Female Sexual Function in Women with Suspected Deep Infiltrating Endometriosis

Função sexual feminina em mulheres com suspeita de endometriose infiltrativa profunda

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Rev Bras Ginecol Obstet 2018;40:115–120.

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Abstract

Objective   To evaluate the quality of the sexual function of women with suspected deep infiltrating endometriosis.

Methods   A cross-sectional, observational and prospective study was conducted between May 2015 and August 2016, in which 67 patients with deep infiltrating endometriosis, suspected or diagnosed, were assessed for epidemiological and clinical characteristics, such as pain level through a visual analog scale (VAS), features of deep infiltrating endometriosis lesions and score on the Female Sexual Function Index (FSFI) before the onset of treatment. The statistical analysis was performed using the software STATA version 12.0 (StataCorp LLC, College Station, TX, USA) to compare the variables through multiple regression analysis.

Results   The average age of the patients was 39.2 years old; most patients were symptomatic (92.5%); and the predominant location of the deep infiltrating lesions was on the rectosigmoid colon (50%), closely followed by the retrocervical region (48.3%). The median overall score on the FSFI was 23.4; in 67.2% of the cases the score was $\leq$ 26.5 (cutoff point for sexual dysfunction). Deep dyspareunia ($p = 0.000$, confidence interval [CI]: 0.64–0.83) and rectosigmoid endometriosis lesions ($p = 0.008$, CI: 0.72–0.95) showed significant correlation with lower FSFI scores, adjusted by bladder lesion, patients' age and size of lesions. Deep dyspareunia ($p = 0.003$, CI: 0.49–0.86) also exhibited significant correlation with FSFI pain domain, adjusted by cyclic bowel pain, vaginal lesion and use of gonadotropin-releasing hormone (GnRH) analog. These results reflect the influence of deep dyspareunia on the sexual dysfunction of the analyzed population.

Conclusion   Most patients exhibited sexual dysfunction, and deep dyspareunia was the pelvic painful symptom that showed correlation with sexual dysfunction.

Keywords
► endometriosis
► sexuality
► deeply infiltrating endometriosis

Resumo

Objetivo   Avaliar a qualidade da função sexual em pacientes com suspeita de endometriose profunda infiltrativa.

Métodos   Foi realizado um estudo observacional transversal prospectivo entre maio de 2015 e agosto de 2016, no qual foram analisados os dados clínicos e

epidemiológicos de 67 pacientes com endometriose profunda presuntiva ou diag-
nosticada, níveis de dor através de escala visual analógica (EVA) e Índice de Função
Sexual Feminina (questionário IFSF) antes do início do tratamento. A análise estatística
foi realizada utilizando o programa estatístico STATA, na versão 12.0 (StataCorp LLC,
College Station, TX, USA), para comparar as variáveis por meio de regressão múltipla.
Resultados   A idade média foi de 39,2 anos; houve predominância de mulheres
sintomáticas (92,5%) e da localização de lesões de endometriose profunda em
retossigmoide (50%) seguida pela topografia retrocervical (48,3%). A pontuação total
no IFSF mostrou uma mediana de 23,4, e em 67,2% das mulheres a pontuação
foi ≤ 26,55 (*cut-off* que indica disfunção sexual). Dispareunia (*p* = 0.000, intervalo
de confiança [IC]: 0.64–0.83) e lesão endometriótica em retossigmoide (*p* = 0.008, IC:
0.72–0.95) exibiram uma relação estatisticamente significante com valores baixos de
pontuação no IFSF, ajustados por lesão em bexiga, idade da paciente e tamanho da
lesão. A dispareunia de profundidade também mostrou correlação significante com o
domínio dor do IFSF ajustado por dor cíclica intestinal, lesão vaginal e uso de análogo de
hormônio liberador de gonadotrofina (GnRH). Os resultados refletem a influência da
dispareunia de profundidade na disfunção sexual da população do estudo.
Conclusão   A maioria das pacientes apresentava disfunção sexual e o sintoma mais
relacionado a esta disfunção foi dispareunia de profundidade.

