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Questionnaire based evaluation of sexual life after laparoscopic surgery for endometriosis: A systematic review of prospective studies

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Abstract

Introduction: Endometriosis is a benign disease, which affects women of reproductive age. Laparoscopic excision of endometriotic implants is considered one of the most effective therapeutic options. The disease and its treatment can have major impact on psychosexual well-being but this is often overlooked as most studies focus on pain instead of sexuality in a holistic approach. The aim of this study was to review the current literature regarding the effect of laparoscopic surgery for endometriosis on quality of sexual life (QoSL). *Material and methods:* Following the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" guidelines we conducted a systematic review which involved searching PubMed and Embase databases for prospective studies evaluating the effect of laparoscopic surgery for endometriosis on QoSL, using validated questionnaires. *Results:* Of 357 papers, 17 were selected for full text evaluation. Twelve studies using seven different questionnaires fulfilled the inclusion criteria. All studies reported improvements in QoSL following laparoscopic surgery for endometriosis. A meta-analysis could not be done due to substantial heterogeneity among the included studies arising from differences in questionnaires, follow-up duration, stages of endometriosis, use of hormonal treatment and missing data. *Conclusions:* Laparoscopic excision of endometriosis can improve QoSL. However, there is a need for randomized controlled trials based on a new validated questionnaire regarding specifically QoSL in association with endometriosis. As sexual functioning is a complex phenomenon driven by multiple physical, psychological and social factors, QoSL should be holistically evaluated by a team of different healthcare providers, implementing individualized treatment programs to every woman.

Keywords

Endometriosis, sexual function, laparoscopy, questionnaire, systematic review.

Abbreviations

DIE: Deep infiltrating endometriosis

SAQ: The Sexual Activity Questionnaire

MFSQ: The McCoy Female Sexuality Questionnaire

SHOW-Q: The Sexual Health Outcomes in Women Questionnaire

EHP-30: The Endometriosis Health Profile Questionnaire

SVQ: The Sexual Function-Vaginal Changes Questionnaire

FSFI: The Female Sexual Function Index

FSDS: The Female Sexual Distress Scale

COC: Combined oral contraceptives

GnRH: gonadotropin-releasing hormone

QoSL: Quality of sex life

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

GRADE: Grading of Recommendations Assessment, Development, and Evaluation

Key Message

This systematic review suggests that sexual function improves substantially following laparoscopic excision of endometriotic lesions. Due to heterogeneity of the questionnaires used randomized controlled trials based on a new validated questionnaire regarding quality of sex life in association with endometriosis is needed.

Introduction

Sexuality is a complex phenomenon driven by social, psychological and hormonal factors (1). It is an essential part of human life, with major implications on global quality of life (2). In women, sexual dysfunction can be expressed as pain during intercourse (dyspareunia), lack of desire, arousal difficulties, decreased lubrication and orgasm disorders (3). These symptoms often overlap and one can lead to the other, as pain for example may result in decreased desire.

Endometriosis is a common chronic benign gynecological disorder, defined as endometrial glands and stroma outside the uterine cavity. Is present in 3-10% of fertile women (4-7), of which approximately two thirds experience some form of sexual dysfunction (8). Symptoms of endometriosis include reduced fertility and pain, such as dysmenorrhea, dyspareunia and non-cyclic chronic pelvic pain (7,9). Sexual function may be compromised due to these symptoms leading to reduced frequency of intercourse, feelings of guilt and lower self-esteem (7,9-13). Consequently,

dyspareunia and sexual dysfunction associated with endometriosis represent a major clinical problem, as well as, an important outcome of endometriosis treatments.

Currently, several treatment options exist including both medical and surgical approaches. Based on previous studies, a recent review by Barbara et al. (14) suggested that endometriosis surgical and/or pharmacological treatments can lead to medium-/long-term improvement, but not necessarily to a definitive resolution of female sexual dysfunction. Moreover, according to the study of Vercellini et al. (15) and the recent guidelines from “The National Institute for Health and Care Excellence” (NICE) for endometriosis (16), both medical and surgical treatments have advantages, as well as, side effects and complications respectively, for which women should be thoroughly informed. Moreover, recurrence for both medical and surgical treatments is not uncommon (9,17-19) and, with the exception of infertility, both should be offered as an option to women with endometriosis (20). Regarding laparoscopic approach for surgical management of endometriosis, it has become a safe and effective approach in resection of endometriosis and is more widely used, in comparison to the open approach, than in the past (21,22).

Unfortunately, improvements on sexual function and quality of sexual life (QoSL) is often overlooked, as most studies on endometriosis treatment tend to focus mainly on “pain scale” as indicator and “pain relief” as outcome for the effectiveness of treatment (12). Since female sexuality is a complex phenomenon, it is difficult to be appraised in a holistic way. However, when conducting clinical studies, one of the main tools used to measure QoSL is questionnaires (23). Presently, there exist several questionnaires evaluating sexual well-being in women, assessing different aspects of sexuality. Some are designed to assess sexual function of women during perimenopause and menopause like the McCoy Female Sexuality Questionnaire (MFSQ) (24), while others, such as Endometriosis Health Profile questionnaire (EHP-30) (25), are designed specifically for women with endometriosis. Interestingly, in some cases the originally designed questionnaire referred to women with serious diseases, such as the Sexual Activity Questionnaire (SAQ) (26), which was firstly designed for women at high risk of developing breast cancer. Consequently, the fitness of those questionnaires to evaluate the sexual function of women with endometriosis is, at least, questionable.

