Do women with suspected endometriosis benefit from pelvic examination to improve diagnostic and management strategy?

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Conflicts of interest :

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CRJ *déclare être consultante pour Bristol Myers Squibb, Novartis, Organon,, Roche, Theramex ;*

XD *déclare être actionnaire de Sanofi et Nanobiotix, être expert pour la HAS et le Haut conseil pour la nomenclature et consultant pour Astellas, Coloplast, Hologic, IBSA Pharma, Laborie, Mylan, Pierre-Fabre et être auteur pour Elsevier-Masson, Regimedia et HealthEvents ;*

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Abstract

Objective: To analyze the literature and expose best evidence available regarding the benefit of pelvic examination for women with suspected endometriosis

Methods: the AGREE II and GRADE systems for grading scientific evidence.

Results: Endometriosis is characterized by the heterogeneity in its clinical presentation with many different symptoms reported by patients. In the literature, questioning for each symptom has a high sensitivity, reaching 76–98%, but lacks specificity (20 – 58%). The symptom-based approach is limited by its low specificity, the absence of external validation for most of the models developed and the inability to characterize the extent of the disease, which could have major implications in the decision – making process. The latest systematic review and meta-analysis included a total of 30 studies with 4,565 participants, compared the diagnostic performance of several modalities for endometriosis. Physical examination had a pooled sensitivity of 71% and a specificity of 69%, with an average diagnostic accuracy of 0.76. Overall, the value of pelvic examination is conferred by its high positive likehood ratio and specificity. Besides its diagnostic value, pelvic examination improves patients' management by allowing the identification of a possible myofascial syndrome as a differential diagnosis. It also increases the quality of the preoperative workup and influences the quality of surgical excision and decreases the time to diagnosis.

Conclusion: Despite the lack of studies in the primary care context, pelvic examination (vaginal speculum and digital vaginal examination) increases the diagnostic value for suspected endometriosis in association with questioning for symptoms.

Keywords: Endometriosis; Pelvic Examination; Symptoms; Diagnostic ;

Introduction

Recent international guidelines have modified gynecological follow-up in asymptomatic women by limiting the indications for pelvic examination [1]. Systematic follow-up consisted of symptom questioning and pelvic examination including vulvar inspection, speculum vaginal examination, and digital vaginal examination. Studies have reported that these medical examinations can be stressful and are perceived as intrusive with negative experiences [2]. However, when symptomatic, most women will accept pelvic examination if required for diagnosis purpose and if the procedure is performed by a qualified health professional [3].

Endometriosis, particularly in its advanced stages, is a well-known cause of disabling pelvic pain and infertility [4]. It is estimated that up to 10% of women of reproductive age and 50% of infertile women have a huge impact on quality of life in some cases [5,6]. In patients with chronic pelvic pain, 11 studies ranged the prevalence of endometriosis with great disparities between 2 and 74% [7]. This disease represents a public health issue with considerable cost at both individual and society levels [8].

Endometriosis diagnosis is a matter of concern. As diagnosis is often the gatekeeper to treatment, the faster the diagnosis, the sooner appropriate treatment can be introduced. The latest “state of the art” review by Pascoal et al. perfectly underlines the diagnostic difficulties of this pathology and the imperfect nature of each method, with its strengths and weaknesses, from which the questioning and pelvic examination do not escape [23]. Indeed, women can present with great disparities of non-specific symptoms and some of them are even completely asymptomatic (independently of the extent of anatomic lesions). Pelvic examination is currently part of first line diagnostic strategy in women with suspected endometriosis in both European and French HAS Guidelines [9,10]. Whenever possible,

pelvic examination associated with the questioning is the first step of the diagnostic algorithm. Several authors reported a benefit of clinical examination to improve diagnostic strategy [11]. The question of the benefit of pelvic examination in patients with suspected endometriosis is all the more relevant that it usually also aims to identify painful spots that could indicate endometriosis. The French college recently issued guidelines on the benefit of pelvic examination in various situations, in either gynecology or obstetrics [12]. This examination must be carried out with particular caution, especially in the context of endometriosis because of its painful nature in these patients and women should be informed of the modalities and expectations prior consent to be examined.

The aim of this work was to analyze the literature and expose best evidence available regarding the benefit of pelvic examination for women with suspected endometriosis

Methods

In collaboration with the methodologist in charge of the aforementioned guidelines, a search strategy was designed using key terms and keywords. The search was limited to human studies written in English or in French. The PubMed platform was used to search MEDLINE. MeSH terms and non-MeSH terms were used. Search equations used "AND" and "OR" on MEDLINE/PubMed. Key words used for this PICO were: “endometriosis”; “deep endometriosis”; “vaginal endometriosis”; “pelvic examination” ; “physical examination” ; “vaginal speculum”; “vaginal examination”; “imaging”; “MRI”; “pelvic ultrasound”.
Each study was evaluated independently, and an overall level of evidence was processed once the review completed.

In this work, pelvic examinations referred to vulva inspection, speculum examination of the vagina and the cervix and palpation through manual examination of internal genital organs (vagina and cervix, uterus corpus, adnexa) and hypogastric region. The question of rectovaginal examination was not considered in these guidelines due to the limited data available in the literature.

