

REVIEW ARTICLE

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Medical and surgical interventions to improve the quality of life for endometriosis patients: a systematic review

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Abstract

Endometriosis impairs the quality of life (QoL) of many women, including their social relationships, daily activity, productivity at work, and family planning. The aim of this review was to determine the instruments used to examine QoL in previous clinical studies of endometriosis and to evaluate the effect of medical and surgical interventions for endometriosis on QoL. We conducted a systematic search and review of studies published between January 2010 and December 2020 using MEDLINE. Search terms included “endometriosis” and “quality of life.” We only selected studies that used a standardized questionnaire to evaluate QoL before and after medical or surgical interventions. Only articles in the English language were examined. The initial search identified 720 results. After excluding duplicates and applying inclusion criteria, 37 studies were selected for analysis. We found that the two scales most frequently used to measure QoL were the Short Form-36 health survey questionnaire (SF-36) and the Endometriosis Health Profile-30 (EHP-30). Many medical and surgical treatments demonstrated comparable benefits in pain control and QoL improvement. There is no clear answer as to what is the best treatment for improving QoL because each therapy must be personalized for the patient and depends on the woman's goals. In conclusion, women must be informed about endometriosis and given easily accessible information to improve treatment adherence and their QoL.

Keywords: Quality of life, QoL, Endometriosis, Medical, Surgical, Interventions

Introduction

Endometriosis is a benign chronic disease caused by the presence of ectopic endometrial tissue, which reacts to changes in ovarian steroids by differentiation, proliferation, and bleeding [1, 2]. It occurs principally during one's reproductive age, most commonly between the ages of 25 and 35 [3, 4]. Its prevalence of 7–10% makes endometriosis one of the most common gynecological chronic inflammatory diseases, and it often affects quality of life (QoL) and fertility [5–9]. Recent literature has shown that many factors contribute to the etiopathogenesis of endometriosis:

genetic, hormonal, and immunological factors play a role, while even intestinal permeability may also be involved [10–13]. Symptomatic endometriosis can be extremely debilitating, leading to dysmenorrhea, chronic pain, dyspareunia, bleeding disorders, and infertility [14, 15]. These painful symptoms can affect physical, mental, and social well-being to a remarkable degree. Infertility itself may also induce psychological stress, low self-esteem, and depression [16]. Endometriosis affects the QoL of many women, including social relationships, daily activity, productivity at work, and family planning [17]. According to the clinical context and the patient's needs, the treatment of this pathology can be medical or surgical [8, 18]. In both blocking the progression of lesions and causing their regression, medical treatment has been demonstrated to

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be effective, resulting in improved symptoms. Moreover, pharmacotherapy has a major role in improving surgical treatment, either in the time preceding it or, more specifically, after surgery. Progestogens, combined oral contraceptives (COCs), gonadotrophin-releasing hormone analogs (GnRHa), and aromatase inhibitors are treatments available today [15, 19–22]. Furthermore, it is important to emphasize that an adequate lifestyle, a diet rich in vegetables and omega-3 polyunsaturated fatty acids, and a simultaneous reduction in red meat intake, coffee, and alcohol may effectively support and improve the benefits of medical therapy [23, 24]. Surgical management may be necessary for patients who do not respond to medical therapy and have important severe symptoms (such as hydronephrosis caused by ureteral stenosis or intestinal obstruction) [8, 25]. The aim is to completely remove the pathology, obtain good long-term results regarding pain relief and recurrence rates, and respect the functional anatomy of the organs involved [25–27].

The World Health Organization (WHO) has defined QoL as a “multi-dimensional construct of the individual perception of one’s position in life in the context of culture and value systems in relation to goals, expectations, standards, and concerns” [28].

Many studies have underlined the damaging results of pelvic pain on women’s mental health and QoL [29]. However, few studies have methodically analyzed whether the QoL of women with endometriosis is primarily affected by the disease itself, which is chronic and distinguished by unpredictable development (leading to uncertainty about the future in general and often triggering concerns about sexuality and infertility, among other vital moments of a woman’s life), or only by the effect of pelvic pain [30–32]. However, in a randomized study, Facchin et al. demonstrated that pain is likely the main problem affecting the QoL of women with endometriosis, showing that patients with endometriosis, who reported overall pelvic pain among other symptoms, are more likely to report poor QoL than those with asymptomatic endometriosis [33].

Since endometriosis has been identified as a social scourge, many systematic reviews of clinical studies on QoL in women with endometriosis have been published [16, 34–36]. The aim of this review was, firstly, to identify the instruments used to examine QoL in previous clinical endometriosis studies, and, secondly, to evaluate the influence of medical and surgical interventions for endometriosis on QoL. We searched MEDLINE databases for relevant studies on QoL in patients with endometriosis, excluding case reports studies and review articles. Relevant, frequently cited articles in the English language published over the last 10 years were examined in more detail.

QoL instruments and measures for endometriosis

Many instruments for assessing the QoL of patients with endometriosis have been previously described. The Short Form-36 health survey questionnaire (SF-36) is the most common questionnaire that measures general QoL in patients with endometriosis; it may be useful during diagnosis, treatment, and follow-up [37, 38]. It consists of 36 items organized into eight domains: physical functioning; role—physical; bodily pain; general health; vitality; social functioning; role—emotional; and mental health.