Therefore, the aim of this study was a) to evaluate the effect of laparoscopic surgery on QoSL in women with endometriosis by identifying all available prospective studies using validated questionnaires, b) to highlight the heterogeneity of questionnaires used by categorizing the included studies according to which questionnaire was used and c) to address a discussion on which method could represent a holistic approach to evaluate QoSL in women with endometriosis, apart from the single use of a questionnaire.

Material and methods

This systematic review was conducted according to the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) guidelines for systematic reviews and we ensured compliance by completing the PRISMA checklist (27). The quality of evidence of the selected studies was assessed by using the "Grading of Recommendations Assessment, Development, and Evaluation" (GRADE) criteria (28). Only published studies were used, so the present review was not subject to Institutional Review Board approval.

Sources and data extraction

A database search (PubMed, Medline) was conducted on April 5, 2017 on the effect of laparoscopic surgery for endometriosis on QoSL, including prospective studies using validated questionnaires. Studies specifically focusing on the effect of laparoscopic surgery on dyspareunia were not taken into consideration since it is well examined and documented by previous reviews that laparoscopy improves the overall pain score (9,19). The search terms were constructed by reviewing titles, abstracts, and keywords of a sample of articles examining sexual dysfunction in women with endometriosis.

The search string used, included the terms "(endometriosis OR endometrioma OR endometriomas) AND (sexuality OR sex behavior OR sexual behavior OR sexual OR sex) AND (laparoscopy OR laparoscopies OR laparoscopic OR resection OR resections OR excision OR excisions)" with language restricted to English, resulting in 128 hits. Furthermore, on April 6, 2017 an Embase search was conducted using the search string "endometriosis.mp. or endometriosis/ OR endometrioma.mp. or

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endometrium tumor/ OR endometriomas.mp. AND sex/ or sex.mp. OR sexuality.mp. or sexuality/ OR sex behavior.mp. or sexual behavior/ AND laparoscopy/ or laparoscopy.mp. OR laparoscopic.mp. OR laparoscopies.mp. OR resection.mp. OR resections.mp. OR excision/ or excision.mp. OR excisions.mp.” with no filters, resulting in 229 hits (Figure 1). All relevant studies were retrieved and their reference lists were systematically examined to identify additional articles, as well as, the original validated questionnaires and their validated modification, if there was any. No attempt was made to identify unpublished studies. The searches were last updated on May 31, 2017 and January 30, 2018 where no additional studies were identified.

Inclusion criteria for full text evaluation were prospective studies with women of reproductive age with endometriosis, laparoscopy as surgical intervention and QoSL assessed using validated questionnaires. Furthermore, only studies in English were included. Studies were excluded if they were reviews, case reports, cross-sectional, retrospective, conference abstracts or non-randomized trials. Additionally, studies were excluded if they used either a non-validated questionnaire or a non-validated version of the original questionnaire.

Two authors (C.F. and M.H.P.) conducted an independent screening of all titles and abstracts retrieved from peer-reviewed journals to exclude irrelevant or duplicate citations. The same authors designed a predetermined data extraction form, which was applied to each paper to independently extract data in relation to author, year of publication, location, sexual functioning questionnaire, study design, time to follow up, number of individuals, inclusion and exclusion criteria, type of surgical or pharmacological intervention, histological confirmation, stage of endometriosis according to the “ Revised American Fertility Society (AFS) Classification of Endometriosis” (29) and outcomes. The quality of evidence of the included studies for the outcome of interest was assessed following the criteria described by the GRADE method. According to the GRADE criteria, the quality of evidence is divided into four categories: high, moderate, low, and very low (27).

Results

Totally, 357 articles were identified by database search as potentially relevant. After removal of duplicates and identification of one additional article (30) from references of relevant studies, 17 articles were selected for full text evaluation (Figure 1). Five articles were excluded because they

used either a non-validated questionnaire or a non-validated version of the original one (7,10,31-33). Complete author agreement (C.F. and M.H.P.) regarding included and excluded studies was achieved. The remaining 12 studies used seven different questionnaires and were subsequently divided into groups based on the questionnaire (4,6,11,13,30,34-40). Four groups of studies, using the same validated questionnaire, were identified while the remaining two studies used one and two questionnaires, respectively (Figure 1). In general, as all studies except one (35) included in this review are prospective cohort studies, the final assessment – according to the GRADE criteria (27) – was low level of quality.

The questionnaires used by the 12 studies included in this review (4,6,11,13,30,34-40) were the SAQ, the MFSQ, the Sexual Health Outcomes in Women Questionnaire (SHOW-Q), the EHP-30, the Sexual Function-Vaginal Changes questionnaire (SVQ), the Female Sexual Function Index (FSFI) and the revised Female Sexual Distress Scale (FSDS).

The SAQ is a questionnaire designed for the evaluation of the effect of long-term tamoxifen treatment on the sexual functioning of women at high risk of developing breast cancer in addition to women without such risk. It consists of three sections concerning hormonal status, reasons for sexual inactivity and sexual functioning, which is named SAQ-F. Thirlaway et al. (26) developed the SAQ and explored the psychometric properties of the SAQ-F, which showed good test/retest reliability and high internal consistency. Only the last section (SAQ-F), consisting of 10 questions, nine of which are rated on a 4-point Likert scale (0 not at all, and 3 very much), evaluating pleasure, habit and discomfort with sexual intercourse during the last 4 weeks, was used in the original studies. Pleasure is scored to a maximum of 18 (6 questions with 0-3 points), habit to a maximum of 3 (1 question with 0-3 points) and discomfort to a maximum of 6 (2 questions with 0-3 points).

