Positive Predictive Value of Clinical Diagnosis of Endometriosis

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Objective : *To determine the positive predictive value of the combined symptoms of severe dysmenorrhea with the sign of tenderness and/or nodularity of the cul-de-sac and/or uterosacral ligament(s) in diagnosing endometriosis clinically.*

Material and Method : *In this prospective study, 116 patients with severe dysmenorrhea, after excluding urinary and gastrointestinal disease, underwent pelvic examination by the same investigator. Women having adnexal mass on pelvic examination were excluded. Tenderness, and also nodularity, of the cul-de-sac, right and left uterosacral ligament were recorded separately. The laparoscopist did not know the findings of the pelvic examination. The diagnosis of endometriosis was made visually when lesions were typical and all other lesions were biopsied.*

Results : *The prevalence of endometriosis was 78.4%. Tenderness, nodularity, tenderness and nodularity, and also tenderness or nodularity of cul-de-sac and/or uterosacral ligament(s) were all statistically significantly associated with the presence of endometriosis (P = .048, .005, .004, and .004 respectively). The positive predictive values were 85.5%, 94.0%, 94.6% and 86.7%, respectively.*

Conclusion : *The positive predictive value of severe dysmenorrhea with nodularity of the cul-de-sac and/or uterosacral ligament(s) was 94.0%.*

Keywords : *Diagnosis, Dysmenorrhea, Endometriosis*

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The prevalence of endometriosis in the general population is hard to determine. Nevertheless, it was found to be 71-87% in patients with chronic pelvic pain[1-3]. The gold standard for the definitive diagnosis of endometriosis is laparoscopy[4]. However, there are significant risks associated with laparoscopy. A review of large surveys and individual series totalling more than 200,000 laparoscopies suggests that serious complications resulting in surgical intervention or death can be expected in one in 660 cases[5]. Moreover, the accuracy of the diagnosis is dependent on the abilities of the surgeon[6], and the cost of performing laparoscopy is expensive. These problems associated with laparoscopy challenges the clinicians' approach in terms of making a laparoscopic diagnosis of endometriosis in every case.

It is well acknowledged that the symptoms and signs of endometriosis are extremely variable. However, if we consider only the group of patients who have severe dysmenorrhea, it may be different. There was a trend for increasing risk for endometriosis to be associated with increasing menstrual pain[7]. Furthermore, focal tenderness was found to be strongly associated with the presence of endometriosis in cul-de-sac and uterosacral ligaments[8]. Koninckx et al[9]. reported that painful nodularities in cul-de-sac found at pelvic examination during menstruation strongly correlated with the presence of deep endometriosis, cystic ovarian endometriosis and severe cul-de-sac disease.

Currently, the only reliable method to diagnose endometriosis is surgery via laparoscopy or

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laparotomy, and no noninvasive tool could be substituted. In the present study, the authors do not try to develop a diagnostic model which is comparable to laparoscopy, but try to identify a group of patients who are very likely to have endometriosis and laparoscopy could be reasonably omitted. Hence, the purpose of this study was to determine the positive predictive value of the combined symptom of severe dysmenorrhea with the sign of tenderness and/or nodularity of the cul-de-sac and/or uterosacral ligament(s) in diagnosing endometriosis clinically. Moreover, the sensitivities and specificities of the tests are less important in this perspective.

Material and Method

This prospective study was conducted from October 2002 to November 2003, in a university hospital. Women 18-45 years of age were eligible for enrollment if they had menstrual pain of at least 6 months' duration, causing them to be in bed for at least 3 days during the previous 6 months. Their pain was incompletely relieved with nonsteroidal anti-inflammatory drugs.

