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Does surgery for deep infiltrating bowel endometriosis improve fertility? A review

Running Head: Bowel endometriosis and fertility

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Conflict of interest

The authors have no conflicts of interest in connection with this study.

Abstract

Introduction: Reduced fertility is a major concern in women with endometriosis. The influence of surgery of deep infiltrating endometriosis (DIE) affecting the bowel wall on fertility is controversial and the literature on this field is heterogenous. In this review we addressed if surgery for bowel DIE improves spontaneous pregnancy rate and results of in vitro fertilization (IVF), and the potential risk

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of such surgery. *Material and methods:* We conducted a literature search including the terms “deep”, “deep infiltrating”, “bowel”, rectovaginal”, “endometriosis”, “fertility”, “infertility” and “IVF” in Pubmed. *Results:* No randomized controlled studies were found. Other publications of relevance included four retrospective and three prospective observational studies. Moreover, one retrospective study compared results of IVF treatment with or without previous surgery for bowel DIE. All studies included reported detailed data on surgical complications. The poor data quality precluded firm conclusions. The results indicate, however, the possibility that surgery for bowel DIE may improve the spontaneous pregnancy rate, and positive effects on IVF outcome cannot be excluded. Such surgery will be associated with risk of major complications. *Conclusion:* The lack of proper data preclude conclusions on the potential role for bowel DIE surgery to improve the spontaneous pregnancy rate and results of IVF treatment. Positive effects cannot be excluded, but the definite risk of major complications must be taken into account

Key words

Deep infiltrating endometriosis, bowel endometriosis, colorectal endometriosis, fertility, infertility, rectovaginal endometriosis, bladder endometriosis, ureteral endometriosis, and colorectal resection.

Abbreviations

DIE: deep infiltrating endometriosis

IVF: in vitro fertilization

SPR: spontaneous pregnancy rate

TPR: total pregnancy rate

ICSI intracytoplasmic sperm injection

Key message

Available data on the effects of surgery for deep infiltrating endometriosis affecting the bowel wall to improve spontaneous pregnancy rate and results of IVF treatment are sparse and of poor quality. Positive effects cannot be excluded but such surgery will be associated with risk of major complications.

Introduction

Endometriosis affects 10 % of women of reproductive age and 25-40 % of clients in fertility clinics suffer from this disease (1, 2). Etiologies for the reduced fecundity depend on the phenotype, which includes peritoneal, ovarian and deep infiltrating endometriosis (DIE). DIE is an advanced form that affects up to 12 % of women with endometriosis (3, 4).

In DIE the disturbed anatomy with severe intraabdominal adhesions interferes with gamete transport. However, women with minimal or mild disease and no adhesions also have reduced fecundity and the disturbance of the reproductive process seems to include ovulation, fertilization, implantation and increased risk of miscarriage(5).

Endometriosis patients undergoing in vitro fertilization (IVF) treatment suffer from reduced fertilization, implantation and pregnancy rates compared to women without the diagnosis. Results seem worst for patients with advanced disease(6), and DIE may exert a specific negative impact on IVF- intracytoplasmic sperm injection (ICSI) outcomes (7).

Treatment modalities include medical and surgical interventions, each with different clinical effects and risks of complications. The medical options have contraceptive effects and cannot be used when pregnancy is attempted. Patients with wish for pregnancy are therefore left with the surgical option except for gonadotropin-releasing hormone analogues (GnRHa), that are used for pretreatment before IVF treatment(8).

Infertility patients with minimal to mild endometriosis benefit from surgery with low rate of complications(9). The situation is more complex for advanced disease where evidence is sparse and the risk of severe complications must be taken into account. However, recent data might indicate a role for surgery in DIE patients with wish for pregnancy(10).

The aim of this review is therefore to uncover the literature on the effects of surgery for DIE on fertility and pregnancy rate. We focus on the following, so-called PICO questions(11) with reference to study design, Participants, Interventions, Comparisons and Outcomes: 1. Should surgery for bowel DIE be performed to improve the spontaneous pregnancy rate (SPR)? and 2. Should surgery for DIE be performed prior to IVF treatment to improve outcome? In addition, we addressed the risk of major complications for such surgery.

Material and methods

We performed an electronic database search in Pubmed for publications on fertility and advanced endometriosis published between 2006 and December 2016. The MESH terms “deep endometriosis”, “deep infiltrating endometriosis”, “bowel endometriosis”, colorectal endometriosis”, “rectovaginal endometriosis”, were combined with “fertility”, “infertility” and “IVF”.

