Original Article

Negative sliding sign during dynamic ultrasonography predicts low endometriosis fertility index at laparoscopy

Sukainah Alfaraj, M.D., Heather Noga, M.A. , Catherine Allaire, M.D, Christina Williams, M.D, Sarka Lisonkova M.D, Ph.D., Paul J. Yong, M.D., Ph.D., Mohamed A. Bedaiwy, M.D., Ph.D.

Division of Reproductive Endocrinology and Infertility, Department of Obstetrics & Gynecology, University of British Columbia, Vancouver, Canada.

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Corresponding author and person to whom reprint requests should be addressed:

Mohamed A. Bedaiwy, MD, PhD

Department of Obstetrics & Gynecology,

University of British Columbia,

D415A-4500 Oak Street, Vancouver, BC, V6H 3N1, Canada

Phone: +1-604-875-2000 ext 4310, Fax: +1-604-875-2725

Email: mohamed.bedaiwy@cw.bc.ca

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Précis: A low endometriosis fertility index can be predicted, without surgery, by using dynamic ultrasonography.

ABSTRACT

Study Objectives: Endometriosis fertility index (EFI) is a robust tool to predict pregnancy rate in endometriosis patients who are attempting non-in vitro fertilization conception. However, EFI calculation requires laparoscopy. Newly established imaging techniques such as sliding sign, that is used to diagnose Pouch of Douglas obliteration, could provide a promising alternative. The objective of this study is to investigate the practicality of using ultrasound data to predict low EFI (score ≤6).

Design: Observational study from a prospective registry (Endometriosis Pelvic Pain Interdisciplinary Cohort (EPPIC), ClinicalTrials.gov#NCT02911090). Analyzed data was captured from December 2013 to June 2017.

Setting: Tertiary referral center at British Columbia Women's Hospital.

Patients or Participants: We analyzed data for 2583 participants from EPPIC. In this cross-sectional study, we included eighty-six women who are less than 40 years old.

Interventions: Dynamic ultrasonography for the sliding sign testing and EFI calculation during laparoscopic surgery

Measurements and Main Results: Logistic regression was used to obtain ROC area under the curve (AUC) for the prediction models. Significance was $p<0.05$. Patients with a negative sliding sign were older, had severe endometriosis and longer duration of infertility. Patients with a negative sliding sign had significantly lower total EFI score and lower surgical factors' scores than patients with a positive sliding sign. Logistic regression showed that a negative sliding sign and EFI historical factors score can predict an EFI score ≤6 (sensitivity= 87.9%, specificity= 81.1%, AUC= 0.93 (95% CI 0.88–0.98). Adding the diagnosis of endometrioma to the previous prediction model resulted in AUC = 0.95 (95% CI 0.90–0.995), sensitivity = 84.8%, and specificity = 92.5%.

Conclusion: The sliding sign could be a potential alternative to the EFI surgical factors, and it could be used in combination with EFI historical factors and the diagnosis of endometrioma to predict an EFI score ≤6 for patients who are not scheduled for immediate surgery.

Keywords: Endometriosis; fertility index; infertility; in vitro fertilization; IVF; sliding sign.

INTRODUCTION

Endometriosis is a challenging gynecological condition responsible for up to 30% of female infertility cases and 11% of in vitro fertilization (IVF) cycles in the United States[1,2]. It can affect every aspect of a woman's reproductive function, whether at the molecular or the anatomical level[3]. The endometriosis fertility index (EFI) is the most current effective approach for formulating treatment plans for infertile patients with endometriosis and for predicting the pregnancy rate (PR) of patients attempting spontaneous conception or intrauterine insemination[4]. It has been validated in 11 studies, showing a high predictive power for non-IVF or IVF outcomes in infertile endometriosis patients[4-14]. The highest score of 10 is associated with the best fertility prognosis, and the lowest score of 0 has the poorest fertility prognosis. Patients assigned a low EFI score can, therefore, be referred immediately for IVF if they wish to conceive without delay; patients with a high EFI score can be expectantly managed for up to 12 months, allowing for natural conception[3,15].

The EFI is calculated during surgery by considering historical and surgical fertility prognostic factors as defined by age, duration of infertility, pregnancy history, least function (LF) score, and total and endometriosis revised American Society for Reproductive Medicine (r-ASRM) scores. Historical factors account for 50% of the EFI score,[13] with nulliparity, increasing age, and increasing duration of infertility resulting in a lower EFI score. Surgical factors, calculated using the LF score (30%) and the r-ASRM endometriosis and total r-ASRM scores (20%), account for the other 50% of the EFI score[13]. Although the LF score is subjective, relying on the surgeon's evaluation of the function of the ovaries, tubes, and fimbria, it is considered a reliable measure[6]. A cut-off of 71 for the total r-ASRM and a score of 16 for the endometriosis r-ASRM have been selected by considering the negative effect of large endometrioma and complete Pouch of Douglas (POD) obliteration on fertility[4].