The MFSQ was developed from a questionnaire used in a longitudinal study of the menopausal transition and designed to measure aspects of female sexuality likely to be affected by changing sex hormone levels. Modified by Wiklund et al. (24,41,42), it consists of 19 questions evaluating sexual satisfaction, sexual problems and satisfaction with partner during the last 4 weeks. Eighteen items use 7-point Likert scales and one item request frequency of activity. Sexual satisfaction is ranged between 5-35; sexual problems are ranged between 2-14; and satisfaction with partner is ranged between 2-14.

The SHOW-Q was developed to assess the impact of pelvic problems on sexual desire, frequency, satisfaction, orgasm and discomfort. It consists of 12 questions assessing sexual satisfaction, orgasm, sexual desire and pelvic problem interference with intercourse. The latter involves to which extent bleeding and pelvic pain interfered with sexual activity (43). Sexual satisfaction consists of two questions, orgasm of four questions, sexual desire of three questions and pelvic problem interference of three questions.

The EHP-30 is the only questionnaire developed specifically for the evaluation of women with endometriosis. It is divided in two parts. Part one is made up of 30 core questions, while part two is a modular questionnaire consisting of sections A to F. Interestingly, only a small section of five questions (Module C) assesses sexual function regarding pain, worriedness about pain, avoidance, guilt and frustration during the last 4 weeks (25).

The FSFI consists of 19 questions comprising six domains (desire, arousal, lubrication, satisfaction and pain) for the measurement of overall female sexual function. It is developed for women who are sexually active, have a partner and measures sexual function during the last 4 weeks (44,45).

The FSDS was developed to provide a standardized, quantitative measure of sexually related personal distress in women with sexual dysfunction using 13 questions regarding for instance guilt, frustration, stress, inadequateness and embarrassment over the last 4 weeks (46).

Finally, the SVQ is a 27-item questionnaire assessing intimacy, sexual interest, sexual satisfaction, vaginal changes (lubrication, pain and bleeding) and sexual functioning (47,48). It was developed to provide a standardized, quantitative measure of sexually related personal distress assessed by the European Organization for Research and Treatment of Cancer Quality of life Questionnaire Core-30 (49).

Characteristics of studies

Characteristics of included studies are reported in Table 1. In general, apart from the heterogeneity regarding questionnaires used for the evaluation of QoSL, substantial differences were found in study design, population, stage of endometriosis, operative intervention and use of pre-/postoperative hormonal treatment.

In nine of 12 studies, the diagnosis of endometriosis was confirmed histologically. Lyons et al. (38) included women with previous histological verification of endometriosis though the current state was unknown. Garry et al. (39) evaluated tissue histologically but did not report the findings, while Setälä et al. (40) did not report any histological information.

The four studies using the SAQ included in total 219 women (36-39). Follow-up periods ranged between four months and two to five years. Three studies included women with all four stages of endometriosis where all endometriotic tissue was resected (36,37,39). Lyons et al. (38) included only women with stage IV endometriosis who in addition underwent bowel resection. Abbott et al. (37) and Garry et al. (39) reported an increase in sexual pleasure and habit as well as a decrease in discomfort during sexual intercourse (Table 2). Data on hormonal treatment was reported by two of the four studies (36,37). None of these included preoperative hormonal treatment. Abbott et al. (36) prescribed combined oral contraceptives (COC) postoperatively to 5% (1/20), while Abbott et al. (37) prescribed unspecified hormonal therapy to 26.7% (36/135). All relevant authors (37-39) were contacted to clarify which hormonal treatment was prescribed and to how many women, but no answer was received.

The two studies using the MFSQ included in total 48 women (6,40). Both studies had 12 months' follow-up, included women with deep infiltrating endometriosis (DIE) and performed radical resection. Kössi et al. (6) performed rectosigmoid resection and Setälä et al. (40) resection of DIE in the posterior fornix of the vagina. Both observed an increase in sexual satisfaction while only Setälä et al. (40) reported a decrease in sexual problems (Table 3). COC was used by 36% both pre- and postoperatively in the study by Kössi et al. (6) while 31% and 23%, respectively, received contraceptive pills in the study by Setälä et al. (40).

The two studies using the SHOW-Q included in total 356 women (4,13). Both studies included women with DIE who had follow-up at six months after radical resection. Mabrouk et al. (13) used a nerve-sparing technique in addition to segmental or nodular excision of intestinal DIE. Both reported an increase in sexual satisfaction and desire as well as a decrease in pelvic problem interference (Table 4). Di Donato et al. (4) prescribed hormonal therapy preoperatively to all women whereas no information about preoperative hormonal treatment was given by Mabrouk et al. (13). In both studies, all women received COC postoperatively. Both authors were contacted to clarify questions regarding hormonal therapy, but no answer was received.

The two studies using the EHP-30 included 235 women (30,35). The follow-up periods were six and 12 months, respectively. Kent et al. (35) included only women with stage IV endometriosis and performed radical resection in a two-stage surgical procedure with interval down-regulation using gonadotropin-releasing hormone (GnRH)-analogues whereas Meuleman et al. (30) included women with stage III and IV and performed radical resection with or without bowel resection. Both studies reported an improvement in sexual life (Table 5). GnRH-analogues were prescribed preoperatively in both studies. Postoperatively, Kent et al. (35) only prescribed hormonal treatment to women who underwent pelvic clearance and Meuleman et al. (30) to women without desire of pregnancy.

Riiskjaer et al. (34) used the SVQ and included 123 women who in addition to radical resection underwent bowel resection for rectosigmoid endometriosis. After a follow-up period of 12 months, significant improvements were seen in for instance desire for sexual intercourse, frequency of sexual intercourse, worries about and satisfaction with sexual life, as well as, lack of lubrication and ability to have intercourse (table not available).