Reference lists from the relevant publications were searched for additional studies on the subject. In case of several publications on the same patient series developing over years only the latest was included. Only publications containing specific information on SPR and results of assisted reproductive technology in patients operated for bowel DIE were included. Case reports were excluded. Only papers in English language were included. Included studies concerned patients undergoing laparoscopic discoid transmural excision or segmental resection for DIE infiltrating the bowel wall, where specific data on postoperative leakage from anastomosis and stapler lines, ureter lesions and other major complication could be identified together with information on postoperative fertility. The number of grade C anastomosis leakage(12) (leakage or fistula with need for re-laparotomy) was registered. The postoperative SPR and total pregnancy rate (TPR) were noted. TPR and SPR were defined as the number of women achieving pregnancy with or without IVF treatment relative to the number with wish for pregnancy. In order to answer if DIE surgery should be performed prior to IVF treatment, specific data on pregnancy outcome in relation to the operative complications were specifically searched for.

Results

The selection of studies included in the analysis is shown in the Flow Chart (Fig 1). Although we found 69 publications our strict selection criteria reduced studies for analysis to only 9 publications. These publications are divided into retrospective observational studies, prospective observational studies and controlled studies.

Retrospective observational studies (Table 1)

We found four retrospective observational studies on laparoscopic bowel surgery for DIE with complete data on operative complications, SPR and TPR. Malzoni et al performed laparoscopic segmental colorectal resection in all patients(13), while Kavalleris et al used a combined laparoscopic and vaginal approach for en bloc resection of the affected bowel segment, cul de sac, rectovaginal septum and vaginal wall(14). Meuleman et al(15) and Jelenc et al (16) performed laparoscopic segmental resection in 89% and 93%, respectively, with local discoid excision in the remaining cases. SPR after surgery ranged from 21% to 69%, with 49% for the four retrospective studies added together. For the highest SPR, pregnancies were achieved within a mean period of less than nine months(13). TPR ranged from 48% to 71%. Grade C leakage occurred in 4% for the four studies together, with 9% major complications in total. Ureter injuries were rare.

Prospective observational studies (Table 2)

We found three prospective observational studies reporting laparoscopic bowel surgery for DIE with complete data on postoperative complications, SPR and TPR. Minelli et al (17) and Daraï et al (18) applied laparoscopic segmental resection, while Roman et al (19) used the novel Rouen technique introduced by this group for transanal stapler excision(20) in 20 patients. In the remaining 30 patients the transanal circular stapler method(21) was used .

Taken together, the three studies indicated a SPR of 21% with a TPR of 55%. Grade C leakage occurred in 5% of patients, with ureteral injuries in less than 1%. Total, major complications amounted to 13% in all. Roman et al specifically reported bladder atony in 16% requiring autocatheterization for up to 6 months. More than 70% of the total material was from the Minelly study(17), where a low SPR of 8% was found, as opposed to 39% in the study by Daraï et al(18), and 50% in Roman et al(19)

Controlled studies

No randomized controlled studies were found, and we also failed to identify studies with control groups for assessment of the potential effects of DIE surgery on SPR. One retrospective study presented controlled data on IVF outcome with or without prior surgery for bowel DIE(22), and one prospective study compared PR and TPR after local surgery (shaving or full thickness discoid excision) and segmental colorectal resection(23).

Stepniewska et al(22) compared IVF results for three groups where all patients had laparoscopy performed prior to treatment: Sixty women with bowel DIE who underwent colorectal resection because of severe pain (group A) and 40 patients with bowel DIE where endometriosis surgery was performed except for the bowel due to lack of patient's consent (group B). In group C, 55 women had stage III-IV endometriosis including DIE and at least one endometrioma, but no.

Spontaneous PR was less for group A and B compared with group C, but for patients with bowel endometriosis, surgery improved this parameter. IVF results were also better for group A compared to group B. Surgical complications in group A included two cases of group C leakage (3%) and the total rate of major complications in this group was 8%. Bladder retention was seen in 25% but resolved over time in the majority.

In a recent two-center study, Ballester et al reported assisted reproductive technology outcomes in 60 patients after surgery for colorectal DIE(23). In total, a clinical pregnancy rate of 78% was achieved after up to three cycles. Patients undergoing local excision (shaving or full thickness disc resection) had a higher CPR compared to cases where segmental resection was performed. However the two groups were not comparable, since patients undergoing segmental resection had larger nodules removed.

Discussion

Severe pain that does not respond to usual medical treatment represents the usual background for bowel surgery in DIE patients (24). Improvement of SPR and results of IVF treatment represent new, less compelling indications where surgical risk related to the potential benefits must be given special attention. Firm evidence, preferably from randomized controlled studies, is needed in

this situation, but with few exceptions, data in this field are based on retro- and prospective observational studies. Still, some conclusions may be justified.