Results

The main studies reporting on the relevance of physical examination for the diagnostic of endometriosis are reported in Table 1.

Value of the questioning for symptoms in the diagnostic strategy of patients with suspected endometriosis

Elements of the systematic questioning in women with suspected endometriosis

Many studies evaluated the relevance of the questioning for symptoms in women with suspected endometriosis. Painful symptoms of deep endometriosis have characteristics that distinguish them from pain of other origins [13]. These pains may be specific to the involvement of a precise anatomical location or a precise organ by the deep endometriosis implants [14]. A detailed clinical history should search for the most common symptoms and their severity, including gynecological symptoms on one side, such as dysmenorrhea [13], cyclical and non-cyclical pelvic pain, deep dyspareunia (and impaired sexual function)[15] and infertility, and non-gynecological cyclical symptoms on the other side, such as dyschezia [16], dysuria [17], hematuria, flank pain, rectal bleeding [14] and shoulder pain [9]. The visual analog scale (VAS) is a well-adapted tool for measuring pain in endometriosis [18]. Eventually, physicians should evaluate the potential overall reduction in the quality of life of patients with suspected endometriosis [19,20].

Performance of the questioning in women suspected with endometriosis

Overall, questioning for each symptom has a high sensitivity, reaching 76–98%, but lacks specificity (20 – 58%) as summarized by Pascoal et al. [21–23]. In a literature review on chronic pelvic pain, Vercellini et al. discussed the frequent non – endometriotic causes, such as irritable bowel syndrome, myofascial syndrome, pelvic adhesions, pelvic venous congestion, and interstitial cystitis [24]. Several authors developed models with different

148 symptoms to predict the presence of endometriosis. Chapron et al. recently [25] identified
149 eight interrogation elements and proposed several diagnostic thresholds for their score:
150 between 1 and ≥ 25: (i) highly specific, correctly identifying patients without the disease; (ii)
151 highly sensitive, identifying the patients with the disease; and (iii) a level maximizing
152 sensitivity and specificity for the best classification of the whole population. They reported
153 the following performance of their model: score 1: specificity of 91% (95% CI [89-93]); score
154 < 11: sensitivity of 91% (95% CI [89-93]); score ≥ 18: specificity of 75% (95% CI [72-78]), and
155 sensitivity of 73% (95% CI [70-76]). Fauconnier et al. reported a standardized self-
156 questionnaire developed from the patients' verbatim (built specifically for diagnosis) with
157 21-item yes/no questions about painful symptoms [26]. They included 105 cases and 197
158 controls, and the full question set prediction model, including age, had an area under the
159 receiver operating characteristic curve of 0.92 (95% confidence interval, 0.87-0.95) after
160 internal validation. The high-risk classification rule had a specificity of 98.0% and a positive
161 likelihood ratio of 30.5. The low-risk classification rule had a sensitivity of 98.1% and
162 negative likelihood ratio of 0.03. Eventually, Bendifallah et al. investigated the use of
163 machine learning algorithms (MLA) in the diagnosis and screening of endometriosis based on
164 16 key clinical and patient-based symptom features [27]. In their work, the sensitivity,
165 specificity, F1-score, and AUCs of the MLA to diagnose endometriosis in the training cohort
166 from the Ziwig Health Platform were 0.82 to 1, 0-0.8, 0-0.88, 0.5-0.89. They performed
167 validation on a 100 – patients prospective cohort with similar performance.
168 Overall, the symptom-based approach is limited by its low specificity and the absence of
169 external validation for most of the models developed. The “paradox” of the aforementioned
170 models is that they were developed in expert centers but aim to increase the diagnostic
171 performance in primary care. Future research could focus on testing their performance in

primary care as well as refining their use to help prescribing MRI imaging or guide the patients toward specific pathways of care.

Another issue with this approach to diagnose endometriosis is its inability to characterize the extent of the disease, which could have major implications in the decision – making process.

Value of the pelvic examination in patients with suspected endometriosis

Elements and timing of pelvic examination in women with suspected endometriosis

Studies report that between 15% and 30% of women with endometriosis have deep infiltrating disease [13]. Speculum examination may reveal bluish spot characteristic of endometriosis in the retrocervical area and the upper part of the posterior vaginal wall. Vaginal digital examination in women with suspected endometriosis aims to identify deep posterior infiltration of the retrocervical area [28] i.e vaginal nodules vagina (figure 1), uterosacral ligaments, or pouch of Douglas; as well as adnexal masses [29]. One may also palpate induration or nodularity in the anterior area which may be related to deep endometriosis of the bladder or uterine anterior serosa. The painful nature of palpated lesions is characteristic. Pelvic examination also allows the identification of a possible myofascial syndrome [30]. Hypersensitivity phenomenon have been largely documented in women with endometriosis and the association with a myofascial syndrome is frequent, with around 60% of patients having both myofascial syndrome and endometriosis [31]. Allodynia, contact hyperpathia with tight clothing, and provoked vulvodynia should be tested as evidence of cutaneous and vulvar hypersensitivity [32,33]. These patients often have hyperpathy or real trigger points found in the muscles of the perineum or the deep part of