An even shorter version of this questionnaire is the Short Form-12 (SF-12), which more briefly investigates the same domains as the SF-36, focusing on two domains: the physical component summary (PCS) and the mental component summary (MCS) [39].

Another useful, specific, and validated questionnaire developed by clinicians for the study of QoL in women with endometriosis is the Endometriosis Health Profile-30 (EHP-30) [40] and its short version, the Endometriosis Health Profile-5 (EHP-5) [41]. It consists of two sections. The first section applies to all women with endometriosis and addresses five domains: pain, control and powerlessness, emotions, social support, and self-image. The second section is not suitable for all women and addresses six domains: work life, relationship with children, sexual intercourse, the medical profession, treatment, and infertility.

Other instruments used to assess QoL include the WHO Quality of Life BREF (WHOQOL-BREF). This is a shorter form (26 items) of the original WHOQOL and it investigates QoL in terms of social relationships, as well as physical, psychological, and environmental health [42, 43].

The European Quality of Life-5 Dimensions questionnaire (EQ-5D) is a descriptive instrument invented in Europe, which contains one item for five domains: mobility, self-care, daily activities, pain, and emotional well-being [44].

Methods

Search strategy

We performed a systematic literature search on the electronic database PubMed/Medline to identify all studies that evaluated the effect of medical and surgical interventions for endometriosis on QoL. The key search terms included “endometriosis” and “quality of life.” The search was limited to full-text articles in the English language published between January 2010 and December 2020. A systematic review was conducted following PRISMA guidelines [45]. Additional articles were manually identified, as we searched references from the retrieved eligible articles to avoid missing relevant publications. Two independent reviewers (MND and SS) screened the

studies identified from the literature search based on the keywords described above.

Selection criteria

All studies that assessed the QoL of reproductive-aged women with a diagnosis of endometriosis, using standardized questionnaires administered before and after surgical or medical interventions have been included. Articles studying QoL in women with adenomyosis or in adolescents were excluded. No restrictions for geographic area were applied. We included prospective studies, controlled and randomized controlled trials, and multicenter studies. Retrospective studies, opinion articles, editorials, case reports, pilot studies, review articles, letters to the editor, and comments were excluded. Articles specifically analyzing sexual dysfunction, mental disorders, and work productivity were excluded.