Women were excluded if they had a previous diagnosis of the cause of dysmenorrhea confirmed by laparoscopy, laparotomy, or histology. Women whose pelvic pain might be related to chronic or recurrent urinary or gastrointestinal disease, including irritable bowel syndrome, were also excluded. Urinary and gastrointestinal diseases were screened by history taking and routine urinary analysis. Each patient gave medical and menstrual histories, including infertility, deep dyspareunia, nonmenstrual pain and dyschezia. The pelvic examination of all the patients was performed by the same investigator (SC). Women having adnexal mass on pelvic examination were also excluded. Tenderness of the cul-de-sac and/or uterosacral ligament(s) was defined as positive pain during palpation that was expressed on the patients' face and also by her words. Nodularity in the present study meant irregular thickening or a nodule. Tenderness, and also nodularity, of the cul-de-sac, right and left uterosacral ligament were recorded separately.

Laparoscopy was scheduled for each woman. The laparoscopist was one of the investigators (KD). The laparoscopists did not know the findings of the pelvic examination. The diagnosis of endometriosis was made visually when lesions on the peritoneum or ovarian surface were typical lesions of endometriosis. Typical lesions were defined as brownish, bluish, or purplish hemorrhagic areas associated with stellate scarring. All other lesions were biopsied and histologically confirmed diagnosis was made. The extent of endometriosis was graded according to the revised American Fertility Society classification (rAFS)[10].

The association between tenderness and/or nodularity and the presence of endometriosis was analyzed by Chi-Square test. The positive predictive values of signs related to the presence of endometriosis were calculated. Correlation between the number of sites of nodularity and stage of endometriosis was analyzed by non parametric test of trend. P-value < .05 was considered statistically significant.

Results

One hundred and sixteen patients were enrolled. The ages (mean $\pm$ SD) of all the patients were 32.8 $\pm$ 5.1 years. Infertility was the complaints of 65 patients (56.0%). The prevalence of endometriosis was 78.4% (91 patients). According to rAFS, 45.0%, 17.6%, 15.4%, and 22.0% of the patients had minimal, mild, moderate, and severe stage of endometriosis, respectively. No ovarian endometrioma were found. Laparoscopic findings are presented in Table 1. Dyspareunia and dyschezia were not associated with the presence of endometriosis. Interestingly, endometriosis was statistically significantly related to not having non-menstrual pain (P = .002).

Table 2 shows the association between findings during pelvic examination and presence of endometriosis. Tenderness, nodularity, tenderness and nodularity, and also tenderness or nodularity of the cul-de-sac and/or uterosacral ligament(s) were all statistically significantly associated with the presence of endometriosis (P = .048, .005, .004, and .004, respectively). Positive predictive values, sensitivities and specificities of signs of the cul-de-sac or uterosacral ligament(s) are presented in Table 3.

Table 1. Laparoscopic findings (n = 116)

	Patients n (%)
Endometriosis	91 (78.4)
Chronic pelvic inflammatory disease	6 (5.2)
Adhesions	3 (2.6)
Leiomyoma	2 (1.7)
Adenomyosis	1 (0.9)
Pelvic congestion syndrome	1 (0.9)
No visible pathology	12 (10.3)

Table 2. Association between the presence of endometriosis and findings of cul-de-sac and/or uterosacral ligament(s) (116 cases)

Findings	With endometriosis (n = 91) n (%)	Without endometriosis (n = 25) n (%)	P-value X^2 test
Tenderness			.048
positive	53 (58.2)	9 (36.0)	
negative	38 (41.8)	16 (64.0)	
Nodularity			.005
positive	47 (51.6)	3 (12)	
negative	44 (48.4)	22 (88)	
Tenderness and nodularity			.004
positive	35 (38.5)	2 (8.0)	
negative	56 (61.5)	23 (92.0)	
Tenderness or nodularity			.004
positive	65 (71.4)	10 (40.0)	
negative	26 (28.6)	15 (60.0)	

Table 3. Positive predictive values, sensitivities and specificities of signs of cul-de-sac and/or uterosacral ligament(s)

	Positive predictive value (%)	Sensitivity (%)	Specificity (%)
Tenderness	85.5	58.2	64.0
Nodularity	94.0	51.6	88.0
Tenderness and nodularity	94.6	38.5	92.0
Tenderness or nodularity	86.7	71.4	60.0

There was statistically significant correlation between the number of sites of nodularity and stage of endometriosis ($P < .005$).