196 the buttocks [34]. Vaginal digital examination can reveal painful tension in the bundles of the
197 levator ani muscle and the pelvic portions of the internal obturator muscles. Painful tension
198 of the piriformis muscles and the gluteal portions of the internal obturator muscles can be
199 sought in the prone position. These pains may be indicative of a regional myofascial
200 syndrome, but are often part of a diffuse pain with extra-pelvic trigger points suggestive of a
201 central hypersensitivity syndrome such as fibromyalgia [35]. These hypersensitization
202 phenomena sustain the pain in patients with endometriosis and explain the persistence of
203 certain pains after surgical management of endometriosis [36]. The myofascial syndrome can
204 also be a differential diagnostic in women with chronic pelvic pain, with no concurrent
205 endometriosis.
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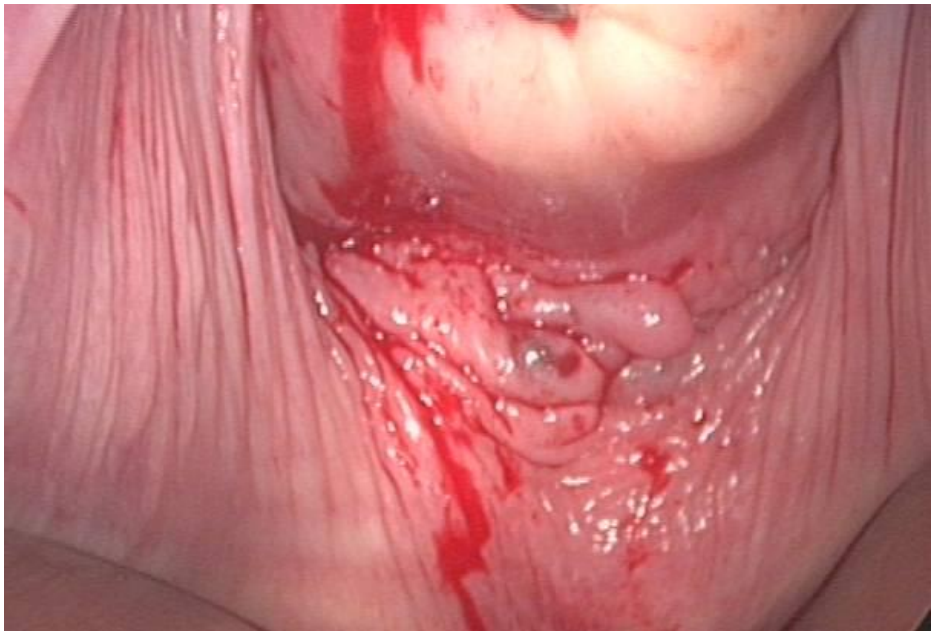

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208 Figure 1: bluish endometriosis spots of the posterior vaginal cul de sac

209 Regarding the most opportune moment of physical examination, several studies have shown
210 an improvement in the diagnostic relevance of pelvic examination during menstruation. A

previous study by Koninckx et al. showed a much greater diagnostic performance than during a routine examination outside of menstruation [37]. This better diagnostic performance must be balanced against the discomfort of a pelvic examination during the menstrual period in some women.

As stated in the latest ESHRE guidelines [9], vaginal examinations might be inappropriate in certain situations and in adolescents. Furthermore, it can be painful for some women. In these women, with high burden/discomfort (adolescents, due to religion, painful examination, sexual abuse in the past, virgo intacta, etc.), vaginal examination should ideally be omitted, and other medical technologies, as described below, should be used as a first step towards diagnosis.

Performance of pelvic examination in women with suspected endometriosis

Unlike questioning, clinical examination has a low sensitivity for the diagnosis of endometriosis, and it is therefore well established that a normal clinical examination does not eliminate the diagnosis: more than 50% of patients with laparoscopically proven endometriosis have a normal clinical examination [21]. A recent review by Pascoal et al. reported that the sensitivity and specificity of pelvic examination for the diagnosis of endometriosis were 18 – 88% and 76 – 100%, respectively [23]. The relevance of pelvic examination depends on the locations of endometriosis as highlighted by the work of Bazot et al. [38].

The main performances of pelvic examination according to endometriosis location is detailed in Table 1. The larger cohorts are those of Hudelist et al. reporting on 129 women [39] and the one of Bazot et al. reporting on 92 consecutive women [38]. In this last cohort, the sensitivity, LR + and LR - values of physical examination were, respectively, 73.5%, 3.3,

for uterosacral ligament endometriosis; 50%, 3.88, and 0.57, for vaginal endometriosis; and 46%, 1.67, and 0.75 for intestinal endometriosis. Eventually, the latest systematic review and meta-analysis by Zhang et al., that included a total of 30 studies with 4,565 participants compared the diagnostic performance of several modalities for endometriosis [40]. Physical examination had a pooled sensitivity of 71% (95% CI, 60- 80%) and a specificity of 69% (95% CI, 54- 82%), with an average diagnostic accuracy of 0.76 (95% CI, 0.66- 0.83).

