The Formation of a Scoring System to Diagnose Endometriosis

By Adibah Ibrahim, Pang Suk Chin & Wan Zahiruddin Wan Mohd

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Abstract- Endometriosis is diagnosed by direct visualization of the lesion, with or without histopathology confirmation, which is often declined by the patients. A non-invasive diagnostic scoring system was formulated to identify patients high likely to have endometriosis, who refused to undergo surgery for diagnosis confirmation.

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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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 Ca125 via 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 dysmenorrhea, 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.

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.

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

Area under ROC curve = 0.8989
Table 1: The association of clinical, biochemical and imaging variables with endometriosis using Simple Logistic Regression test

<table>
<thead>
<tr>
<th>Variable</th>
<th>b</th>
<th>Crude OR (95% CI)</th>
<th>Wald Statistic (df)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>-0.03</td>
<td>0.97 (.93,1.02)</td>
<td>1.49(1)</td>
<td>0.222‡</td>
</tr>
<tr>
<td>Parity</td>
<td>-0.23</td>
<td>0.80 (.69, 0.92)</td>
<td>10.14 (1)</td>
<td>0.001†</td>
</tr>
<tr>
<td>Presence of subfertility</td>
<td>0.79</td>
<td>2.20(1.19,4.06)</td>
<td>6.41(1)</td>
<td>0.011‡</td>
</tr>
<tr>
<td>Subfertility years</td>
<td>0.05</td>
<td>1.05 90.99,1.11</td>
<td>2.59(1)</td>
<td>0.108‡</td>
</tr>
<tr>
<td>Presence of dysmenorrhoea</td>
<td>1.06</td>
<td>2.90(0.52,16.27)</td>
<td>1.46(2)</td>
<td>0.227‡</td>
</tr>
</tbody>
</table>

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: -3.19 0.04 (0.01,0.31) 9.56 (1) 0.002†
- Not thickened: 1.30 3.68 (1.69,8.02) 1.00 1.00

POD
- Normal: 1.49 4.46 (1.34,14.06) 5.94 (1) 0.015†
- Oblitrate: 2.04 7.67 (2.30,25.58) 11.00 (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)

<table>
<thead>
<tr>
<th>Variable</th>
<th>b</th>
<th>Adjusted OR (95% CI)</th>
<th>LR statistic (df)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA125</td>
<td>0.03</td>
<td>1.03 (1.02, 1.05)</td>
<td>22.44 (1)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Dysmenorrhoea Severity
- No pain: 0.30 1.35 (0.13, 13.64) 0.06 (1) 0.800
- Mild: 2.78 16.04 (4.41, 58.34) 1.34 (1) 0.248
- Moderate: 3.33 27.89 (1.89, 411.95) 5.87 (1) 0.015

Content of ovarian mass
- No cyst: -2.66 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†

Severe dysmenorrhoea was significantly associated with increased likelihood of having endometriosis. Those patients with severe dysmenorrhoea 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.
The Diagnostic Clinical Scoring System for Endometriosis

Name: .................................  Registration No.: .................................

Date: .................................

Total Score: .................................  Recommended treatment: .................................

Endometriosis: Yes  No

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<table>
<thead>
<tr>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysmenorrhoea:</td>
<td></td>
</tr>
<tr>
<td>• No dysmenorrhea</td>
<td>0</td>
</tr>
<tr>
<td>• Mild dysmenorrhea</td>
<td>1</td>
</tr>
<tr>
<td>• Moderate dysmenorrhea</td>
<td>2</td>
</tr>
<tr>
<td>• Severe dysmenorrhea</td>
<td>3</td>
</tr>
<tr>
<td>Ultrasonographic findings:</td>
<td></td>
</tr>
<tr>
<td>• Solid ovarian mass or cystic ovarian mass with papillary projections</td>
<td>0</td>
</tr>
<tr>
<td>• Uniloculated, serous ovarian cyst</td>
<td>1</td>
</tr>
<tr>
<td>• Multiloculated cyst with thick sedimentations (ground glass appearance)</td>
<td>2</td>
</tr>
<tr>
<td>Level of serum Ca125:</td>
<td></td>
</tr>
<tr>
<td>• &lt;50 u/ml or &gt;200 u/ml</td>
<td>0</td>
</tr>
<tr>
<td>• 50-200 u/ml</td>
<td>2</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td></td>
</tr>
</tbody>
</table>

The CliEndomet formula:

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

Risk of having endometriosis:

<table>
<thead>
<tr>
<th>Total score</th>
<th>Possibility of endometriosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score 0-2</td>
<td>Unlikely</td>
</tr>
<tr>
<td>Score 4-6</td>
<td>Low possibility</td>
</tr>
<tr>
<td>Score 8-10</td>
<td>Moderate possibility</td>
</tr>
<tr>
<td>Score 12-14</td>
<td>High possibility</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th></th>
<th>Direct Visualisation</th>
<th></th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Endometriosis</td>
<td>No endometriosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endometriosis</td>
<td>90</td>
<td>7</td>
<td></td>
<td>97</td>
</tr>
<tr>
<td>No endometriosis</td>
<td>13</td>
<td>66</td>
<td></td>
<td>79</td>
</tr>
<tr>
<td>Total</td>
<td>103</td>
<td>73</td>
<td></td>
<td>176</td>
</tr>
</tbody>
</table>

Prevalence of endometriosis = 103/176 x 100% = 58.6%
Observed % agreement = (90 + 66)/176 x 100% = 88.6%
Chance-expected % agreement = \[(97\times103) + (79\times73)\] x \[\frac{100}{176}\]
Kappa coefficient (K) = \[\frac{(Perfect \% \text{ agreement}) - (\text{chance-expected \%} \text{ agreement})}{(\text{Observed \%} \text{ agreement}) - (\text{chance-expected \%} \text{ agreement})}\] = 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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References