Early identification of women with endometriosis by means of a simple patient-completed questionnaire screening tool: a diagnostic study

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Objectives: To assess the value of a self-completed questionnaire based on patients' verbal descriptors of pelvic painful symptoms to identify women with endometriosis.
Design: Prospective 1:2 nonmatched case-control study.
Setting: Three French endometriosis referral centers.
Patient(s): Endometriosis cases were women aged 18–45 years with endometriosis confirmed by histology. Controls were as follows: asymptomatic women attending a gynecologic consultation for routine examination; women without evidence of endometriosis consulting for pain/infertility; and population-based controls from the same urban locations.
Intervention(s): All women completed the 21-item yes/no questionnaire about painful symptoms.
Main Outcome Measure(s): The area under the receiver operating characteristic curve of the full question set model based on binary logistic regression and the diagnostic accuracy of low- and high-risk classification rules based on selected threshold of the prediction model.
Result(s): We included 105 cases and 197 controls (45 asymptomatic consultation-based controls, 66 women without endometriosis consulting for pain/infertility, and 86 population-based controls). The full question set prediction model, including age, had an area under the receiver operating characteristic curve of 0.92 (95% confidence interval, 0.87–0.95) after internal validation. The high-risk classification rule had a specificity of 98.0% and a positive likelihood ratio of 30.5. The low-risk classification rule had a sensitivity of 98.1% and a negative likelihood ratio of 0.03. For a hypothesized pretest prevalence of 10%, the high- and low-risk prediction rules ascertained endometriosis with posttest probability rates of 77.2% and 0.3%, respectively.
Conclusion(s): A self-completed patient-centered questionnaire can identify women at low or high risk of endometriosis with a high diagnostic accuracy and, thus, may help early identification of women with endometriosis. (Fertil Steril® 2021;116:1580-89. ©2021 by American Society for Reproductive Medicine.)
El resumen está disponible en Español al final del artículo.

Key Words: Endometriosis, pelvic pain, questionnaires, diagnostic accuracy, screening

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The prevalence of endometriosis is between 5% and 11% in women of childbearing age (1, 2). Both disease expression and disease progression can vary markedly (3). Consequently, treatment options vary from occasional use of painkillers to multiple extensive surgeries including organ resection (4).

The gold standard for the diagnosis of endometriosis is visual inspection with histologic confirmation of macroscopic lesions, usually by laparoscopy (5, 6). However, over the past two decades, imaging examinations such as specialized ultrasound (US) and magnetic resonance imaging (MRI) have been shown to be accurate in diagnosing the most severe forms of endometriosis, including endometrioma or deep infiltrating endometriosis (DIE) (7), marking a shift toward noninvasive diagnosis (8). Nevertheless, the unlimited use of these examinations is not applicable in primary care due to cost-effectiveness concerns and the serious consequences of false positives incurring unnecessary laparoscopy (7, 9).

Most women report having to see a doctor five times or more before being diagnosed or referred to a specialized center (10). Misdiagnosis or referral to inappropriate secondary care and a lack of knowledge or awareness of endometriosis are barriers to accurate diagnosis at the primary care level (11). Thus, improving these parameters could help the primary care physician to correctly identify women with endometriosis.

Preliminary studies based on questioning suggested that assessing endometriosis symptoms in a standardized fashion helps diagnose DIE (12, 13). However, a 2017 literature review did not identify any fully validated, symptom-based, patient-reported questionnaires to screen women for endometriosis (14). From the perspective of patient empowerment and in collaboration with the French Association of Patients with Endometriosis (EndoFrance, http://www.endofrance.org/), we developed a self-completed questionnaire based on patients' verbal descriptors to measure the painful symptoms of endometriosis, the ENDOPAIN-4D questionnaire (15, 16), which could constitute a solid basis to develop an effective screening tool to diagnose endometriosis.

The present study aimed to assess the value of the ENDOPAIN-4D questionnaire to identify women with endometriosis. For this purpose, we designed a prospective non-matched case-control study, comparing women with a primary biopsy-proven diagnosis of endometriosis to control women without endometriosis within the same age range and from the same urban locations.

