Review Article

Endometriosis surgery in young women: a narrative review

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Objective: To describe the optimum approach to surgery in young women.

Background: Endometriosis is frequently diagnosed in young women who present with pelvic pain, particularly when it is resistant to medical therapies and surgery is frequently considered. Infertility is an infrequent presenting symptom in this age group but future concerns on fertility raises many questions during consultations.

Methods: A Medline and Embase search was carried out to determine the relevant articles. Data related to indications, type, timing and outcomes of surgery, as well as risk of recurrence and strategies for prevention after surgery were summarised.

Conclusions: All stages of endometriosis including deep endometriosis (DE) are found in young women. The data from this young age group are limited but suggest the benefit of surgery for the treatment of pain symptoms. It is debatable whether surgery should be performed as early as diagnosis is made before more severe lesions develop or a more conservative approach should be adopted due to high recurrence rates. Long-term data collection is needed to determine which approach would offer a better long-term outcome. There is even less data on long term fertility outcome following surgery. Due to high recurrence rates postoperative hormonal therapies are recommended to reduce the need for repeated operations.

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Introduction

Endometriosis affects women throughout their reproductive years starting from adolescence. Its prevalence reaches a peak in early 40's but many women trace the beginning of their symptoms back to their teenage years, suggesting that the disease process starts in young ages (1,2). Endometriosis is considered a chronic condition with a high risk of recurrence after treatment (3). This is of particular significance in young women in their teens or 20s who have many more years ahead of them before they become menopausal. It is quite common to treat young women with cyclical pain symptoms such as dysmenorrhoea with hormonal contraceptives alone or in combination with analgesics. This may improve the pain in a significant proportion whether they have endometriosis associated pain or primary dysmenorrhoea so that further intervention may not be needed at that point. However, some will have

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persistence of their pain and may eventually be diagnosed with endometriosis following positive findings on imaging or at laparoscopy (4).

Due to a significant proportion of women experiencing recurrence, surgical treatment of endometriosis poses a specific challenge in young women. Recurrence may lead to repeated operations. In addition to possible surgical morbidity from multiple operations, repeat operations may create further problems such as reduced ovarian reserve and adhesion formation.

In this narrative review article, we will aim to describe the optimum approach to surgery in young women. Indications, type, timing and outcomes of surgery, as well as risk of recurrence and strategies for prevention after surgery will be summarised. Published literature on surgical treatment of endometriosis specifically on young women is relatively limited. There are a small number of publications on surgical treatment of endometriosis in teenagers or adolescents. The definition of 'young women' would probably go beyond the 'teen' years, hence we will try to extrapolate data whenever possible beyond these years. The article is presented in accordance with the Narrative Review reporting checklist (available at https://gpm.amegroups.com/article/view/10.21037/gpm-20-57/rc) (5).

Methods

We searched MEDLINE (through PubMed) and EMBASE (through Embase.com) for potentially eligible records using a combination of MeSH (Medical subject Headings) and relevant index terms. We used MeSH or index terms for the following keywords: "endometriosis", "adolescent endometriosis" and "adolescents", "teenagers", "young women", "surgery", "recurrence", "prevention". The search was limited to humans and papers in the English language. Relevant articles were chosen by the authors and additional relevant references were included from the reference list of these articles.

Indications for surgery

Pelvic pain is the common presenting symptom in young women, although infertility may also be an additional or the primary symptom in a smaller proportion. An article from France on adolescent endometriosis reported five of 55 (9%) girls aged between 12 and 19 years had a history of infertility (6). The most common type of pain in teenagers with endometriosis is the classical dysmenorrhoea and chronic pelvic pain (CPP) (6,7). Dysmenorrhoea is a common symptom affecting 40–50% of young women and is quite often considered to be due to primary dysmenorrhoea that is not associated with an identifiable pathology (8). For this reason, delayed diagnosis which is still thought to be over 8 years may be a bigger issue for younger women (9). Adult women with endometriosis are more likely to experience cyclical pain but teenagers may present with non-cyclical pain (10). Other symptoms include dyschezia, constipation, intestinal cramps, exercise pain and bladder pain. Sexually active teenagers may report dyspareunia (11). Adolescents and young women with endometriosis were twice more likely to report dyspareunia compared to those without endometriosis (79% *vs.* 40%) and have lower quality of life scores (12).

A systematic review of 15 published articles showed that the overall prevalence of visually confirmed endometriosis was 62% in all teenagers undergoing laparoscopic investigation for pain, 75% in girls with CPP resistant to treatment, 70% in girls with dysmenorrhoea and 49% in girls with CPP that was not necessarily resistant to treatment (4). An updated review on the same subject confirms these figures (13). These results indicate high likelihood of endometriosis in this group of young women with pain symptoms, particularly in those resistant to medical treatment.