Finally, Fritzer et al. (11) used the FSFI and FSDS questionnaires and included 96 women who underwent radical resection with or without resection of the posterior fornix of the vagina as well as bladder and rectal resection. The women were subsequently divided into two groups of DIE and peritoneal endometriosis, respectively. For the FSFI, no significant improvement in sexual function was observed while the FSDS showed a significant change in sexual distress only for women with DIE (table not available).

Discussion

Overall, our review demonstrates that endometriosis negatively affects several domains of female sexual functioning, such as pleasure, frequency of sexual intercourse, comfort, desire, orgasm and satisfaction with sex. On the contrary, six of the seven validated questionnaires used in the 12 studies included in our analysis, identified improvements in sexual function following laparoscopic surgery for endometriosis regardless of location, severity of the disease and hormonal treatment.

Nevertheless, an overall meta-analysis among the 12 studies that fulfilled the inclusion criteria could not be performed due to substantial heterogeneity arising mainly from the use of different questionnaires, stages of endometriosis, variation in duration of follow-up, use of different categories of hormonal treatment pre-/postoperatively and missing data.

An innovative aspect of our review is the subdivision of included studies in groups based on the type of sexual questionnaire used (Figure 1, tables 2-5). This methodological approach was driven by the fact that when analyzing the effect of laparoscopy on QoSL of women with endometriosis, the main tool used in most studies is questionnaires. This way, we clearly highlighted the weakness of a questionnaire group-based meta-analysis between and/or among studies using the same questionnaire, mainly due to differences on stages of endometriosis, duration of follow-up, use of different kinds of hormonal treatment pre-/postoperatively and missing data.

Our results are in accordance with the conclusion of previous reviews examining the effect of laparoscopy on QoSL of women with endometriosis (8,9,14,19,50). In the most recent one by Barbara et al. (14), the key message was that “endometriosis surgical and pharmacological treatments can lead to medium-/long-term improvement, but not necessarily to a definitive resolution of female sexual dysfunction”. In comparison to this review and regarding the “surgical intervention group” our analysis identified two additional articles (34,35), which were included in our analyses. Two more reviews on QoSL following surgery for endometriosis, have previously been published both by Fritzer et al. (9,19). Inclusion criteria were prospective studies that used both a validated questionnaire estimating QoSL and a validated pain scale such as Visual Analog Scale (VAS) estimating dyspareunia. Both reviews concluded that laparoscopic excision of endometriosis was feasible, offered pain relief and improved QoSL. Nevertheless, it must be emphasized that complete radical excision of DIE is frequently associated with a not negligible risk of major intra- and postoperative complications, such as ureteral, bladder, or bowel injuries, rectovaginal fistula formation, anastomotic dehiscence in case of bowel resection, or potential risk of pelvic denervation (13-15, 50). Consequently, patients should be exhaustively informed about all these risks as well as about the incidence of possible complications, in order to obtain a fully informed consent.

Our analysis indicates core weaknesses on methodology of available studies to evaluate QoSL taking into consideration all possible factors that can influence sexuality, apart from the score of a single questionnaire. For example, data on complications were given in 10 of 12 studies except for the ones

from Di Donato et al. (4) and Fritzer et al. (11). Major complications included for instance temporary colostomy or ileostomy and rectovaginal or ureterovaginal fistula. Such complications might lead to lower sexual self-esteem and feelings of femininity, making improvements in sexual function less explicit. To the best of our knowledge, only Riiskjaer et al. (34) has examined in which way sexual function was influenced by complications and showed that having a short-term surgical complication did not affect overall sexual function after one year. However, the link between major complications and change in QoSL has never been investigated in-depth. Therefore, future studies should aim to explore how the type and the severity of complications interfere with sexual function and QoSL.

Another core weakness when evaluating effectiveness of laparoscopy on QoSL in women with endometriosis, which is clearly highlighted in our review (Table 1), is the short follow-up postoperative period. Apart from the study of Abbot et al. (25) with a follow-up period of two to five years all other studies followed women for four to 12 months. As endometriosis is a chronic progressive disease, surgical treatment may be useful, but may not necessarily lead to long-term resolution of women's sexual dysfunction. Taking also into consideration that recurrence is not unusual, and that it is usually developed in medium-/long-term time space, future studies with longer follow-up period are needed.

Moreover, the 12 included studies varied greatly regarding hormonal treatment. Furthermore, the kind of hormones used also varied between COC, contraceptive pills, GnRH-analogues as well as unspecified hormonal treatment, making a direct comparison problematic. Despite these variations, most studies reported substantial improvements in QoSL following laparoscopic surgery for endometriosis. However, when surgical treatment is combined with postoperative hormonal treatment it is impossible to distinguish between the effects of the two. Therefore, well-designed randomized controlled trials comparing surgical vs hormonal treatment, as well as, different kinds of hormonal treatments are needed.

Another limitation is that the 12 included studies used seven different questionnaires of which only the EHP-30 questionnaire was developed specifically for the evaluation of women with endometriosis. However, even that questionnaire includes only a small section of five questions assessing sexual function, making it unsuitable for an in-depth evaluation of sexual life. Interestingly, the six other questionnaires (24,26,43-48) were developed for the evaluation of sexual life in other

populations than women with endometriosis, such as, menopausal women or women with cancer. Hence, they may not be ideal for evaluating women with endometriosis since the questions might address topics that are not relevant for these women while overlooking other important aspects of the disease. For example, only some of the questionnaires (MFSQ, FSFI and SVQ) address questions regarding the partner and the sexual function of the couple in a more holistic approach. Moreover, the majority of the questionnaires used (SAQ, MFSQ, EHP-30, FSFI and FSDS) evaluate sexual function and QoSL during the last 4 weeks and not for a longer time period. As endometriosis is a chronic disease with great impact not only on woman, but her partner as well, its effect on the relationship of the couple should be thoroughly examined. Likewise, the time period of the last 4 weeks for the evaluation of QoSL seems to be at least inadequate for women with endometriosis.

