Presurgical diagnosis of posterior deep infiltrating endometriosis based on a standardized questionnaire

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BACKGROUND: To derive a diagnostic model based on symptoms and history as assessed by a standardized questionnaire to predict posterior deep infiltrating endometriosis (DIE) among women with chronic pelvic pain symptoms. METHODS: 134 women scheduled for laparoscopy for chronic pelvic pain symptoms completed a standardized self-administered questionnaire, specifically designed for the study. We compared the symptoms of the women with posterior DIE diagnosed at laparoscopy with those of the women with other disorders, and used multiple logistic regression analysis to select the best combination of symptoms for predicting posterior DIE. Cross-validation was performed with the jackknife method. RESULTS: 51 women (38.1%) were diagnosed with posterior DIE and 83 with other disorders (61.9%). The following variables were independent predictors for posterior DIE: painful defecation during menses, severe dyspareunia (visual analogic scale ≥8), pain other than noncyclic, and previous surgery for endometriosis. The cross-validation procedure leads to a simplified diagnostic model that uses two independent predictors: painful defecation during menses and severe dyspareunia. The sensitivity of this model for diagnosing posterior DIE was 74.5%, its specificity was 68.7%, its positive likelihood ratio was 2.4, and its negative likelihood ratio was 0.4. It correctly classified 70.9% of our sample into a high-risk (with either severe dyspareunia or painful defecation during menses) and a low-risk (neither symptom) group. CONCLUSIONS: Standardized evaluation of painful symptoms is useful for screening women so that they may have adequate exploration and counselling before laparoscopic surgery for pelvic pain symptoms.

Key words: deep infiltrating endometriosis/diagnosis/dyspareunia/pelvic pain/questionnaires

Introduction

Deep infiltrating endometriosis (DIE) is a particular form of endometriosis that penetrates deeply under the peritoneal surface (Martin et al., 1989; Koninckx et al., 1991). These lesions are strongly associated with chronic pelvic pain symptoms, including severe dysmenorrhea (DM), deep dyspareunia and nonmenstrual pain (Koninckx et al., 1991). Reports indicate that DIE is found in about one third of the laparoscopies performed because of pelvic pain symptoms (Koninckx and Martin, 1994). DIE implants are found in specific locations, primarily the posterior area (Cornillie et al., 1990; Chapron et al., 2003). Posterior DIE can involve uterosacral ligaments (USL), the torus uterinus, the posterior vaginal wall and the anterior rectal wall (Redwine, 1992; Martin and Batt, 2001; Chapron et al., 2003).

Treatment of posterior DIE may require extensive surgery (Redwine, 1992; Garry et al., 2000), which may include USL resection (Chapron and Dubuisson, 1996), partial colpectomy (Martin, 1988; Donnez and Nisolle, 1995) and resection of rectal endometriosis (Coronado et al., 1990). Because these surgical procedures are time-consuming and require that patients receive specific information and appropriate preparation, presurgical diagnosis is very important.

Routine clinical examination cannot be used alone to diagnose DIE (Koninckx et al., 1996a; Chapron et al., 2002). Magnetic resonance imaging is an interesting tool for presurgical diagnosis (Kinkel et al., 1999), but its diagnostic accuracy has not been evaluated. Rectal endoscopic ultrasonography has excellent diagnostic value for posterior DIE (Ohba et al., 1996; Fedele et al., 1998). It requires bowel preparation as well as a skilled radiologist. Because its invasiveness, however, it may not be proposed to all women before laparoscopic evaluation and treatment of pelvic pain. A previous study of retrospective data (Fauconnier et al., 2002) showed that the various specific anatomic locations of DIE are related to specific pain symptoms. These findings suggest that questioning may be helpful for predicting posterior DIE. That study, however, did not assess symptoms in a standardized fashion, with, for example, a questionnaire. The aim of the present study was thus to evaluate...
prospectively the diagnostic accuracy of medical history and symptoms, collected with a standardized questionnaire, in predicting posterior DIE.