Apart from the DIE-induced disturbance of pelvic anatomy, these patients represent a relatively homogenous group of otherwise healthy younger women, irrespective of the individual indication for surgery. Observational data on surgical risks for bowel DIE in general may therefore be imputed some value in the special situation where fertility is of importance.

Major complications to DIE surgery amounted to 9% in the retrospective studies, and to 13% for the prospective, more rigorously collected data. Grade C leakage represents the most serious of these problems and amounted to 5%, and the risk of bladder atony should also be taken into account. However, recent data indicate that most of these patients have a good long term clinical outcome, irrespective of the complication (25). Still, surgery for DIE to improve SPR and results of IVF treatment will be associated with significant risk of major complications, even in subspecialized referral centers.

Severe endometriosis is associated with a very low, crude pregnancy rate and the European Society of Human Reproduction and Embryology (ESHRE) guidelines allow clinicians to consider operative laparoscopy to improve the situation (26). The majority of observational studies in the present review indicate a postoperative SPR from 40% and up to more than 60%. The highest value was reported from a large volume, single surgeon center, with a low risk of grade C leakage and of major complications in general (13). These results may not be generally applicable but they reflect that DIE surgery should be restricted to subspecialized centers where results are monitored to provide proper data for the decision process. Taken together, available data are of poor quality but it seems that surgery for bowel DIE does improve SPR. Clinical consideration in these patients should embrace the total situation, including the local possibilities for IVF treatment, the chance of success and possibilities for public funding, together with the actual risk of surgical complications in the regional endometriosis center.

In the absence of randomized controlled trials, comparative studies including control groups are needed as a minimum to assess the effects of DIE bowel surgery prior to IVF-ICSI. Only one such study was available(22). Although the results indicated that surgery might improve results of IVF treatment, further studies are needed to establish the role for this approach. The data on local excision versus segmental resection do not permit any conclusion on the optimal technique in terms of IVF outcome, but the method that allows for sufficient DIE excision combined with the lowest rate of complications will always be the clinical choice.

Taken together, available data indicate that surgery prior IVF might be considered in cases of concomitant pain and repeated IVF failure, after careful clinical assessment and in cooperation with the regional endometriosis center. The risk of disease progression with bowel obstruction secondary to ovarian hyperstimulation in patients with large DIE nodules should also be kept in mind in this process (27).

In conclusion, data quality on the potential role for surgery for bowel DIE to improve SPR and results of assisted reproductive technology treatment is poor, but positive effects on both parameters cannot be excluded. Such surgery will be associated with risk of major complications and should be performed in subspecialized centers. Detailed information to the patient is mandatory if this approach is considered. Unfortunately, randomised controlled studies will be difficult to perform in this field since patients with pain and wish for pregnancy will be reluctant to leave the important decision about surgery to chance. A realistic alternative would be prospective studies based on shared decisions with detailed clinical data that allow for proper matching of cases and controls.

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Legends

Fig 1. Flow Chart.

Table 1: Retrospective observational studies on postoperative complications and pregnancy rates after colorectal surgery for deep infiltrating endometriosis.

Table 2: Prospective studies on postoperative complications and pregnancy rates after colorectal surgery for deep infiltrating endometriosis.

Table 1: Retrospective observational studies on postoperative complications and pregnancy rates after colorectal surgery for deep infiltrating endometriosis.

	N	Wish for pregnancy n	Spontaneous PR	Overall PR	Grade C leakage	Ureter lesions	Total major complications
Malzoni et al 2016 (13)	248 ^a	72	61%	69%	4%	0	8%
Kavallaris et al 2011 (14)	55 ^b	17	41%	65 %	4%	0	11%
Meuleman et al 2009 (15)	56 ^{a,c}	33	21%	48 %	4%	0	11%
Jelenc et al 2012 (16)	56 ^{a,c}	14	57%	71 %	5%	2%	12%
Total	415	136	49%	63%	4%	<1%	9%

^alaparoscopic segmental; ^ben bloc resection; ^clocal discoid excision.

PR, pregnancy rate.

Table 2: Prospective studies on postoperative complications and pregnancy rates after colorectal surgery for deep infiltrating endometriosis.

	N	Wish for pregnancy N	Spontaneous PR	Overall PR	Grade C leakage	Ureter lesions	Total major complications
Minelli et al 2009 (17)	357 ^a	113	8%	42 %	5%	0.6%	12%
Darai et al 2010 (18)	83 ^a	51	39%	47%	8,00%	0	12%
Roman et al 2015 (19)	50 ^b	20	50%	80 %	4%	0	26%
Total	490	184	21%	55%	5%	<1%	13%

^alaparoscopic colorectal resection; ^bDisc excision by use of the Rouen technique.

PR, pregnancy rate.

Figure 1