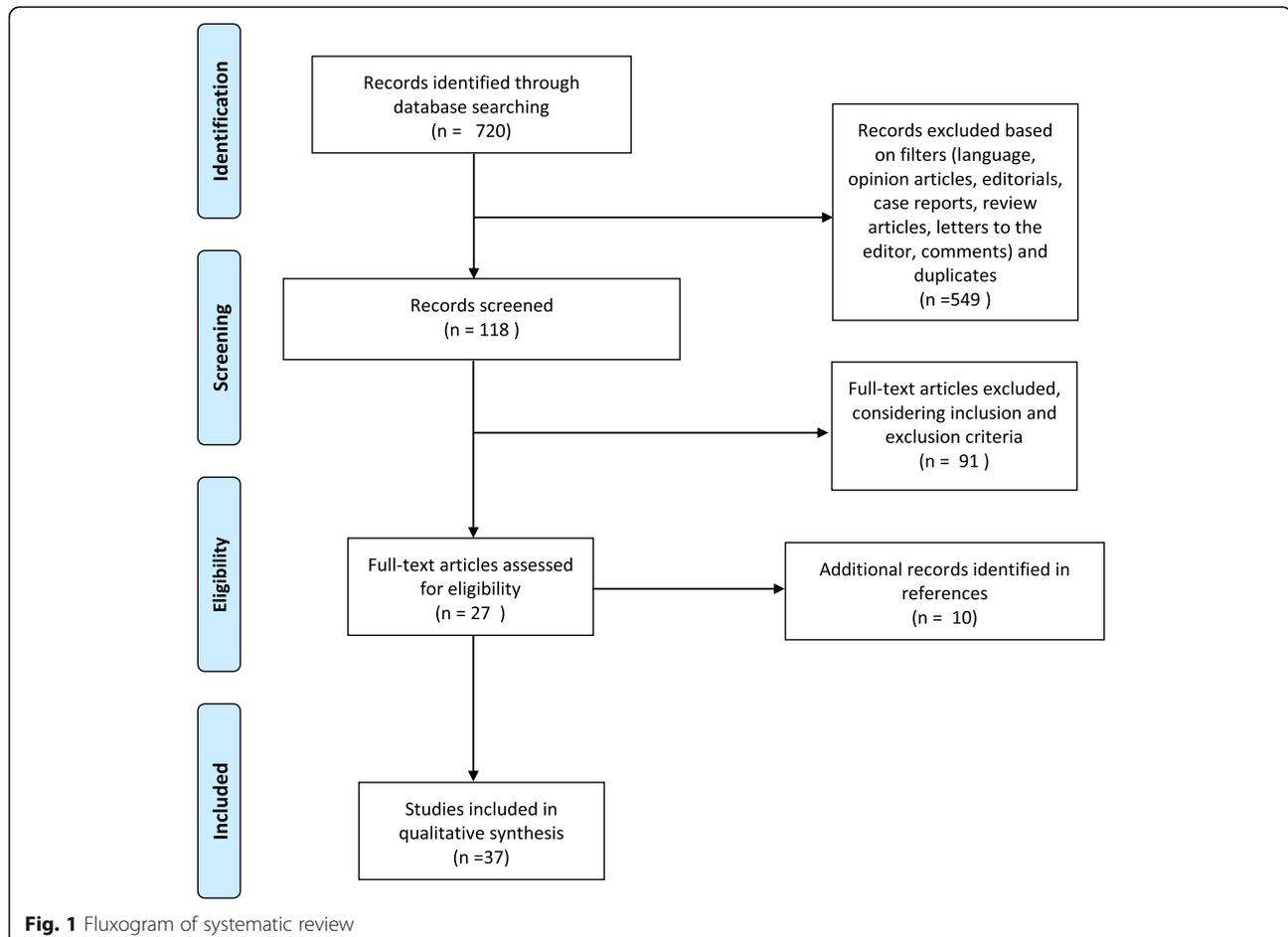
Results

The initial search identified 720 articles. After excluding duplicates and applying inclusion criteria, 27 full-text studies were assessed for eligibility. We selected 10 additional articles from a systematic review of the references

of retrieved eligible articles. Thus, 37 studies were included in our qualitative synthesis. The selection process is shown in Fig. 1.

Of these studies, 18 aimed to evaluate the effect of the medical treatment for endometriosis on QoL [46–63]. The remaining 19 studies aimed to evaluate the impact of surgical treatment upon QoL in endometriosis [64–82]. Moreover, 18 studies reported QoL on patients with all types of endometriosis [46–54, 57, 59, 60, 62–65, 80, 81], 2 with deep infiltrating endometriosis (DIE) [55, 67], 5 with DIE and bowel involvement [68, 72, 73, 77, 79], 5 with bowel endometriosis [69, 70, 74–76], 1 with bladder endometriosis [82], 2 with endometrioma [56, 61], and 3 with rectovaginal endometriosis [58, 71, 78]. One study involved patients with minimal endometriosis (revised American Fertility Society score < 6) [66, 83].

In the 37 studies included in this review, six standardized QoL questionnaires were used. In general, the two scales most frequently used to measure QoL are the SF-36 and the EHP-30. The SF-36 survey questionnaire was used in 25 studies [46, 47, 51, 53, 54, 57–61, 63–70, 72–76, 78, 82]; its short version, the SF-12, was used in 3 studies [52, 64, 81]. The EHP-30 was used in 5 studies [62,



77, 79–81]; its short version, the EHP-5, was used in 2 studies [49, 50]. Three studies used the WHOQOL-BREF questionnaire [48, 55, 56] and two studies used the EQ-5D questionnaire [71, 77].

The main characteristics of studies included in this review are summarized in Tables 1 and 2.

Outcomes of the included studies

Medical interventions

The effect of various medical treatments on the QoL of women with endometriosis was assessed. Medical treatments for endometriosis include hormonal and non-hormonal therapies, which can improve general health, reduce pain, and improve vitality and physical and physiological function.

Zhao et al. showed that after 12 weeks of therapy with gonadotrophin-releasing hormone agonists (GnRHa), women with endometriosis experienced improvement in almost all QoL parameters. Only anxiety and depression worsened, but these parameters improved after treatment with progressive muscle relaxation [46]. Another study also reported increased anxiety and depression during the use of GnRHa (perhaps for hypoestrogenic and genitourinary syndrome) to treat endometriosis [47]. In that study, additional benefits occurred after add-back therapy with estradiol and testosterone, leading to an improvement in all QoL parameters [47]. Besides this, GnRHa with add-back therapy proved as useful as a dienogest or dienogest plus estradiol valerate for preventing the recurrence of pain after a laparoscopic intervention for endometriosis, improving all QoL parameters without differences between the two therapies [48, 49].

The newest gonadotrophin-releasing hormone antagonists (GnRHant) (elagolix) in the US market have demonstrated excellent results after 6 months of treatment, improving all QoL variables. This treatment particularly improved the fatigue experienced by women with endometriosis. Women receiving this treatment reported significant improvement compared to the placebo control group [50].

Treatment with progestins has also been shown to significantly improve the QoL of women with endometriosis. In particular, dienogest has been shown to improve many domains of SF-36 and EHP-30 [51–53] more than GnRHa or other progestins, such as leuprolide acetate, when used to treat symptomatic endometriosis [54]. Dienogest has even been proposed as a conservative therapy for bladder endometriosis and deep infiltrating (DIE) endometriosis decreasing pain and improving QoL [55]. Dienogest is considered to be an option for long-term postoperative management. Seo et al., in a prospective cohort study, compared long-term use of dienogest with combined oral contraceptive (COC) after gonadotropin-releasing hormone (GnRH) agonist plus add-back therapy

as medical treatments after surgery for ovarian endometrioma. No difference was found in values of the psychological, physical, environmental, and social components of QoL between the two groups. Both COC and dienogest have proven to be tolerable options for long-term maintenance [56].