**Materials and methods**

**Study population**

For this study, we recruited all premenopausal women who were younger than 46 years and scheduled for laparoscopy for chronic pelvic pain symptoms in our department between January and December 2000. Women presenting a history suggesting sexual abuse, severe depression or psychotic disease were not included in the study. Exclusion criteria were the following: previous resection of a DIE nodule; amenorrhea (including due to hysterectomy); diagnosis of myoma larger than 40 mm in size.

Each woman who agreed to participate was asked to complete a written self-administered questionnaire. A.F. and C.C. developed this questionnaire at our institution to evaluate endometriosis-related pain symptoms. The list of symptoms we included came from a comprehensive review of the literature and from our previous practice. Sentences were constructed from oral interviews during which we asked women who had pelvic pain symptoms and confirmed DIE to describe their pain. A draft questionnaire was tested on 12 women (three without and nine with pain) and modified to improve its comprehensibility. The questionnaire included items to evaluate the intensity and frequency of DM, dyspareunia and nonmenstrual pain, as well as the disability associated with each. The intensity of each painful symptom was evaluated according to either a 10 cm visual analogue scale (VAS) (Peveler et al., 1996) or a semiquantitative assessment (not at all; yes a little; yes a lot). Patients also recorded whether various symptoms (of the urinary or gastrointestinal tracts) occurred or increased during menses. The appendix includes several items from the questionnaire, which also asked for sociodemographic data, height, weight, body mass index, previous pelvic surgery, gravidity, parity, infertility (failure to conceive for more than 1 year), menstrual cycle characteristics and sexual activity. This questionnaire was given at the pre-operative consultation and completed during the month before before surgery.

Posterior DIE was diagnosed during laparoscopy (The American Fertility Society, 1993), which included thorough bidualt palpation of the retrocervical area under laparoscopic guidance. The diagnosis was based on the macroscopic appearance of the lesion, according to the following criteria: (1) obvious deep infiltration during excision (Koninckx and Martin, 1994), requiring either USL resection, partial colpectomy or resection of the rectal wall to remove the implant; (2) visible nodule or infiltration associated with palpable induration (Martin et al., 1989; Cook and Rock, 1991; Reich et al., 1991; Chapron and Dubuisson, 1996; Possover et al., 2000) at any of the following locations: torus uterinum, USL, posterior vaginal wall or anterior rectal wall at laparoscopy; (3) visible dark blue nodule of the posterior vaginal fornix on speculum examination (Vercellini et al., 1996). In case of complete cul-de-sac obliteration, the surgeon had to perform a complete adhesiolysis to analyse the posterior area.

The diagnoses of the other patients were grouped as follows: (1) not endometriosis (e.g. ovarian cysts, tubal pathology, adhesions without evidence of endometriosis), (2) superficial endometriosis, (3) endometriomas (including one woman with anterior DIE).

**Statistical methods**

Women with posterior DIE were compared with the other patients. Pearson’s $t$-test for the qualitative variables and Student’s $t$-test for the quantitative variables. The variables were dichotomized to simplify their use in constructing the diagnostic model as follows: the diagnostic accuracy of each possible cut-off point for the quantitative or ordinal variables was assessed by analyzing the receiver operating characteristics (ROC). Sensitivity, specificity, positive and negative likelihood ratios were calculated and the best cut-off points were considered to be those that maximized the sum of specificity and sensitivity.

Dichotomized variables associated with the presence of posterior DIE (at a threshold of $P < 0.10$) were then entered into a multiple logistic regression model to select the best combination for predicting posterior DIE. A backward stepwise procedure was then used to remove variables so that the final model included only those variables independently associated with posterior DIE at the threshold of $P < 0.05$. The model’s predictive ability was then assessed by calculating the probability of posterior DIE for the overall study population, with its mathematical equation. Observed and predicted values were compared with the Hosmer and Lemeshow goodness-of-fit test (Hosmer and Lemeshow, 1989). We then calculated overall sensitivity, specificity and positive and negative likelihood ratios for the diagnostic value of the model.