Special mention should be given to the FSFI questionnaire. It is a brief self-report instrument and provides a cutoff score indicating sexual dysfunction or not (44,45). It has been utilized by clinicians and researchers in several clinical drug trials for the treatment of sexual problems. Therefore the experience and pool of data using this instrument is large and it is the “golden standard” in the evaluation of women’s sexual function (23). Nevertheless, a major limitation of the FSFI is that it is developed for women with a sexual partner and having been sexually active within the last 4 weeks. If this is followed strictly all women not fulfilling these criteria need to be excluded. On the contrary, if they are included then the FSFI questionnaire does not allow discrimination between “lack of a partner” versus “sex avoidance due to endometriosis-associated dyspareunia”. As a consequence, the risk of including these patients is on one hand to overestimate sexual dysfunction, in case the reason for not having intercourses is the lack of a partner, and on the other hand to underestimate the problem by excluding women without sexual activity, in case the reason for not being sexually active is endometriosis-associated pain.

Finally, all seven questionnaires evaluate sexual function, but only two of them, the FSDS and the FSFI provide a cutoff-value defining clinical relevance. The remaining five questionnaires use as “outcome measure” the postoperative changes in either the overall questionnaire score or the score of each question/domain of the questionnaire. Consequently, no predefined values are available for what is considered clinically relevant. This is a crucial weakness as sexual function may be improved significantly after surgery as score, while the woman still experiences a dysfunctional sexual life. This problem is partially equalized in the MFSQ and SHOW-Q questionnaires, as both evaluate sexual

satisfaction, which can be considered as an alternative measurement of clinical relevance. Interestingly, studies have shown that sexual problems and distress do not necessarily lead to dissatisfaction with sexual life (51). If the woman reports improvements in sexual satisfaction, it suggests that she is pleased with her sex life, which is of high clinical importance. Due to those weaknesses, a new validated questionnaire developed specifically for women with endometriosis is needed. For each evaluated domain the impact on the woman's life and satisfaction should be addressed and a predefined measure for clinical relevance should be determined.

Furthermore, sexual functioning is a complex phenomenon driven by multiple physical, psychological, and social factors, resulting to different types of sexual dysfunction, which may co-exist. Therefore, we recommend that every woman with endometriosis should be holistically evaluated by a team of different healthcare providers, such as sexologists, gynecologists, psychologists and physiotherapists, providing individualized treatment programs. This comprehensive medical approach should be provided in high experienced reference centers, as women with endometriosis are treated and followed for years and surgical management of DIE requires high-level of technical competence and is strictly operator-dependent.

Our review has some strengths. Firstly, we only included prospective studies that used validated questionnaires to secure the highest level of evidence. Secondly, by grouping the studies based on questionnaires used, a direct comparison of the outcomes within the groups was possible. To our knowledge, no other previous review has followed this methodology, which highlighted clearly the weakness to conduct a meta-analysis. Furthermore, we thoroughly reviewed the available bibliography and critically analyzed the advantages and limitations of every questionnaire.

This review has also several limitations, reflecting the limitations of the relevant studies in this field. Firstly, due to the heterogeneity among the included studies a meta-analysis could not be conducted. Secondly, out of seven questionnaires, only one was developed specifically for the evaluation of women with endometriosis. Thirdly, the included studies varied extensively regarding hormonal treatment, which may bias the effect of laparoscopy on QoSL. In this way, it is impossible to distinguish between the effect of surgery alone and the effect of hormonal treatment on QoSL of women with endometriosis.

Conclusion

This review of prospective studies provides evidence that laparoscopic excision of endometriosis improves QoSL and should be provided to women as treatment alternative alongside with pharmacological approach. That is why, healthcare professionals should address the topic of QoSL when consulting women with endometriosis, as it is an important part of human life and improvements following surgery can be expected. Unfortunately, the heterogeneity among the included studies excludes a meta-analysis. Consequently, there is a need for RCT based on a new validated questionnaire regarding sexual function in association with endometriosis. Finally, as human sexuality is a complex phenomenon, influenced by multiple aspects including biological/hormonal mechanisms, psychological factors and social parameters, a holistic approach to evaluate QoSL in women with endometriosis should be applied.

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Legends

Figure 1: Flowchart. N: Number of articles. n: Number of participants in the study. Irrelevant intervention: for instance, medical treatment or laparotomy. Irrelevant population: for instance, animals or children/adolescents. SVQ: The Sexual Function-Vaginal Changes Questionnaire. FSFI: The Female Sexual Function Index. FSDS: The revised Female Sexual Distress Scale. SAQ: The Sexual Activity Questionnaire. MFSQ: The McCoy Female Sexuality Questionnaire. SHOW-Q: The Sexual Health Outcomes in Women Questionnaire. EHP-30: The Endometriosis Health Profile Questionnaire.

Table 1: Characteristics of included studies.

Table 2: Results from the Sexual Activity Questionnaire (SAQ).

Table 3: Results from the McCoy Female Sexuality Questionnaire (MFSQ).

Table 4: Results from the Sexual Health Outcomes in Women Questionnaire (SHOW-Q).