Caruso et al. found that a continuous COC regimen is more effective than a cyclical one for improving all aspects of QoL measured with SF-36 [57]. Moreover, for patients with recurrent migraines without auras, progestogen-only contraceptive pills (POPs) are more effective than COCs [58]. Both etonogestrel-releasing contraceptive implant and levonorgestrel-releasing intrauterine system have proven to be effective in treating symptoms associated with endometriosis and improving all QoL domains measured by the SF-36 and EHP-30 [59–61]. Carvalho et al. compared the two systems in a noninferiority randomized clinical trial and found no significant differences between reductions in endometriosis-associated pain and improvement in QoL [62]. Even non-hormonal therapies such as palmitoylethanolamide (PEA) and α -lipoic acid (LA) have been shown to improve QoL in selected patients with endometriosis [63].

Surgical interventions

Surgical treatments for endometriosis have a positive postoperative effect on pelvic pain and dyspareunia, improving patients' physical and mental QoL (physical pain, social and physical functioning, and mental and general health) and providing patients with years of healthy functioning [64, 65]. However, in cases of minimal endometriosis surgery is seldom a good treatment for improving QoL [66].

Many studies have investigated the outcomes of various surgical treatments for DIE. In a prospective cohort study, Mabrouk et al. demonstrated that the laparoscopic excision of DIE lesions improves all domains of the SF-36 within 6 months after surgery, regardless of the surgical procedure performed (segmental bowel resection or rectal shaving) or the medical therapy recommended after surgery [67]. The same results have been confirmed by many other authors, especially those who focus on intestinal surgery in patients with bowel endometriosis [68–71]. No authors have found any correlation between QoL improvements and the type of surgical technique (i.e., segmental bowel resection rather than laparoscopic shaving or discoid excision) [72–74].

Two studies compared QoL improvement after laparoscopically assisted or open surgery colorectal resection and no difference was observed between groups [75, 76].

With regard to the role of a hysterectomy with bilateral salpingo-oophorectomy for QoL improvements, Kent et al. found that this procedure improved all domains of the SF-36 [77].

Table 1 Characteristics and outcomes of the included studies evaluating the effect of the medical treatment for endometriosis on QoL

First author and study period	Type of study	Sample size	Range of age	Type of medical treatment	Type of endometriosis treated	Results	Instruments
Ács et al. 2015 [50]	Multicenter randomized controlled study	180 n = 45 Oral elagolix 150 mg once daily n = 45 Elagolix 250 mg n = 45 placebo n = 45 LA 1-month depot 3.75 mg intramuscularly	18-45	GnRH antagonist: Elagolix vs leuprorelin acetate (LA) and placebo	Not specified	There were improvements from baseline to week 12 in all 5 dimensions of the EHP-5 in all treatment groups. The differences between elagolix 150 mg, elagolix 250 mg vs. LA were statistically significant ($p = 0.006$ and $p = 0.0204$, respectively), which indicated a higher efficacy of LA in the pain dimension of EHP-5.	EHP-5
Agarwal et al. 2015 [47]	Randomized, multicenter, open-label clinical trial	20 n = 5 D + E ₂ transdermal n = 7 D + E ₂ nasal n = 8 D + E ₂ + T nasal	25-45	Gonadotropin-releasing hormone agonist (GnRHa) deslorelin (D) with low-dose estradiol ± testosterone (E ₂ ± T) add-back	Not specified	There were statistically significant improvements relative to baseline for five of the ten quality of life domains: physical functioning, role physical, bodily pain, social functioning, and vitality; those that were unaffected by treatment were already within normative ranges for women of similar age at baseline. Quality of life issues with everyday problems was significantly improved with treatment.	SF-36
Caruso et al. 2015 [51]	Prospective study	92	18-37	Dienogest	Not specified	At 3 months follow-up, women reported QoL improvement in physical function, physical role, body pain, general health, social function and emotional role categories ($p < 0.05$); at 6 months follow-up, they reported improvement in all categories ($p < 0.001$).	SF-36
Caruso et al. 2015 [63]	Prospective study	56	18-31	Palmitoylethanolamine and α -lipoic acid	Not specified	No changes were observed in QoL at the 3rd month follow-up. By the 6th and 9th month all categories of the QoL ($P < 0.001$) improved.	SF-36
Caruso et al. 2016 [57]	Comparative, open-label prospective study	96 n = 63 Study group (continuous regimen) n = 33 Control group (21/7 regimen)	18-35	2 mg dienogest/30 μ g ethinyl estradiol continuous vs 21/7 regimen oral contraceptive	Not specified	At 3 and 6 months, the Study group reported QoL improvements in all categories ($p < 0.001$). The Control group reported QoL improvements in all categories at the second follow-up ($p < 0.05$). The QoL of the Control group improved slightly at the second follow-up. The intergroup statistical comparison analysis between each follow-up showed a better efficacy of the continuous regimen than the 21/7 conventional regimen in all the QoL aspects.	SF-36
Carvalho et al. 2018 [62]	Randomized clinical trial	103 n = 52 ENG implant n = 51 LNG-IUS	18-35	Etonogestrel-releasing contraceptive implant vs 52 mg levonorgestrel-releasing intrauterine system	Not specified	Health-related quality of life improved significantly in all domains of the core and modular segments of the Endometriosis Health Profile-30 questionnaire, with no difference between both treatment groups.	EHP-30
Granese et al. 2015 [49]	Multi-center randomized trial	78 n = 39 Dienogest +	18-45	Gonadotrophin-releasing hormone analog vs dienogest plus estradiol valerate after	Not specified	At the 9-month follow up, the questionnaire results showed a considerable increase of scores	EHP-5