Currently, the r-ASRM stage and EFI score can only be determined surgically; however, newly established imaging techniques offer a promising alternative. Endometrioma and POD

obliteration with adhesion can be detected with a high degree of accuracy using transvaginal ultrasound (TVS). Endometriomas appear as regular cystic lesions containing materials with ground glass appearance[16] and are diagnosed with 90% sensitivity and 96% specificity through a routine TVS[17,18]. Moreover, dynamic imaging can assess the sliding movement between the uterus or cervix against the colon to determine the extent of adhesion in the posterior uterine compartment[19]. The negative sliding sign can predict POD obliteration with 93% accuracy, with a sensitivity of 83.3%, and a specificity of 97.1%[19].

The objective of our study was to explore the possibility of using ultrasound data, specifically evaluating for negative sliding sign and endometrioma to predict an EFI score ≤6.

MATERIALS AND METHODS

Patient Selection

This study analyzed data (n=2583) from the Endometriosis Pelvic Pain Interdisciplinary Cohort (EPPIC), a prospective endometriosis registry (clinicaltrials.gov, NCT02911090) established in December 2013 at a tertiary referral center for endometriosis and pelvic pain clinic in British Columbia, Canada. The registry was approved by the University of British Columbia ethics committee and the BC Women's Hospital and Health Centre (H16-00264). Data for the EPPIC registry is managed by the Research Electronic Data Capture (REDCap) data management platform at BC Children's Research Institute[20].

EPPIC contains a large dataset of women with endometriosis and/or pelvic pain, and details of its procedures have been previously published[21,22]. After providing informed consent, participants were asked to complete an online baseline questionnaire, which included information about their demographic characteristics, pain assessment, and past medical and surgical history. When new or re-referred patients presented to the pelvic pain clinic, they had a physical examination and a TVS performed by an endometriosis specialist in the pelvic pain clinic. If patients required surgery, surgical data, including staging, were entered prospectively by a gynecologist.

Inclusion Criteria

In this cross-sectional study, we included consenting participants (n=86) enrolled between December 2013 to June 2017 who matched the following inclusion criteria: 1) seen by a gynecologist in the pelvic pain clinic; 2) were ≤ 40 years old at the time of enrollment; 3) had visualized endometriosis, completed r-ASRM scoring and EFI calculated via laparoscopy; 4) had preoperative sliding sign tested at the pelvic pain clinic (Figure 1).

Gynecological Assessment

In the pelvic pain clinic, a routine gynecological examination for endometriosis patients included palpating for DIE nodules of the POD, sliding sign assessment, and visualization of endometrioma by TVS. Sliding sign testing requires real-time dynamic imaging of uterine movement. This is part of the evaluation of POD obliteration status and pelvic adhesions, and it was performed at the pelvic pain clinic by gynecologists with more than five years of experience with dynamic ultrasonography. The sliding sign was tested in two locations: (1) between the rectum and cervix, where gentle pressure was applied on the cervix using the transvaginal ultrasound probe to observe the anterior rectum freely sliding over the posterior cervix; and (2) between the recto-sigmoid and the uterus, where the gynecologist applied pressure using a hand on the lower abdominal wall to observe the recto-sigmoid freely sliding over the posterior upper uterus. The sliding sign is considered positive when free movement is observed in both locations (posterior cervix and posterior upper uterus). The sliding sign is considered negative when the colon is attached to the uterus and the cervix at one or both sites. Neither the ultrasonographers nor the surgeons were blinded to the patients' history, their pelvic exams, and the ultrasound data going into the surgery.

Endometriosis Fertility Index

The EFI was determined only in patients with complete r-ASRM scoring information. EFI (Appendix 2**)** [23] and r-ASRM (Appendix 1**)** [24] scores were prospectively collected for EPPIC as

an integral part of the registry surgical data[4,24]. The r-ASRM form was completed when lesions consistent with endometriosis were observed during surgery.

For the analysis, we created a binary variable of low versus high EFI score. A review of six studies showed the optimal EFI cut-off for IVF referral is between 5.5 and 7.5[6,8,10,12-14]. The calculated mean of the suggested cut-off points was 6.5. Accordingly, we chose EFI score of ≤6 as a cut-off, with EFI ≤6 being indicative for an immediate IVF referral.

Statistical analysis

We compared two groups, women with positive sliding sign and women with negative sliding sign, according to the dynamic TVS results. The comparisons were made with respect to:

1) Demographic and clinical factors including age, body mass index (BMI), ethnicity and smoking.
2) Pelvic and ultrasonographic examination with endometriosis-specific findings (e.g., presence of endometrioma, endometrioma size and laterality, and palpation of DIE nodules) and antral follicular count (AFC).
3) R-ASRM staging (stage I–IV); and
4) Each element of the EFI, such as historical factors (age divided into three groups, history of parity, and duration of infertility) and surgical factors (LF score, total r-ASRM, and endometriosis score) in addition to the total score (historical factors score + surgical factors score = total EFI score).