MATERIALS AND METHODS

Setting

The present study was part of a prospective observational study conducted in three French endometriosis referral centers (Centre Hospitalier de Versailles, Centre Hospitalier Intercommunal de Poissy-Saint-Germain, and Centre Hospitalier Universitaire de Poitiers) between January 1, 2017, and June 30, 2019. These centers work together with similar preoperative assessments, including a standardized self-completed pelvic pain symptom and quality of life questionnaire, a standardized clinical examination, and systematic specialized US examination (performed according to a US-based endometriosis staging system [17]) and MRI examination. Whenever possible, surgical treatment consists of complete excision of the endometriosis lesions. The type of surgery depends on the lesion characteristics and locations. We systematically use a description sheet for the anatomical locations of the endometriosis lesions, which reports the localization of endometriosis implants and the subtype (endometriosis with or without DIE and the depth of infiltration). Patients are also classified according to the revised American Society for Reproductive Medicine (r-ASRM) score (18).

The cases were consecutive premenopausal women aged 18–45 years who had undergone primary laparoscopic surgery with histologically confirmed endometriosis and who gave their consent to participate to the registry. All women had an imaging-confirmed diagnosis of endometriosis as part of their preoperative workup (19). Women with incidental endometriosis discovered at laparoscopy were not included. Women with a negative histology, those with amenorrhea of more than 3 months, and those who did not respond to the preoperative questionnaire, or who responded to fewer than 50% of the items, were excluded. Patients with previous surgery for endometriosis were also excluded.

The controls were recruited during the same period. They were premenopausal women within the same age range as the cases and resident in the same geographical setting as the cases (i.e., the west suburb of Paris and Poitou-Charentes, France). The women were recruited as follows: consultation-based controls comprising women from the same areas as the cases consulting either for a routine gynecologic examination or request for contraception; women consulting for gynecologic symptoms including pain or infertility with specialized imaging (i.e., MRI examination or specialized US) or laparoscopy excluding endometriosis; and population-based controls comprising women recruited by social networks, friends or relations of the patients, or relational networks of the staff at the participating centers and of EndoFrance members. The exclusion criteria for the controls were a previous diagnosis of endometriosis, either by surgery or by imaging, or ongoing examination for a clinical suspicion of endometriosis; current treatment to stop menstruation; or amenorrhea of more than 3 months.

Predictors

Each woman who agreed to participate in the study completed a self-completed questionnaire containing the ENDOPAIN-4D. This questionnaire was developed according to the Food and Drug Administration recommendations for patient-reported outcome (PRO) measures (20). It was initially based on women's verbal descriptions of the pain symptoms of endometriosis (15). It was then developed further through a modified Delphi survey of patients and physicians that demonstrated content validity. The ENDOPAIN-4D comprises 21 items divided into four subparts: *Spontaneous pelvic pain and dysmenorrhea* (questions 1 to 10); *Dyspareunia* (questions 11 to 13); *Intestinal pain symptoms* (questions 14 to 16); and *Other symptoms* (questions 17 to 21). The questionnaire has two forms: a short form with yes/no answers

(specifically designed for diagnostic purposes) and an expanded form with pain intensity measured on an 11-point numerical rating scale as recommended by the World Endometriosis Research Foundation Endometriosis Phenome and Biobanking Harmonisation Project (WERF-EPHect) (for research purposes) (21). The initial version of the questionnaire was in French, and appropriate translation and back translation of the questionnaire were performed to obtain the English version of the ENDOPAIN-4D. The questionnaire is available online at https://ars.els-cdn.com/content/image/1-s2.0-S2468784717302271-mmc2.docx. For the present study, we used the short form (yes or no) questionnaire. The questionnaire was provided to the patients in a paper version and filled in by pencil during the 3-month time frame before surgery for the cases. The questionnaire had no role in the decision to perform the surgery.

Sample Size

We aimed to develop at least one clinical decision rule to diagnose patients at high risk of endometriosis using the questionnaire. We aimed for a specificity (Sp) of the classification algorithm of at least 95% and a positive likelihood ratio (LR+) of at least 10 (22). We planned to enroll approximately one case for two controls to simulate a prevalence of 33%, similar to the prevalence in women consulting for gynecologic symptoms (i.e., menstrual disorders, pain, and/or infertility) (2). The number of required patients with endometriosis was estimated as follows: we hypothesized that the classification algorithm would be clinically useless if its LR+ was under 5 (23). Based on the calculation of the lower bound of the 95% confidence interval (95% CI) of the LR, approximately 84 cases and 168 controls were required. Based on this estimation, we calculated that the precision of the area under receiver operating characteristic curve (ROC-AUC) of the classification algorithm would be of ±0.04 for a hypothesized ROC-AUC of 0.90.