Discussion

Noninvasive diagnostic techniques for endometriosis potentially could reduce the number of laparoscopic procedures and provide a rational basis for initiating medical treatment. Noninvasive tools for diagnosis of endometriosis may include symptoms, pelvic examination, transvaginal ultrasonography, magnetic resonance imaging, and endometrial and serum markers[11]. Eskenazi et al[12]. have developed a predictive model for endometriosis based on symptoms, signs, and transvaginal ultrasound findings. They reported that ovarian endometriosis, but not nonovarian endometriosis, could be reliably predicted with noninvasive tools; ultrasound and examination best predicted ovarian endometriosis, correctly classifying 100% of cases with no false positive diagnoses. After excluding ovarian endometriosis by ultrasound, 19 (43.2%) of 44 patients with dysmenorrhea and dyspareunia in their study had nonovarian endometriosis, and 14 patients (31.8%) had positive pelvic examination. The positive predictive value of pelvic examination was 71.4% (10 of 14 patients). In the present study, the prevalence of endometriosis was 78.4% and the positive predictive values of signs of cul-de-sac and/or uterosacral ligament(s) were 85.5-94.6% (Table 3). The different definitions of dysmenorrhea of their and the present study may partly account for the difference of prevalences of endometriosis. Furthermore, since positive predictive values are influenced by the frequency of disease[13], the presented higher positive predictive values may be due to a higher prevalence of endometriosis.

In a retrospective study, Chapron et al[14]. reported that a classic, painful, spheric nodule was palpated in 69 (43.1%) of 160 patients with histologically proved deeply infiltrating endometriosis. In other words, the sensitivity of this test was only 43.1%. They concluded that routine clinical examination is not sufficient for diagnosing deeply infiltrating endometriosis. In the present study, tenderness with nodularity of the cul-de-sac and/or uterosacral ligament(s) were found in 35 (38.5%) of 91 patients with endometriosis, but the positive predictive value of this finding was 94.6%, which is useful.

Ripps and Martin[8] observed that focal tenderness was strongly associated with the presence of endometriosis in the cul-de-sac and uterosacral ligaments. In their study, endometriosis was found in 59 (63%) of the 94 patients studied and the positive predictive values of these findings were 75.0-87.0%. Our positive predictive value of tenderness finding (85.5%) is comparable to theirs. In a prospective study, Koninckx et al[9]. found that pelvic painful nodularities were detected in 22 (37.9%) of 58 women by clinical examination during menstruation, with the positive predictive value of 88%. The authors preferred to perform a pelvic examination when the patients first came to the outpatient clinic and the presented positive predictive value of tenderness and nodularity finding was 94.6%, with 37 (31.9%) of 116 patients having a positive finding.

Among four findings of our pelvic examination (Table 2,3), the tenderness and nodularity of the cul-de-sac and/or uterosacral ligament(s) had the highest positive predictive value (94.6%). However, only 31.9% of the patients had this positive finding. Seventy-five (64.7%) of all the patients had a positive sign of tenderness and/or nodularity, but the positive predictive value was only 86.7%. So the authors decided to choose the nodularity of the cul-de-sac and/or uterosacral ligament(s) to be the most appropriate sign for clinical diagnosis of endometriosis. According to this model, laparoscopy could be reasonably omitted in 50 (43.1%) of 116 patients with the probability of 94.0% to have endometriosis and 6.0% to have misdiagnosis.

The clinical and economic consequences of the misdiagnosis of these patients should be considered thoroughly. Among the 3 patients misdiagnosed, one had pelvic adhesions and the other two had no visible pathology. All were benign diseases, and early detection was not crucial. Stones and Mountfield[15] reviewed studies of treatment of chronic pelvic pain extensively. They included studies of patients having chronic pelvic pain with no known cause but excluded studies of patients having chronic pelvic pain known to be caused by endometriosis, primary dysmenorrhea, active chronic pelvic inflammatory disease or irritable bowel syndrome. They reported that progestogen (medroxyprogesterone acetate) was associated with a reduction of pain during treatment. Then, if all of the presented patients with severe dysmenorrhea and nodularity of cul-de-sac and/or uterosacral ligament(s), in the absence of infertility, were treated with depot medroxyprogesterone acetate, the patients without endometriosis might have the benefit of pain relief during treatment at low cost, while patients with endometriosis might have been treated with the proper drug[16].