Table 1 Characteristics and outcomes of the included studies evaluating the effect of the medical treatment for endometriosis on QoL (Continued)

First author and study period	Type of study	Sample size	Range of age	Type of medical treatment	Type of endometriosis treated	Results	Instruments
		E2V n = 39 GnRH-a		laparoscopic surgery for endometriosis		for all women compared with before surgery, demonstrating an improvement in the QoL and an equal health-related satisfaction with both treatments	
Lee et al. 2016 [48]	Prospective, comparative study	64 n = 28 GnRHa + add back group n = 36 Dienogest group	18-45	GnRHa plus add back therapy vs dienogest in the treatment of pain recurrences after laparoscopic surgery for endometriosis	Not specified	In this study, there are no differences in QoL according to treatment option.	WHOQOL-BREF
Leonardo-Pinto et al. 2017 [55]	Prospective cohort study	30	18-45	Dienogest	DIE (intestinal and posterior fornix)	Treatment with dienogest for 12 months positively affected several domains of QoL, with significant improvement in the physical, psychological, as well as a self-assessment of QoL and health.	WHOQOL-BREF
Luisi et al. 2015 [52]	Prospective observational multicenter cohort study	142		Dienogest	Not specified	Quality-of-life assessments in the present study showed improvements in both physical and mental indices within 12 weeks, also confirming the decrease of endometriosis-associated pain.	SF-12
Morotti et al. 2014 [58]	Prospective patient preference trial	144 n = 82 COC group n = 62 Desogestrel group		COCs vs POPs in patients with migraine without aura	Symptomatic rectovaginal endometriosis and migraine without aura	Regarding the quality of life, the baseline values of physical component summary (PCS) and mental component summary (MCS) were similar for both groups while after 6 months of treatment a statistical improvement was observed in both components in group POP ($p < 0.001$ for both PCS and MCS) compared to group COC ($p = 0.154$ and $p = 0.640$ for PCS and MCS respectively)	SF-36
Sansone et al. 2018 [61]	Multicenter prospective observational study	25	18-45	Etonogestrel implant	Ovarian endometrioma	After 12 months, the bodily pain, general health, vitality, social functioning, and mental health domains of the QoL score were significantly improved.	SF-36
Seo Jong-Wook 2019 [56]	Prospective cohort study	52 women n = 20 GnRHa+ COC n = 32 Dienogest (28.1 5.9)		Combined oral contraceptive (COC) after gonadotropin-releasing hormone (GnRH) agonist plus add-back therapy vs dienogest (DNG) treatment as medical treatments after surgery	Ovarian endometrioma	Physical, psychological, social, and environmental components of QoL were not significantly different across treatment options.	WHOQOL-BREF
Strowitzki et al. 2010 [53]	Randomized, double-blind, placebo-controlled study	188 n = 90 Placebo n = 98 Dienogest	18-45	Dienogest at a dose of 2 mg daily for 12 weeks	Not specified	Quality-of-life analyses indicated greater improvements in the dienogest group for two of eight SF-36 categories: bodily pain and role emotional Mental sum scale and physical sum scale scores showed similar improvements in both groups.	SF-36
Strowitzki et al. 2010 [54]	Randomized, multicenter, open-label trial	186 n = 90 DNG group n = 96 LA	18-45	Dienogest vs leuprolide acetate for 24 weeks	Not specified	Compared with LA, DNG was associated with pronounced improvements in specific quality-of-life measures. In	SF-36

Table 1 Characteristics and outcomes of the included studies evaluating the effect of the medical treatment for endometriosis on QoL (Continued)

First author and study period	Type of study	Sample size	Range of age	Type of medical treatment	Type of endometriosis treated	Results	Instruments
		group				particular, DNG produced greater improvements in the categories "physical functioning," "vitality," and "social functioning."	
Tanmahasamut et al. 2012 [59]	Double-blind randomized controlled trial	54 n = 28 Levonorgestrel-releasing intrauterine system n = 26 Control group		Postoperative Levonorgestrel-releasing intrauterine system	Not specified	The Short Form-36 scores improved in the levonorgestrel-releasing intrauterine system group but did not change in the expectant management group	SF-36
Yucel et al. 2018 [60]	Prospective, cross-sectional and non-comparative study	42	18-50	Levonorgestrel-releasing intrauterine system	Not specified	Regarding the SF-36 health questionnaire, the calculated physical health scores and the mental health scores increased by the end of 12 months.	SF-36
Zhao et al. 2012 [46]	Controlled, randomized, open-label study	100 n = 50 GnRHa +PMR n = 50 Control group: only GnRHa therapy	18-48	Progressive muscle relaxation training on patients under GnRHa	Not specified	After 12 weeks of therapy with gonadotrophin-releasing hormone agonists (GnRHa), women with endometriosis experienced improvement in almost all QoL parameter. Between-group comparisons of the improvement in scores after intervention showed that the PMR group had significantly better improvement in the scores of anxiety, depression and overall/ domain QOL than the control group ($P < 0.05$)	SF-36

