Bowel surgery as a fertility-enhancing procedure in patients with colorectal endometriosis: methodological, pathogenic and ethical issues

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ABSTRACT: Bowel surgery for colorectal endometriosis is being promoted to infertile women without severe sub-occlusive symptoms, with the objective of improving the likelihood of conception. Contrary to rectal shaving, bowel surgery involving full-thickness disk excision and segmental resection entails opening of the intestinal lumen thus increasing the risk of postoperative infectious complications. About 1 in 10 patients undergoing colorectal resection for intestinal endometriosis will experience severe sequelae, including anastomotic dehiscence, rectovaginal fistula formation, and bladder and bowel denervation. Similar to other surgical procedures aiming at enhancing fertility in women with endometriosis, bowel surgery has been introduced into clinical practice without adequate evaluation through randomized controlled trials. According to systematic literature reviews based mainly on case series, the incremental gain of adding bowel procedures to standard surgery appears uncertain in terms of pregnancy rate after both natural attempts and IVF. Considering the methodological drawbacks and the high risk of bias in the available observational studies, it is not possible to exclude the suggestion that the benefit of colorectal surgery has been overestimated. Given the risk of harms to women’s health and the important ethical implications, less emphasis should be put on strict statistical significance and more emphasis should be placed on the magnitude of the effect size. In this regard, the published data may not be generalizable, as the surgeons publishing their results may not be representative of all surgeons. Until the results of adequately designed and conducted RCTs are available, colorectal surgery with the sole intent of improving the reproductive performance of infertile patients with intestinal endometriosis should be performed exclusively within research settings and by highly experienced surgeons. Women should be informed about the uncertainties regarding the harms and benefits of bowel surgery in different clinical conditions, and preoperative counselling must be conducted impartially with the objective of achieving a truly shared medical decision.

Key words: endometriosis / colorectal endometriosis / surgery / infertility / IVF

Introduction

Bowel surgery for colorectal endometriosis is gaining momentum as a fertility-enhancing intervention (Ballester et al., 2017). Elective bowel procedures are suggested in women without severe sub-occlusive symptoms, where the surgery would be optional to improve fertility, rather than mandatory to preserve health (Abrão et al., 2015). Whereas rectal shaving entails subserosal and superficial muscularis excision, full thickness discoid excision and segmental colorectal resection entail opening of the bowel lumen (Abrão et al., 2015; Daraï et al., 2017; Donnez and Roman, 2017; Nezhat et al., 2017). This may cause postoperative infectious complications such as suture/anastomotic dehiscence and rectovaginal fistula formation. In addition, segmental colorectal resection increases the risk of neurogenic bladder and bowel dysfunction due to iatrogenic denervation and may also result in
stenosis of the anastomosis (Vercellini et al., 2009a; De Cicco et al., 2011; Kupelian and Cutner, 2016).

Although disk excision seems associated with a lower complication rate compared with segmental resection (Roman et al., 2016, 2018; Donnez and Roman, 2017; Nezhat et al., 2017), the former procedure is not always feasible, and not all colorectal surgeons are prone to choose it (Vercellini et al., 2018a). In fact, segmental colorectal resection is still frequently performed (Risgaard et al., 2016), especially in case of sub-occlusive stenosis of the rectosigmoid junction or multiple rectosigmoid nodules. As an example, in the recent study by Ballester et al. (2017), 15 out of 60 patients (25%) underwent rectal shaving, three (5%) full thickness underwent disc excision and 42 (70%) underwent segmental colorectal resection. Overall, about 1 woman out of 10 will be harmed by colorectal resection (Vercellini et al., 2009a; De Cicco et al., 2011; Kondo et al., 2011; Iversen et al., 2017; Bouazz and Soriano, 2017).

Currently, bowel surgery is being promoted not only to infertile women seeking conception via natural attempts (Cohen et al., 2014; Darai et al., 2017; Iversen et al., 2017), but also to those scheduled for IVF (Cohen et al., 2016; Ballester et al., 2017; Bendifallah et al., 2017). Bendifallah et al. (2017) maintain ‘although first-line ART remains a good option [for infertile women with colorectal endometriosis], our results suggest that first-line surgery should be systematically considered’.