The diagnostic model was then tested with the jackknife method (Efron and Gong, 1983); especially useful for assessing its stability. The method was applied as follows (Efron et al., 1999): (1) the study population was randomly stratified into 10 subgroups of 13 ($\pm$1) women; (2) for each subgroup (i), a new prediction model ($M_i$) was constructed with the entire study sample except those in subgroup (i); (3) the model $M_i$ was then used to predict the outcome of the women omitted in constructing it. These steps were repeated for each subgroup. All analyses were performed with Stata 6.0 software (Stata Corporation).

**Results**

During the study period 249 women met the inclusion criteria and 174 (69.9%) completed the questionnaire. Responders and non responders were of the same age ($32.1 \pm 6.0$ vs $33.3 \pm 6.3; P = 0.18$) and had similar diagnoses at laparoscopy ($x^2$ with three degrees of freedom $= 1.29; P = 0.73$). Thirty women met at least one of the exclusion criteria: amenorrhea, eight women (3.2%); previous resection of DIE, six women (2.4%); myoma larger than 4 cm, 16 women (6.4%). Finally 10 women (4.0%) did not have accurate laparoscopic evaluation of the retrocervical area, so that no definitive diagnosis of posterior DIE was possible. These women were thus excluded from the analysis. Accordingly, the final study population included 134 women: 51 (38.1%) were diagnosed with posterior DIE and 83 (61.9%) with other disorders. Table I provides a complete list of the laparoscopic diagnoses.

Table II summarizes the associations between the variables considered and posterior DIE. No item dealing with DM was associated with posterior DIE. Variables associated with posterior DIE at a threshold of $P > 0.10$ at their best cut-off point are listed in Table III. One (fewer than two previous pregnancies) had high sensitivity but low specificity. Four (any previous surgery for endometriosis, dyspareunia always, aparunia and VAS for dyspareunia $\geq$ 8) had high specificity but low sensitivity. Three (age $< 32$ years, painful defecation and pain other than noncyclic) had rather high sensitivity and specificity.
The final multiple regression logistic model is reported in Table IV. Any painful defecation during menses, VAS for dyspareunia ≥ 8, pain other than noncyclic and previous surgery for endometriosis were independently associated with a diagnosis of posterior DIE. The model’s predictive ability was excellent (area under ROC curve = 0.77; Hosmer–Lemeshow statistic = 2.90 with six degrees of freedom, $P = 0.82$). Because of the strong correlation between dyspareunia always, apareunia and VAS for dyspareunia ≥ 8, these variables were not entered into the multiple logistic regression analysis together. VAS for dyspareunia ≥ 8 was chosen because its sensitivity and specificity had the highest sum. Two similar models, but with slightly lower predictive value, were obtained when VAS for dyspareunia ≥ 8 was replaced by either dyspareunia always or apareunia.

Table V reports the model’s sensitivity, specificity, positive likelihood ratio, negative likelihood ratio and diagnostic accuracy for the overall population. The jackknife procedure, however, yielded a lower diagnostic value than expected. In this procedure, five subgroup models were the same as the complete model, while five did not contain all four variables of the complete model. All 10 included painful defecation and VAS for dyspareunia ≥ 8. We therefore constructed a simplified model (Table IV) with these two variables (women not sexually active were not considered to have dyspareunia). The simplified model had good predictive ability (area under ROC curve = 0.72; Hosmer–Lemeshow statistic = 2.11 with two degrees of freedom, $P = 0.35$) and a diagnostic value that was both satisfactory and stable (Table V). It can be illustrated simply in a diagnostic tree constructed by successively dichotomizing the population according to the presence or absence of each symptom (Figure 1). This diagnostic tree allowed us to identify one low-risk group (neither symptom) of 70 women (52.2% of the study population) and one high-risk group (either severe dyspareunia or painful defecation during menses) of 64 women (47.8% of the study population). The probability of diagnosing posterior DIE at laparoscopy in patients in the high-risk population was 59.4% (95% confidence interval = 47.3–71.4%) and in the low-risk group, 18.6% (95% confidence interval = 9.5–27.7%).
This study shows that standardized questioning has an acceptable diagnostic value in the presurgical diagnosis of posterior DIE in a group of women suffering from pelvic pain. Painful defecation during menses and severe dyspareunia (i.e. VAS $\geq 8$ cm, apareunia or always having dyspareunia) are both rather reliable predictors of posterior DIE.