Some studies evaluated the performance of models combining questioning symptoms and pelvic examination signs, increasing the performance of questioning alone models. The study by Chattot et al. established a predictive score for recto sigmoidal involvement comprising 4 parameters including a questioning component (the presence of blood in the stool at the time of menstruation) and a clinical examination component (palpation of a nodule on vaginal touch) [41]. Eskenazi et al. included 90 women with a scheduled laparoscopy or laparotomy [21]. Ultrasound and examination best predicted ovarian endometriosis, correctly classifying 100% of cases with no false positive diagnoses in the study sample.

Overall, the value of pelvic examination is conferred by its high positive likehood ratio and specificity. Its performance overpass these of questioning alone for diagnostic purpose. The value of pelvic examination is always compared with that of ultrasound and MRI. The low negative predictive value of "routine" ultrasound for the diagnosis of deep endometriosis has been reported in several studies [38,40,42]: it is relevant mainly for the diagnosis of endometrioma and cannot therefore replace clinical examination. Concerning the value of MRI, the great variability of the MRI protocols described in the literature and the absence of standardized reports limit the reproducibility of this examination in this indication [43]. In addition, the expertise of the radiologist and the location of the lesions

(lower agreement for determining damage to the utero sacral ligaments) have an influence on the performance of MRI [44,45]. No study has evaluated the sensitivity and specificity of pelvic MRI for the diagnosis of endometriosis without prior clinical examination.

Other benefits of the pelvic examination for the management

It is well established that the quality of the preoperative workup influences the quality of surgical excision and minimizes the risk of incomplete excision or an unplanned procedure [46]. Soliman et al 2017 showed that clinical diagnosis (non-invasive) also decreases the time to diagnosis [47]. Similar conclusions were drawn from the recent review by Agarwal et al 2019 in the American Journal of Obstetrics and Gynecology (AJOG) [11].

Limits

Some bias in the available literature deserves to be underlined, as it could influence the magnitude of the benefit of both medical questioning and pelvic examination. Most published data concern expert centers and clinicians with great experience in diagnosing endometriosis, with an increased prevalence among patients tested when compared to the general population [48].

There is also probably a bias linked to the duration of the evolution of symptoms at the time of the consultation and a verification bias inherent in the pathology (the comparator used is always laparoscopy; therefore, only patients with an indication for surgery have formal confirmation of the diagnosis).

Furthermore, as underlined in the latest recommendations of the CNGOF – HAS 2018 [48], there are no data from the 1st line clinical examination for the diagnosis of deep

endometriosis (primary care) since all the studies relate to the performance of examinations by expert - clinicians or highly experienced. In addition, studies are often conducted in "expert" centers, where the prevalence of the disease is probably higher than in the general population. Therefore, it is possible that the diagnostic relevance of clinical examination is overestimated in light of the literature. Eventually, it is possible that the performances of both physical examination and questioning are biased since only patients exhibiting a positive screening test (i.e., intense symptoms and / or positive physical examination) with undergo a laparoscopy to confirm the diagnostic in case of negative or indeterminate imaging. This bias could be responsible for an increased sensitivity and decreased specificity.

Another point is that of the bias associated with the duration of the evolution of symptoms at the time of the consultation, which may have implications for the findings of the clinical examination and history and modify their relevance. Finally, there is a verification bias inherent in the pathology and valid for all the studies included; the comparator used is always laparoscopy + / - histological analysis; therefore, only patients with an indication for surgery have formal confirmation (if possible) of the diagnosis.

To date, no study has evaluated the diagnostic relevance of history alone compared with pelvic examination alone. No study has assessed the diagnostic relevance of history alone compared with the combination of history and pelvic examination.

Conclusion

In women with suspected endometriosis, pelvic examination (vaginal speculum and digital vaginal examination) when positive increases the diagnostic value in association with questioning for symptoms. Informing patients on the usefulness of this examination will allow its realization within the framework of an empathetic relationship.

References

[1] US Preventive Services Task Force, Bibbins-Domingo K, Grossman DC, Curry SJ, Barry MJ, Davidson KW, et al. Screening for Gynecologic Conditions With Pelvic Examination: US Preventive Services Task Force Recommendation Statement. JAMA 2017;317:947–53. https://doi.org/10.1001/jama.2017.0807.

[2] Yilmaz FT, Demirel G. The relationship between body privacy and anxiety in women having gynecological examination. J Obstet Gynaecol J Inst Obstet Gynaecol 2021;41:1112–5. https://doi.org/10.1080/01443615.2020.1835845.

[3] Carugno J, Timmons D, Lederer M, Grady MM. Impact of using words with unpleasant emotional connotations on perceived patient discomfort during vaginal speculum examinations: A randomized controlled trial. Eur J Obstet Gynecol Reprod Biol 2020;247:203–6. https://doi.org/10.1016/j.ejogrb.2020.02.034.