LA leuprorelin acetate, GnRHa gonadotrophin-releasing hormone agonists, D deslorelin, E2 estradiol, T testosterone, ENG etonogestrel, LNG-IUS levonorgestrel-releasing intrauterine system, DIE deep infiltrating endometriosis, GnRHant gonadotrophin-releasing hormone antagonists, E2V estradiol valerate, COCs combined oral contraceptives, POPs progestogen-only contraceptive pills, PCS physical component summary, MCS mental component summary, PMR progressive muscle relaxation training

Other studies have evaluated the role of post-surgical medical treatment with GnRHa in patients with DIE who received complete or incomplete laparoscopic surgical excision. Administration of GnRHa was followed by a temporary improvement in pain and QoL in patients with incomplete surgical treatment. Therefore, this appears to play no role in post-surgical pain when the surgeon was able to completely excise the DIE implants [78]. Recent studies have also considered whether new technologies could improve surgical treatments for endometriosis; several have already found that the use of plasma or CO₂ lasers may improve QoL in selected case [79]. Instead, laparoscopic treatment of mild-to-moderate endometriosis with a helium thermal coagulator was not found to be superior to treatment with electrodiathermy in improving QoL measures [80].

No difference in QoL improvement has been demonstrated even between laparoscopic and robotic surgical techniques [81]. Studies have also examined whether surgical treatment of bladder endometriosis can lead to QoL improvements. Pontis et al. found that the innovative

combined transurethral and laparoscopic approaches improved QoL 12 months after surgery [82].

Discussion

This review shows that endometriosis can adversely influence patients' QoL; the two most common problems affecting QoL are chronic pain and infertility. The connection between inflammatory diseases and mood disorders has been confirmed by medical research [84]. Associations between immunopathogenetic factors (imbalanced production of pro- and anti-inflammatory cytokines) and severe shifts in mood and mental health have been established in patients with endometriosis. Peripheral immunological alterations may induce the central neural system to cause a response that includes behavioral changes (such as fatigue, anhedonia, or sadness), which may negatively affect social interactions and relationships [85]. Furthermore, women with chronic pelvic pain related to endometriosis have pain hypersensitivity due to central and peripheral sensitization. This has been demonstrated in animal models and it is also

Table 2 Characteristics and outcomes of the included studies evaluating the effect of the surgical treatment for endometriosis on QoL

First author and study period	Type of study	Sample size	Range of age	Type of surgical intervention performed	Type of endometriosis treated	Results	Instruments
Angioni et al. 2015 [78]	Randomized clinical trial	159		Laparoscopic en-block resection of DIE vs. incomplete surgical treatment with or without GnRHa administration after surgery	Deep infiltrating endometriosis of the cul-de-sac and of the rectovaginal septum	At 1-year follow-up patients treated with en-block resection showed significant improvement in physical function ($p < 0.01$), general health ($p < 0.01$) and vitality ($p < 0.01$) in comparison to baseline and to 12 months follow-up of the patients who underwent an incomplete surgical treatment. GnRHa administration is followed by a temporary improvement of pain in patients with incomplete surgical treatment.	SF-36
Bassi et al. 2011 [68]	Prospective study	151		Laparoscopic segmental rectosigmoid resection	Deep infiltrating endometriosis with bowel involvement	One year after the bowel resection, there was a significant increase ($p < 0.01$) in scores in all SF-36 domains, as well as in the sum of the components comprising both physical health and mental health recorded before and after the surgical procedure.	SF-36
Byrne et al. 2018 [71]	Multicenter prospective cohort study	4721	25.9-44.8	Laparoscopic surgical excision of rectovaginal endometriosis requiring dissection of the pararectal space.	Rectovaginal endometriosis	Global quality of life significantly improved at 6 months. There was a significant improvement in quality of life in all measured domains and in quality-adjusted life years. These improvements were sustained at 2 years.	EQ-5D
Comptour et al. 2019 [65]	Prospective and multicenter cohort study	981	15-50	Laparoscopic treatment	Not specified	Improvement was observed for all the SF-36 dimensions at 6 months after surgery, and this improvement remained stable over several years.	SF-36
Darai et al. 2010 [75]	Randomized trial	52 n = 26 laparoscopically assisted n = 26 open surgery group	25-44	Laparoscopically assisted vs open colorectal resection	Colorectal endometriosis	The median follow-up was 19 months. Except for physical functioning, all the items of the SF-36 questionnaires were improved after surgery for the whole population. An improvement in PCS ($P = 0.0001$) and MCS ($P < 0.0001$) scores of the SF-36 questionnaire was noted after surgery. No difference in delta of PCS and MCS scores of the SF-36 questionnaire was observed between the groups.	SF-36
Deguara et al. 2013 [64]	Prospective study	21	18-50	Laparoscopic surgery	Not specified	Therapeutic laparoscopic surgery shows benefits in the symptoms and psyche of patients with endometriosis.	SF-36; SF-12
Kent et al. 2016 [77]	Prospective Cohort Study	137 patients had surgery, of which 100 completed follow-up		Laparoscopic surgery: 2-stage procedure with interval downregulation using GnRH analogs.	Severe rectovaginal endometriosis compromising the bowel	Surgery by an experienced multidisciplinary team results in significant improvement in pain, sexual function, and quality of life up to 1 year postoperatively. Pelvic clearance improves outcome.	EHP-30; EQ-5D
Mabrouk et al. 2011 [67]	Prospective cohort study	100	23-39	Laparoscopic surgery	DIE	Six months postoperatively all the women had a significant improvement in every scale of the SF-36 ($p < 0.0005$).	SF-36
Meuleman et al. 2014 [79]	Prospective Cohort study	203 n = 76 Study group: patients with DIE receiving bowel	20-47	CO2 laser ablative surgery with bowel resection and without bowel resection	Extensive DIE with colorectal extension	In both groups, EHP30 scores improved significantly and remained stable for 24 months after surgery. No differences were observed between study and	EHP-30