Statistical Analysis

The endometriosis cases and the controls were compared for each yes/no variable of the ENDOPAIN-4D, using a χ^2 test. The diagnostic performance of each of these variables ($P<.05$) was assessed using sensitivity (Se), Sp, LR+, negative likelihood ratio (LR−), and diagnostic odds ratio. Multiple logistic regression analysis was then used to estimate the predictive ability of the questions associated with endometriosis ($P<.05$). To respect the PRO instrument format used during the instrument development process (20), we used the full model approach, that is, all candidate variables were included in the logistic prediction (further referred as the full question set model) (24). Multiple imputations were performed to account for missing data in the analysis (25). Adjusted diagnostic odds ratios were calculated with their 95% CI. The discrimination performance of the model in the diagnosis of endometriosis was specified by calculating the ROC-AUC (26).

We performed an internal validation of the prediction model with the leave-one-out cross-validation procedure to correct for overoptimism in the predictive performance of the model (27). In this method, each of the n observations of the entire sample was individually assigned to the test set, out of the calibration data set, recalibrating the model omitting the case, and predicting the observation that was left out. This was repeated n times, and the results of the n-th iterations were then pooled (28). We also conducted sensitivity analyses to test the discriminative ability of the model according to the subset of controls whether symptomatic (i.e., women without evidence of endometriosis consulting for pain/infertility) or not (i.e., asymptomatic consultation-based controls and population-based controls).

To find the best clinically applicable model to classify women as being at high or low risk of endometriosis, we derived classification rules from the prediction score: first, a *rule-out* classification by selecting a cutoff with an Se of >95% and an LR− of <0.10 and, second, a *rule-in* classification by another cutoff with an Sp of >90% and an LR+ of >10 (22). The predictive value of endometriosis according to the low- and high-risk classification rules were calculated for the actual prevalence of endometriosis (i.e., the predetermined prevalence of 1:2). We also assessed the predictive value of the classification rules according to the different subset of controls. To emulate the impact of our decisions rule at the population level, we estimated the posttest probability of endometriosis following a hypothetical prevalence of endometriosis of 10% reflecting the expected prevalence in the general population (2).

All statistical analyses were performed with R Studio 3.5.2 software.

All women received written information about the study and agreed to participate. The Institutional Review Board, *Comité de protection des personnes-IV Sud-Est*, approved the research protocol (n°18/002).

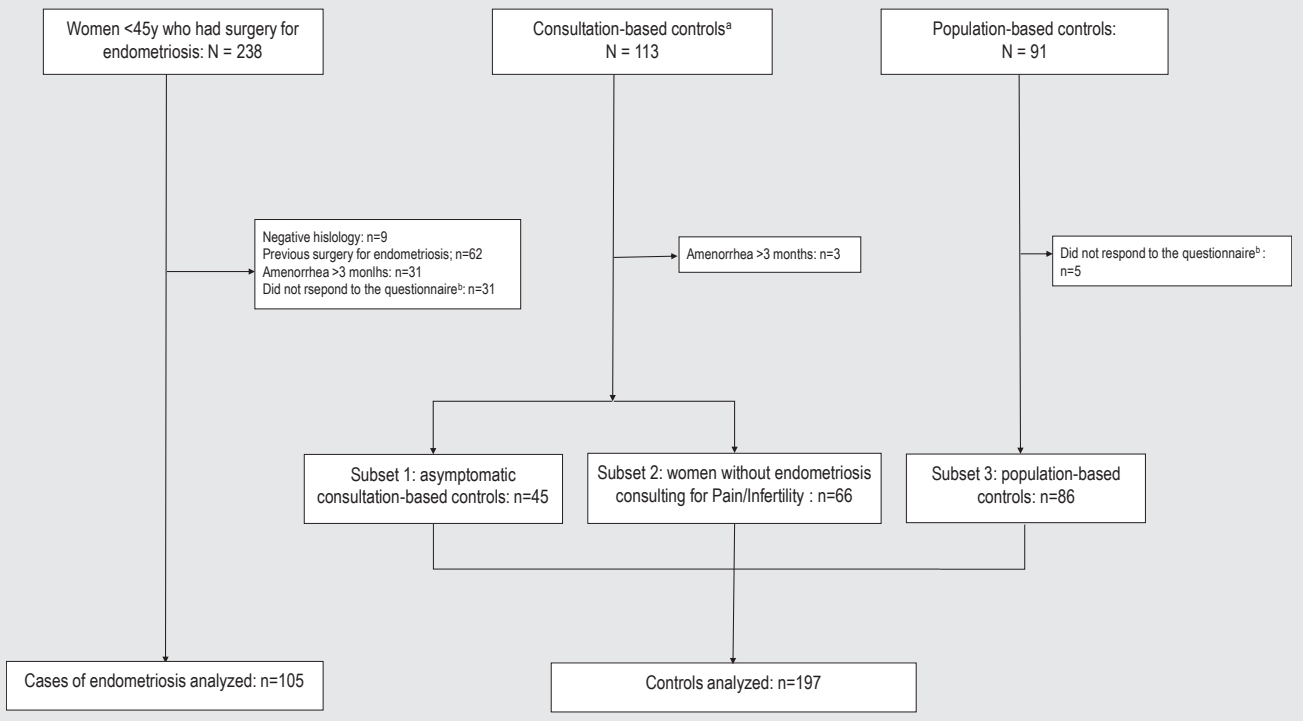
This study was performed with involvement of women with endometriosis who contributed to the development of the ENDOPAIN-4D questionnaire (16). Two members of the French Association of Patients with Endometriosis (Endo-France) were invited to comment on the study design and participated in the interpretation of the results and the writing of the manuscript.