[4] Gordts S, Koninckx P, Brosens I. Pathogenesis of deep endometriosis. Fertil Steril 2017;108:872-885.e1. https://doi.org/10.1016/j.fertnstert.2017.08.036.

[5] Eskenazi B, Warner ML. Epidemiology of endometriosis. Obstet Gynecol Clin North Am 1997;24:235–58. https://doi.org/10.1016/s0889-8545(05)70302-8.

[6] Meuleman C, Vandenabeele B, Fieuws S, Spiessens C, Timmerman D, D'Hooghe T. High prevalence of endometriosis in infertile women with normal ovulation and normospermic partners. Fertil Steril 2009;92:68–74. https://doi.org/10.1016/j.fertnstert.2008.04.056.

[7] Borghese B, Santulli P, Marcellin L, Chapron C. [Definition, description, clinicopathological features, pathogenesis and natural history of endometriosis: CNGOF-HAS Endometriosis Guidelines]. Gynecol Obstet Fertil Senol 2018;46:156–67. https://doi.org/10.1016/j.gofs.2018.02.017.

[8] Soliman AM, Surrey E, Bonafede M, Nelson JK, Castelli-Haley J. Real-World Evaluation of Direct and Indirect Economic Burden Among Endometriosis Patients in the United States. Adv Ther 2018;35:408–23. https://doi.org/10.1007/s12325-018-0667-3.

[9] ESHRE 38th Annual Meeting of ESHRE, ESHRE 2022 | Official Site n.d. https://www.eshre.eu/ESHRE2022 (accessed February 9, 2022).

[10] Collinet P, Fritel X, Revel-Delhom C, Ballester M, Bolze PA, Borghese B, et al. Management of endometriosis: CNGOF/HAS clinical practice guidelines - Short version. J Gynecol Obstet Hum Reprod 2018;47:265–74. https://doi.org/10.1016/j.jogoh.2018.06.003.

[11] Agarwal SK, Chapron C, Giudice LC, Laufer MR, Leyland N, Missmer SA, et al. Clinical diagnosis of endometriosis: a call to action. Am J Obstet Gynecol 2019;220:354.e1-354.e12. https://doi.org/10.1016/j.ajog.2018.12.039.

[12] Deffieux X, Rousset-Jablonski C, Gantois A, Brillac T, Maruani J, Maitrot-Mantelet L, et al. [Pelvic exam in gynecology and obstetrics: Guidelines for clinical practice]. Gynecol Obstet Fertil Senol 2023;51:297–330. https://doi.org/10.1016/j.gofs.2023.04.001.

[13] Fauconnier A, Chapron C. Endometriosis and pelvic pain: epidemiological evidence of the relationship and implications. Hum Reprod Update 2005;11:595–606. https://doi.org/10.1093/humupd/dmi029.

[14] Fauconnier A, Chapron C, Dubuisson J-B, Vieira M, Dousset B, Bréart G. Relation between pain symptoms and the anatomic location of deep infiltrating endometriosis. Fertil Steril 2002;78:719–26. https://doi.org/10.1016/s0015-0282(02)03331-9.

[15] De Graaff AA, D'Hooghe TM, Dunselman G a. J, Dirksen CD, Hummelshoj L, WERF EndoCost Consortium, et al. The significant effect of endometriosis on physical, mental and social wellbeing: results from an international cross-sectional survey. Hum Reprod Oxf Engl 2013;28:2677–85. https://doi.org/10.1093/humrep/det284.

