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GENERAL GYNECOLOGY

Agreement between the preoperative findings and the operative diagnosis in patients with deep endometriosis

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Abstract
Introduction During the evaluation of patients with endometriosis, recognizing the location and characteristics of lesions is fundamental to define the type and evaluate the response of treatment, as well as for the preoperative surgical planning. However, the non-invasive diagnostic tests have specific limitations making the diagnostic laparoscopy been recommended as a tool necessary for the diagnosis of endometriosis lesions despite the high cost and the risks involved in this procedure.
Objective To evaluate the feasibility of mapping endometriosis lesions using clinical signs and image evaluation, comparing the pre- and postoperative findings of patients submitted to surgical treatment.
Method A retrospective and prospective study included all patients who underwent surgical treatment for deep endometriosis between March 2011 and November 2014, at two centers of endometriosis in Rio de Janeiro. The positive finds registered during the clinical and image evaluation were compared with the surgical and histopathological results using a new instrument: the Lasmar's MAP of endometriosis
Results 46 patients were included, age ranging from 23 to 47 years. For each site of endometriosis lesions, sensitivity, specificity, positive and negative predictive value, the positive and negative likelihood ratios and accuracy were calculated.
Discussion The results show a high sensitivity, specificity and accuracy of the preoperative clinical evaluation to identify the main sites of endometriosis lesions without the use of diagnostic laparoscopy.

Keywords Endometriosis map · Treatment · Laparoscopy · Diagnosis · Endometriosis

Introduction

Endometriosis is defined as the presence of endometrial tissue outside the uterine cavity [1] and it is found in approximately 10–15 % of women during the reproductive period [2]. Endometriosis can be classified as deep endometriosis when the lesions are at least 5-mm deep in the affected structure [3].

In the follow-up of a patient with endometriosis, identifying the sites and characteristics of the lesions is essential to define the management, to assess the response to the treatment and to determine the preoperative surgical planning.

In most cases, a presumptive diagnosis of endometriosis is made by the signs and symptoms observed in the clinical history and physical examination. Then, imaging studies complement the investigation of the location of the disease, commonly with the use of magnetic resonance imaging (MRI) and/or ultrasound (US) [4].

However, this model of lesion mapping may be flawed due to some interference factors, such as obesity, size of the lesions and experience of the examiner, resulting in lower sensitivity and specificity of the clinical investigation.

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As a result, some authors now consider diagnostic laparoscopy as a sine qua non tool for the diagnosis of endometriosis lesions, because it enables direct visualization and biopsy of the lesions [5, 6].

However, diagnostic laparoscopy is an expensive surgical procedure, requires general anesthesia and is inevitably associated with rare but potentially severe complications [7].

In 2012, Lasmar et al. developed a diagram to map endometriosis lesions found in the pelvis of patients with deep endometriosis, called "MAP", [8] through which the sites of the disease can be recorded by medical history, physical examination and imaging tests, with no need of diagnostic laparoscopy.

The main objective of the study was to evaluate the possibility of preoperative clinical mapping of deep endometriosis lesions, compared to the operative diagnosis, using the Lasmar MAP as an instrument.

Materials and methods

This was a retrospective and prospective study which included all patients who underwent surgery for deep endometriosis from March 2011 to November 2014, at the Endometriosis Service of the Hospital Universitário Antônio Pedro, Federal Fluminense University, in the city of Niteroi, State of Rio de Janeiro, Brazil.

The patients were referred from the primary care network to the outpatient endometriosis service and evaluated by the same team that performed the surgery. History taking and the gynecological pelvic examination, including digital rectal examination, were carried out by at least two surgeons. With the aid of imaging studies—pelvic transabdominal or transvaginal ultrasound (TA-US or TV-US), and/or magnetic resonance imaging (MRI) of the pelvis, cystoscopy and colonoscopy—the endometriosis lesions were diagnosed, located and recorded in the MAP, about 30 days before surgery.

The surgical indications were disabling pain, unsatisfactory response or contraindication to drug treatment, and functional impairment of organs by endometriosis lesions.

In all cases, the preoperative diagnostic evaluation, the surgical indication and the laparoscopic surgeries included the same surgeon, Professor Ricardo Lasmar, the head of the endometriosis sector. The operative confirmation of the location of lesions was made by visual perioperative analysis and histopathological study, and only positive histopathological tests for endometriosis were considered as lesion sites. All suspect lesions were excised. After surgery, a new MAP was created and compared with the preoperative MAP, to establish the correlation between the findings.