Table 5: Results from the Endometriosis Health Profile Questionnaire (EHP-30).

Table 1: Characteristics of included studies

Author Country; year	Question- naire	Study design Follow-up	Individuals (n)	Inclusion and exclusion criteria	Procedures performed (histological confirmation)	Stage (rAFS)	
Abbott et al. (24) United Kingdom; 2004	SAQ	Cross-over RCT 6 months	20 ^a	Included: Women with clinical symptoms and signs suggestive of endometriosis. Excluded: Patients with suspected gynecologic malignancy or its precursors, current or chronic pelvic inflammatory disease, or pregnancy preoperatively.	Radical resection (+)	Stage I: Stage II: Stage III: Stage IV:	1 (5%) 9 (45%) 2 (10%) 8 (40%)
Abbott et al. (25) United Kingdom; 2003	SAQ	Cohort 2-5 years	135	Included: Women with symptoms and signs suggestive of endometriosis. Excluded: N.A.	Radical resection (+)	Stage I: Stage II: Stage III: Stage IV:	19 (14%) 39 (28%) 23 (17%) 54 (41%)
Lyons et al. (26) Australia; 2006	SAQ	Cohort 12 months	7	Included: Consecutive patients undergoing laparoscopic colorectal surgery for intestinal endometriosis. Excluded: N.A.	Radical resection with bowel resection (+) ^b	Stage IV:	7 (100%)
Garry et al. (27) United Kingdom; 2000	SAQ	Cohort 4 months	57	Included: Consecutive patients who were referred for radical laparoscopic excision of endometriosis. Excluded: N.A.	Radical resection (+) ^c	Stage I + Stage II: Stage III + Stage IV:	21 (37.8%) 36 (63.2%)
Kössi et al. (4) Finland; 2013	MFSQ	Cohort 12 months	26	Included: Women who underwent laparoscopic bowel resection for colorectal endometriosis Excluded: N.A.	Radical resection with rectosigmoid resection (+)	DIE	26 (100%)

Setälä et al. (28) Finland; 2012	MFSQ	Cohort 12 months	22	<p>Included: Consecutive patients scheduled for endometriosis surgery with resection of the posterior fornix of the vagina.</p> <p>Excluded: Patients with previous hysterectomy, previous surgery for DIE or undergoing concomitant hysterectomy at the index surgery.</p>	<p>Radical resection including resection of DIE in the posterior fornix of the vagina (N.A.)</p>	DIE	22 (100%)
Mabrouk et al. (10) Italy; 2012	SHOW-Q	Cohort 6 months	106	<p>Included: Consecutive patients aged 20-40 with diagnosis of DIE who were sexually active.</p> <p>Excluded: Women with major medical conditions, psychiatric disorders, use of drugs affecting cognition, vigilance and/or mood, pelvic inflammatory disease, interstitial cystitis, contraindications to hormonal therapy or desire to conceive.</p>	<p>Radical nerve-sparing resection with segmental or nodular excision of intestinal DIE (+)</p>	DIE:	106 (100%)
Di Donato et al. (2) Italy; 2015	SHOW-Q	Cohort 6 months	250	<p>Included: Consecutive patients aged 18-40 with a diagnosis of DIE who were sexually active.</p> <p>Excluded: Women with previous or current gynecological cancer, interstitial inflammatory disease, history of pelvic radiotherapy or systemic chemotherapy, history of gynecological infection in the last three months, history of psychiatric disorder and use of psychotropic medications.</p>	<p>Radical resection (+)</p>	DIE:	250 (100%)
Kent et al. (23) United Kingdom; 2016	EHP-30	Cohort 12 months	100	<p>Included: Patients who required surgery for stage IV endometriosis with bowel involvement and an obliterated Pouch of Douglas after laparoscopic diagnosis.</p> <p>Excluded: Women who declined or were unable to complete the questionnaire and had less severe disease without bowel involvement.</p>	<p>2-step surgical procedure with interval GnRH-analogues for 3-6 months: If bowel involvement by deep endometriosis is diagnosed, any peripheral visible disease is excised. Removal of any residual endometriosis is deferred to the second procedure. (+)</p>	Stage IV:	137 (100%)

Meuleman et al. (18) Belgium; 2014	EHP-30	Cohort 6 months	135	Included: Women requiring laparoscopic excision of stage III or stage IV endometriosis with (study group) or without (control group) bowel resection and reanastomosis. Excluded: N.A.	CO ₂ -laser radical resection with or without bowel resection and reanastomosis (+)	Stage III: Stage IV:	67 (33%) 136 (67%)
Riiskjaer et al. (22) Denmark; 2016	SVQ	Cohort 12 months	123	Included: Women undergoing bowel resection for rectosigmoid endometriosis. Excluded: N.A.	Radical resection with bowel resection (+)	N.A.	
Fritzer et al. (8) Austria; 2016	FSFI + FSDS	Cohort 10 months	96	Included: Consecutive symptomatic women scheduled for surgical excision of endometriosis who were heterosexual, above 18, had dyspareunia for at least six months and without any hormonal treatment within a period of three months before study enrollment. Excluded: Women with previous surgery for endometriosis, pain symptoms of other origin (chronic disease other than endometriosis possibly causing pain symptoms) or history of gynecological malignancy/internal disease.	Radical resection with or without resection of the posterior fornix of the vagina, partial bladder and rectal resection. (+)	Stage I: Stage II: Stage III: Stage IV:	27 (28%) 20 (21%) 25 (26%) 24 (25%)

SAQ: The Sexual Activity Questionnaire. **MFSQ:** The McCoy Female Sexuality Questionnaire. **SHOW-Q:** The Sexual Health Outcomes in Women Questionnaire. **EHP-30:** The Endometriosis Health Profile Questionnaire. **SVQ:** The Sexual Function-Vaginal Changes Questionnaire. **FSFI:** The Female Sexual Function Index. **FSDS:** The revised Female Sexual Distress Scale.