[16] Nnoaham KE, Hummelshoj L, Kennedy SH, Jenkinson C, Zondervan KT, World

Endometriosis Research Foundation Women's Health Symptom Survey Consortium. Developing symptom-based predictive models of endometriosis as a clinical screening tool: results from a multicenter study. Fertil Steril 2012;98:692-701.e5. https://doi.org/10.1016/j.fertnstert.2012.04.022.
[17] Tirlapur SA, Kuhrt K, Chaliha C, Ball E, Meads C, Khan KS. The "evil twin syndrome" in chronic pelvic pain: a systematic review of prevalence studies of bladder pain syndrome and endometriosis. Int J Surg Lond Engl 2013;11:233–7. https://doi.org/10.1016/j.ijsu.2013.02.003.
[18] Bourdel N, Alves J, Pickering G, Ramilo I, Roman H, Canis M. Systematic review of endometriosis pain assessment: how to choose a scale? Hum Reprod Update 2015;21:136–52. https://doi.org/10.1093/humupd/dmu046.
[19] Marinho MCP, Magalhaes TF, Fernandes LFC, Augusto KL, Brilhante AVM, Bezerra LRPS. Quality of Life in Women with Endometriosis: An Integrative Review. J Womens Health 2002 2018;27:399–408. https://doi.org/10.1089/jwh.2017.6397.
[20] Gao X, Yeh Y-C, Outley J, Simon J, Botteman M, Spalding J. Health-related quality of life burden of women with endometriosis: a literature review. Curr Med Res Opin 2006;22:1787–97. https://doi.org/10.1185/030079906X121084.
[21] Eskenazi B, Warner M, Bonsignore L, Olive D, Samuels S, Vercellini P. Validation study of nonsurgical diagnosis of endometriosis. Fertil Steril 2001;76:929–35. https://doi.org/10.1016/s0015-0282(01)02736-4.
[22] Nawrocka-Rutkowska J, Szydłowska I, Rył A, Ciećwież S, Ptak M, Starczewski A. Evaluation of the Diagnostic Accuracy of the Interview and Physical Examination in the Diagnosis of Endometriosis as the Cause of Chronic Pelvic Pain. Int J Environ Res Public Health 2021;18:6606. https://doi.org/10.3390/ijerph18126606.
[23] Pascoal E, Wessels JM, Aas-Eng MK, Abrao MS, Condous G, Jurkovic D, et al. Strengths and limitations of diagnostic tools for endometriosis and relevance in diagnostic test accuracy research. Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol 2022;60:309–27. https://doi.org/10.1002/uog.24892.
[24] Vercellini P, Somigliana E, Viganò P, Abbiati A, Barbara G, Fedele L. Chronic pelvic pain in women: etiology, pathogenesis and diagnostic approach. Gynecol Endocrinol Off J Int Soc Gynecol Endocrinol 2009;25:149–58. https://doi.org/10.1080/09513590802549858.
[25] Chapron C, Lafay-Pillet M-C, Santulli P, Bourdon M, Maignien C, Gaudet-Chardonnet A, et al. A new validated screening method for endometriosis diagnosis based on patient questionnaires. EClinicalMedicine 2022;44:101263. https://doi.org/10.1016/j.eclinm.2021.101263.
[26] Fauconnier A, Drioueche H, Huchon C, Du Cheyron J, Indersie E, Candau Y, et al. Early identification of women with endometriosis by means of a simple patient-completed questionnaire screening tool: a diagnostic study. Fertil Steril 2021;116:1580–9. https://doi.org/10.1016/j.fertnstert.2021.07.1205.
[27] Bendifallah S, Puchar A, Suisse S, Delbos L, Poilblanc M, Descamps P, et al. Machine learning algorithms as new screening approach for patients with endometriosis. Sci Rep 2022;12:639. https://doi.org/10.1038/s41598-021-04637-2.
[28] Dc M, Re B. Retrocervical, retrovaginal pouch, and rectovaginal septum endometriosis. J Am Assoc Gynecol Laparosc 2001;8. https://doi.org/10.1016/s1074-3804(05)60543-9.
[29] Riazi H, Tehranian N, Ziaei S, Mohammadi E, Hajizadeh E, Montazeri A. Clinical diagnosis of pelvic endometriosis: a scoping review. BMC Womens Health 2015;15:39. https://doi.org/10.1186/s12905-015-0196-z.
[30] Kapurubandara SC, Lowes B, Sansom-Daly UM, Deans R, Abbott JA. A systematic review of diagnostic tests to detect pelvic floor myofascial pain. Int Urogynecology J