Although infertility is a less common symptom in young women, future fertility concern is a frequent subject raised by the young woman with endometriosis or by her relatives during consultations. Questions on future chances of fertility, best treatment to preserve fertility, impact of surgery on future fertility, potential damage surgery may cause on fertility and fertility preservation are frequently asked. Young women who are diagnosed with endometriosis are known to have an increased risk of infertility. Prospective data from the Nurses' Health Study II showed that women aged 24–40 years who were diagnosed with laparoscopically confirmed endometriosis had a 2-fold greater risk of infertility compared to those without endometriosis (14). This evidence based information is useful in counselling young women with endometriosis about their future risk of infertility. Based on this data, pre-emptive surgery to improve future fertility may come up during discussion with patients. Currently, we do not have evidence to support this approach (i.e., pre-emptive surgery to enhance future fertility) in young women who have not tried for pregnancy yet. However, the possibility of a long-term

fertility benefit cannot be ruled out altogether and we need prospective long-term data to answer this question.

Ovarian cyst accidents due to endometriomas may be another indication for surgery. Rupture of endometriomas or haemorrhage into cysts causing sudden enlargement can cause severe pain and may warrant emergency surgery. Endometriotic cyst torsions are unlikely, as ovaries tend to be adherent in the presence of endometriosis and this probably makes them less likely to twist. Surgery for asymptomatic endometriomas in young women is controversial and there is no overall consensus when surgery should be performed in this situation. It is generally accepted that asymptomatic endometriomas in the absence of pain, infertility or concern over malignancy do not need treatment regardless of their size (15). There is increasing evidence that presence of endometriomas per se reduces ovarian reserve and this may raise concern about future fertility. However, surgery itself appears to have a detrimental impact on ovarian reserve, hence preventive surgery to protect ovarian reserve may be difficult to justify.

Hydronephrosis due to ureteric obstruction is an obvious indication for surgery and requires immediate action to prevent damage to renal function. This is an uncommon complication of endometriosis in young women but has been reported (16).

Clinical features

Prevalence

Endometriosis is estimated to affect 6–10% women of reproductive age. Epidemiological data from Germany demonstrated 0.05%, 1.93% and 6.1% of patients were in 10–14, 15–19 and 20–24 years age groups, respectively (17). These numbers suggest that endometriosis is less likely to be diagnosed in young women, compared to general reproductive age women. This may be due to lack of awareness amongst patients, their families or medical professionals, as well as clinicians having a higher threshold in agreeing to and carrying out a laparoscopy in the younger age group. As explained above, endometriosis is much more likely to be diagnosed in young women who have CPP symptoms, particularly when it does not respond to medical treatment.

Extent of disease

Endometriosis in young women is not limited to early or superficial disease and all stages of endometriosis are found in this group. This includes deep endometriosis (DE) affecting bowel, bladder and ureters, as well as endometriomas. Certain studies suggest endometriosis in teenagers is mostly early or superficial disease (10,18). This is likely to be due to the patient population looked after by the group that publishes data. A systematic review by Janssen *et al.* (4) found approximately a third of teenagers had advanced disease (revised American Society of Reproductive Medicine Stage, rASRM Classification Stage III and IV). Later studies showed that a much higher proportion of young girls have advanced endometriosis; the series by Davis *et al.* (19) reported 50%, Vicino *et al.* (20) 68.4% and Yang *et al.* (7) 88.9% advanced endometriosis. The recent report from France showed 40% of 55 adolescents had stage III or IV disease, including 6 girls with DE (6). It is quite likely that publications that report a high proportion of ovarian endometriomas originate from centres that operate on symptomatic young women following ultrasound detection of these cysts.

Endometriosis and adenomyosis may co-exist in 20–50% women (21,22). It appears that adolescents with endometriosis are less likely to have co-existing adenomyosis compared to older women (23).

Natural history of endometriosis in young women

Some groups believe that endometriosis in teenagers is a progressive disease (24). However, in prospective randomised controlled trials (RCT) on all age women repeat laparoscopies with an at least six months interval showed spontaneous resolution in 42% of the participants and progress was seen only in 29% of patients (25). Audebert *et al.* (6) reported valuable follow-up data from 50 adolescents on progress; in addition to the initial diagnosis of six DE cases, nine more patients were found to have developed DE at repeat laparoscopy. Furthermore, three (50%) of the original six patients later developed recurrent DE, giving a total of 12 cases with DE during follow-up. The same report also showed five new cases and seven recurrent (35.84%) endometriomas during the follow-up period.