RESULTS

Figure 1 shows the study flowchart. A total of 105 cases of endometriosis and 197 controls were included. The control group included three subsets: 45 asymptomatic consultation-based controls (23%), 66 women without evidence of endometriosis consulting for pain/infertility (34%), and 86 population-based controls (44%). Among the 66 symptomatic controls with pain/infertility, endometriosis was excluded by laparoscopy in 8 women (12%), by MRI in 23 (35%), and by transvaginal US-based endometriosis staging system in 35 (53%).

The characteristics of the endometriosis cases and controls are shown in Table 1. The cases were older than the controls.

FIGURE 1



Flowchart of the study participants.

Fauconnier. Questionnaire for endometriosis screening. Fertil Steril 2021.

On bivariate analysis, all 21 questions were significantly associated with endometriosis (Supplemental Table 1, available online).

For logistic regression modeling, we included all 21 questions according to the "full model method" as planned. As there was a linear relationship between age and the risk of endometriosis, we also included age in the prediction model. The logistic coefficients of the full question set model are shown in Supplemental Table 2. Age, nonmenstrual pelvic pain, worsening pain, disabling pain, interruption of sexual intercourse, painful bowel movements, pain when urinating, and infertility were independently related to endometriosis ($P<.05$). The item *dyspareunia* (Supplemental Table 2) showed a counterintuitive change in the coefficient sign between the unadjusted coefficient (significant positive effect) and adjusted coefficient (negative effect) due to collinearity between this item and the item *interruption of sexual intercourse* (adjusted odds ratio, 18.5; 95% CI, 10.0–34.3).

The ROC-AUC (Fig. 2) of the full question set model was 0.95 (95% CI, 0.93–0.98). Using the leave-one-out validation procedure, the ROC-AUC decreased slightly to 0.92 (95% CI, 0.87–0.95). When assessing the ROC-AUC separately for symptomatic and asymptomatic controls (Fig. 2), the discriminant value of the model decreased for symptomatic controls only (0.93; 95% CI, 0.89–0.97) vs. the asymptomatic controls (0.96; 95% CI, 0.94–0.99).

Two risk groups of endometriosis were then derived from the prediction model equation. First, a low-risk group (rule-out decision) of endometriosis was based on a threshold of predicted probability of <0.11. This classification rule had an Se of 98.1%, LR− of 0.03, and observed probability of 1.4%. These results remained unchanged when using asymptomatic controls only (Table 2). Second, a high-risk group (rule-in decision) was based on a threshold of prediction score ≥ 0.83. This threshold had an excellent diagnostic accuracy (Sp, 98.0%; LR+, 30.5) and an observed probability of endometriosis of 94.1% (Table 2). When using the subset of symptomatic controls (i.e., women without evidence of endometriosis consulting for pain/infertility), the diagnostic value of the high-risk classification decreased but stayed above the expected level (Table 2).

For a hypothesized pretest prevalence of 10% of endometriosis, representing the prevalence in the general population, the high- and low-risk prediction models would ascertain endometriosis with posttest probability rates of 77.2% (lower bound 95% CI, 55.9%) and 0.3% (upper bound 95% CI, 1.2%), respectively. We created a free interactive web app, called shinyDEVA (https://arnaudfauconnier.shinyapps.io/shinyDEVA/), that determines the risk group for individual patients with their predicted probability of endometriosis.