Palavras-chave
► endometriose
► sexualidade
► endometriose
   profunda infiltrativa

Introduction

Endometriosis is characterized by the presence of endome-
trium-like functional tissue located outside the uterine
cavity, most often on the pelvic peritoneum and ovaries. It
might present as deep and infiltrating lesions in the organs
adjacent to the uterus—the bladder in the anterior pelvic
compartment, retrocervical region, rectovaginal septum,
vaginal fornices, rectosigmoid colon and cecal appendix in
the posterior compartment.[1,2] While the etiopathogenesis of
the disease is not well known, some evidences suggest that a
combination of retrograde menstrual flow with genetic,
hormonal and immune factors and the cell response of the
eutopic endometrium might contribute to the formation and
development of endometriosis lesions.[3]

According to the available studies, the prevalence of this
disease is 10–20% among women of reproductive age,[4] but it
might vary to be as high as 50% in populations of patients
with specific clinical characteristics, such as infertility and
chronic pelvic pain.[5]

With the help of laparoscopy, endometriosis might be
classified according to its anatomical localization and exten-
sion. Among the available classification systems is the one
formulated by the American Society of Reproductive Medi-
cine, which is based on the appearance, size and depth of
peritoneal and ovarian implants, presence, extension and
type of adhesions, and degree of cul-de-sac obliteration.[6]
More recently, the ENZIAN classification was developed for
deeply infiltrating lesions, in which the stages of disease are
defined according to their localization and size.[7,8] The bowel
is frequently affected in the deep form of the disease, defined
as endometriosis infiltrating deeper than 5 mm under the
peritoneum.[7]

Deep infiltrating lesions can be identified by physical
examination,[1] but transvaginal ultrasound[9] and magnetic
resonance imaging[10] have been used for definition of the
extension of the lesions with adequate accuracy.

There is no confirmed correlation between extension of
the disease and severity of symptoms, reproductive progno-
sis or recurrence of pain in the long run.[11]

The clinical presentation of the disease is quite variable.
Up to 25% of the patients might be asymptomatic,[12] 30–50%
might report infertility,[12,13] and up to 80% complain of
chronic pelvic pain (severe dysmenorrhea, deep dyspareunia
and painful ovulation).[14] In addition, perimenstrual urinary
or rectal symptoms and chronic fatigue are common clinical
complaints.[12,15]

The quality of life of patients with endometriosis is
significantly impaired, while deep dyspareunia considerably
affects their sexual life.[16] In addition, dyspareunia is associ-
ated with anxiety,[17,18] reduced frequency of sexual inter-
course, reduction of sexual desire and arousal, and less
orgasmic experiences.[19,20] While these are subjective phe-
nomena, assessment of the sexual function through validat-
ed questionnaires affords a better understanding of the
impact of endometriosis on the quality of female sexuality.
One of the best-established questionnaires for this purpose is
the Female Function Sexual Index (FSFI), which has been
validated for the Brazilian Portuguese language.[21–23]

Laparoscopic excision of endometriotic nodules, pharma-
cological treatment and the combination of both proved to be
efficacious to reduce deep dyspareunia.[24–28]

Considering the intimate relationship between endome-
triosis and sexual dysfunction,[17–20] we sought to assess the
quality of the sexual function of women with suspected deep
infiltrating endometriosis (DIE).

Methods

The present prospective, observational and cross-sectional study was approved by the Brazilian national ethics committee.

On their first appointment at the endometriosis and chronic pelvic pain outpatient clinic of Hospital do Servidor Público Estadual Francisco Morato de Oliveira (HSPE-FMO), 67 consecutive patients with clinical suspicion of DIE were invited to participate in this study from May of 2015 to August of 2016.

We included sexually active women of reproductive age with suspected DIE at gynecological examination, ultrasonography (US) or magnetic resonance (MR) images and who agreed to participate in the study by signing an informed consent form. The participants were assured as to the confidentiality of the data and were informed they could withdraw their consent at any time.

All women were treated by means of continuous contraceptive or gonadotropin-releasing hormone (GnRH) analog to induce amenorrhea, and the surgical procedure was determined by non-responsive pain symptoms[1] or intestinal and urinary risk of complications. The surgical procedures were performed laparoscopically with the aim of complete resection of DIE's lesions and histological exam was conducted in all specimen. The exclusion criteria consisted of incomplete filling out of the sexual function questionnaire and the withdraw of the informed consent.