Table 2 Characteristics and outcomes of the included studies evaluating the effect of the surgical treatment for endometriosis on QoL (Continued)

First author and study period	Type of study	Sample size	Range of age	Type of surgical intervention performed	Type of endometriosis treated	Results	Instruments
		resection n = 127 Control group: subgroup with or without DIE not receiving bowel resection				control groups.	
Misra et al. 2020 [80]	Parallel-group randomized controlled trial.	192 patients n = 96 Diathermy n = 96 Helium	16-50	Laparoscopic ablation or excision with helium thermal coagulator vs hook electrodiathermy	Not specified	Small but statistically significant differences in some quality-of-life measures (pain, emotional well-being and self-image) also favored the use of electrodiatherm.	EHP-30
Pontis et al. 2016 [82]	Prospective observational study	16		Combined transurethral and laparoscopic approach	Symptomatic bladder endometriosis	At one year follow up, patients showed significant improvement in physical function ($p < 0.01$), in general health ($p < 0.00021$), in physical ($p < 0.0003$) and emotional roles ($p < 0.03$), in mental health ($p < 0.004$), and vitality ($p < 0.0013$), in comparison to baseline (pre-surgery)	SF-36;
Ribeiro et al. 2014 [74]	Prospective observational cohort study	45		Laparoscopic colorectal segment resection	Intestinal deep endometriosis	At 6 months post-operatively and 1 year post-operatively significant improvements were observed in all domains of the SF-36 ($p < 0.05$). Physical health-related QOL domains showed greater improvement than mental health domains.	SF-36
Riiskjær 2018 [70]	Prospective observational study	175		Laparoscopic bowel resection	Rectosigmoid endometriosis	A total of 97.1% of the women completed the 1-year follow up (170). A significant improvement on all quality-of-life scores was observed ($p = 0.0001$).	SF-36
Roman et al. 2018 [72]	2-arm randomized controlled trial	60 n = 27 Conservative surgery n = 33 Segmental resection	27-36	Conservative surgery, by shaving or disk excision, vs radical rectal surgery, by segmental resection	Deep endometriosis infiltrating the rectum	The intention-to-treat comparison of the overall scores on SF36 did not reveal significant differences between the two arms 2 years postoperatively.	SF-36
Roman et al. 2019 [73]	2-arm randomized controlled trial	60 n = 27 Conservative surgery n = 33 Segmental resection	27-36	Conservative surgery, by shaving or disk excision, or radical rectal surgery, by segmental resection	Deep endometriosis infiltrating the rectum	There is an overall improvement in pelvic pain and quality of life after surgery, which is comparable between the two arms and remains constant during the 5 years of follow-up.	SF-36
Silveira da Cunha Araújo et al. 2014 [69]	Observational prospective cohort study	36		Laparoscopic treatment for deep infiltrative endometriosis with colorectal resection	Bowel endometriosis	Analysis of each domain revealed improved quality of life when comparing the period before surgery with 12 and 48 months after surgery. There was a significant increase ($p < 0.001$) in the scores in all of the SF-36 domains when comparing T0 vs T12 and T0 vs T48, with higher average scores at T48 corresponding to the domains of physical functioning, role physical, and social functioning	SF-36
Soto et al. 2017 [81]	Multicenter randomized controlled trial	73 n=38 Laparoscopic group		Laparoscopic versus robotic surgery	Not specified	EHP-30: all parameters improved compared with baseline at 6 weeks and 6 months. No statistical differences were found between	SF-12; EHP-30

Table 2 Characteristics and outcomes of the included studies evaluating the effect of the surgical treatment for endometriosis on QoL (Continued)

First author and study period	Type of study	Sample size	Range of age	Type of surgical intervention performed	Type of endometriosis treated	Results	Instruments
		n=35 Robotic group				groups when each parameter was compared at baseline, 6 weeks, or 6 months on univariate analysis. The physical and mental health component of the SF-12 did not change significantly compared with baseline. When compared across all time points using a linear mixed model, there were no differences between groups	
Touboul et al. 2015 [76]	Randomized controlled trial	40 n = 20 laparoscopically assisted group n = 20 open surgery group	25-44	Laparoscopically assisted vs open colorectal resection	Colorectal endometriosis	QoL was significantly improved after surgery and remained stable over 4 years. All dimensions of the SF-36 were increased postoperatively and remained steady over 4 years except for physical functioning (PF) which increased without reaching statistical significance. No difference in QoL was observed between the groups	SF-36
Valentin et al. 2017 [66]	Prospective and multicenter observational study	161	15-50	Laparoscopic procedure	Minimal endometriosis (rAFS score < 6)	The study shows 86% of failure of surgery to improve QoL. Surgery is seldom a good option to increase QoL for patients with minimal endometriosis.	SF-36

DIE deep Infiltrating endometriosis, *GnRH* gonadotrophin-releasing hormone, *PCS* physical component summary, *MCS* mental component summary, *rAFS* revised American Fertility Society

present in other painful syndromes such as irritable bowel syndrome and painful bladder [86]. This state of chronic inflammation and hypersensitivity to pain overlap with other painful syndromes, which can thus lead to anxiety, depression, and chronic fatigue, affecting patients' social lives and leading to a deterioration in QoL [5, 6].