RCT: Randomized controlled trial. **rAFS:** Revised American Fertility Society classification of endometriosis.

N.A.: Data not available. **DIE:** Deep infiltrating endometriosis. **GnRH:** Gonadotropin-releasing hormone analogues.

^a The women were randomized into two groups: an Immediate Surgery Group (ISG) consisting of 20 women who had radical resection of endometriosis performed in the beginning of the study period and a renewed laparoscopy after six months as well as a Delayed Surgery Group (DSG) consisting of 19 women who had a diagnostic laparoscopy performed at the beginning and radical resection after six months. The DSG was excluded in the current review in order to minimize the risk of bias from the placebo effect. Only data on the ISG from the six months' follow-up after radical resection was included in this review.

^b All women had previously been diagnosed with histologically confirmed endometriosis but the current state is unknown.

^c All tissue is subsequently examined histologically but no data on histological findings is reported.

Table 2: Results from the Sexual Activity Questionnaire (SAQ)

Reference	Individuals (n)	Follow-up	Hormonal treatment		Results from SAQ					
			Preoperative	Postoperative	Pleasure		Habit		Discomfort	
					Preoperative (IQR/SD)	Postoperative (IQR/SD)	Preoperative (IQR/SD)	Postoperative (IQR/SD)	Preoperative (IQR/SD)	Postoperative (IQR/SD)
Abbott et al. (24) ^a	20	6 months	None	CP: 5%	8.8 (3.7)	10.4 (4.8)	0.64 (1.08)	1.12 (1.02)	3.3 (1.9)	2.4 (1.9)
Abbott et al. (25) ^b	135	2-5 years	None	Unspecified hormonal treatment: 26%	10 (5-12)	12* (9-16)	1 (0-1)	1* (1-1)	3 (1.5-5)	2* (1.5-3)
Lyons et al. (26) ^b	7	12 months	N.A.	N.A.	13 (6-14)	15 (13-16)	1.00 (0.75-1.00)	1.00 (0.00-1.00)	1.00 (0.00-2.00)	0.00 (0.00-0.50)
Garry et al. (27) ^{b, c}	57	4 months	N.A.	N.A.	11 (6-13)	13* (9-16)	1 (0-1)	1* (1-2)	3 (1-5)	1* (0-3)

Pleasure is scored to a maximum of 18 (6 questions with 0-3 points), habit to a maximum of 3 (1 question with 0-3 points) and discomfort to a maximum of 6 (2 questions with 0-3 points) where higher scores for pleasure and habit indicate higher sexual functioning while higher scores for discomfort indicate lower sexual functioning.

^a Results are presented as mean and standard deviation (SD).

^b Results are presented as median and interquartile ranges (IQR).

^c Statistical analysis was only performed on paired data for n = 32 for pleasure, n = 33 for habit and n = 30 for discomfort.

CP: Contraceptive pills. **N.A.:** Data not available.

* Significant data, p <0.05.

Table 3: Results from the McCoy Female Sexuality Questionnaire (MFSQ)

Reference	Individuals (n)	Follow-up (months)	Hormonal treatment		Results from MFSQ					
			Preoperative	Postoperative	Sexual satisfaction		Sexual problems		Satisfaction with partner	
					Preoperative (SD)	Postoperative (SD)	Preoperative (SD)	Postoperative (SD)	Preoperative (SD)	Postoperative (SD)
Kössi et al. (4)	26	12	COC: 31%	COC: 23%	20.2 (5.0)	Change: 2.8 (5.2)*	7.0 (2.9)	Change: -1.1 (3.6)	12.1 (1.9)	Change: -0.7 (1.8)
Setälä et al. (28)	22	12	CP: 36%	CP: 36%	21.1 (5.4)	Change: 2.1 (4.2)*	6.3 (2.8)	Change: -1.4 (2.9)*	12.1 (1.5)	Change: -0.8 (2.1)

Sexual satisfaction is ranged between 5-35; higher scores indicate more satisfaction. Sexual problems are ranged between 2-14; higher scores indicate more problems. Satisfaction with partner is ranged between 2-14; higher scores indicate more satisfaction.

Results are presented as mean and standard deviation (SD).

COC: Combined oral contraceptives. **CP:** Contraceptive pills.

* Significant data, $p < 0.05$.

Table 4: Results from the Sexual Health Outcomes in Women Questionnaire (SHOW-Q)

Reference	Individuals (n)	Follow-up (months)	Hormonal treatment		Results from SHOW-Q							
					Sexual satisfaction		Orgasm		Sexual desire		Pelvic problem interference	
			Pre-OP	Post-OP	Pre-OP	Post-OP	Pre-OP	Post-OP	Pre-OP	Post-OP	Pre-OP	Post-OP
Mabrouk et al. (10) ^a	106	6	N.A.	COC: 100%	51 (45-56)	65 (60-70)*	57 (52-62)	59 (53-64)	55 (50-60)	64 (58-69)*	59 (53-65)	26 (21-31)*
Di Donato et al. (2) ^b	250	6	Hormonal therapy: 100%	COC: 100%	50 (37-75)	75 (50-87)*	63 (45-79)	62 (50-81)	58 (41-75)	72 (50-83)*	66 (33-75)	16 (0-41)*

Sexual satisfaction consists of two questions, orgasm of four questions, sexual desire of three questions and pelvic problem interference of three questions. After appropriate reverse scoring, all sexual function item responses were converted to a scale of 0-100 points. Higher scores indicate higher sexual functioning or fewer sexual problems, except for items measuring pelvic problem interference, in which higher scores indicate more interference.