We first collected data on the patients' age, number of pregnancies, surgical history of endometriosis, previous treatment, fertility condition, urinary and intestinal complains and pain symptoms: dysmenorrhea, dyspareunia and non-cyclic pelvic pain, which were quantified by means of the visual analog scale (VAS). Also, the characteristics of the endometriotic lesions on imaging tests (size, location and degree of infiltration) were described and classified preoperatively according to the ENZIAN classification, as it affords a satisfactory morphological description per affected compartment and lesion size.[8]

At first, before any surgical treatment, the participants filled out the FSFI questionnaire; some of them had already received clinical treatment previously but that information was taken into account as a possible confounding factor toward statistical analysis. The FSFI is a short, specific and multidimensional scale, previously adapted to the Portuguese language, with significant reliability and validity,[21] which transforms subjective assessments into objective, quantifiable and analyzable data.[23] The FSFI includes 19 questions corresponding to 6 domains— desire, arousal, lubrication, orgasm, satisfaction and pain or discomfort; the questions are scored from 0 to 5. We calculated the overall score by adding the scores of the individual items in each domain, then we multiplied the sum by the domain factor— provided by the scale authors— and finally added the six domain scores. The overall score might vary from 2 to 36, being that the higher the score the better the sexual function.[21,22] Scores equal to or lower than 26.55 indicate sexual dysfunction.[29]

The collected data were entered in a Microsoft Excel for Windows spreadsheet (Microsoft Corp., Redmond, WA, USA). The statistical software STATA version 12.0 (StataCorp LLC, College Station, TX, USA) was used to perform descriptive and comparative analysis by means of Poisson's or logistic regression to investigate the correlation of the epidemiological and clinical data with the scores on the FSFI.

The categorical variables were expressed as percentages and the numerical ones as mean and standard deviation, when parametric distribution was observed, or as median and quartiles when their distribution was nonparametric.

For the logistic and Poisson regression models, we employed the forward stepwise method to select the variables potentially correlated with the outcomes. After univariate correlation analysis, the variables with $p \leq 0.20$ or others with clinical relevance were selected to perform the multiple regressions. To improve the model fit, the significance level for the final correlations and adjusted multiple analysis was set at $p \leq 0.05$ with 95% confidence interval (CI). We subjected the final models to reliability tests to establish their goodness-of-fit, to wit, the Hosmer-Lemeshow test was used for the logistic regression model and the Pearson goodness-of-fit test for the Poisson regression model.

Results

From the 67 patients selected to participate in the study, none matched the exclusion criteria. Data corresponding to 67 women with age varying from 20 to 52 years old (mean: 39.19 ± 6.67) were analyzed. Relative to the obstetrical history of the participants, 47.8% (32) had never been pregnant and 52.2% (35) had one to three children. The most prevalent delivery route was cesarean section, corresponding to 65.6% (21) of the cases, information that was found in patients' the medical records. About 19.4% (13) of the sample had history of miscarriage, and 52.2% (35) had history of infertility. Finally, 26.2% (17) of the participants had history of pelvic gynecological surgery.

About 92.5% (62) of the participants were symptomatic, the median duration of symptoms being 84 months (24–120), that is, 7 years, varying from 1 to 420 months (35 years). The most prevalent symptoms included dysmenorrhea (94%), dyspareunia (71.2%) and non-cyclic pain (67.2%). The distribution of painful symptoms according to the VAS scores is described on ►Table 1.

Table 1 Distribution of painful symptoms on the VAS of women with deep infiltrating endometriosis

VAS	Dysmenorrhea n (%)	Dyspareunia n (%)	Non-cyclic pain n (%)
0–4 (mild)	4 (6)	24 (36.9)	32 (47.8)
5–6 (moderate)	9 (13.5)	14 (21.5)	14 (20.9)
7–10 (severe)	54 (80.5)	29 (41.6)	21 (31.3)

Abbreviations: n, number of subjects; p, p-value; VAS, visual analog scale.

Specific bowel and urinary symptoms were reported by the patients, and the most common clinical presentation of these specific symptoms is the non-cyclic variety: constipation (28.4%), non-cyclic dyschezia (20.9%), cyclic dyschezia (16.4%), non-cyclic abdominal bowel pain (16.4%), cyclic abdominal bowel pain (9%), non-cyclic hematochezia (7.5%), cyclic hematochezia (6%), non-cyclic urinary pain (3%), cyclic urinary pain (1.5%). About 28.4% of the sample reported constipation, with an average interval of 2.28 days between stools.

Some patients (34.3%) were referred to the outpatient clinic already receiving treatment, which included combined oral contraceptives (COC) (17.9%), progestin alone (11.9%), and GnRH analog (4.5%).