2022;33:2379–89. https://doi.org/10.1007/s00192-022-05258-7.
[31] Margueritte F, Afraoucene A, Furdui R, Armengaud C, Fauconnier A. [Assessment of neuropathic pain among women with suspected endometriosis based on two specific surveys]. Gynecol Obstet Fertil Senol 2023;51:111–6. https://doi.org/10.1016/j.gofs.2022.12.004.
[32] Ploteau S, Labat JJ, Riant T, Levesque A, Robert R, Nizard J. New concepts on functional chronic pelvic and perineal pain: pathophysiology and multidisciplinary management. Discov Med 2015;19:185–92.
[33] Jarrell J, Arendt-Nielsen L. Allodynia and Dysmenorrhea. J Obstet Gynaecol Can JOGC J Obstet Gynecol Can JOGC 2016;38:270–4. https://doi.org/10.1016/j.jogc.2016.02.001.
[34] Stratton P, Khachikyan I, Sinaii N, Ortiz R, Shah J. Association of chronic pelvic pain and endometriosis with signs of sensitization and myofascial pain. Obstet Gynecol 2015;125:719–28. https://doi.org/10.1097/AOG.0000000000000663.
[35] Clauw DJ, Schmidt M, Radulovic D, Singer A, Katz P, Bresette J. The relationship between fibromyalgia and interstitial cystitis. J Psychiatr Res 1997;31:125–31. https://doi.org/10.1016/s0022-3956(96)00051-9.
[36] Riant T, Rigaud J, Delavierre D, Sibert L, Labat J-J. [Predictive factors and prevention of chronic postoperative pelvic and perineal pain]. Progres En Urol J Assoc Francaise Urol Soc Francaise Urol 2010;20:1145–57. https://doi.org/10.1016/j.purol.2010.08.054.
[37] Koninckx PR, Meuleman C, Oosterlynck D, Cornillie FJ. Diagnosis of deep endometriosis by clinical examination during menstruation and plasma CA-125 concentration. Fertil Steril 1996;65:280–7.
[38] Bazot M, Lafont C, Rouzier R, Roseau G, Thomassin-Naggara I, Daraï E. Diagnostic accuracy of physical examination, transvaginal sonography, rectal endoscopic sonography, and magnetic resonance imaging to diagnose deep infiltrating endometriosis. Fertil Steril 2009;92:1825–33. https://doi.org/10.1016/j.fertnstert.2008.09.005.
[39] Hudelist G, Ballard K, English J, Wright J, Banerjee S, Mastoroudes H, et al. Transvaginal sonography vs. clinical examination in the preoperative diagnosis of deep infiltrating endometriosis. Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol 2011;37:480–7. https://doi.org/10.1002/uog.8935.
[40] Zhang X, He T, Shen W. Comparison of physical examination, ultrasound techniques and magnetic resonance imaging for the diagnosis of deep infiltrating endometriosis: A systematic review and meta-analysis of diagnostic accuracy studies. Exp Ther Med 2020;20:3208–20. https://doi.org/10.3892/etm.2020.9043.
[41] Chattot C, Huchon C, Paternostre A, Du Cheyron J, Chouillard E, Fauconnier A. ENDORECT: a preoperative score to accurately predict rectosigmoid involvement in patients with endometriosis. Hum Reprod Open 2019;2019:hoz007. https://doi.org/10.1093/hropen/hoz007.
[42] Eskenazi B, Warner M, Bonsignore L, Olive D, Samuels S, Vercellini P. Validation study of nonsurgical diagnosis of endometriosis. Fertil Steril 2001;76:929–35. https://doi.org/10.1016/S0015-0282(01)02736-4.
[43] Pascoal E, Wessels JM, Aas-Eng MK, Abrao MS, Condous G, Jurkovic D, et al. Strengths and limitations of diagnostic tools for endometriosis and relevance in diagnostic test accuracy research. Ultrasound Obstet Gynecol n.d.;n/a. https://doi.org/10.1002/uog.24892.
[44] Saba L, Sulcis R, Melis GB, Ibba G, Alcazar JL, Piga M, et al. Diagnostic confidence analysis in the magnetic resonance imaging of ovarian and deep endometriosis: comparison with surgical results. Eur Radiol 2014;24:335–43. https://doi.org/10.1007/s00330-013-3013-9.
[45] Jaramillo-Cardoso A, Shenoy-Bhangle A, Garces-Descovich A, Glickman J, King L, Mortele KJ. Pelvic MRI in the diagnosis and staging of pelvic endometriosis: added value of

structured reporting and expertise. Abdom Radiol N Y 2020;45:1623–36. https://doi.org/10.1007/s00261-019-02199-6.
[46] Leonardi M, Gibbons T, Armour M, Wang R, Glanville E, Hodgson R, et al. When to Do Surgery and When Not to Do Surgery for Endometriosis: A Systematic Review and Meta-analysis. J Minim Invasive Gynecol 2020;27:390-407.e3. https://doi.org/10.1016/j.jmig.2019.10.014.
[47] Soliman AM, Fuldeore M, Snabes MC. Factors Associated with Time to Endometriosis Diagnosis in the United States. J Womens Health 2002 2017;26:788–97. https://doi.org/10.1089/jwh.2016.6003.
[48] Fauconnier A, Borghese B, Huchon C, Thomassin-Naggara I, Philip C-A, Gauthier T, et al. [Epidemiology and diagnosis strategy: CNGOF-HAS Endometriosis Guidelines]. Gynecol Obstet Fertil Senol 2018;46:223–30. https://doi.org/10.1016/j.gofs.2018.02.012.
[49] Chapron C, Lafay-Pillet M-C, Santulli P, Bourdon M, Maignien C, Gaudet-Chardonnet A, et al. A new validated screening method for endometriosis diagnosis based on patient questionnaires. EClinicalMedicine 2022;44. https://doi.org/10.1016/j.eclinm.2021.101263.
[50] Nawrocka-Rutkowska J, Szydłowska I, Rył A, Ciećwież S, Ptak M, Starczewski A. Evaluation of the Diagnostic Accuracy of the Interview and Physical Examination in the Diagnosis of Endometriosis as the Cause of Chronic Pelvic Pain. Int J Environ Res Public Health 2021;18:6606. https://doi.org/10.3390/ijerph18126606.
[51] Arion K, Aksoy T, Allaire C, Noga H, Williams C, Bedaiwy MA, et al. Prediction of Pouch of Douglas Obliteration: Point-of-care Ultrasound Versus Pelvic Examination. J Minim Invasive Gynecol 2019;26:928–34. https://doi.org/10.1016/j.jmig.2018.09.777.
[52] Lafay Pillet MC, Huchon C, Santulli P, Borghese B, Chapron C, Fauconnier A. A clinical score can predict associated deep infiltrating endometriosis before surgery for an endometrioma. Hum Reprod Oxf Engl 2014;29:1666–76. https://doi.org/10.1093/humrep/deu128.
[53] Fedele L, Bianchi S, Carmignani L, Berlanda N, Fontana E, Frontino G. Evaluation of a new questionnaire for the presurgical diagnosis of bladder endometriosis. Hum Reprod Oxf Engl 2007;22:2698–701. https://doi.org/10.1093/humrep/dem236.
[54] Hudelist G, Oberwinkler KH, Singer CF, Tuttlies F, Rauter G, Ritter O, et al. Combination of transvaginal sonography and clinical examination for preoperative diagnosis of pelvic endometriosis. Hum Reprod Oxf Engl 2009;24:1018–24. https://doi.org/10.1093/humrep/dep013.

