The Formation of a Scoring System to Diagnose Endometriosis

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Objectives: To evaluate the reliability of a non-invasive diagnostic scoring system to diagnose endometriosis.

Results: A non-invasive diagnostic tool named CliEndomet was formulated based on clinical presentation, ultrasound findings and serum Ca125 of patients.

Conclusion: CliEndomet scoring system is a reliable diagnostic tool to diagnose endometriosis in patients who refuse to undergo surgical diagnosis and intervention.

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THEFORMATIONOFASCORINGSYSTEMTODIAGNOSEENDOMETRIOSIS

Strictly as per the compliance and regulations of:

The Formation of a Scoring System to Diagnose Endometriosis

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I. Introduction

Endometriosis is a common gynecology disorder affecting women of reproductive age. It is a disease characterized by the presence of tissue that is biologically and morphologically similar to the endometrium, containing endometrial glands and stroma, in ectopic locations outside the uterine cavity. The diagnosis of endometriosis cannot be made based on clinical manifestations due to its variable manifestation. Biological markers such as serum Ca125 and IL6 are non-specific and may not reflect the disease well. Ultrasound has limited value to diagnose endometriosis, but it may be helpful to exclude ovarian endometrioma (Moore J, 2002). At present, visualization of the endometriotic lesion, either via laparoscopic or laparotomy, remains the gold-standard to diagnose endometriosis. However, the lack of experience and skill of the surgeon to recognize the lesion limits its accuracy as diagnostic tool (Razvan et al., 2010). Also the fact that there is a high prevalence of women with pelvic pain who refuse to undergo the operation in this region made the accurate diagnosis nearing impossible.

Because of the above reasons, we try to look into a non-invasive method to diagnose endometriosis, by combining the clinical manifestation, ultrasound finding and the level of serum Ca125, and later forming a scoring system to diagnose endometriosis.

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II. Objectives

The objective of this study is to formulate a diagnostic scoring system to diagnose endometriosis, and subsequently test its reliability and validity, to diagnose endometriosis, by comparing it with the gold-standard method by direct visualization of the endometriotic lesion.

III. Methodology

All women who came to the general gynecology and Infertility Clinic of Hospital USM with pelvic pain within the age of 18 to 45 years old were randomized to participate in the study, using the computer-generated block-of-ten randomization. We excluded women who were previously diagnosed to have endometriosis. We obtained written consent from the patients.

The pelvic pain was assessed using the modified version of Andersch and Milsom's multidimensional verbal rating scale. This scale defines pain according to the limitation of ability to work (unaffected = 0, rarely affected = 1, moderately affected = 2, clearly affected = 3), co-existing of systemic symptoms (absent=0, present=1), and the need for analgesia (no=0, yes=1), and rank the total sum in three groups (1-2=mild, 3-4=moderate, 5=severe) (Konincky PR, 1996). The severity of deep dyspareunia and dyschezia was evaluated using a 10-point linear analog scale in which 0 indicated no pain and 10 indicated unbearable pain.

We determined the presence of any pelvic mass by performing the abdominal examination and bimanual vaginal examination. In the presence of a mass, we determined its site, margin, surface, consistency, mobility and tenderness.

Using a transvaginal scan, we further evaluated the features of the mass. We collected the late luteal phase serum Ca125via venipuncture.

All women underwent laparoscopic surgery, where the presence of any endometriotic lesion was documented and staged using the revised American Fertility Society scoring system, and tissue biopsy were performed and sent for histology examination and diagnosis.

The diagnosis of endometriosis was made based on the positive findings of endometriotic lesions during the operation, with or without the confirmation of tissue histology biopsy.

An analysis was made on the data of the women. The simple logistic regression test is used to analyze the clinical symptoms, physical examination findings, ultrasound findings and the level of serum Ca125 of the patients. From this, we selected the significant variables for further analysis using the multiple logistic regression tests to predict the presence of endometriosis. From this, the presence of dysmenorrhoea, pelvic mass and the level of serum Ca125 between 50 to 200u/ml were significantly associated with the presence of endometriosis. Subsequently, a diagnostic scoring system was formulated and tested for its reliability and validity.