Our study was specifically designed to evaluate the usefulness of questioning in diagnosing posterior DIE. Medical history and symptoms were assessed prospectively. Following the appropriate procedures (Falissard, 2001), we developed a questionnaire designed to assess pain symptoms related to endometriosis. The exhaustiveness of the symptoms studied was ensured by basing the list on a comprehensive literature review and on our previous practice (Fauconnier et al., 2002). Finally, the study population was fairly large and included 51 women with posterior DIE.

This study nonetheless has several weaknesses. First, 30.1% of the women asked to participate did not answer the questionnaire. This may weaken the generalizability of the results. However, responders and non responders had similar age and similar diagnosis at laparoscopy.

The second limitation is that the diagnosis of posterior DIE was based on laparoscopic evaluation (The American Fertility Society, 1993) and not on histological results, as some authors recommend (Howard, 1993; Redwine, 1999). We chose to base inclusion of the women on macroscopic diagnosis of DIE because the posterior implants were not systematically removed during the study. Some women had DIE discovered incidentally at laparoscopy or did not want extensive surgery. Limiting inclusion to the cases which had laparoscopic removal of their posterior DIE would have led to indication bias. Nonetheless, the macroscopic criteria we used are very reliable for the diagnosis of posterior DIE (Martin et al., 1989; Cornillie et al., 1990; Koninckx and Martin, 1994; Vercellini et al., 1996; Possover et al., 2000; Chapron et al., 2001, 2002; Fedele et al., 2001; Bonte et al., 2002).

Third, we performed no cross-validation studies on independent samples. There is accordingly a risk that we overfit the data when we developed the prediction model (Altman

<table>
<thead>
<tr>
<th>Table III.</th>
<th>Diagnostic value of the variables found to be predictive of posterior DIE at univariate analysis at their best cut-off point</th>
</tr>
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<tbody>
<tr>
<td><strong>No</strong></td>
<td><strong>% with Posterior DIE</strong></td>
</tr>
<tr>
<td>Age $&lt; 32$ years</td>
<td>70</td>
</tr>
<tr>
<td>Fewer than two previous pregnancies</td>
<td>107</td>
</tr>
<tr>
<td>Any previous surgery for endometriosis</td>
<td>36</td>
</tr>
<tr>
<td>Having any painful defecation</td>
<td>51</td>
</tr>
<tr>
<td>Pain other than noncyclic</td>
<td>72</td>
</tr>
<tr>
<td>Dyspareunia always$^b$</td>
<td>22</td>
</tr>
<tr>
<td>Apareunia$^a$</td>
<td>11</td>
</tr>
<tr>
<td>Dyspareunia always or apareunia$^b$</td>
<td>24</td>
</tr>
<tr>
<td>VAS for dyspareunia $\geq 8^b$</td>
<td>19</td>
</tr>
</tbody>
</table>

DIE, deep infiltrating endometriosis; Se, sensitivity; Sp, specificity; LR +, Positive Likelihood Ratio; LR −, Negative Likelihood Ratio.  
$^a$Chi square for heterogeneity.  
$^b$Nine women were not sexually active.

<table>
<thead>
<tr>
<th>Table IV.</th>
<th>Complete and simplified models for prediction of posterior DIE using multiple logistic regression analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logistic model</td>
<td>Variables</td>
</tr>
<tr>
<td><strong>Complete model</strong></td>
<td>Any painful defecation</td>
</tr>
<tr>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>3.9</td>
</tr>
<tr>
<td>VAS for dyspareunia $\geq 8$</td>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
<td>4.6</td>
</tr>
<tr>
<td>Not sexually active</td>
<td>0.6</td>
</tr>
<tr>
<td>Any previous surgery for endometriosis</td>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
<td>2.6</td>
</tr>
<tr>
<td>Pain other than non cyclic</td>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
<td>2.5</td>
</tr>
<tr>
<td><strong>Simplified model</strong></td>
<td>Any painful defecation</td>
</tr>
<tr>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>4.9</td>
</tr>
<tr>
<td>VAS for dyspareunia $\geq 8$</td>
<td>No$^a$</td>
</tr>
<tr>
<td>Yes</td>
<td>4.5</td>
</tr>
</tbody>
</table>

DIE, deep infiltrating endometriosis; VAS, visual analog scale.  
$^a$Together with the women who were not sexually active.

