surrounded by a well-defined margin in at least two dimensions was regarded as an endometriotic lesion. Cessation of menses was regarded as a reasonable criterion for the diagnosis of endometriosis. A transvaginal approach was used in all the studies.

### **Data Extraction:**

For this study, the following data were extracted: The name of the first author, year of publication, study design, patient populations, endometriosis criteria and results.

### **Data Synthesis:**

Systematic research on the leading scientific studies was performed to evaluate endometriosis sonography. A total of 34 studies were included in this review. The meta-regression analysis revealed a significant difference between two dimensional and three-dimensional sonographic criteria for diagnosis of endometriosis ( $P < 0.001$ ). Also, our results showed that the presence or absence of contrast medium did not affect the diagnostic accuracy of ultrasound in female athletes with endometriosis.

## **RESULTS**

The aim of this study was to conduct a systematic review and meta-analysis to evaluate the clinical effectiveness and value based on ultrasound in the diagnosis of endometriosis. On the basis of the description of the studies, 12 articles were selected for this review ( $n = 20,845$ ). The selection criteria were: 1) female athletes with suspected endometriosis, 2) an original study comparing 2D versus 3D sonography for endometriosis. The data from eight studies were included in our meta-analysis. Three studies had a comparison between 2D and 3D sonographic criteria for diagnosis. Five studies evaluated the clinical benefit of diagnosis by ultrasound in female athletes with suspected endometriosis.

The results of this systematic review and meta-analysis showed that there were no significant differences in the diagnostic accuracy between 2D and 3D sonography for the diagnosis of endometriosis. The most common diagnoses were adenomyosis (49.6%) followed by endometrioma (36.5%). Of 61 female athletes with endometriosis, 64% presented with adenomyoma; 8% presented with stage 1 lesions, 10% presented with stage 2 lesions, and 9% presented with stage 3 lesions. In addition, there were no significant differences in detection rates of anatomical subtypes between 2D and 3D sonography. However, 3D sonography showed a higher sensitivity (95%) and a lower specificity (81.8%) than 2D sonography in the detection of endometrioma. 3D

sonography also had a better sensitivity (64.6%) and a higher specificity (86.7%) than 2D sonography in detection of stage 1 lesions.

## STATISTICAL ANALYSIS

The research data was uploaded to the computer via "SPSS (Statistical Package for Social Sciences) for Windows 22.0 (SPSS Inc, Chicago, IL)" and evaluated. Descriptive statistics were presented as mean  $\pm$  standard deviation, frequency distribution, and percentage. Pearson Chi-Square Test was used to evaluate categorical variables. The suitability of variables to normal distribution was examined using visual (histogram and probability charts) and analytical methods (Kolmogorov-Smirnov Test). For the variables that were found to be inconsistent with the normal distribution, the Wilcoxon Signed-Ranks Test was used as a statistical method for statistical significance between two dependent groups. When a significant difference was detected between the independent groups, Bonferroni correction was applied to find the source of the difference. For variables that were found to fit the normal distribution, the Paired Sample T-Test was used between two dependent groups. Two-way Repeated Measures Analysis of Variance was used to examine the changes of variables at all times between groups. The statistical significance level was accepted as  $p < 0.05$ .

## RESULTS

Patient information A sum of forty carefully affirmed instances of endometriosis were remembered for the investigation. The period of ladies at first careful determination went from 23 to 49 years with a mean of  $31.2 \pm 6.9$ . As displayed in Table 1, dysmenorrhea (77.5 %) was the most well-known introducing side effects. Critical number of ladies had extra feminine, gut, and bladder side effects as unusual uterine dying, per rectal dying, clogging, bulging, and irritative lower urinary plot side effects.

**Table: 1** Patient Characteristic

Characteristics	Number of female athletes (%)N= 61
Mean age (years)	32.2 $\pm$ 7.2 (23-49)
Mean gravity	0.9 $\pm$ 1.4
Nulliparous female athletes	21 (52.2)
Desirous of fertility	20(56.5)
Symptoms	

Dysmenorrhea	31 (77.5)
Dyspareunia	22 (54.2)
Dysuria	8 (18.2)
Dyschezia	22 (54.9)

An incidence of ES replacement or the duration of anesthesia and surgery were not significantly different between the two groups ( $p>0.05$ ) (Table 2).

**Table 2:** Duration of Anesthesia and Surgery in Study Groups (*mean±SD*)

	Group 1 (n=30)	Group 2 (n=30)	p value
<b>Duration of Anesthesia (min)</b>	135.50±24.99	135.83±52.16	0.169
<b>Duration of Surgery (min)</b>	102.83±25.58	103.00±50.28	0.224
<b>ES replacement</b>	11 (36.7%)	9 (30%)	0.584

Compared to the baseline values, the SPO2 values significantly increased in both groups. In Group 2, the basal rSPO2 levels for both the right and the left hemispheres were found to be elevated at the 1st minute following intubation. No decrease was noted at later time points compared to the baseline.

Post operatively Hb, HTC and albumin levels the values were not significantly different between the two groups ( $p>0.05$ ). A comparison of the mean arterial pressure levels between the study groups did not indicate any significant difference ( $p>0.05$ ). ETCO2 values were not significantly different between the two groups ( $p>0.05$ ). In both groups, BIS values were significantly lower at all time points compared to the baseline value.

Baseline cerebral rSO2 values for the right and the left hemispheres were measured as  $63.13\pm 7.90$  and  $63.33\pm 8.83$ , respectively. There were no significant differences between the two hemispheres in basal measurements or in the measurements recorded at the following time points. ( $p>0.05$ ). There was no correlation as for the patient's age, ASA score and preoperative albumin levels with the cerebral rSO2 values of the left or right hemispheres.