Continuous variables (i.e., age, historical factors score, surgical factors score, and total EFI scores) were compared using the Mann-Whitney test, and categorical variables were compared using chi-square or Fisher exact tests. We used logistic regression to create predictive models for low EFI (≤6) and to calculate the receiver operating characteristic (ROC) area under the curve (AUC). The predictive model included the historical factors score, sliding sign, DIE, and presence of endometriomas. A size threshold of 3cm as well as unilateral versus bilateral were considered (no endometrioma, unilateral endometrioma <3cm, and unilateral or bilateral

endometrioma ≥3cm). We used the McNemar test to find whether adding the sliding sign to the model built from EFI historical factors and endometrioma would significantly improve the sensitivity[25].

There were 33 cases with EFI≤6 and 53 cases with EFI>6. To statistically compare the sensitivity, we looked at the cases with EFI ≤6 (Table 6)

All analyses were performed using SPSS version 24; $P<0.05$ was considered statistically significant.

RESULTS

Eighty-six patients met the inclusion criteria; 60 participants had a positive sliding sign and 26 had a negative sliding sign (Table 1).

Clinical Examination Findings

Endometriomas were found in 29.1% of the participants (25/86); of these women, 60% (15/25) were in the negative sliding sign group and 40% (10/25) were in the positive sliding sign group. Endometriomas in the negative sliding sign group were more likely to be ≥ 3 cm (P<0.001). Women with negative sliding sign were more likely to have DIE ($P<0.001$). AFC testing in 53 participants found that most women with positive sliding sign (82%, 32/39) had a normal AFC, at least in one side, with a measurement of ≥ 5 ($P=0.033$). An equal number of negative sliding sign women were in the normal and low AFC groups (bilaterally < 5 AFC) (Table 2)

Surgical Findings

Women with negative sliding sign had higher r-ASRM scores (Table 3); we found that 92% (24/26) of women in this group had stage IV endometriosis, 3.8% (1/26) had stage III, 3.8 (1/26) had stage II, and none of the women had stage I. In contrast, women with positive sliding sign had lower r-ASRM scores; and 10% (6/60) of women in this group had stage IV, 23.3% (14/60) had stage III, 35% (21/60) had stage II, and 31.7% had stage I ($P<0.001$).

Women with negative sliding sign had lower overall EFI scores (median = 5, IQR = 4–6, versus median = 7, IQR = 5–9; $P<0.001$; Figure 2, Table 4). Women with negative sliding sign also had

lower scores for all surgical factors, including the LF score (*P*<0.001), a higher proportion of r-ASRM endometriosis scores over 16 (*P*<0.001), and a higher proportion of total r-ASRM over 71(*P*<0.001). Overall, women with negative sliding sign had a lower median for the total surgical factor score (median = 2, IQR = 1–3 versus median=5, IQR=4–5, *P*<0.001). With respect to medical historical factors, women with negative sliding sign were more likely to report a history of infertility lasting > 3 years (*P*=0.03). The median total historical factors score was not significantly different between negative and positive sliding sign.

Predictive models

Logistic regression results are shown in Table 5 and Figure 3. Using the historical factors score alone to predict an EFI score ≤6 resulted in AUC = 0.85 (95% CI 0.77–0.94), sensitivity = 63.6%, and specificity=90.6%. In prediction model A, we used the EFI historical factors score and the diagnosis of endometrioma, considering size and laterality (Figure 3A), resulting in AUC=0.87(95% CI 0.78–0.94), sensitivity = 69.7%, and specificity = 88.7%. In model C, we used the EFI historical factors score and the sliding sign without the endometrioma variable, resulting in AUC= 0.93 (95% CI 0.878–0.983), sensitivity = 87.9%, and specificity = 81.1% (Figure 3C). In model B, we used DIE and endometrioma with the historical factors score (Figure 3B), resulting in AUC = 0.89(95%CI 0.82–-0.96), sensitivity=72.7, and specificity= 84.9. In model D, we used endometrioma and sliding sign with the EFI historical factors score (Figure 3D), resulting in AUC = 0.95 (95% CI 0.90– 0.995), sensitivity = 84.8%, and specificity = 92.5%, Additionally, the same results were achieved when the diagnosis of DIE was added as a predictor to model D. Finally, the McNemar test results showed insignificant results (p=0.12) when the sensitivities of model A and model D were compared (Table 6).

DISCUSSION

In this study of women with endometriosis who were referred to a tertiary center, we found that EFI for women with a negative sliding sign was lower than for those with a positive sliding sign.

Participants in the negative sliding sign group were more likely to have severe endometriosis and endometriomas. The negative sliding sign was associated with a lower EFI surgical factors score than the historical factors score. The McNemar test result did not show a significant change in sensitivity when sliding sign was added to the model built from EFI historical factors and endometrioma. However, it is expected to show statistical differences with a larger sample size due to the high difference in magnitude. The median age of the negative sliding sign group was slightly higher in our study than the group with a positive sliding sign; however, the calculated medians of both groups were less than 35 years old, which did not produce a significant difference when the three EFI age categories were compared. Results of the regression analysis suggest that a negative sliding sign can be combined with simple fertility prognostic measures (the EFI historical factors score and the diagnosis of endometrioma) to predict a low EFI score. The sliding sign could add value to counseling infertile women when surgery is not immediately planned. However, it does not provide a substitute to the currently used EFI, given the fact that EFI has been validated for endometriosis patients who have undergone surgical treatment for infertility.