IV. Results

A total of 176 women at the age of 35.41 ± 6.90 years, with parity 2.10 ± 2.30, were recruited into the study. 106 women (60.22%) had fertility issues, with the mean duration of subfertility of 4.12 ± 5.41 years. A total of 103 women (58.52%) were diagnosed to have endometriosis during operation, in which 92 of them (89.32%) confirmed by histology examination.

Among the 176 women, 169 women (96.00%) had dysmenorrhea with equal distribution of severity. Out of the 169 women, 100 of them (59.17%) were confirmed to have endometriosis. A total of 26 women had dyspareunia, in which 19 women (73.08%) confirmed to have endometriosis. Only four women had dyschezia and two confirmed to have endometriosis.

158 women were noted to have pelvic masses, confirmed by ultrasound. 75 of them (47.47%) were uniloculated while the rest were multiloculated. 42 women with uniloculated ovarian cyst (56.00%) were noted to have endometriosis, as compared to 57 women with multiloculated cyst (68.67%). Among all ovarian cyst noted 107 of them (67.72%) had the typical feature of endometrioma, which is the ground glass appearance, in which 98 women (91.59%) had endometriosis confirmed.
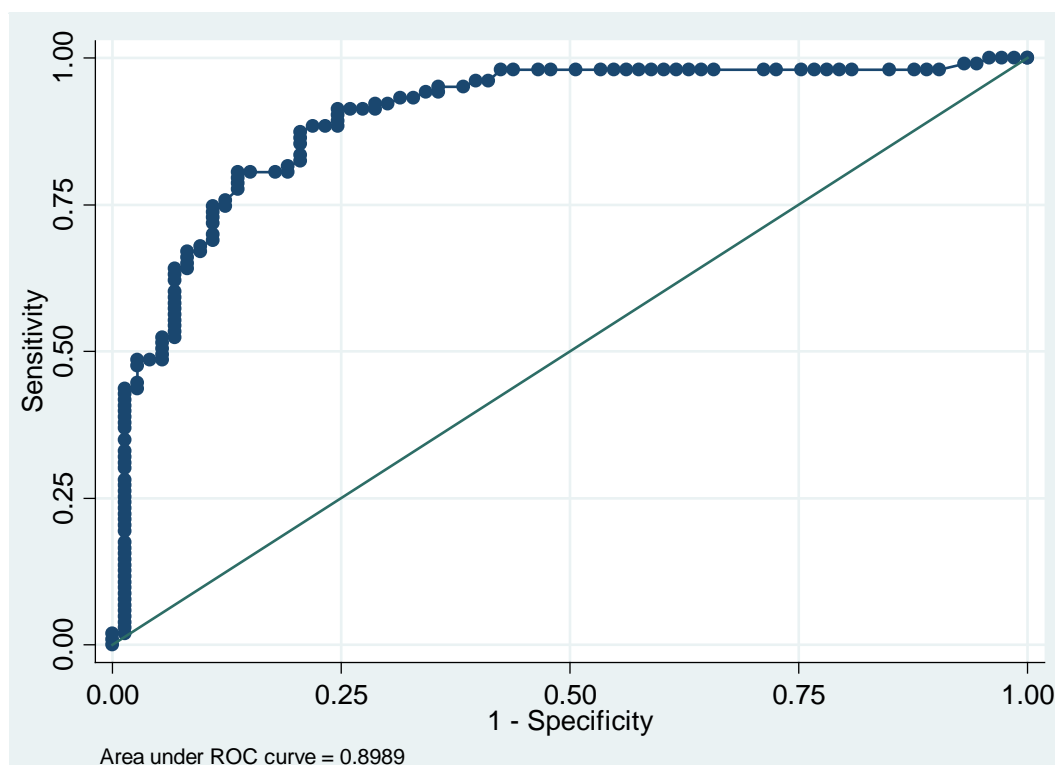