Is the available evidence sufficiently robust to accept that bowel surgery entailing intestinal lumen opening is routinely proposed to infertile women with non-sub-occlusive colorectal endometriosis with the sole intent of improving reproductive performance? During recent years, we have already witnessed the gradual fading of early enthusiasm for purportedly fertility-enhancing surgical procedures aimed at removing superficial peritoneal, ovarian, and deep lesions, as soon as the preliminary low-quality findings were integrated with better quality data (De Ziegler et al., 2010; Vercellini et al., 2009b, 2012; Somigliana and Garcia-Velasco, 2015; Brink Laursen et al., 2017; Somigliana et al., 2017). According to theESHRE guideline on management of women with endometriosis, ‘overall, the evidence for performing surgery with the sole intent of increasing live birth rate is limited’ (Dunselman et al., 2014, p. 60). Avoiding overestimation of the effect is of particular clinical importance because, compared with surgery for other endometriosis forms, the consequences of radically removing intestinal endometriotic lesions are not limited to future fertility or equitable allocation of healthcare resources, but include potential harms to women’s health.

Addressing some methodological, pathogenic and ethical aspects regarding surgery for bowel endometriosis in infertile women, may help clarify whether disk excision or segmental resection should be implemented in standard practice or whether these procedures should be performed only within research settings until the results of comparative effectiveness trials can be published.

Methodological Issues: The Quality of the Evidence Supporting Colorectal Resection as a Fertility-Enhancing Procedure

Colorectal endometriosis can be categorized into occlusive, sub-occlusive and non-sub-occlusive. The occlusive form is rare and requires emergency surgery. The sub-occlusive form is not rare and requires elective surgery or, in selected cases, medical treatment. Colorectal procedures for infertility, by definition, refer to the relatively frequent non-sub-occlusive forms, when surgery is not mandatory, but constitutes a therapeutic option specifically aimed at increasing the likelihood of conception. In fact, in women not seeking pregnancy, bowel symptoms associated with non-sub-occlusive colorectal endometriosis can be successfully managed with medications in the majority of cases (Egelkvist et al., 2017; Vercellini et al., 2018a, 2018b). Importantly, disk excision and segmental resection performed for non-sub-occlusive colorectal endometriosis are not less risky than when performed for the sub-occlusive forms.

The impact of bowel surgery for colorectal endometriosis on reproductive performance of infertile women has been recently evaluated in two systematic reviews (Darai et al., 2017; Iversen et al., 2017). Darai et al. (2017) highlighted the absence of RCTs conducted to verify the effect of bowel surgery for colorectal endometriosis on the likelihood of postoperative conceptions achieved naturally or via IVF. In this systematic review, the overall postoperative pregnancy rate in infertile patients undergoing colorectal surgery in addition to deep genital-pelvic lesion removal was 31% (95% CI: 28–35%), compared with 26% (95% CI: 14–39%) in women undergoing resection of deep endometriosis but leaving in-situ colorectal lesions (additional gain = + 5%). The overall pregnancy rate observed in infertile women undergoing IVF after surgery including removal of colorectal lesions was 21% (95% CI: 18–25%), compared with 27% (95% CI: 19–35%) in patients undergoing IVF with in-situ colorectal lesions.

Iversen et al. (2017) included in their review four retrospective and three prospective observational, uncontrolled studies. Again, no RCT was identified. The postoperative natural pregnancy rate varied from 21 to 61% in retrospective studies, with a mean of 49%, and from 8 to 50% in prospective studies, with a mean of 21%. Major postoperative complications were observed in 9% of patients included in the retrospective studies and in 13% of those included in prospective studies. Overall, grade C anastomotic leakage was reported in 5% of the women who underwent segmental colorectal resection.

A previous review by Cohen et al. (2014), reported an equal aggregate pregnancy rate of 29% in 1320 women who underwent surgery with removal of bowel lesions and sought conception with natural attempts, and in 115 women who underwent IVF without removal of bowel endometriotic lesions.