One strength of our study was the use of a standardized, prospective data registry. Additionally, we used a validated technique (sliding sign testing) that can be done in a gynecologist's office without the need for a fertility specialist. The study's main limitation was the small sample size, which was a consequence of the restrictive inclusion criteria (complete EFI calculation and sliding sign testing). Additionally, since the r-ASRM and EFI scores can be calculated only when the patients have visualized endometriosis, the study and the regression analysis only included endometriosis patients. Furthermore, these findings require a prospective validation by linking the sliding sign to the clinical pregnancy rate.

Endometriosis is a progressive disease that, in the severe stage, may be associated with infertility through mechanical disruption of the reproductive organs. Increasing size of endometriotic cysts, DIE, and complete POD obliteration are markers of disease advancement[26,27]. In our study, a negative sliding sign was also associated with the diagnosis of endometriomas and DIE nodules. Reid et al. reported a higher percentage of unilateral endometriomas, bilateral endometriomas, and rectal DIE in their negative sliding sign group than in the positive sliding sign group (34%, 27%, and 66% vs. 12%, 3%, and 7%, respectively).[28] However, their research focused on the sliding sign's prediction of DIE during laparoscopy, which showed a high specificity (90.3%) and sensitivity (73.7%). Accuracy of the sliding sign's prediction of POD obliteration status during surgery has been validated in a previous study[19]. It has also been validated in a study using our data; the sensitivity was 73.2% (95% CI 57.1%–85.8%) and the specificity was 93.9% (95% CI 89.9%–96.6%)[29]. Furthermore, negative sliding sign consider a marker for severe pelvic adhesions without the presence of endometrioma or DIE. In another study, sliding sign was used to evaluate the intra-abdominal adhesion status in women who had undergone repeated caesarean section deliveries. The negative sliding sign had a sensitivity of 56% (95% CI 35–76) and specificity of 95% (95% CI 93–97) in predicting severe intra-abdominal adhesions[30].

Endometriomas hamper fertility as they exert a pressure effect on the ovary and create a barrier to oocyte retrieval at the fimbria[31]. In addition, toxic agents that can have a detrimental effect on folliculogenesis and oocyte fertilization can potentially diffuse through the cyst wall of the endometrioma[32]. A 2008 Cochrane review indicated that the complete removal of endometriomas resulted in an increased rate of spontaneous pregnancy[33]. However, a cystectomy should be carefully considered because of the negative effect on ovarian reserve, especially in bilateral endometriomas[34,35]. The relationship of DIE to infertility is controversial due to the high rate of association with other forms of the disease (endometrioma, adhesions, and adenomyosis)[36]. Surgical treatment of DIE without the association of other forms resulted in

a 46.7% spontaneous PR[37]. However, Vercellini et al. reported that surgical management of DIE and expectant management resulted in similar pregnancy rates (44.9% and 46.8%, respectively)[38]. The existence of endometrioma with DIE lowers the PR with or without surgical treatment[39]. Posterior compartment DIE is usually associated with adhesions and POD obliteration that could affect tubal function and prevent spontaneous conception[40]. In one study, surgical treatment of complete POD obliteration resulted in viable intrauterine pregnancy in 70% of 46 women with infertility[41]. This suggests that endometriomas and/or POD obliteration have a significantly greater effect on fertility than DIE alone. In our study, using sliding sign and endometrioma with historical factors resulted in the highest predictive power of a low EFI score (AUC=.95). Moreover, sliding sign appeared more important than endometrioma and DIE (together) in predicting the EFI score, suggested by the higher AUC when sliding sign and the historical factors score were used in the prediction of EFI ≤6 (Table 5, Figure 3C).

Options for the treatment of endometriosis-associated infertility are conservative management, IVF, or surgery[3,42]. Conservative management is reserved for young women who have the mild form of the disease, a normal ovarian reserve, and whose partner has normal semen. In other cases, IVF bypasses and surgery aim to restore the distorted pelvic anatomy. Evidence to support the superiority of either method (IVF or surgery alone) in treating infertility is lacking, and there is no consensus on whether surgery or IVF should be offered first for patients with advanced endometriosis[43]. IVF is less invasive than surgery, but advanced endometriosis reduces the chance of successful IVF according to a recent study analyzed the Society for Assisted Reproductive Technologies [44] database[2]. Surgical excision of endometriosis improves the chance of spontaneous pregnancy,[45] which has a more favorable outcome than pregnancy resulting from IVF[46]. Patient who forgoes surgery to excise endometriosis loses the benefits of pain management, possible improvement of non-IVF clinical pregnancy rate or successful oocytes retrieval with large endometrioma. However, increasing maternal age among infertile women and the negative effect of endometriosis on ovarian reserve should be taken into

consideration when offering surgical treatment. Scheduling a surgical procedure in a specialized endometriosis center, ensuring adequate post-operative recovery, and allowing a period of natural pregnancy contribute to a reduced probability of pregnancy in a given time period. Although the EFI is a robust tool for the prediction of natural PR and IVF outcomes, it mandates surgery and cannot resolve this debate.