Area under ROC curve = 0.8989

Figure 1: The association between serum Ca125 and the diagnosis of endometriosis

The ROC curve as in Figure 1 shows the association between the level of serum Ca125 and the diagnosis of endometriosis. The AUC was 0.8989, which indicated a good correlation. From the curve, the value of Ca125 equal or more than 50u/ml had a sensitivity of 80% and a specificity of 86%. There is higher likelihood of endometriosis with higher level of Ca125. However, Ca125 level more than 200u/ml had low sensitivity (7.7%) but high specificity at 98.6%.Thus, Ca125 levels were divided into three categories, from 50u/ml to 200u/ml (50–200u/ml) and either less than 50u/ml or more than 200u/ml.

We use the simple logistic regression test to evaluate the association of each clinical feature, ultrasound finding and the serum Ca125 with the diagnosis of endometriosis, as shown in Table 1. From this table, variables with significant association were taken and tested using the multiple logistic regression tests, to predict endometriosis, as shown in Table 2.

Table 1: The association of clinical, biochemical and imaging variables with endometriosis using Simple Logistic Regression test

Variable	b	Crude OR (95% CI)	Wald Statistic (df)	p value
Age (year)	-0.03	0.97 (.93,1.02)	1.49(1)	0.222‡
Parity	-0.23	0.80 (0.69, 0.92)	10.14 (1)	0.001†
Presence of subfertility	0.79	2.20(1.19,4.06)	6.41(1)	0.011‡
Subfertility years	0.05	1.05 90.99,1.11)	2.59(1)	0.108‡
Presence of dysmenorrhoea	1.06	2.90(0.52,16.27)	1.46(2)	0.227‡
Dysmenorrhoea Severity				
Mild	-0.90	0.91 (0.91,4.46)	0.01 (1)	0.912
Moderate	0.62	1.85 (0.39,8.86)	0.59 (1)	0.492
Severe	2.68	14.67 (2.18,98.78)	7,62 (1)	0.006†
Presence of deep dyspareunia	0.48	1.61 (0.68,3.79)	1.18 (1)	0.277
Presence of dyschezia	-0.35	0.70 (0.09,5.11)	0.12 (1)	0.728
Presence of abdominal mass	-0.21	0.81 (0.45,1.49)	0.49 (1)	0.503
Uterus Ligaments				
Thickened			1.00	
Not thickened	-3.19	0.04 (0.01,0.31)	9.56 (1)	0.002†
POD				
Normal			1.00	
Obliterate	1.30	3.68 (1.69,8.02)	10.78 (1)	0.001†
Locule of ovarian mass				
Uniloculated	1.49	4.46 (1.34,14.06)	5.94 (1)	0.015†
Multiloculated	2.04	7.67 (2.30,25.58)	11.00 (1)	0.001†
Content of ovarian mass				
Serous	-2.65	0.07 (0.01,0.68)	5.27 (1)	0.220‡
Thick with sediments	3.64	38.11(10.34,140.42)	29.93 (1)	<0.001†
CA125	0.04	1.04 (1.03, 1.05)	37.24 (1)	<0.001†

Table 2: Association between variables with endometriosis using Multiple Logistic Regression (n=176)

Variable	b	Adjusted OR (95% CI)	LR statistic (df)	p value
CA125	0.03	1.03 (1.02, 1.05)	22.44 (1)	<0.001
Dysmenorrhoea Severity				
No pain		1.00	14.27 (3)	0.003
Mild	0.30	1.35 (0.13, 13.64)	0.06 (1)	0.800
Moderate	2.78	16.04 (4.41, 58.34)	1.34 (1)	0.248
Severe	3.33	27.89 (1.89, 411.95)	5.87 (1)	0.015
Content of ovarian mass				
No cyst		1.00	55.30 (2)	<0.001
Serous	-2.66	0.07 (0.01, 0.68)	5.27 (1)	0.022
Thick with sediments	3.64	38.11 (10.34, 140.42)	29.93 (1)	<0.001

Severe dysmenorrhea was significantly associated with increased likelihood of having endometriosis. Those patients with severe dysmenorrhea will have 27 times higher risk of having endometriosis. Ca125 values and the ultrasound scan findings of thick sediments or ground-glass appearance were highly significant in the diagnosis of endometriosis.