This review considered a number of instruments used to measure QoL in women with endometriosis. The two most common scales are the SF-36 and the EHP-30. The SF-36 is an excellent questionnaire for evaluating QoL in the general population and for comparing the effect of various pathologies on its domains, but it is insufficient for the specific assessment of the pain and infertility associated with endometriosis. Instead, the EHP-30 validated questionnaire is recommended by the American Society for Reproductive Medicine and the European Society for Human Reproduction and Embryology for measuring QoL in patients with endometriosis. This questionnaire investigates some more specific domains of the disease (e.g., infertility, sexual intercourse, trust in the doctor) and is considered more reliable and specific for assessing the QoL of women with endometriosis [87].

Many medical and surgical treatments for endometriosis demonstrate comparable benefits in pain control and improvement in QoL. Medical therapy can control the symptoms of endometriosis and stop the development of

pathology. However, long-term treatment may come with various side effects and a risk of recurrence when treatment is suspended. Surgical treatment should be proposed only when it is strictly necessary. Whenever possible, a conservative approach performed by a multidisciplinary team should be preferred.

Trying to compare medical therapy with surgical therapy to understand which is more effective for improving the QoL parameters is impossible in several aspects: (1) the data cannot be meta-analyzed because the articles considered in this review used different questionnaires; (2) the localization and stage of endometriosis in many papers are not specified, especially those in which medical therapy is used; (3) the sample of women studied in the articles have different ages and socio-anthropological characteristics or are not reported.

In the articles that have studied the effects of medical therapy on QoL in our systematic review, the localization is not mentioned, except in 4 papers, of which two focused on DIE [55, 58] and two on endometrioma treatment [56, 61]. Instead, since 14 out of 19 articles investigated the effects of surgery on QoL focused on DIE treatment, it seems that the surgical treatment is the most used for treating the most insidious form of endometriosis improving QoL. Logically from these results, we cannot assume that surgical therapy is better than medical one in improving the QoL of women with

DIE. However, we can certainly state that the literature has focused attention on the surgical treatment of this form of endometriosis, which may particularly affect the QoL of our patients for his insidious clinical history.

Surgical treatment is recommended for patients who have severe endometriosis-associated symptoms, such as chronic pelvic pain, with a visual analog scale for pain symptoms (VAS) > 7, hydronephrosis caused by ureteral stenosis, or subocclusive bowel syndrome cause by intestinal obstruction [88]; women who decline or have contraindications to the use of hormones; those who experienced a failure of medical treatment; cases of two or more in vitro fertilization (IVF) failures [89].

Although medical therapy could improve DIE-associated symptoms, it never offers a definite treatment for symptomatic patients, who often require surgical treatment. Moreover, it is not fully clear whether medical treatment is effective in preventing the progression of the disease, as discontinuous treatment commonly entails symptoms recurrence [90]. For these reasons, a surgical approach for severe DIE may be, overall, more effective and decisive, despite the possible complications associated with it [90]. The rationale behind DIE surgical treatment is to achieve the complete removal of all lesions through a one-step surgical procedure; to obtain promising long-term results for pelvic pain, recurrence rate, and fertility; and to protect the functionality of the involved organs. Achieving these results depends on the total removal of the pathology from the pelvis, in an attempt to preserve, as much as possible, the healthy tissues surrounding the site of the disease [91].

Conclusions

Which treatment best improves QoL in patients with endometriosis? There is no clear answer because therapy must be personalized for each patient and depends on the woman's goals.

Particular attention must be paid to the management of the patient with DIE, trying to take into account the natural history of the disease and book the surgery at the right time that matches the needs and desires of the woman, always following the guidelines provided by scientific societies.

Therefore, women should be educated about endometriosis and given easily accessible information to improve treatment adherence and, consequently, the QoL of patients with endometriosis.

Acknowledgements

This publication was created as part of a research project financed with the resources of P.O.R. SARDEGNA F.S.E. 2014-2020 - Asse III "Istruzione e Formazione, Obiettivo Tematico: 10, Obiettivo Specifico: 10.5, Azione dell'accordo di Partenariato: 10.5.12" Avviso di chiamata per il finanziamento di Progetti di ricerca - Anno 2017.

Authors' contributions

MND corresponding author, contributed to study conception and design, preparation of final manuscript, and writing of the manuscript. SP and MA contributed to the design and wrote the initial draft. The revision process was made by SA, ASL, and MN. E S-L and AF contributed to the English editing and approved the final draft. The authors read and approved the final manuscript.

Funding

Not funded

Availability of data and materials

Not applicable

Declarations

Ethics approval and consent to participate

Not required

Consent for publication

Not required

Competing interests

The authors declare that they have no competing interests.

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Received: 26 February 2021 Accepted: 26 May 2021

Published online: 03 June 2021

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