The study was approved by the Research and Ethics Committee of the Hospital Universitário Antônio Pedro.

We excluded patients who had previously undergone surgery for endometriosis by any other staff, patients who did not accept to undergo the surgical procedure, patients who were lost to follow-up, and patients with malformations of pelvic organs.

The following data were analyzed for each patient: age, parity, skin color, the complaint of each patient (dysmenorrhea, hypermenorrhea, pelvic pain not related to menstrual cycle, dyspareunia, dyschezia or urinary symptoms), and the pre- and postoperative MAP.

The following changes in the physical examination were considered consistent with the diagnosis of endometriosis: nodules or thickening in the vaginal mucosa, Douglas pouch, uterosacral ligaments and parametrium, palpable adnexal cyst, little or no uterine mobilization, globular and hardened aspect of the uterus suggestive of adenomyosis, or the presence of bluish or purplish visible lesions.

In all cases, the lesions were completely resected, including when a complete obliteration of the cul-de-sac (frozen pelvis) was found, increasing the accuracy of the gold standard test.

Statistical analysis was performed using STATA® version 8. For each deep lesion site eligible for recording in MAP (ovaries, uterus, cervix, adenomyosis, round ligaments, uterosacral ligaments, retrocervical region, rectovaginal septum, bladder, vesicouterine fold, rectum, sigmoid appendix, cecum and ureters), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LHR +) and negative likelihood ratio (LHR-), and accuracy were calculated. A MAP was created for each patient including all preoperative findings compared with a postoperative MAP with the pathological diagnosis of the surgical specimens. The χ^2 test was used, considering a p value < 0.05 as statistically significant.

Results

The mean age and epidemiological characteristics of the patients are shown in Table 1, and the pre-existing symptoms are described in Table 2.

Out of 273 patients referred for evaluation and follow-up with clinical endometriosis, 52 (19 %) had indication for surgical treatment and met the inclusion criteria. However, four were excluded for loss to follow-up and two did not agree to undergo surgery, resulting in 46 operated patients.

The mean age was 34 years (range 23–47 years). All patients operated on had at least one anatomic site with a focus of endometriosis confirmed by histopathological

Table 1 Basic characteristics of patients undergoing surgery ($n = 46$)

Characteristics	Values	Percentage
Age (years)[a]	34 ± 5.5 (range 23–47)	
Skin color (*n*/%)		
White	28	60.9
Mixed race	13	28.3
Black	4	8.7
Non declared	1	2.1
Pregnancies (*n*/%)		
0	29	63.0
1	10	21.7
≥2	7	15.2
Parity (*n*/ %)		
0	34	73.9
1	8	17.4
≥2	4	8.7
Abortion		
0	36	78.3
1	8	17.4
≥2	2	4.3

[a] Mean ± standard deviations

Table 2 Symptoms of patients undergoing surgery ($n = 46$)

Symptoms	Number of patients	Percentage
Dysmenorrhea	43	93.5
Dyspareunia	27	58.7
Infertility	23	50.0
Menorrhagia	18	39.1
Chronic pelvic pain	17	37.0
Disquezia	14	30.4
Urinary symptoms	5	10.9

examination. Two patients had only one focus of endometriosis (both in the ovary), and others showed an average of 4 (range 3–8) anatomical regions with endometriosis foci. There were 184 sites with clinical suspected endometriosis, and 194 sites that were positive for endometriosis at the histologic analysis (Table 3).

Table 3 also summarizes sensitivity and specificity, PPV, NPV, LHR+, LHR− and the accuracy of the clinical assessment, separated by anatomical regions.

In the assessment of the uterosacral ligaments (USL), there were 42 suspected cases preoperatively, and 39 positive results for endometriosis in the histopathological examination. There was one case in which uterosacral ligament endometriosis was not identified in the preoperative assessment.

Similarly, in the assessment of retrocervical nodular disease, there were 36 suspected cases preoperatively, 34 confirmed by histopathological examination and one false negative (a 0.5-cm nodule that was found only during histopathology analysis).

Of the 33 patients with suspected ovarian disease preoperatively, 31 were confirmed postoperatively. Overall, the histopathological examination revealed the presence of ovarian endometriosis in 34 patients.