DISCUSSION

Using a simple "yes or no" questionnaire based on patients' verbal descriptors of painful symptoms of endometriosis, we developed a clinical prediction model with two classification

TABLE 1

Demographic features and disease characteristics of the study participants.

Characteristics	Endometriosis cases (N = 105)	Control women N (= 197)			*P* value
		Subset 1: Asymptomatic consultation-based controls (N = 45)	Subset 2: Women without endometriosis consulting for pain/infertility (N = 66)	Subset 3: Population-based controls (N = 86)	
Center, n (%)					
Center 1 (CHV)	38 (36)	5 (11)	0 (0)	0 (0)	
Center 2 (CHIPS)	59 (56)	15 (33)	47 (71)	19 (22)	
Center 3 (CHU Poitiers)	8 (8)	25 (56)	3 (5)	14 (16)	< .001
West-Paris suburb office-based practices	0 (0)	0 (0)	16 (24)	0 (0)	
EndoFrance network	0 (0)	0 (0)	0 (0)	53 (62)	
Age (years ± 1 SD)	33.0 ± 6.0	28.6 ± 6.3	32.7 ± 6	29.6 ± 5.8	< .001
BMI (kg/m^2 ± 1 SD)	24.1 ± 5.6	23.1 ± 3.8	26.3 ± 6.1	23.2 ± 4.0	< .001
Gravidity, median (interquartile range)	0 (1)	0 (2)	0 (1)	0 (1)	.6
Parity, median (interquartile range)	0 (1)	0 (1)	0 (0)	0 (1)	.2
Prior pelvic surgery, n (%)[a]	23 (22)	2 (4)	16 (24)	28 (14)	.011
Infertility, n (%)	46 (44)	0 (0)	45 (68)	0 (0)	< .001
r-ASRM stage, n (%)					
I	14 (13)				
II	30 (29)				
III	22 (21)				
IV	39 (37)				
Cases with endometrioma	41 (39)				
Cases with intestinal DIE	38 (36))				

Note: BMI = body mass index; DIE = deep infiltrating endometriosis; CHIPS = Centre Hospitalier Intercommunal de Poissy-Saint-Germain; CHU Poitiers = Centre Hospitalier Universitaire de Poitiers; CHV = Centre Hospitalier de Versailles; SD = standard deviation; r-ASRM = Revised American Society for Reproductive Medicine.

[a] Women with previous surgery for endometriosis were excluded.

Fauconnier. Questionnaire for endometriosis screening. Fertil Steril 2021.

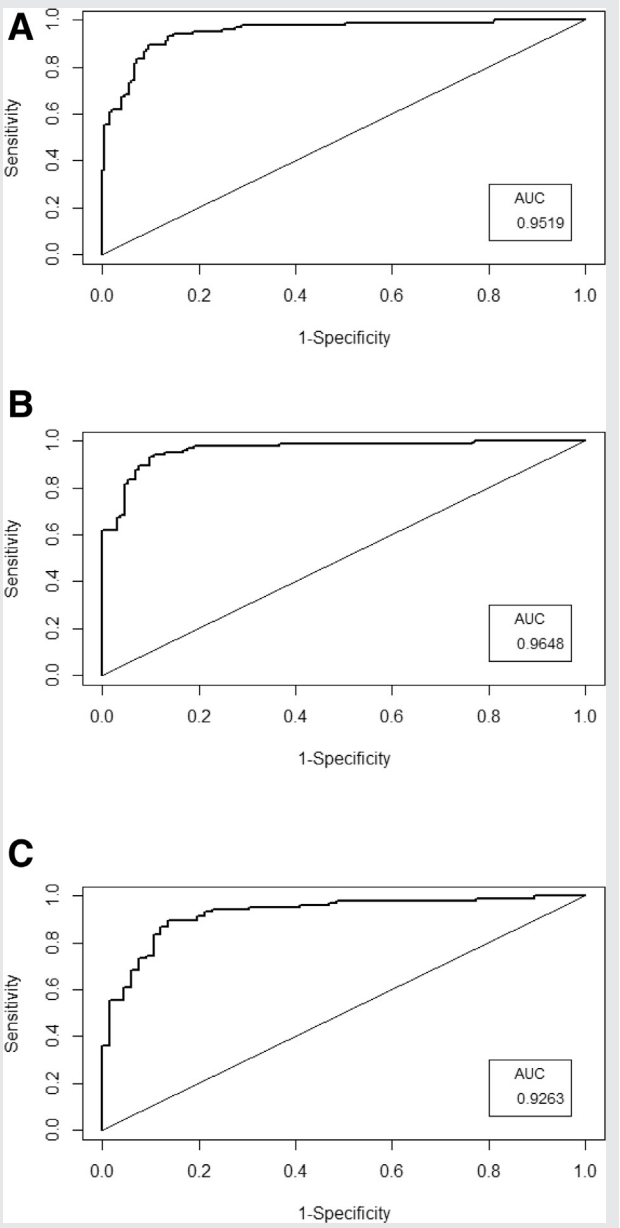
rules. The first one, the low-risk classification, rules out a diagnosis of endometriosis with a high accuracy even in a medium prevalence population. The second, the high-risk classification, rules in a diagnosis of endometriosis with a high probability even in a low prevalence population. These classification rules may help screen for endometriosis among women of childbearing age in the general population or at the primary care level.