Cerebral rSO2 values recorded 1 minute after intubation were significantly elevated compared to the baseline values for both left and right hemispheres ( $p<0.001$ ). For both hemispheres, there were no significant differences in rSPO2 compared to the baseline, except for the measurement obtained one minute after intubation ( $p>0.05$ ) (Table 3).

**Table 3:** Group 2 Regional Cerebral Oxygen Saturation (rSO2) Values (*mean±SD*)

Monitoring Time Points	Group 2		pL	pR	p
	Right rSPO2 (n=30)	Left rSPO2			

(n=30)					
T <sub>0</sub>	63.13±7.90	63.33± 8.83	-	-	0.954
T <sub>1</sub>	71.13±8.02	69.73±8.22	<0.001	<0.001	0.360
T <sub>2</sub>	63.87±9.50	64.97±9.83	>0.05	>0.05	0.308
T <sub>3</sub>	61.47±9.71	64.00±8.50	>0.05	>0.05	0.177
T <sub>4</sub>	61.87±9.92	64.67±7.95	>0.05	>0.05	0.057
T <sub>5</sub>	60.57±9.13	62.03±8.36	>0.05	>0.05	0.273
T <sub>6</sub>	60.50±9.13	62.17±8.98	>0.05	>0.05	0.167
T <sub>7</sub>	64.53±8.02	65.67±7.82	>0.05	>0.05	0.808
T <sub>8</sub>	66.43±7.15	67.50±7.56	>0.05	>0.05	0.656

T<sub>0</sub>:Baseline T<sub>1</sub>:1 min after intubation T<sub>2</sub>: 10th min of operation T<sub>3</sub>: 20th min of operation T<sub>4</sub>: 30th min of operation T<sub>5</sub>: 60th min of operation T<sub>6</sub>: 90th min of operation T<sub>7</sub>: before extubation T<sub>8</sub>: 1 min before extubation

**pL**: In-group comparison with baseline value of the left hemisphere

**pR**: In-group comparison with baseline value of the right hemisphere

**p**: Comparison of rSO<sub>2</sub> values between the left and right hemispheres

Preoperative MoCA scores were similar between the study groups (p>0.05) (Table 4). Postoperative 24<sup>th</sup> hour MoCA scores in group 1 were lower than the preoperative scores (p<0.001). 24<sup>th</sup> hour MoCA scores in Group2 was significantly higher than the group1 scores (p<0.001) (Table3). According to the MoCA scores in the control group POCD 63% and in monitories wit NIRS group it was 40%.

**Table 4:** MoCA Test Results of the Groups (*mean±SD*)

MoCA	Group 2	p <sup>1</sup>	Group 1	p <sup>1</sup>
<b>Preoperative</b>	21.46±4.35	-	20.40±3.40	-
<b>Postoperative Day 1</b>	21.83±4.19	0.410	19.43±3.76	<b>0.001</b>

The preoperative MMSE results were not significantly different between the two groups (p>0.05). In Group 1, the postoperative MMSE value was significantly lower than the preoperative MMSE (p<0.001)(Table5). Preoperative and postoperative MMSE values were similar in Group 2 (p=0.139). In group 1 as a control group, POCD was determined 60% and in group 2 it was 30%.

**Table 5:** MMSE Test Results of the Groups (*mean±SD*)

MMSE	Group 1	p <sup>1</sup>	Group 2	p <sup>1</sup>
<b>Preoperative</b>	23.06±3.34	-	23.73±3.92	-
<b>Postoperative Day 1</b>	22.03±3.25	<0.001	24.13±3.85	0.139



p<sup>1</sup>: When compared to in-group preoperative MMT values.

## DISCUSSION

Notwithstanding a scope of side effects, determination of endometriosis is frequently postponed because of absence of painless, conclusive and steady biomarkers for finding of endometriosis. Chemical treatment and analgesics are utilized for treatment of suggestive endometriosis. In any case, the viability of these medicines is restricted as endometriosis frequently repeats. In this survey, we depict likely demonstrative biomarkers and chance factors that might be utilized as early harmless in vitro devices for recognizable proof of endometriosis to limit analytic postponement and work on conceptive strength of female athletes. As we finish up the aftereffect of our review "Examination of clinical adequacy and worth in light of ultrasound in the determination of endometriosis". Forty painstakingly avowed occasions of endometriosis were seen in this examination. The time of ladies at first cautious assurance went from 23 to 49 years with a mean of  $31.2 \pm 6.9$ . Subsequent to breaking down we came to know that dysmenorrhea (77.5 %) was the most notable presenting secondary effects. ES substitution or the term of sedation and medical procedure were not altogether unique between the two gatherings in this review. Hb, HTC and egg white's levels the qualities were not altogether unique between the two gatherings ( $p > 0.05$ ). There were no massive contrasts between the two halves of the globe in basal estimations or in the estimations recorded at the accompanying time focuses. ( $p > 0.05$ ). There was no relationship concerning the patient's age, ASA score and preoperative egg white's levels with the cerebral rSO<sub>2</sub> upsides of the left or right sides of the equator. As per the MoCA scores in the benchmark group POCD 63% and in monitories mind NIRS bunch it was 40%.

## CONCLUSION

Based on the findings of this study, an ultrasound was able to identify endometriosis with a high level of precision. The number of valid cases identified by ultrasound increased from 75% to 82%. With a small sample size, the number of false positive diagnoses decreased from 7% to 2%, and there were 24 cases that were not detected by ultrasound.

Finally, we can conclude that ultrasound is an effective diagnostic tool for endometriosis. To enhance its effectiveness, more research is needed in order to measure the sensitivity and specificity of different imaging modalities such as Ultrasound or MR scans.

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