Commentary

Women's Health

Surgery for endometriosis-related pain

"Surgery for endometriosis-associated pain can be targeted either on the endometriotic lesions or nerve pathways."

Keywords: adhesiolysis • adhesions • bilateral ovariectomy • breast cancer • deep endometriosis • endometrioma • endometriosis • excision • gestagen • hormonal treatment • hormone replacement treatment • laparoscopy • multidisciplinary approach • ovary • pain • pelvic anatomy • peritoneal lesions • progestin • recto-sigmoid resection • removal • surgery • uterosacral nerve ablation • uyterus

Murat Api
muratapi@hotmail.com

Endometriosis is defined as the presence of endometrial glands and stroma outside the uterine cavity. Most of the women with endometriosis seek treatment for pelvic pain, infertility or both. The leading cause for women presenting to the gynecologist's office is pelvic pain. Endometriosis is believed to be one of the major causes of chronic pelvic pain in reproductive age women. Pain symptoms related to the endometriosis include dysmenorrhea, dyspareunia and nonmenstrual pelvic pain. Since pathophysiology and underlying mechanism of endometriosis has not been fully understood, endometriosis-related pain still stays to be a dilemma. As the surgery is accepted to be failure of medicine, all efforts should be tried to reduce the pain with different types of medication. However, endometriosis-related pain sometimes cannot be managed by any means of medical treatment, and surgery becomes the last resort. There is a strong evidence that the surgery is effective in endometriosis-related pain obtained [1]. The purpose of surgery is to excise or coagulate all visible endometriotic peritoneal lesions, endometriotic ovarian cysts, deep rectovaginal endometriosis and associated adhesions, and to restore normal anatomy. Depending upon the severity of disease, ideal practice is to diagnose and remove endometriosis surgically at the same time, provided that preoperative informed consent has been obtained [2–5]. There are no data to justify hormonal treatment prior to surgery to improve the success of surgery [6,7]. Laparoscopy is accepted to be the most effective tool in the diagnosis and treatment of endometriosis. This technique decreases skin scar, length of hospital stay, cost, morbidity and postoperative adhesions. If there is no deep endometriotic lesion, laparoscopic operation can be performed as a day surgery. On the other hand, if the laparoscopic skill or competence of surgeon is not enough to perform such a complex procedure, laparotomy should be the way of surgery in patients with advanced stage disease. Although the amount of pain was thought to be correlated to the extent of the disease, it has been shown that the revised classification of endometriosis of the American Fertility Society [8,9] is not associated consistently with severity of pelvic pain symptoms.

Surgery for endometriosis-associated pain can be targeted either on the endometriotic lesions or nerve pathways. Disrupting the afferent nerves around the pelvic organs in different techniques is reported to be effective in relieving pain symptom. Laparoscopic uterine nerve ablation (LUNA) and removal of endometriotic lesions in minimal-moderate disease reduces endometriosis-associated pain at 6 months compared with diagnostic laparoscopy [10]. Other reports suggest that LUNA is ineffective in addition to endometriosis surgery [11], and LUNA by itself has no effect on dysmenorrhea-associated with endometriosis [12]. In selected cases presacral

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neurectomy is found to be effective especially in severe dysmenorrhea [13]. In persistent cases hysterectomy can be performed and all visible lesions should be removed during the operation [14]. In severe cases of endometriosis all visible and deeply infiltrating lesions have to be removed. Adding bilateral salpingo-oophorectomy to primary radical surgery may result in pain relief and a reduced chance of repeated surgery [15].

Surgery in peritoneal endometriosis

Peritoneal endometriotic lesions can be visualized in different forms from small red flame-like lesions to black or yellowish spots. If the lesions take place 5 mm or more deep into the subperitoneal location, it is called deep infiltrating endometriosis (DIE). All these lesions can be removed during laparoscopy by excision, ablation using laser or electrical energy. There is no evidence demonstrating that a one energy modality is better than the others. The surgical ablation of peritoneal endometriosis lesions has been shown to be effective for pain management in randomized controlled trials where the control group underwent a laparoscopy without surgical ablations of lesions. The ablation group had a statistically significant reduction of pain symptoms that persisted for 12 [16] and 18 months [17,18]. Addition of LUNA to these ablative procedures has not been proved to be effective in pain relief [9].