^a Results are presented as mean and 95% confidence intervals for mean.

^b Results are presented as median and quartile values.

Pre-OP: Preoperative. **Post-OP:** Postoperative. **N.A.:** Data not available. **COC:** Combined oral contraceptives.

* Significant data, $p < 0.05$.

Table 5: Results from the Endometriosis Health Profile Questionnaire (EHP-30)

Reference	Individuals (n)	Follow-up (months)	Hormonal treatment		Results from EHP-30		
			Preoperative	Postoperative	Preoperative	12 months postoperative	6 months' postoperative change
Kent et al. (23) ^a	100	12	GnRH-analogues 3-6 months before second procedure: 100%	Combined hormones after pelvic clearance: 33.3%	70.0 (40-94.1)	17.5 (0-56.3)*	
Meuleman et al. (18) ^b	135	6	GnRH-analogues 3 months preoperatively if clinical and/or radiological evidence of DIE: 100 %	COC, oral progesterone or IUD if no pregnancy was desired: 7%			3.2 (0.4)*

The EHP-30 consists of two parts. Part one is made up of 30 core questions. Part two is a modular questionnaire consisting of sections A to F. Section C concerns the effect endometriosis has had on sexual relationships during the last four weeks. It is made up of five questions regarding pain, worriedness, avoidance, guilt and frustration about sexual intercourse. Scores are reported as a percentage, with a lower score indicating a better result.

^a Results are presented as median and interquartile ranges (IQR). 100 of 137 women completed 12 months' follow-up.

^b Results are presented as mean difference and standard error (SE). 135 of 203 women completed six months' follow-up.

GnRH-analogues: Gonadotropin-releasing hormone analogues. **COC:** Combined oral contraceptives. **IUD:** Intrauterine device (levonorgestrel-releasing).

* Significant data, $p < 0.05$.

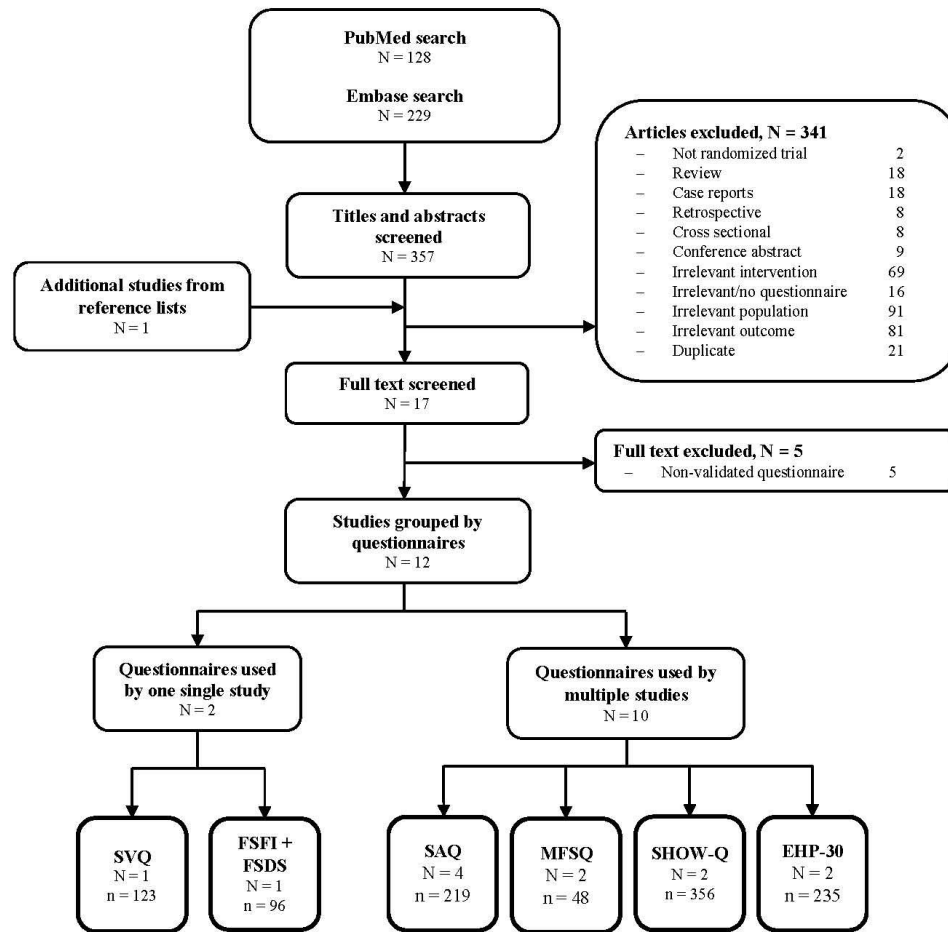


Figure 1. Flowchart. N: Number of articles. n: Number of participants in the study. Irrelevant intervention: for instance, medical treatment or laparotomy. Irrelevant population: for instance, animals or children/adolescents. SVQ: The Sexual Function-Vaginal Changes Questionnaire. FSFI: The Female Sexual Function Index. FSDS: The revised Female Sexual Distress Scale. SAQ: The Sexual Activity Questionnaire. MFSQ: The McCoy Female Sexuality Questionnaire. SHOW-Q: The Sexual Health Outcomes in Women Questionnaire. EHP-30: The Endometriosis Health Profile Questionnaire.