Author	Type of study	Population included	Intervention	Gold standard	95% CI
Zhang, 2020 [40]	Systematic review and meta - analysis	30 studies including a total of 4565 women.	Physical examination, ultrasound, MRI	Laparoscopy + / - histology	Se 0.71 (0.6 – 0.8) Sp 0.69 (0.54 – 0.82) Diagnostic Odds Radio 5 (3 – 12) LR+ 2.3 (1.5 – 3.6) LR- 0.42 (0.29 – 0.61) AUC 0.76 (0.66 – 0.83) Post-test probability (+ 37%, - 10%) significantly different from the pre-test probability (20%)
Nnoaham, 2012 [16]	Prospective, observational including 19 hospitals in 13 countries	771 women phase I (including 360 with endometriosis) et 625 women phase II (including 364 with endometriosis)	Questionnaires 25 questions	Laparoscopy	Without ultrasound: LR+ 1.5 LR- 0.35 With ultrasound: LR+ 5.39 LR- 0.47
Chapron, 2022 [49]	Case - Controles	2005 - 2018 3 levels of analysis: development cohort (N = 1675 inlcuding 880 with endometriosis), internal validation cohort (N = 842 including 395 with endometriosis) and an external validation cohort (N = 308 including 220 with endometriosis)	Questioning	Laparoscopy	For score 1 >=25 Sp 91% (CI 95% 89 – 93)
Nawrocka-Rutkowska J, 2021 [50]	Prospective cohort	148 women hospitalized in a Polish gynecological department with chronic pelvic pain and at least one symptom suggestive of endometriosis for more than 6 months.	Questioning and physical examination	Diagnostic laparosocpy	The association of “catamenial increased pain and painful sexuel intercourse: Se 63.34%, Sp 65.69%, PPV 12.96% et NPV 95.74%
Bazot, 2009 [38]	Cohort study	92 women with endometriosis	Questioning, physical examination, ultrasound, endorectal ultrasound and MRI	Laparoscopy	For the utero-sacral ligaments, LR+ 3.3 (0,95 – 11.1) and LR- 0.34 (0.22 – 0.58) For the vagina: LR+ 3.88 (1.85 – 8.11) et LR – 0.57 (0.40 – 0.83) For the recto-vaginal pouch, LR+ 4.91 (0.92 – 26.2) et LR- 0.85 (0.64 – 1.13) For digestive lesions, LR+ 1.67 (0.87 – 3.19) and LR – 0.75 (0.54 – 1.03)
Arion, 2019 [51]	Data from a prospective cohort	269 women incluing 41 with Douglas pouch with endometriosis	Physical examination	Endovaginal ultrasound « sliding sign »	Se 0.24 (0.12 – 0.40) Sp 0.93 (0.89 – 0.96) PPV 0.40 (0.24 – 0.58) NPV 0.87 (0.85 – 0.89) LR+ 3.7 (1.8 – 7.7) LR- 0.81 (0.68 – 0.97)
Lafay Pillet, 2014 [52]	Cohort study	326 women with ovarian endometriosis operated between january 2005 and octobre 2011 : 164 with deep infiltrating endometriosis and 162 without deep infiltrating endometriosis. patientes avec endométriome opérées entre Janvier 2005 et Octobre 2011 : 164 avec endométriose profonde et 162 sans endométriose profonde	Questioning	Laparoscopy + / - histology	No LR+/- on the VAS except for urinary pain LR + = 4
Fauconnier, 2021 [26]	Prospective case – controls	105 with endometriosis and 197 controls with no endometriosis	Questionnaire ENDOPAIN-4D.	Laproscopy + / - histology	LR+ 30.5 / LR- 0.03 With pre-test prevalence of 10%, post-test + 77.2% / - 0.3%
Fedele, 2007 [53]	Cohort study	157 women operated with chronic pelvic pain including 127 with endometriossi and 14 bladder endometriosis. The objective was to predict bladder endometriosis.	Questionnaire American Urologic Association Symptom Index modified partially	Laparoscopy or laparotomy	With a threshold set at 9, max Se (93%) and Sp (88%)

Hudelist, 2009 [54]	Prospective cohort	200 consecutive women with symptoms suggestive of endometriosis. Eventually, 135 cases (68%) of endometriosis.	Questioning, physical examination and ultrasound	Laparoscopy + / - histology	Physical examination alone Sp 89 – 100% Se 23 – 88%, PPV 65 – 100%, NPV 85 – 99%, Accuracy 86 – 99%. Physical examination and endovaginal ultrasound Se 67 – 100%, Sp 86 – 100%, PPV 50 – 100%, NPV 93 – 100, Accuracy 86 – 100%

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