Late diagnosis of endometriosis is now recognized as being a major problem. The average time to diagnosis varies from 3 to 11 years (29). The consequences of late diagnosis are prolonged patient uncertainty inducing unnecessary distress and delayed treatment (30, 31). Furthermore, as for cancer, it has been suggested that delay in diagnosis may contribute to disease progression and result in more complex treatment modalities (13). Several teams have sought to shorten time to diagnosis of endometriosis by various means: biomarkers (32); standardized questioning (33); or symptom-based predictive models (14). Predictive models based on a combination of examination and first-level pelvic US have also been developed (34, 35). Unfortunately, these methods are of limited value in terms of discrimination and are, therefore, not applicable in the general population or in a primary care setting where the prevalence of endometriosis is moderate. An algorithm for clinical diagnosis of endometriosis based on a detailed review of signs and symptoms has also been proposed to reduce time to diagnosis (13). However, it does not allow for the collection of clinical predictors in a standardized fashion and requires clinical experience of the disease, which would tend to rule it out for use in a primary care setting. In contrast, our prediction algorithm is based on answers to questions from the patients themselves without amendment or interpretation by a clinician or other health care provider (20, 36). In 2010, an international meeting on evidence-based practice in endometriosis and pain scoring (37) suggested developing a new patient-derived pain scale. However, the suggestion was not retained. We selected to do so because the existing questionnaires (33, 35, 38) do not have sufficient content validity and, most of all, had not been subjected to patient-centered development as recommended by the Food and Drug Administration guidelines for PROs. The ENDOPAIN-4D meets these criteria. The questionnaire was initially based on women's verbal descriptions of the pain symptoms of endometriosis and was further developed through a modified Delphi survey of patients and physicians. The final questionnaire, thus, demonstrated content validity, that is, that it measures the subjective experiences of women with pain from endometriosis. The questionnaire was developed according to a rigorous methodological process and with proven content validity (16). We, thus, provide here a standardized and inexpensive screening tool to identify endometriosis in women with sufficient accuracy to be used at the primary care level according to a two-step procedure similar to the one proposed for imaging (7).

Strengths

One of the major strengths of the present study is that our cases consisted of women who had undergone surgery for

FIGURE 2



Discriminative ability of the full set model using the area under receiver operating characteristic curve (ROC-AUC), endometriosis cases vs. all control groups **(A)**, vs. asymptomatic (population-based and asymptomatic women attending a gynecologic consultation) control group **(B)**, and vs. women without evidence of endometriosis consulting for pain/infertility **(C)**.

Fauconnier. Questionnaire for endometriosis screening. Fertil Steril 2021.

typical symptoms of endometriosis with positive diagnosis on preoperative imaging and confirmation by laparoscopy with excisional surgery and confirmatory histology. On the other hand, the controls were healthy volunteers from the general population or from gynecologic consultations (i.e., with gynecologic symptoms but with imaging examination excluding endometriosis). We deliberately chose to mix symptomatic and asymptomatic controls to obtain an algorithm that would be valid in different settings including primary care or in the general population (where women can have symptoms and ask for advice). The prediction algorithm was developed a posteriori, and therefore, the questionnaire had no role in the decision to operate, which limits the risk of referral bias (39). Finally, because of the strength of the discrimination power of the prediction model, we could select meaningful classification rules of sufficiently high diagnostic value to remain relevant in the worst possible situations, that is, assessing the low-risk endometriosis value in the subgroups of population-based controls and asymptomatic women and the high-risk endometriosis value in the subgroup of controls with symptoms suggestive of endometriosis. This allowed us to minimize the risk of error in an independent population, including at the general population and the primary care levels and even at the secondary level (23, 40).