Sixty medical records had information on the localization of deep infiltrating endometriosis lesions by means of specialized imaging tests, such as magnetic resonance imaging of the pelvis and transvaginal ultrasound with bowel preparation. About 45% (27) of the sample exhibited lesions suspected of cystic ovarian endometriosis concomitant with bowel lesions, which were bilateral in 16.6% (9) of the cases. As to the distribution of lesions, 50% (30) were located on the rectosigmoid colon, 48.3% (29) in the retrocervical region, 11.7% (7) in the vaginal fornices, 8.3% (5) in the vaginal septum and 5.9% (3) on the bladder reflection.

The mean size of the lesions was 2.3 cm (1.6–3.0 cm), varying from 0.7 to 11.4 cm. Forty-nine cases could be classified according to the ENZIAN system (►Table 2). Lesions on the vaginal fornices, vagina or rectovaginal septum were classified as ENZIAN stage A, retrocervical lesions as stage B and bowel lesions as stage C.

About 80% (24) of the lesions reached the muscle layer of the affected bowel loop wall, while 20% extended into the submucosal layer. Most lesions (73.3%) affected up to 25% of the bowel loop circumference.

The median overall score on the FSFI was 23.4 (18–28.6); the proportion of cases with score ≤ 26.55 was 67.2% (45). The domain scores were: desire 3 (2.4–3.6), arousal 3.9 (2.7–4.5), lubrication 4.8 (3.3–5.7), orgasm 4.4 (2.8–5.6), satisfaction 4.8 (33.2–5.2) and pain 3.6 (2–5.2).

We analyzed the correlation between predictor variables by means of multiple regression analysis to identify possible confounding factors and selected the ones with higher statistical significance or better fit to the model, thus reducing the odds of colinearity or confusion in the final model.

Multiple logistic regression evidenced significant correlation between dyspareunia and sexual dysfunction (FSFI score ≤ 26.55) adjusted by lesion size and patients' age, as shown in ►Table 3.

Table 2 Distribution of deep infiltrating endometriosis lesions according to the ENZIAN classification

Lesion size (cm)	Grade	Compartment		
		A	B	C
< 1	1	1	2	1
1– 3	2	3	14	18
> 3	3	1	4	5

Table 3 Multiple logistic regression of predictor variables and sexual dysfunction corresponding to patients with deep infiltrating endometriosis

Variables	Unadjusted analysis p (CI)	Final adjusted model p (CI)
Dyspareunia	0.002 (0.68–3.01)	0.003 (2.75–140.54)
Lesion size	0.112 (−0.01–0.11)	0.052 (0.991.22)
Age	0.225 (−0.02–0.12)	0.069 (0.99–1.23)

Abbreviations: CI, confidence interval; p, p-value.
Hosmer-Lemeshow = 0.6255.

The Poisson multiple regression detected significant inverse correlation of variables dyspareunia and rectosigmoid localization with higher overall score on the FSFI, adjusted by age, lesion size and presence of lesions in the bladder, as described in ►Table 4.

The Poisson multiple regression was also used to analyze the correlation between the study variables and sexual function domains— desire, arousal, lubrication, orgasm, satisfaction and pain or discomfort. No statistically significant correlation was found between the selected predictor variables and desire, arousal, lubrication, orgasm or satisfaction. In turn, variable deep dyspareunia exhibited inverse correlation with higher score on the FSFI domain pain, adjusted by cyclic bowel pain, endometriosis lesion on the vaginal fornix and use of GnRH analog (►Table 5).

Discussion

The average age of the patients in the present study corresponds to the age range in which endometriosis is usually diagnosed, that is, the fourth decade of life.[30,31] Relative to the obstetrical history, the prevalence of women with no previous pregnancy and primary or secondary infertility was

Table 4 Poisson multiple regression analysis of predictor variables and overall score on FSFI corresponding to patients with deep infiltrating endometriosis

Variables	Unadjusted analysis p (CI)	Adjusted analysis p (CI)
Dyspareunia	0.000 (−0.34–0.13)	0.000 (0.64–0.83)
Rectosigmoid lesion	0.041 (−0.21–0.00)	0.008 (0.72–0.95)
Bladder reflection lesion	0.052 (−0.35–0.00)	0.151 (0.43–0.13)
Lesion size	0.059 (−0.007–0.00)	0.470 (0.99–1.00)
Age	0.067 (−0.01–0.00)	0.174 (0.98–1.00)

Abbreviations: CI, confidence interval; FSFI, female sexual function index; p, p-value.
Pearson goodness-of-fit = 0.2304.