Surgery for ovarian endometriosis

There is an ongoing debate about the size of endometriotic ovarian cysts to be removed surgically. In cases with superficial ovarian surface endometriosis lesions can be ablated. However, any intervention to the ovary of a reproductive age women could either create adhesion formation or decreases ovarian reserve. These issues should be kept in mind for the future reproductive capacity of a young woman. Although it is rare, in young ages, the primary indication for surgery of an endometrioma is to exclude malignancy. Most of the guidelines suggest that small ovarian endometriomas (<3 cm in diameter) can be aspirated, irrigated and inspected for intracystic lesions [1]. If possible, stipping of the mucosal lining can be performed but commonly interior wall is handled by coagulation or vaporization. Larger ovarian endometriomata >3 cm was advised to be removed entirely [19]. Sometimes fibrosis around the cyst wall makes the stripping procedure difficult. This technical difficulty can be solved by two-step application of marsupialization and rinsing followed by hormonal treatment and surgery 3 months later [20]. In any type of surgical intervention, ovarian reserve destruction should be minimized to preserve reproductive capacity of the ovary [21] and some authors suggest fenestration and coagulation of inner cyst wall [22] but a case–control study [23] and a randomized controlled trial [24] have demonstrated that pain and subfertility, related to ovarian endometriomas, were improved more by cystectomy than by fenestration plus coagulation. Based on the current evidence, ovarian endometrioma surgery should be performed by stripping of the internal wall lining [19]. Removal of endometrioma has also decreased the risk of recurrence [25].

Adhesiolysis

In the general concept of infertility surgery, we have to avoid adhesion formation. During the endometriosis surgery all adhesions should be dissected carefully to restore pelvic anatomy. It is unclear whether adhesiolysis *per se* is effective in the treatment of endometriosis-related pain. During the endometriosis surgery less tissue trauma, minimal invasive surgical approach, minimal destruction to the peritoneal surfaces and small amount of blood coagulum left in the peritoneal cavity are recommended to avoid surgery-related *de-novo* adhesions. There is no publication demonstrating the beneficial effect of adhesion barriers in any form [26].

Deep rectovaginal & rectosigmoidal endometriosis

Women with a persistent pain after several surgical intervention for symptomatic endometriosis most probably have a DIE in the rectovaginal area. In inexperienced hands, either preoperative evaluation is incompletely performed or during the laparoscopic or open surgery the DIE is overlooked. Repeated operations for symptomatic endometriosis are undesired [27,28]. Therefore, detailed examination before the operation is imperative to avoid repetitive operation. In some cases a rectal involvement may necessitate partial bowel resection. Because of the fact that management of deeply infiltrating endometriosis is complex, referral to a center with expertise to offer all available treatments in a multidisciplinary approach is strongly recommended. This complex operations should be applied only for symptomatic deeply infiltrating endometriosis. Asymptomatic patients must not be surgically treated. Asymptomatic rectovaginal endometriosis is found to be not a progressive disease [29]. When the surgical treatment option has to be chosen, the entire lesion should be removed in the rectovaginal septum. Sometimes rectal lesion is shaved but in severe cases discoid excision or segmental rectal resection and anastomosis need to be done. In severe cases, segmental resection relieves the pain symptom without affecting the chance of reproductive capacity of patients [30].

Since the surgery bears a lot of risk, preoperatively the patients' written signed consent must be obtained. This complex procedure might comprise of the resection of the uterosacral ligaments, the excision of the upper part of the posterior vaginal wall, discoid or segmental bowel resection followed by end-to-end anastomosis, partial cystectomy and ureterolysis, eventually resection, reanastomosis and reimplantation. All these intensive surgical interventions can be completed by laparoscopy or laparoscopy-assisted vaginal route, or by laparotomy [31]. Operative approach to the deep rectovaginal and rectosigmoidal endometriosis is difficult and can be associated with major complications such as bowel perforations with resulting peritonitis [32]. Full bowel preparation with preoperative laxatives, starch-free diet are needed to allow preoperative bowel suturing, if needed. A bowel contrast enema should be performed preoperatively if deep endometriosis is suspected by clinical exam and bowel symptoms. In such cases preoperative evaluation of DIE by transvaginal ultrasound or MRI might be performed. For nongynecologic involvement of endometriosis to the urinary tract or gastrointestinal system, interdisciplinary surgical teams such as bowel surgeons and urologists sometimes have to be included. Rectosigmoid resection has to be discussed preoperatively when indicated and planned accordingly. Ureteric catheters are not required before ureteric dissection. Our experience suggests that ureteric catheters are associated with even harmful for the ureters during periureteric endometriosis removal. Complexity of the disease necessitates the subspeciality of the surgical team not only for handling but also to get rid of the medico-legal issues. Since symptomatic endometriosis creates multiple health problems, multidisciplinary approach is necessary.

Oophorectomy & hysterectomy

When the persistent pain remains in previous treatments in cases without the need for fertility sparing, total hysterectomy is performed. Since the cervix and uterosacral ligaments are common location for endometriosis subtotal hysterectomy is not recommended. For women younger than 30 years of age, hysterectomy should not be a procedure of choice. Addition of oophorectomy is contraversial. Radical extirpation of all endometriosis lesions is an effective treatment for rectovaginal endometriosis. Addition of hysterectomy to recto-sigmoid resection is associated with a better response and quality of life [1].