Of the 26 cases of suspected intestinal lesion preoperatively, there was histopathological confirmation in 25. However, in two cases in which no intestinal endometriosis was suspected, superficial foci of endometriosis were identified in the sigmoid, totaling up 27 cases with intestinal disease.

Of 10 patients diagnosed with adenomyosis preoperatively, nine cases were confirmed after surgery.

Out of 18 patients with confirmed rectovaginal septum lesions, in 16 of them endometriosis was suspected preoperatively, and in two the lesion was identified only during the surgery.

In the anterior compartment, there were 8 cases of suspected endometriotic lesions in the vesicouterine fold and 6 in the bladder. Eleven cases were confirmed after surgery in the vesicouterine fold and 6 in bladder. In the assessment of the round ligament, 7 patients presented lesions in the preoperative period, and 14 were identified and confirmed after surgery.

Discussion

The results show high sensitivity and specificity of the preoperative clinical evaluation in identifying the main sites where endometriosis can be found.

The clinical evaluation of the round ligament had lower sensitivity to identify endometriotic lesion, but with high specificity. This can be explained, in part, because it is an area of difficult access for the bimanual physical examination and low sensitivity for TV-US. It is likely that some signs and symptoms, not yet established as clinical markers, may indicate involvement of the region, increasing the sensitivity of the clinical investigation. The coincidence of round ligament lesions with laterally deflected uterus and/or bladder lesions was frequent in our study.

In the assessment of uterosacral ligaments, high sensitivity (97.5 %), moderate specificity (50 %), and high accuracy (92 %) were observed. The USL are easily accessible by digital cervical examination and better evaluated by digital rectal examination. Even when only slightly thickened, they can still be identified by ultrasonography and MRI. Of the 46 patients evaluated, only six had no ligament disease, and among these, three were evaluated as false positive, explaining the specificity found in this study. In these three cases, the histopathological

Table 3 Topographic diagnosis of lesions in preoperative and postoperative with the sensitivity, specificity, PPV, NPV, LHR+, LHR− and Accuracy

Anatomical location	PRE-OP[a]	POS-OP[b]	Sensitivity (%)	Specificity (%)	*p* value [c]	VPP (%)	VPN (%)	LHR +	LHR −	Accuracy (%)
Usl	42	40	97.5	50	<0.01	75	92.8	1.94	0.06	92.8
Retovaginal septum	16	18	88.8	100	<0.01	100	93.3	–	0.12	95.6
Retrocervical lump	36	35	97.1	81.8	<0.01	94.4	90	5.1	0.03	93.4
Ovary	33	34	91.1	83.3	<0.01	93.9	76.9	5.35	0.10	89.1
Intestine	26	27	92.5	94.7	<0.01	96.1	90	15.3	0.08	93.4
Adenomyosis	10	9	100	97.2	<0.01	90	100	33.3	–	97.8
Round ligament	7	14	42.8	96.8	<0.01	85.7	79.4	0.5	0.6	80
Vesico-uterine peritoneum	8	11	72.7	100	<0.01	100	92.1	–	0.28	93.4
Bladder	6	6	100	100	<0.01	100	100	–	–	100
Total	184	194	–	–	–	–	–	–	–	–

VPP positive predictive value, *VPN* negative predictive value, *LHR+* positive likelihood ratio, *LHR−* negative likelihood ratio, *USL* uterosacral ligament

[a] Numbers of patients with diagnosis after anamnesis, physical examination and evaluation by USG and/or MRI of the pelvis

[b] Numbers of patients with operative diagnosis and positive histopathology

[c] χ^2 Pearson's test

examination only revealed the presence of fibrosis probably secondary to the inflammatory and scarring processes of the endometriotic lesions. Nevertheless, these cases were not considered as positive in the final analysis, due to the need of histopathological evidence as gold standard.

The same was true for the evaluation of nodular lesions in the retrocervical region. Of the 36 patients evaluated with lesions in this region, 34 (94 %) were confirmed postoperatively, and these two cases of false negative were also considered as fibrous tissue by pathologists. There was one false-negative case, due to an enlarged resection of the upper vaginal third, in which the histopathological report revealed the presence of a small (0.5 cm) nodule adjacent to the resected vaginal tissue.