Table 5 Poisson multiple regression of predictor variables and domain pain in patients with deep infiltrating endometriosis

Variables	Unadjusted analysis p (CI)	Adjusted analysis p (CI)
Dyspareunia	0.000 (0.45–0.75)	0.003 (0.49–0.86)
Cyclic bowel pain	0.065 (0.97–2.12)	0.256 (0.84–1.87)
Lesion on vaginal fornix	0.152 (0.43–1.13)	0.236 (0.46–1.21)
Use of GnRH analogue	0.159 (0.24–1.25)	0.291 (0.06–2.29)

Abbreviations: CI, confidence interval; GnRH, gonadotropin-releasing hormone; p, p-value.
Pearson goodness-of-fit = 0.99.

high, which might be explained by the effect of immune cells and the hostile environment caused by the disease.[32]

As the sample was composed of women cared for at an outpatient clinic for treatment of chronic pelvic pain, the high prevalence of symptomatic patients (92.5%) is easy to understand.

In the present study, the prevalence of dysmenorrhea and dyspareunia was 94% and 71.2%, respectively. These rates are much higher than the ones reported by Bellelis et al (2010);[29] however, these authors only considered severe painful symptoms. Despite the low prevalence, specific bowel and urinary symptoms were also reported by the patients.

As the present study also shows, bowel complaints are common manifestations among patients with DIE and might interfere with the bowel function;[2] and overall quality of life and sexual function. We were not able to establish a direct relationship between lesion size or location and FSFI scores indicative of sexual dysfunction, which agrees with reports by other authors.[11]

As concerns the negative impact of symptoms on the female sexual function, the prevalence of sexual dysfunction among the patients with suspected or confirmed diagnosis of DIE was 67.2%. In the studies by Di Donato et al (2014)[16] and Jia et al (2013),[33] this rate was 58% and 73%, respectively.

We found a direct correlation between dyspareunia and sexual dysfunction, defined as an FSFI score below 26.55.[29]

In addition, we detected an inverse correlation between dyspareunia and bowel lesion with a higher FSFI score. The correlation is inverse in this case because higher FSFI scores indicate better sexual function, therefore, lesion size and dyspareunia correlated with lower scores, which is indicative of sexual dysfunction. Relative to the individual FSFI domains, our models detected a correlation between dyspareunia and the pain domain.

It is a fact well established in the literature that the experience of pain is reinforced in subsequent intercourse experiences, which creates a cognitive pattern characterized by negative expectations, which in turn affects the sexual function and causes suffering, anguish or interpersonal difficulties, making the women unable to participate in intercourse as they would wish.[18,20,34,35]

Rectosigmoid lesions are the most prevalent form of presentation of DIE and usually cause painful symptoms, and its prevalence might account for the inverse correlation found between FSFI scores and lesions in that location.

We did not find a statistically significant correlation between the analyzed predictor variables and the FSFI domains desire, arousal, lubrication, orgasm or satisfaction. Only the variable deep dyspareunia exhibited an inverse correlation with higher scores on the pain domain. Other authors observe that patients with endometriosis develop strategies to cope with pain due, for instance, to a desire to become pregnant, which may have increased the individual scores on the other FSFI domains.[36]

The lack of information on the partners' or relationship status is a limitation of the FSFI. Further limitations of the present study derive from the lack of assessment of other factors, such as comorbidities, family and religious aspects, and the women's personal values, which determine their sexual choices and behaviors.

In addition, the lack of randomization, the study design and the small sample size might limit the interpretation and external validity of the results of the present study. However, we have already developed a research line to continue the longitudinal investigation so as to compare the sexual function outcomes before and after treatment for DIE, as the results might afford a better understanding of the effects of therapeutic interventions on the quality of the female sexual experience.

Conclusion

The results of the present study show that dyspareunia exerts a negative influence on the overall FSFI score and also on the pain domain. These findings reinforce the fact that female sexual dysfunction is a public health problem in women with suspected DIE, thus demanding special attention from gynecologists.

Conflicts to interest
The authors declare that there are no conflicts of interest.

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