Results of surgical treatment

Pain sensation is memorized in the certain brain area. Endometriosis-related pain transduction effects neighborhood nerve pathways and even after the radical surgery pain may remain. The results of surgery in patients with endometriosis and pain are influenced by many psychological factors. Patient's personality, marital and psychosexual issues, social factors are the other confounders. Consequently, it is difficult to evaluate the objective effect of different surgical approaches scientifically. Extirpation or destruction of the pathological tissue can impact on the results but not only surgery *per se*, the doctor–patient relationship, complications, etc. are the other contributing factors to the outcome of the pain management. Diagnostic laparoscopy with incomplete removal of endometriosis lesions has also been found to alleviate pain in 50% of patients [18]. Similar results have been reported using oral placebo medications [34]. The long standing effect of surgery on pain is hard to assess as the follow-up time is short, usually just a few months. The risk of recurrences is strongly correlated to the age of the patients. The younger the patients are at the time of the diagnosis the higher the chance of recurrence. Higher recurrence rates in younger women seem to justify a more radical treatment in this group [29].

The major limitations of surgical treatment in endometriosis-related pain are the lack of prospective, randomized controlled trial (RCT) with a follow-up time long enough to draw clear clinical conclusions. In a prospective, controlled, randomized, double-blind study, surgical therapy has been shown to be superior to expectant management 6 months after treatment of mild and moderate endometriosis [18]. Treatment was least effective in women with minimal disease. One year later, symptom relief was still present in 90% of those who initially responded [17]. In another randomized study, it was reported that laparoscopic excision of endometriosis is more effective than placebo in reducing pain and improving quality of life [16]. Surgery resulted in pain relief in 80% of patients with severe disease who did not respond to medical therapy [35]. It is also important to note that all these studies have very short follow-up period. Medical treatment to suppress the gonadal hormones prior to surgery improves rAFS scores, there is insufficient evidence of any effect on outcome measures such as pain relief [36]. In a comparative study for surgery alone or surgery plus placebo, postoperative hormonal treatment does not produce a significant reduction in pain recurrence at 12 or 24 months, and has no effect on disease recurrence [36]. However, postoperative hormonal suppressive medication (GnRHa) has a tendency to delay recurrence. Postoperative 6 months GnRHa treatment resulted in reduced pain scores, and in a delay of pain recurrence with more than 12 months [37,38] but not if they were administered only for 3 months [39]. Similarly, postoperative hormonal treatment with low dose danazol (100 mg/day) during 12 months after sur-

gery for moderate to severe endometriosis resulted in a significantly lower pain score in the danazol group when compared with a placebo group. Interestingly, high-dose danazol (600 mg/day) for 3 months was not superior to expectant management with respect to pain recurrence in an identical patient population [40]. In an RCT postoperative administration of low-dose cyclic oral contraceptives did not significantly affect the long-term recurrence rate of endometriosis after surgical treatment. A delay in recurrence was evident at life-table analysis [41]. In a RCT with a limited number of participants, the levonorgestrel intrauterine system, inserted after laparoscopic surgery for endometriosis associated pain, significantly reduced the risk of recurrent moderate-severe dysmenorrhea at 1-year follow-up [42]. Although the data are not sufficient, it seems logical to offer hormonal suppression after the surgery for pain because endometriosis is known to be a chronic estrogen dependant disease. Conversely, hormonal replacement therapy is recommended after bilateral oophorectomy in young patients for the quality of life measures [43]. In hysterectomized women, adding to progesteron to estrogen replacement therapy is reported to be unnecessary; however, progesteron is associated with protection of the effect of unopposed estrogen on residual disease. It should balance the risks and benefits of progestogenic compound of HRT, since breast cancer risk is associated with the usage of gestagens [44].

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Executive summary

- Pain symptoms related to the endometriosis include dysmenorrhea, dyspareunia and nonmenstrual pelvic pain.
- Asymptomatic patients must not be surgically treated.
- Laparoscopy is accepted to be the most effective tool in the diagnosis and treatment of endometriosis.
- Laparoscopic uterosacral nerve ablation by itself has no effect on dysmenorrhea associated with endometriosis.
- The surgical ablation of peritoneal endometriosis lesions has been shown to be effective for pain management.
- Larger ovarian endometriomata >3 cm was advised to be removed entirely.
- Removal of endometrioma has also decreased the risk of recurrence.
- Because of the fact that management of deeply infiltrating endometriosis is complex, referral to a center with expertise to offer all available treatments in a multidisciplinary approach is strongly recommended.

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