<table>
<thead>
<tr>
<th>Table V.</th>
<th>Diagnostic value of the complete and simplified models in the overall population and in the validation population using the jackknife method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall population</td>
</tr>
<tr>
<td>Se (%)</td>
<td>68.6</td>
</tr>
<tr>
<td>Sp (%)</td>
<td>77.1</td>
</tr>
<tr>
<td>Correctly classified (%)</td>
<td>73.9</td>
</tr>
<tr>
<td>LR +</td>
<td>3.0</td>
</tr>
<tr>
<td>LR −</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Se, sensitivity; Sp, specificity; LR +, Positive Likelihood Ratio; LR −, Negative Likelihood Ratio.

Discussion

This study shows that standardized questioning has an acceptable diagnostic value in the presurgical diagnosis of posterior DIE in a group of women suffering from pelvic pain. Painful defecation during menses and severe dyspareunia (i.e. VAS $\geq 8$ cm, apareunia or always having dyspareunia) are both rather reliable predictors of posterior DIE.

Our study was specifically designed to evaluate the usefulness of questioning in diagnosing posterior DIE. Medical history and symptoms were assessed prospectively. Following the appropriate procedures (Falissard, 2001), we developed a questionnaire designed to assess pain symptoms related to endometriosis. The exhaustiveness of the symptoms studied was ensured by basing the list on a comprehensive literature review and on our previous practice (Fauconnier et al., 2002). Finally, the study population was fairly large and included 51 women with posterior DIE.

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Third, we performed no cross-validation studies on independent samples. There is accordingly a risk that we overfit the data when we developed the prediction model (Altman
To safeguard against overfitting, we used the jackknife procedure to test for instability of the model. This method is known to yield results similar to those obtained by testing the model in an independent population (Rothpearl, 1989; Ezeh et al., 1999). Nonetheless, validation studies of samples from different centres are important for evaluating the actual predictive ability of our diagnostic model (Coste et al., 1997). Because the prevalence of posterior DIE in our population was particularly high, it is important to verify the diagnostic accuracy of our model in a population with a lower prevalence of DIE. Its negative predictive value will certainly increase.

Painful defecation during menses was the strongest predictor of posterior DIE. This result is consistent with previous series that report significant reductions in painful defecation after surgical (Anaf et al., 2001) or medical treatment (Fedele et al., 2001) of posterior DIE. In a previous retrospective study we found that this symptom was specifically related to infiltration of the posterior vaginal wall (Fauconnier et al., 2002) rather than other DIE locations. In the present study, painful defecation during menses was present in more than half the women with posterior DIE, regardless of the anatomic location of the posterior implant. This finding suggests that posterior DIE is to be viewed more as a continuum of possible locations (e.g. USL, vagina, rectum) than a specific and distinct location.

Although dyspareunia is a well known marker for posterior DIE (Vercellini et al., 1996; Chapron et al., 1999), some form of dyspareunia is also reported frequently in general populations (Jamieson and Steege, 1996) and in women with any type of endometriosis (Mahmood et al., 1991; Fedele et al., 1992; Al-Badawi et al., 1999). With the use of a standardized questionnaire, we found that only severe dyspareunia (i.e. VAS ≥8 cm, apareunia, or always having dyspareunia) and not dyspareunia itself (regardless of its severity) was linked to posterior DIE. Another prospective study (Porpora et al., 1999) compared DIE involving USL with other subtypes of endometriosis and found dyspareunia to have a discriminant value, at the same cut-off point we used.