Our study suggests that EFI could be estimated using ultrasound and historical data. In this cohort, negative sliding sign, endometrioma, and the EFI historical factors score predicted an EFI score ≤6 with a high degree of accuracy. This model could lead to the establishment of a modified fertility index that could benefit patients when surgery is not immediately planned. Consequently, patients could be advised to proceed to IVF or consider reconstructive surgery if they cannot afford IVF. The modified fertility index can be tested with a larger sample size and would require external validation to be applied in practice.

AUTHOR CONTRIBUTIONS

1. Conception and Design

Sukainah Alfaraj, Mohammed A. Bedaiwy, Sarka Lisonkova.

2. Acquisition of Data

Mohammed A. Bedaiwy, Paul Yong, Catherine Allaire, Christina Williams, Heather Noga, Sukainah Alfaraj.

3. Analysis and Interpretation

Sukainah Alfaraj, Mohamed A. Bedaiwy, Sarka Lisonkova.

4. Drafting and revising the Article

Sukainah Alfaraj, Mohamed A. Bedaiwy, Paul Yong, Catherine Allaire, Christina Williams, Sarka Lisonkova, Heather Noga.

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Tables

Table 1. Descriptive statistics of the positive and negative sliding sign groups.

	Total	Positive sliding sign	Negative sliding sign	*P Value*
N	86	60	26	
Age, Median (IQR)	33(30-36)	32(29-35)	34(32-36)	**.010**
BMI	n (%)	n (%)	n (%)	
Underweight (>18.5)	3(3.5)	2(3.4)	1(3.8)	.490
Normal (18.5–24.9)	54(62.8)	37(61.6)	17(65.4)	
Overweight (25–29.9)	14(16.3)	12(20)	2(7.8)	
Obese (≥30)	15(17.4)	9(15)	6(23)	
Ethnicity				
Caucasian	47(54.7)	37(62.7)	10(38.4)	.061
Others	39(45.3)	23(38.3)	16(61.5)	
Smoking				
Yes	7(8.4)	4(7)	3(12)	.425
No	76(91.6)	54(93)	22(88)	

IQR= Interquartile rang

Table 2. Transvaginal ultrasonography assessment and visualization of endometriosis at laparoscopy in the positive and negative sliding sign groups.

Gynecological examination factors	Total	Positive sliding sign	Negative sliding sign	*P Value*
Endometrioma	n (%)	n (%)	n (%)	
None	61(70.9)	50(83.3)	11(42.3)	**<.001**
Unilateral<3	11(12.8)	7((11.7)	4(15.4)	
Unilateral or bilateral ≥3	14(16.3)	3(5)	11(42.3)	
DIE				
Yes	16(30.2)	5(8.4)	11(42.3)	**<.001**
No	70(69.8)	55(91.6)	15(57.7)	
AFC*				
One side ≥5	39(73.6)	32(82)	7(50)	**.033**
<5 bilaterally	14(26.4)	7(18)	7(50)	
Visualized endometriosis at laparoscopy				
Yes	86(100)	60(100)	26(100)	--
No	0	0	0	

***** tested in 53 participants.
DIE=Deep Infiltrating Endometriosis
AFC=Antral Follicular Count

Table 3. R-ASRM scoring for the positive and negative sliding sign groups.

R-ASRM	Total	Positive sliding sign	Negative sliding sign	*P Value*
	n(%)	n(%)	n(%)	
I	19(22.1)	19(31.7)	0	**<.001**
II	22(25.6)	21(35)	1(3.8)	
III	15(17.4)	14(23.3)	1(3.8)	
IV	30(34.9)	6(10)	24(92.4)	

Table 4. EFI total and variable scores in the positive and negative sliding sign groups

EFI	Total	Positive sliding sign	Negative sliding sign	*P Value*
Historical factors				
Age	n (%)	n (%)	n (%)	
≤35	61[47]	45(75)	16(61.5)	.389
36–39	16(18.6)	9(15)	7(27)	
≥40	9(10.5)	6(10)	3(11.5)	
Years of infertility				
>3	31(36)	17(28.3)	14(53.8)	**.030**
≤3	55(64)	43(71.7)	12(46.2)	
Prior pregnancy				
Yes	28(32.6)	19(31.6)	9(34.6)	.806
No	58(67.4)	41(68.3)	17(65.4)	
Historical Factors Score†	4(2–4)	4(2–4)	3.5(2–4)	.051
Surgical factors				
Least function score	n (%)	n (%)	n (%)	
7–8	42(48.8)	41(68.3)	1(3.8)	**<.001**
4–6	31(36)	14(23.3)	17(65.4)	
1–3	13(15.1)	5(8.4)	8(30.8)	
r-ASRM endometriosis score				
<16	48(55.8)	46(76.7)	2(7.7)	**<.001**
≥16	38(44.2)	14(23.3)	24(92.3)	
r-ASRM total score				
<71	70(81.4)	59(98.3)	11(42.3)	**<.001**
≥71	16(18.6)	1(1.7)	15(57.7)	
Surgical factors score†	4(2–5)	5(4–5)	2(1–3)	**<.001**
EFI total score †	7(5–9)	8(7–9)	5(4–6)	**<.001**

†median(IQR)

Table 5. Binominal logistic regression results and factors used to predict EFI<6.