There is now increasing evidence that DE has its origins in adolescence. Many women who are diagnosed with DE have a history of severe dysmenorrhoea and absenteeism from school in teenage years (2). This supports the concept that endometriosis that starts in teenage years progresses to DE in the long-term.

Management of symptomatic suspected or confirmed endometriosis in young women

It is generally accepted that women who present with pain symptoms suggestive of endometriosis and not trying for pregnancy should initially be treated with analgesics and hormonal treatment using combined hormonal contraceptives or progestogens for a period of 3 months. If this approach is not effective, referral and further investigations should be carried out (26). Transvaginal ultrasound examination is usually the first line investigation, however, this may not be appropriate in young women who have never been sexually active. In this situation either a transabdominal or a transrectal ultrasound examination can be considered. Although transabdominal ultrasound would not be sensitive enough to detect many of the markers for endometriosis, transrectal ultrasound would be expected to be a very good alternative to transvaginal scan (27). Diagnostic laparoscopy should be considered in symptomatic young women in whom empirical medical treatment is not effective, as both ultrasound and magnetic resonance imaging would not be sensitive enough to detect superficial endometriosis (26).

Both medical and surgical treatment options can be considered in young women for the treatment of confirmed disease (see section below on 'Timing of surgery'). There are no studies specifically in young women comparing medical treatment with surgery. However, limited data comparing surgery with medical treatment using progestins in all age women suggest that they are both effective in the treatment of pain associated with DE (28). Caution is required before deciding to use gonadotrophin hormone analogues in young women and adolescents, as this group may not have reached maximum bone density (29).

Type of surgery

Surgery for endometriosis aims to eliminate endometriotic lesions, separate adhesions and restore pelvic anatomy. Elimination of the lesions may be achieved by ablating or excising the lesions. In publications specific to teenagers both ablative and excisional approaches have been used. Ablative approaches have been recommended by some groups for the treatment of endometriosis in young women to reduce risk of postoperative pelvic adhesions (30,31). However, a number of other studies in teenagers and/or young women described successful treatment of endometriosis with excisional surgery (6,11,16,32).

There are no direct comparisons of ablative and excisional methods in young women with endometriosis. There are however three RCT from all age women comparing ablation versus excision. A meta-analysis of these RCTs suggest that excisional methods are probably superior to ablation in reducing dysmenorrhoea, dyschezia and CPP (33). For treatment of ovarian endometriomas, excisional treatments have a lower risk of recurrence and higher postoperative spontaneous pregnancy rates compared to drainage and bipolar coagulation (34). It is however possible that ablative methods such as plasma energy or carbondioxide laser may preserve the ovarian reserve better without increasing the risk of recurrence in the long term (35-37).

Timing of surgery

There is no overall agreement as to whether surgery should be delayed or avoided as much as possible, or surgical treatment should be considered at an early stage to prevent progression and should aim to eliminate endometriosis completely, including DE. Whilst some recommend a conservative approach due to high recurrence rates, the others suggest early intervention before more severe lesions develop (24). Long-term data collection is needed to determine which approach would offer a better long-term outcome.

Outcomes

Pain and quality of life

It is generally accepted that surgical treatment of endometriosis is beneficial for the pain symptom of endometriosis and quality of life (29,38). The quality of data that this recommendation is based on has recently been questioned in a recent Cochrane review (39), however the difficulty in performing large scale high quality RCTs explains the lack of good quality evidence.

There are relatively few publications which provide outcome data specific to teenagers and young women. A small case series by Stavroulis *et al.* reported 80% patients had excellent improvement of pain following excisional surgery after a median follow-up of 65 weeks (16). Similarly, Yeung *et al.* (11) and Roman (32) described significant improvement of pain after approximately 2-year follow-up after excisional surgery. It has to be noted that these reports included a small number (11-20) of young women and the follow-up was relatively short (approximately 1–2

years). The larger study by Audebert *et al.* (6) reported that 23.6% of 55 teenagers who underwent ablative or excisional surgery had complete resolution of significant improvement of their symptoms after an average 97-month follow-up.