Bazot et al. [9], in a similar study, including 92 patients assessing USL lesions alone, found sensitivity, specificity and accuracy of 73, 77 and 74 %, respectively, for physical examination with digital rectal examination; 78, 66 and 77 % for TV-US; and 84, 88 and 84 % for MRI. In this study, the high sensitivity and accuracy figures were probably due to the association of history, physical examination and imaging tests in the preoperative period.

Likewise, the workup for investigating ovarian lesions had high accuracy. There were only three false-negative cases, namely, three endometriomas measuring up to 10 mm, that were identified only during surgery, due to the small size of the lesions.

Concurrently, we achieved 100 % accuracy for bladder lesions, and 93 % for intestinal lesions. These percentages are closer to the values found in other studies and the results obtained by centers specialized in imaging evaluation [1, 10–13]. This study included ultrasound and MRI examinations of different places, conducted by different professionals, not necessarily by centers specialized in diagnostic imaging of endometriosis.

Currently, imaging investigation either by US or MRI is consistently supported by the medical literature. Different studies demonstrated near 100 % accuracy for ovarian, intestinal and bladder investigation [1, 13–15]. TV-US is recommended by the European Society of Human Reproduction and Embryology (ESHRE) as the first choice for the evaluation of this site, with level of evidence and grade of recommendation 1A. Although important, it is precisely in the assessment of these sites that the standard physical examination achieves less sensitivity, mainly because the lesions are higher and often inaccessible to touch examination.

In a prospective study conducted in 2011, Hudelist et al. [16] preoperatively evaluated 83 women who underwent laparoscopy for treatment of deep endometriosis. When comparing gynecological examination versus TV-US, they found a sensitivity of 40 % for endometriomas, 38 % for intestinal endometriosis, and 25 % for bladder lesions. It is important to note that in this study the physical examination was performed by five different examiners and did not include digital rectal examination.

Similarly, Eskenazi et al. [15], in 2001, evaluated 120 women, considering the same positivity criteria for physical examination used by Hudelist, and achieved a sensitivity of 74 % for identifying infiltrative lesions of the posterior compartment. In this study, digital rectal examination was not routinely performed, which could further increase the sensitivity of the first physical examination [1].

When analyzing the results found in the assessment of the rectovaginal septum and the vesicouterine fold, the physical examination employed in the study resulted in a sensitivity of 100 % and NPV greater than 90 %, reflecting a superior ability to exclude the disease in these sites.

All patients had endometriosis confirmed by histopathological studies. This fact, along with the high PPV found for each focus, confirms that the preoperative diagnosis is feasible without the need for diagnostic laparoscopy.

The medical history identifies patients at risk for endometriosis by highlighting the associated main complaints. According to Eskenazi et al., the physical examination alone may have a sensibility and specificity of approximately 76 and 74 % [15]. However, it is insufficient for higher lesions that are inaccessible to digital examination, such as small endometriomas, bladder and intestinal lesions, and patients with vaginal malformations or who are virgin [17, 18].

Transvaginal ultrasound is an important tool to identify lesions. It is a reproducible method and the results depend on the examiner's experience. According to Hudelist G. et al., its sensitivity ranges from 98 to 100 % for ovarian, bladder, rectum and retrouterine lesions. And specificity is 90 % for rectovaginal septum and Douglas pouch lesions. However, on average, it has lower sensitivity (up to 25 %) for assessing the round and uterosacral ligaments and is insufficient to evaluate multifocal intestinal disease [16].

Likewise, MRI is an important diagnostic tool, with sensitivity and specificity similar to TV-US, and it has advantages in assessing multifocal intestinal disease, recurrences, previously operated patients [17], and also large tumors (voluminous fibroids and ovarian cysts) that prevent the ultrasound energy from reaching these regions entirely. Its costs are higher than those of TV-US, and it is an examiner-dependent method. Nonetheless, when the images are recorded on a CD or DVD, other professionals can revise the exams in different stages of the clinical evaluation.

In this study, using MAP as an instrument, medical history, physical examination, TA-US, TV-US and/or MRI could be assessed together, in a scenario similar to the reality of several treatment centers in Brazil, where there is no availability of radiologists who are experienced in the evaluation of patients with endometriosis.

Probably no single diagnostic test will be able to identify all lesions, due to the different forms of the disease. But the study results showed that combining the tools available to investigate patients with deep endometriosis; that is, medical history, physical examination and imaging studies—it is possible to map the lesions in the pelvis noninvasively, with high pathological correlation.

Compliance with ethical standards

Conflict of interest None.

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