Limitations

First, the cases we included had all undergone surgery for endometriosis and, therefore, constituted a population with the more severe forms of the disease (41, 42) and having significant pain or infertility symptoms (9). Conversely, on a pragmatic basis, our screening process excluded the silent and minimal forms of the disease and identified women with the "endometriosis syndrome," that is, forms with extensive peritoneal endometriosis, DIE, and/or ovarian cysts, responsible for disabling symptoms that must absolutely be treated (43).

Another weakness lies in the way we constructed the control group. Indeed, the controls were not selected randomly by matching with the cases. Rather, our prospective study was based on the inclusion of voluntary female controls from different settings: healthy controls inside or outside the hospital circuit and from the general population and symptomatic women but without evidence of endometriosis. We aimed to include controls from various entry points to avoid an obvious comparison between totally asymptomatic women and severely affected cases, thus artifactually increasing the contrast between both groups and ultimately being of limited interest (44). Nonetheless, symptomatic patients with pain/infertility without imaging evidence of endometriosis can still include a proportion of women with peritoneal endometriosis and/or small endometriotic nodules that cannot be detected on imaging. Inversely, including only women with negative laparoscopy would have exposed us to serious referral bias as most of the women would have undergone laparoscopy for symptoms mimicking endometriosis (39). We are, nevertheless, confident in our results as the sensitivity analyses demonstrated the robustness of the high-risk classification in the context of a consultation for pain or infertility.

Third, the risk calculation of endometriosis we provide here must be interpreted with caution in other settings. The choice to build a classification algorithm on the full set of the 21 questions, independent of their statistical significance, avoids overfitting and selection bias and, thus, provides correct standard errors that increase its generalizability (45).

TABLE 2

Classification and diagnostic accuracy of the rule-out (cutoff value, < 0.11) and rule-in (cutoff value, ≥0.83) decisions for the overall population and according to the different control subsets.

	Endometriosis cases (n)	Controls (n)	Actual probability of endometriosis (%)	Se (%)	Sp (%)	LR
		All controls: (Subsets 1, 2, and3)				
	105	197	35			
Low risk of endometriosis (rule-out decision)	2	138				
Estimate			1.4	98	70	0.03[a]
Lower bound			0.0	95.5	63.7	0.01[a]
Upper bound			3.4	100.7	76.4	0.11[a]
High risk of endometriosis (rule-in decision)	65	4				
Estimate			94	62	98	30.5[b]
Lower bound			89	53	96	11.4[b]
Upper bound			100	71	100	81.4[b]
Sensitivity analyses						
		Asymptomatic controls only: (Subsets 1 and 3)				
	105	131	44			
Low risk of endometriosis (rule-out decision)	2	105				
Estimate			1.9	98	80	0.02[a]
Lower bound			0.0	95	73	0.01[a]
Upper bound			4.4	100	87	0.09[a]
		Pain/infertility controls only: (Subset 2)				
	105	66	61			
High risk of endometriosis (rule-in decision)	65	4				
Estimate			94	62	94	10.2[b]
Lower bound			89	53	88	3.9[b]
Upper bound			100	71	100	26.7[b]

Note: LR = likelihood ratio; Se = sensitivity; Sp = specificity.
[a] Negative LR.
[b] Positive LR.

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Furthermore, it is significant that a PRO instrument, such as ours, be consistent with the format that is used during the development process (20). However, external validity—confirmation that the model performs as expected in a fresh set of similar patients—is a critical requirement for the present model (26). External validation of the risk models must be provided in the general population and in primary care practice for women consulting for gynecologic symptoms, as different distribution of predictor values ("case-mix") can influence some aspects of the model's performance (46). This was the case here as the diagnostic performance of the high-risk classification faded with the subset of symptomatic controls.

Implications

We suggest that the tool we present here could be used as a sequential stepwise diagnostic strategy at the primary level of care to reduce unnecessary interventions and improve the diagnostic process in conjunction with the appropriate use of noninvasive imaging modalities (7). The prevalence of endometriosis is unknown in primary care settings and may be highly dependent on the reason for consulting: it may be as high as high as 30%–50% in women consulting for pelvic pain or infertility (13, 47, 48). Confirmatory diagnostic examinations are only recommended in high-prevalence populations because a positive result may generate consequences in terms of costs and false-positive rates (7, 8). For example, MRI may generate a false-positive rate of up to 20% (7). Using our high-risk criteria to select women for MRI at the primary care level may have a significant impact on health care value: lower false-negative rates; decreased cost; and improved early diagnosis rates. In this context, we suggest that the primary aim of our model is to reduce time to diagnosis by referring women at high risk of endometriosis for specialized imaging examination, including MRI (8), and/or to a referral center. Inversely, using our low-risk criteria may decrease the need for unnecessary procedures and the potential harm of overdiagnosis. Finally, mild to moderate dysmenorrhea is easy to treat at the primary care level by the simple use of a combined oral conceptive (49), and in the short term, there is no need to conduct further investigations for evidence of peritoneal endometriosis, which might regress spontaneously.