In conclusion, the positive predictive value of combined symptom of severe dysmenorrhea with nodularity of cul-de-sac and/or uterosacral ligament (s) was very high (94.0%). Thus laparoscopy may be reasonably omitted in this group of patients and medical treatment may be initiated appropriately.

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โอกาสที่ผู้มีผลการตรวจเป็นบวกจะเป็นโรคภาวะเยื่อบุโพรงมดลูกเจริญผิดที่ในการวินิจฉัยทางคลินิก

โสภณ ชีวะธนรักษ์, กรัณฑรัตน์ ปิยนันท์จรัสศรี, เกรียงศักดิ์ ธนวรวิบูล, ทิพวรรณ เลียบสื่อตระกูล

วัตถุประสงค์ *: เพื่อหาค่าโอกาสที่ผู้มีผลการตรวจเป็นบวกจะเป็นโรค ของการวินิจฉัยภาวะเยื่อบุโพรงมดลูกเจริญผิดที่ทางคลินิก โดยการใช้อาการปวดระดูอย่างรุนแรงร่วมกับการตรวจพบอาการกดเจ็บและ/หรือคลำได้ขรุขระของ cul-de-sac และ/หรือ uterosacral ligament(s)*

วัสดุและวิธีการ *: เป็นการศึกษาแบบไปข้างหน้า หลังการวินิจฉัยแยกโรคของระบบทางเดินปัสสาวะและทางเดินอาหารออกไปแล้ว ผู้ป่วยที่มีอาการปวดระดูรุนแรงจำนวน 116 ราย ได้รับการตรวจภายในโดยแพทย์คนเดียว หากตรวจพบก้อนที่ปีกมดลูกจะทำการคัดผู้ป่วยออกจากการศึกษา อาการกดเจ็บของ cul-de-sac และ uterosacral ligament ข้างซ้ายและขวาได้รับการบันทึกแยกตำแหน่งกัน อาการคลำได้ขรุขระก็ได้รับการบันทึกแยกตำแหน่งกันด้วยแพทย์ผู้ทำการส่องกล้องตรวจเป็นอีกคนหนึ่งและไม่ทราบผลการตรวจภายใน การวินิจฉัยภาวะเยื่อบุโพรงมดลูกเจริญผิดที่ทำโดยการมองเห็นรอยโรคที่มีลักษณะจำเพาะ สำหรับรอยโรคอื่นแพทย์จะทำการตัดชิ้นเนื้อ*

ผลการศึกษา *: ความชุกของภาวะเยื่อบุโพรงมดลูกเจริญผิดที่มี 78.4% อาการกดเจ็บ อาการคลำได้ขรุขระ อาการกดเจ็บร่วมกับคลำได้ขรุขระ อีกทั้งอาการกดเจ็บหรือคลำได้ขรุขระของ cul-de-sac และ/หรือ uterosacral ligament(s) มีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติกับการตรวจพบภาวะเยื่อบุโพรงมดลูกเจริญผิดที่ (P = .048, .005, .004 และ .004 ตามลำดับ) ค่าโอกาสที่ผู้มีผลการตรวจเป็นบวกจะเป็นโรคมี 85.5%, 94.0%, 94.6% และ 86.7% ตามลำดับ*

สรุป *: ค่าโอกาสที่ผู้มีผลการตรวจเป็นบวกจะเป็นโรคภาวะเยื่อบุโพรงมดลูกเจริญผิดที่มี 94.0% หากใช้เกณฑ์การวินิจฉัยว่ามีอาการปวดระดูรุนแรงร่วมกับการคลำได้ขรุขระของ cul-de-sac และ/หรือ uterosacral ligament(s)*