Based on the significant variables in the prediction of endometriosis found in the multiple logistic regression tests, a scoring system, named as CliEndomet, was formulated as shown in Figure 2.

CliEndomet The Diagnostic Clinical Scoring System for Endometriosis	

Name: …………………………………..

Registration No.: ………………………………

Date: ………………………………………………

Total Score: ………………………………

Recommended treatment: ……………………

Endometriosis: Yes   No

…………………………………………………………..

…………………………………………………………..

Criteria	Score
Dysmenorrhoea: • No dysmenorrhea • Mild dysmenorrhea • Moderate dysmenorrhea • Severe dysmenorrhoea	0 1 2 3
Ultrasonograhic findings: • Solid ovarian mass or cystic ovarian mass with papillary projections • Uniloculated, serous ovarian cyst • Multiloculated cyst with thick sedimentations (ground glass appearance)	0 1 2
Level of serum Ca125: • <50 u/ml or >200u/ml • 50-200u/ml	0 2
TOTAL	

The CliEndomet formula:

Total score = (Dysmenorrhoea + Ultrasonographic findings + serum Ca125) x 2

Risk of having endometriosis:

Total score	Possibility of endometriosis
Score 0-2	Unlikely
Score 4-6	Low possibility
Score 8-10	Moderate possibility
Score 12-14	High possibility

Figure 2: The CliEndomet Scoring System

The reliability of CliEndomet was tested using kappa, as in Table 3. CliEndomet carried a substantial agreement with direct visualization to diagnose endometriosis.

Table 3: The Agreement between CliEndomet and direct visualization for the diagnosis of endometriosis

CliEndomet	Direct Visualisation		
	Endometriosis	No endometriosis	Total
Endometriosis	90	7	97
No endometriosis	13	66	79
Total	103	73	176

Prevalence of endometriosis	= 103/ 176 x 100% = **58.5%**
Observed % agreement	= (90 + 66)/176 x 100% = **88.6%**
Chance-expected % agreement	= $\frac{(97 \times 103)}{176}$ + $\frac{(79 \times 73)}{176}$ x $\frac{100}{176}$ = **50.87%**
Kappa coefficient (K) = $\frac{\text{(Observed \% agreement) – (chance-expected \% agreement)}}{\text{(Perfect \% agreement) – (chance-expected \% agreement)}}$ = $\frac{(88.6 – 50.87)}{(100 - 50.87)}$ = **0.77**	

V. Discussion

Endometriosis associates with pain and infertility, which causes much distress to the women involved. The gold standard diagnostic tool remains visual inspection of the endometriotic lesion, either by laparoscopy or laparotomy, with the preference of histopathological confirmation. Standing alone, none of the non-invasive tests can accurately diagnose this disease, causing a significant delay of its diagnosis and treatment. However, a combination of various non-invasive tests is yet to be tested.

From this study, among all the non-invasive tests tested for the diagnosis of endometriosis, the presence of dysmenorrhea, ovarian cyst at ultrasound and the level of serum Ca125 between 50 to 200 iu/ml showed a significant association with endometriosis. Based on that, a scoring system was formulated and tested for its reliability. The proposed scoring system (CliEndomet) carried a substantial agreement to diagnose endometriosis in comparison to the standard direct visualization of the disease.

Having able to diagnose endometriosis using a non-invasive or less invasive method could provide an advantage to the patient, especially those who are not suitable or agreeable to undergo surgery. Treatments which include hormones can be administered based on this non-invasive diagnosis, thus reducing the patient's pain agony and morbidity. Neoadjuvant medical treatment can also be administered with certainty before surgery to reduce the intraoperative complication.

Though CliEndomet has been shown to be a reliable diagnostic tool, it requires a proper validation test before its usage.

Acknowledgement

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