On the other hand, the prevalence of endometriosis in the general population is generally stated to be at approximately

10% (1, 2). Using this estimate, we ensure that our high-risk model would have a sufficient positive predictive value to be useful in selected population as young adults with mild or moderate dysmenorrhea. However, large population-based studies in developed countries resulted in lower estimate in which 1.1%–1.5% of women are diagnosed with endometriosis (50–52). These prevalence rates may result in an insufficient positive predictive value of our high-risk model at the population level (i.e., for screening) and unduly inflate diagnosis of endometriosis in the asymptomatic population, resulting in avoidable risk of harm and costs (8). While the potential benefits of screening for early asymptomatic endometriosis are unclear, diagnostic labeling carries with it the emotional burden of becoming a "patient" (8). From this point of view, our low-risk model will be of value by classifying asymptomatic women as nonendometriotic, which may also decrease cost and avoid unnecessary treatments. Another approach would, therefore, be to use our model in a selected population of women of particular interest for endometriosis, for example, young female adults from high school or university, as the rate of dysmenorrhea is high in this population and screening may result in early diagnosis of endometriosis and avoid development of more severe forms (13, 53).

CONCLUSION

In conclusion, a simple yes/no self-completed patient-centered questionnaire about painful symptoms helps to identify women at high or low risk of endometriosis with a high diagnostic accuracy. This diagnostic tool may be of benefit for primary care physicians for early identification of endometriosis. External validation is needed in different populations and settings.

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Identificación temprana de mujeres con endometriosis mediante un simple cuestionario completado por el paciente como herramienta de visualización: un estudio diagnóstico.

Objetivos: Evaluar el valor de un cuestionario autocompletado basado en las descripciones verbales de pacientes de síntomas pélvicos dolorosos para identificar mujeres con endometriosis.

Diseño: Prospectivo 1:2 estudio de casos control no emparejados.

Lugar: Tres centros franceses referentes de endometriosis.

Paciente (s): Casos de endometriosis de mujeres de 18-45 años de edad con endometriosis confirmada por histología. Los controles fueron los siguientes: mujeres asintomáticas realizando una consulta ginecológica para examen de rutina, mujeres sin evidencia de endometriosis consultando por dolor/infertilidad; y controles basados en la población de las mismas localidades urbanas.

Intervención (es): Todas las mujeres completaron el cuestionario de 21 ítems por sí/no sobre síntomas dolorosos.

Principal (es) medida (s) de resultado (s): El área bajo la curva característica de funcionamiento del receptor del cuestionario completo del modelo se basó en logística binaria de regresión y la precisión del diagnóstico de bajo y alto riesgo con reglas de clasificación basadas en el umbral seleccionado del modelo de predicción.

Resultado (s): Nosotros incluimos 105 casos y 197 controles (45 controles asintomáticos basados en consulta, 66 mujeres sin endometriosis consultando por dolor/infertilidad, y 86 controles basados en la población). El conjunto de preguntas completo del modelo predictivo, incluyendo edad, tuvo un área bajo la curva característica del operador receptor de 0.92 (95% intervalo de confianza, 0.87–0.95) luego de validación interna. La regla de clasificación de alto riesgo tuvo una especificidad de 98.0% y una razón de probabilidad positiva de 30.5. La regla de clasificación de bajo riesgo tuvo una sensibilidad de 98.1% y una razón de probabilidad negativa de 0.03. Para un pretest hipotetizado una prevalencia del 10%, las reglas de predicción de alto y bajo riesgo confirmaron endometriosis por probabilidad de postest de 77.2% y 0.3% respectivamente.

Conclusión (es): Un cuestionario de autoevaluación y centrada en el paciente puede identificar mujeres con bajo y alto riesgo de endometriosis con una alta precisión diagnóstica y, por lo tanto, puede ayudar a una identificación temprana de mujeres con endometriosis.