Factors	Sensitivity	Specificity	PPV	NPV	AUC (95%CI)
EFI Historical factors score	63.6	90.6	80.8	80	0.85(0.77–0.94)
EFI Historical factors score +Endometrioma	69.7	88.7	79.3	82.5	0.87(0.78–0.94)
EFI Historical factors score +Endometrioma +DIE	72.7	84.9	75.0	83.3	0.89(0.82–0.96)
EFI Historical factors score + Sliding sign	87.9	81.1	74.4	91.5	0.93(0.88–0.98)
EFI Historical factors score + Sliding sign +Endometrioma	84.8	92.5	87.5	90.7	0.95 (0.90-1.00)
EFI Historical factors score + Sliding sign +Endometrioma +DIE	84.8	92.5	87.5	90.7	0.95 (0.90-1.00)

PPV=positive predictive value
NPV=negative predictive value
DIE=Deep infiltrating endometriosis

Table.6 Shows 2 X 2 table to compare the sensitivities of model A and model D

		EFI historical factors' score + endometrioma		Total
		>6	**≤6**	
EFI historical factors score + endometrioma + Sliding sign	**>6**	4	1	5
	≤6	6	22	28
Total		10	23	33

Figures

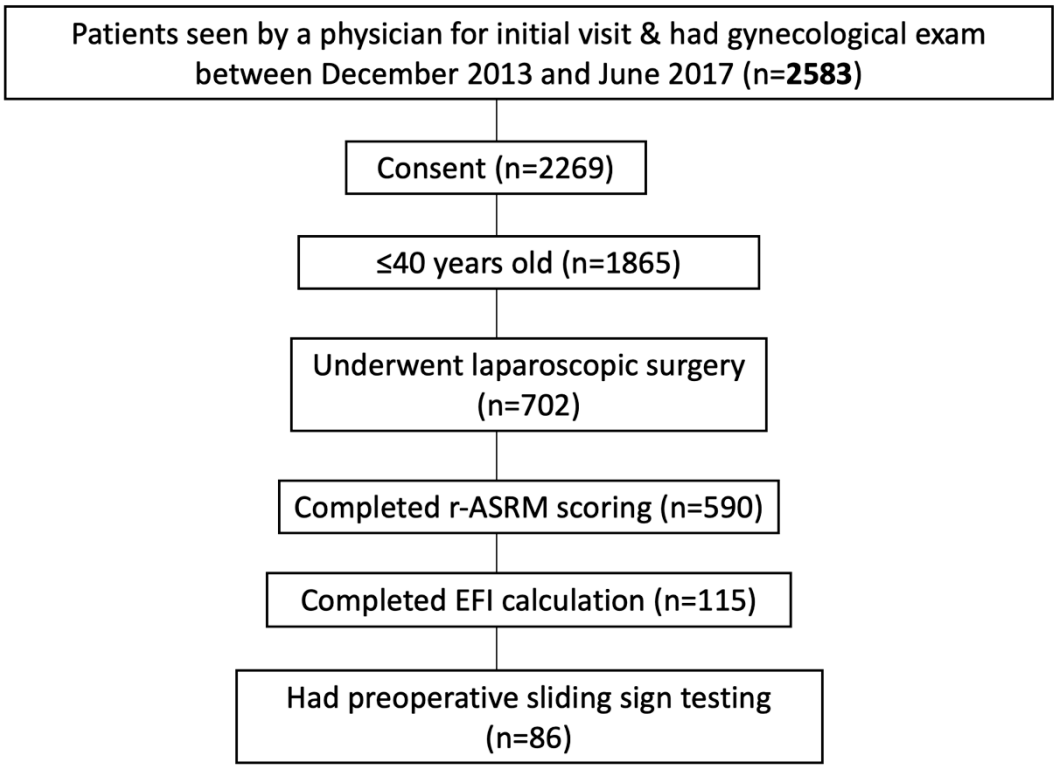


Figure 1. Participant selection flow chart

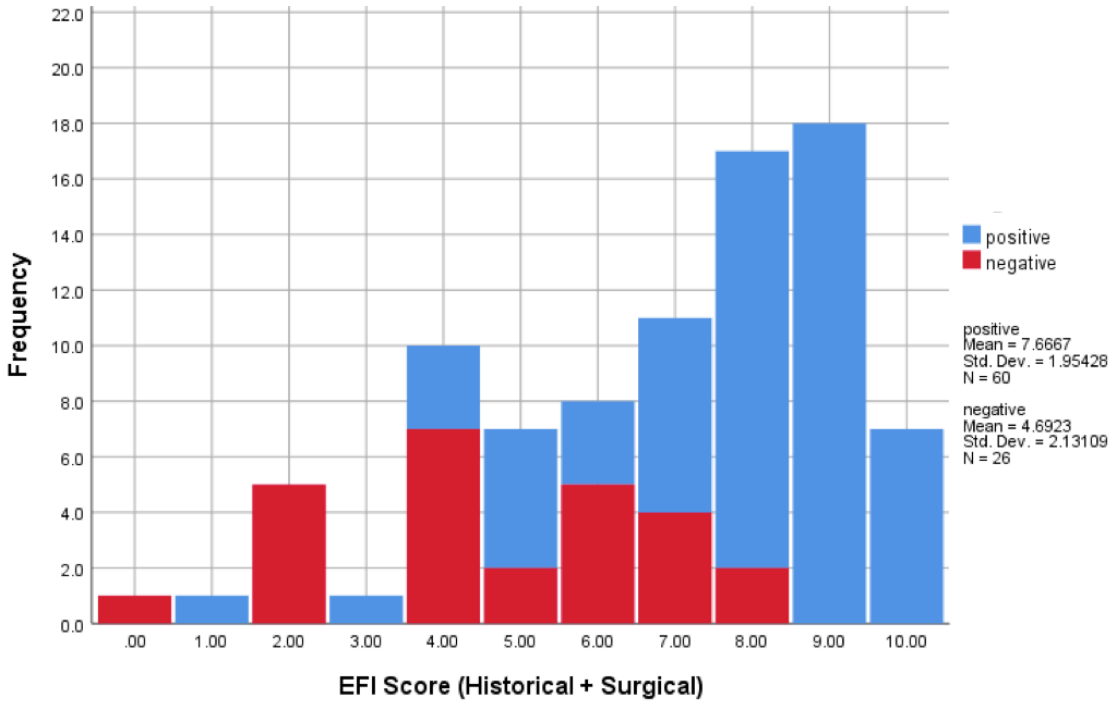


Figure 2. Total EFI score distribution of positive (blue) and negative (red) sliding sign participants

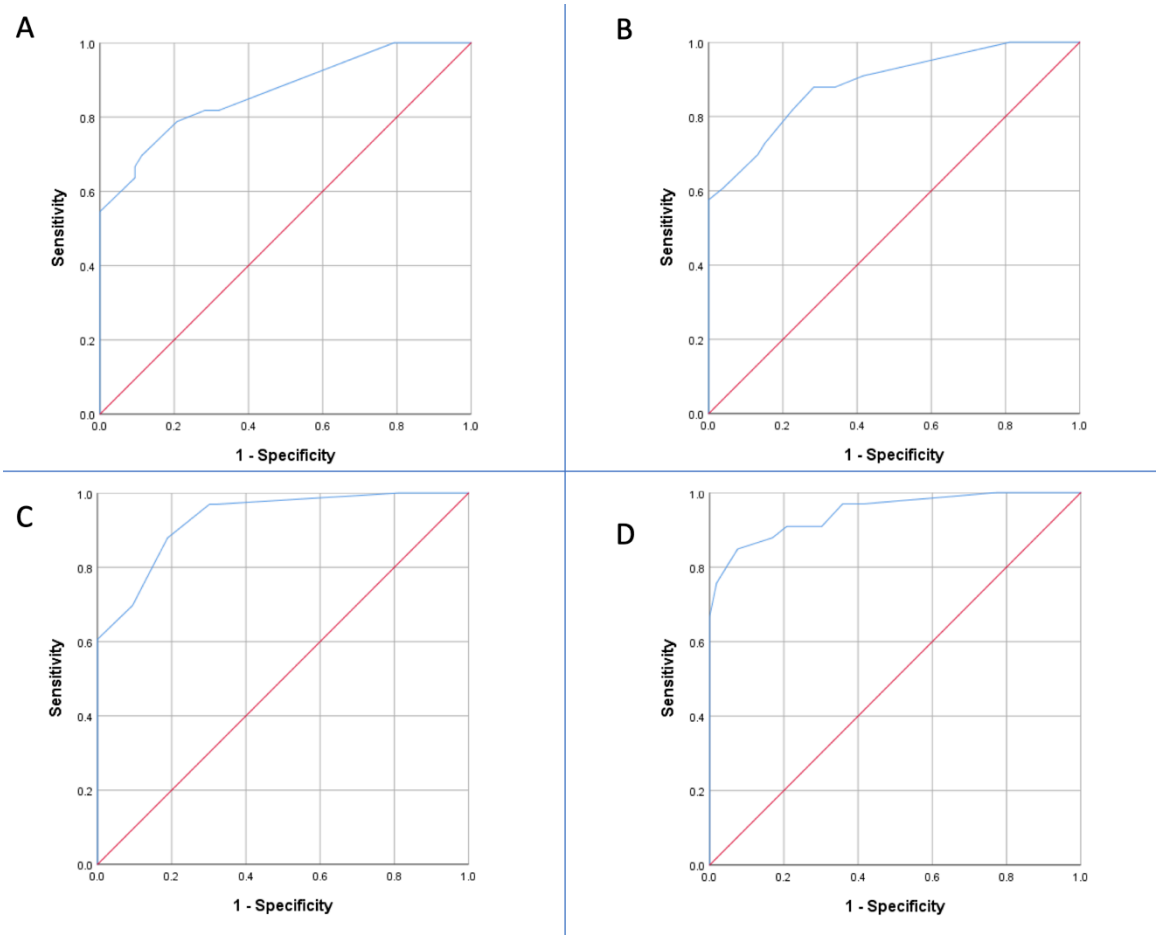


Figure 3. ROC curve (blue line) for EFI≤6 based on the following models: A) historical factors score and endometrioma, B) historical factors score+ endometrioma + DIE, C) historical factors score +sliding sign, D) historical factors score + endometrioma + sliding sign.