Fertility outcome

There is even less data on long term fertility outcome following surgery in young women with endometriosis. Audebert *et al.* (6) reported fertility outcome in 18 out of 55 adolescents aged 12–19 years who wished to become pregnant during the average 97-month follow-up. Thirteen (72.2%) had a successful delivery, nine (69.2%) of the pregnancies were in patients who had stage I or II endometriosis. It is not clear whether some of these pregnancies were following fertility treatment. Eleven out of 55 patients developed infertility, six of these (54.5%) delivered a child, two of these were following *in vitro* fertilisation (IVF) treatment, five apparently had a history of infertility at presentation.

It would be useful to compare these fertility outcomes with data from another report which included young women who were treated with a combined oral contraceptive (OC) which was taken continuously. In this report by Ventolini *et al.* (40) twenty-two of the 27 patients who had laparoscopically confirmed endometriosis had a desire to conceive and were followed up for 8.6 years. The fecundability rate which was defined as the probability of achieving a pregnancy within one year period was found to be related to the stage of endometriosis; 3/3 (100%) in stage I, 6/9 (66.7%) in stage II and 3/10 (30%) in stage III. Six of the 22 patients apparently had additional treatments but these were not specified.

This limited information suggests that the majority of young women with endometriosis will be able to become pregnant either spontaneously or after surgery. Some may need help to become pregnant, including IVF treatment and the likelihood of a successful outcome is probably higher in women with early endometriosis.

Recurrence of endometriosis after surgery

Endometriosis is considered as a chronic condition with a significant risk of recurrence despite complete surgical elimination. 10–47% of patients required repeat laparoscopy in published case series of endometriosis in teenagers (6,11,32,41). Symptom recurrence is even more common; in the series by Tandoi *et al.* (41), 57% experienced recurrent pain during 5-year follow-up, and only 23% had resolution or significant improvement of pain in the series by Audebert *et al.* (6). Recurrence of endometriosis or its symptoms in young women is a bigger challenge for clinicians as they have many years ahead of them with potential risk of recurrence before they become menopausal (42). Recurrence may lead to repeat surgery which may carry risks of higher surgical morbidity, postoperative adhesion formation and higher impact on ovarian reserve. There is considerable amount of data indicating that ovarian reserve is diminished after endometrioma surgery depending on the type of endometrioma and technique used (43-45). The effect is greater in women with bilateral endometriomas. The impact of reduced ovarian reserve on natural fertility is not known but there is evidence that it makes future IVF treatment more difficult without improving the chances of success (46). The detrimental impact of endometrioma surgery may be bigger following repeat surgery.

Postoperative hormonal treatment

Hormonal treatments, particularly those that suppress ovulation are usually recommended to reduce risk of recurrence (or secondary prevention), particularly after endometrioma surgery. This concept is supported by a meta-analysis (47) which concluded that the postoperative OC use dramatically reduced the risk of endometrioma recurrence and is recommended in international guidelines (29). A recent network meta-analysis by Wattanayingcharoenchai *et al.* (48) questioned the benefit of postoperative medical therapies in reducing endometrioma recurrence. It concluded that evidence from RCTs do not support the use of postoperative hormonal therapies, but data from cohort studies indicate a significant protective effect of levonorgestrel intrauterine system (LNG-IUS) followed by dienogest, gonadotrophin releasing hormone agonists (GnRHa) + LNG-IUS, continuous and cyclical OCs. The most effective postoperative therapy (although non-significant) was GnRHa+LNG-IUS, followed by continuous OC and GnRHa based on RCTs. It is very likely that suppression of ovulation and reducing/eliminating menstrual flow in the long-term would reduce recurrences. The current literature is too heterogeneous and fragmented to confirm or refute this (49).

Postoperative secondary prevention using medical treatment has bigger significance in young women by reducing recurrences during many remaining reproductive years ahead of them. For this reason, it is probably sensible

to offer postoperative combined hormonal contraceptives or levonorgestrel intrauterine system to young women who are not planning to become pregnant (29).

Future research

There are many unknowns in the management of endometriosis and treatment of endometriosis in young women is no exception. Increasing evidence that suggest that endometriosis may have its roots in early reproductive years makes it even more important to study diagnosis and management of endometriosis specifically in this age group. Further research is required to determine whether early diagnostic laparoscopy instead of empirical treatment, whether early surgery instead of medical treatment prevents progression and provides better long-term quality of life and fertility outcomes and whether excisional or ablative techniques should be used in young women.

Conclusions

Endometriosis may have its roots in teenage years and the most common symptom it presents with is pelvic pain. All stages of endometriosis including DE are found in young women. The data from this young age group are limited but suggest the benefit of surgery for the treatment of pain symptoms. There is even less data on long term fertility outcome following surgery. Recurrence rates are relatively high and postoperative hormonal therapies are recommended to reduce the need for repeated operations.

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