Surprisingly, no items evaluating DM correlated with the presence of posterior DIE. Most of our controls (some of whom had other subtypes of endometriosis) had similar or higher levels of DM. The severity of DM was in fact strongly related to the presence of any subtype of endometriosis (data not shown), but not to any particular subtype. These findings are consistent with those by Vercellini et al. (1996).

Apart from ours, two studies have previously developed diagnostic models for the presurgical prediction of endometriosis, based on noninvasive tools. One (Koninckx et al., 1996a) developed a diagnostic model to predict deep endometriosis based on two criteria: menstrual examination and CA-125 assay during the follicular phase. This model, with a sensitivity of 83% and a specificity of 87%, had a far better diagnostic value than ours. It has however two important flaws: the study includes only 13 women with DIE lesions; and, contrary to our model, it did not distinguish women with DIE from those with endometriomas. The other study (Eskenazi et al., 2001) was specifically designed to assess the prediction of endometriosis with the use of medical history, clinical examination and transvaginal ultrasonography. Apart from endometriomas, which were accurately predicted by transvaginal ultrasonography, no other subtypes of endometriosis were reliably predicted by any of the variables tested. The originality of our diagnostic model is that it was specifically designed to predict posterior DIE among women with chronic pelvic pain symptoms rather than to predict endometriosis of any subtype, as the other diagnostic models do.

Physical examination, including palpation of the retrocervical area with manual examination and searching for a dark

![Figure 1. Decision tree to determine whether women were at high or low risk of posterior deep infiltrating endometriosis](https://academic.oup.com/humrep/article-abstract/20/2/507/603298/511)
blue nodule at speculum examination is important in assessing women with suspected DIE. However, routine physical examination was not included in the study because it has insufficient diagnostic value for screening women with posterior DIE. Indeed, > 50% of women presenting with posterior DIE may have negative or non-specific findings at physical examination (Koninckx et al., 1996a; Chapron et al., 2002). On the other hand, physical examination performed during menstruation was found to have interesting diagnostic value (sensitivity: 77% and specificity 76%) to diagnose either deep endometriosis, cystic ovarian endometriosis, or cul-de-sac obliteration (Koninckx et al., 1996a). However, physical examination in the context of endometriosis requires skilled practitioners and inter-observer variability may be quite high, contrarily to our diagnostic model whose reproducibility is guaranteed by the fact that it is based on a standardized questionnaire.

Compared with more invasive diagnostic tools, such as laparoscopy (Martin et al., 1989; Cook and Rock, 1991), rectal endoscopic ultrasonography (Ohba et al., 1996; Fedele et al., 1998) or magnetic resonance imaging (Bazot et al., 2004), the diagnostic accuracy of our model can best be categorized as rather moderate. However, it may be appropriately combined with other non-invasive diagnostic tools, such as menstrual examination (Koninckx et al., 1996a), CA 125 sampling (Koninckx et al., 1996a), or transvaginal ultrasonography (Bazot et al., 2003) to improve the pre-operative detection of posterior DIE. Further studies are needed to evaluate the accuracy of these strategies.

We recommend our diagnostic model’s use to help clinicians dealing with endometriosis to screen women who may require more invasive exploration than laparoscopic evaluation and treatment of pelvic pain. The aim of this policy is to promote a one-step surgical procedure for the complete removal of the DIE. Rectosigmoid involvement is rather frequent in women with posterior DIE and may lead the surgeon to perform extensive surgical procedures, including bowel resection (Chapron et al., 2003). Adequate pre-operative evaluation, including rectal endoscopic ultrasonography (Schröder et al., 1997; Bazot et al., 2003; Chapron et al., 2004), magnetic resonance imaging (Kinkel et al., 1999; Bazot et al., 2004; Chapron et al., 2004) profile rectal radiography with barium enema (Donnez et al., 1997), or rectosigmoidoscopy (Anaf et al., 2001) is thus necessary to evaluate the extension of disease. The need for detection of women with posterior DIE before surgery is also important to provide adequate counselling (Garry et al., 2000). Excision of posterior DIE is technically demanding and may be associated with significant surgical risks (Koninckx et al., 1996b). Women must thus be advised of the risks of laparotomy and colostomy (Garry et al., 2000).

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