Appendices

AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE
REVISED CLASSIFICATION OF ENDOMETRIOSIS

Patient's Name _____ Date _____

Stage I (Minimal) - 1-5
Stage II (Mild) - 6-15
Stage III (Moderate) - 16-40
Stage IV (Severe) - >40
Total _____

Laparoscopy _____ Laparotomy _____ Photography _____
Recommended Treatment _____
_____
Prognosis _____

PERITONEUM	ENDOMETRIOSIS	<1cm	1-3cm	>3cm
	Superficial	1	2	4
	Deep	2	4	6
OVARY	R Superficial	1	2	4
	Deep	4	16	20
	L Superficial	1	2	4
	Deep	4	16	20
	POSTERIOR CULDESAC OBLITERATION	Partial		Complete
		4		40
OVARY	ADHESIONS	<1/3 Enclosure	1/3-2/3 Enclosure	>2/3 Enclosure
	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4	8	16
TUBE	R Filmy	1	2	4
	Dense	4*	8*	16
	L Filmy	1	2	4
	Dense	4*	8*	16

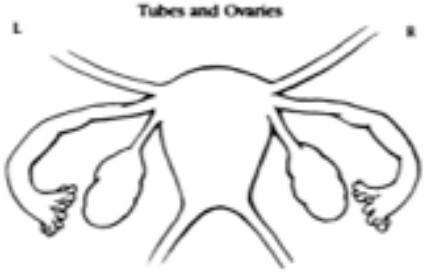
*If the fimbriated end of the fallopian tube is completely enclosed, change the point assignment to 16.

Denote appearance of superficial implant types as red [(R), red, red-pink, flamelike, vesicular blobs, clear vesicles], white [(W), opacifications, peritoneal defects, yellow-brown], or black [(B) black, hemosiderin deposits, blue]. Denote percent of total described as R____%, W____% and B____%. Total should equal 100%.

Additional Endometriosis: _____

Associated Pathology: _____

To Be Used with Normal Tubes and Ovaries



To Be Used with Abnormal Tubes and/or Ovaries

Appendix 1. R-ASRM classification for endometriosis, Reproduced from Revised American Society for Reproductive Medicine classification of endometriosis: 1996. *Fertility and sterility.* 1997;67(5):817-821.Reprinted with permission from Elsevier.

ENDOMETRIOSIS FERTILITY INDEX (EFI)
SURGERY FORM

LEAST FUNCTION (LF) SCORE AT CONCLUSION OF SURGERY

Score		Description		Left		Right		
4	=	Normal	Fallopian Tube					
3	=	Mild Dysfunction						
2	=	Moderate Dysfunction	Fimbria					
1	=	Severe Dysfunction						
0	=	Absent or Nonfunctional	Ovary					

To calculate the LF score, add together the lowest score for the left side and the lowest score for the right side. If an ovary is absent on one side, the LF score is obtained by doubling the lowest score on the side with the ovary.

	Left		Right		LF Score
Lowest Score		+		=	

ENDOMETRIOSIS FERTILITY INDEX (EFI)

Historical Factors			Surgical Factors		
Factor	**Description**	**Points**	**Factor**	**Description**	**Points**
Age			LF Score		
	If age is ≤ 35 years	2		If LF Score = 7 to 8 (high score)	3
	If age is 36 to 39 years	1		If LF Score = 4 to 6 (moderate score)	2
	If age is ≥ 40 years	0		If LF Score = 1 to 3 (low score)	0
Years Infertile			AFS Endometriosis Score		
	If years infertile is ≤ 3	2		If AFS Endometriosis Lesion Score is < 16	1
	If years infertile is > 3	0		If AFS Endometriosis Lesion Score is ≥ 16	0
Prior Pregnancy			AFS Total Score		
	If there is a history of a prior pregnancy	1		If AFS total score is < 71	1
	If there is no history of prior pregnancy	0		If AFS total score is ≥ 71	0
Total Historical Factors			**Total Surgical Factors**		

EFI = TOTAL HISTORICAL FACTORS + TOTAL SURGICAL FACTORS:	Historical	+	Surgical	=	EFI Score

Appendix 2. EFI surgery form created by Adamson GD and Pasta DJ, Reproduce from Endometriosis fertility index: The new, validated endometriosis staging system. *Fertility and sterility.* 2010;94(5):1609-1615. Reprinted with permission from Elsevier.