The objective of a recent retrospective matched cohort study, not included in the above reviews, was to assess whether the results of IVF were improved by prior bowel surgery in infertile women with colorectal endometriosis (Bendifallah et al., 2017). The pregnancy rate was 60% (40/67) in women who underwent colorectal surgery before IVF and 36% (25/69) in those undergoing immediate IVF. The livebirth rate was, respectively, 49% (33/67) in the former group and 20% (14/69) in the latter one. However, the differential gain in live-birth rate was partly due to unequal distribution of miscarriages between the two groups, as 7/40 (17%) pregnancies ended prematurely in the surgery plus IVF group, compared with 11/25 (44%) in the immediate IVF group. This large and statistically significant difference is at odds with literature findings (Clarke et al., 2010).

Recently, Ferrier et al. (2018) reported the reproductive performance of a series of patients who experienced major complications after colorectal surgery for endometriosis, including rectovaginal fistula, anastomotic leakage, deep pelvic abscess, ureterohydronephrosis, urinary fistula and bowel obstruction. A protective diverting stoma was created in more than one-third of cases. A total of 48 women sought conception after surgery and 16 (33%) achieved a pregnancy with natural attempts after a median time period of 3 years. The natural pregnancy rate was lower (27%) in the 26 women with proven subfertility before surgery. Complications resulting in bacterial contamination of the pelvis were a negative determinant of...
fertility outcome. Of interest, major complications were observed in almost 6% of the entire series of patients (53/900).

Overall, the quality of the available evidence regarding the impact of bowel surgery on pregnancy rate of infertile women with colorectal endometriosis is poor, as it originates mostly from uncontrolled case series with substantial quantitative heterogeneity (Cohen et al., 2014; Darai et al., 2017; Iversen et al., 2017). Whether the mean differential gain over standard surgery for endometriosis without removal of intestinal lesions is clinically meaningful, appears currently uncertain when conception is sought via natural attempts. Shifting the endpoint of bowel surgery toward favouring conception via IVF seems to lack a strong rationale when these procedures have not been definitively demonstrated to substantially favour natural conception.

Once again, surgical procedures have been introduced in clinical practice with the aim of enhancing fertility without well-designed and conducted RCTs. In general, non-randomized studies tend to show larger treatment effects than RCTs (Ioannidis et al., 2001). Thus, it is not possible to exclude the possibility that the effect size of bowel lesions removal in infertile women has been overestimated. Johnson et al. (2008) consider that traditionally in surgical specialties, a non-evidence-based approach to practice has been prevalent and warn that introducing new surgical procedures without RCTs is dangerous. In fact, case series and cohort studies may not allow a reliable estimate of the effect of an intervention owing to unacceptable bias (Johnson et al., 2008; Evers, 2018). Salman et al. (2008), when analysing the available literature data, observed a progressive reduction of effect sizes over time as the quality of studies on gynaecological procedures ameliorated. The authors hypothesized that improvement in research methodology limits biasing factors that inflate effects. Producing robust data on surgical innovation seems feasible. Instructions on how to achieve this goal have been provided (Barkun et al., 2009; Ergina et al., 2009) and recommendations have been developed by the Balliol Collaboration (McCullough and Jones, 2009; McCulloch et al., 2009).

A multicentre RCT is ongoing in France comparing the pregnancy rate of infertile women with colorectal endometriosis undergoing IVF with or without prior radical surgical removal of bowel lesions (https://www.clinicaltrials.gov/ct2/show/NCT02948972?term=endometriosis+AND+France&draw=2&rank=8. Accessed on 26 December 2017). Recruitment is expected to be completed by the end of 2020. Therefore, the results will not be available until another three or four years from now. In the meantime, given the low quality of the supporting evidence and the still undefined balance of harms and benefits, disk excision and segmental bowel resection performed solely for the purpose of improving the reproductive performance of infertile women should be considered as experimental procedures to be performed exclusively in high-volume hospitals by experienced surgeons with the objective of limiting complications (Abrão et al., 2015; Bendifallah et al., 2018).

**Pathogenic Issues: The Impact of Colorectal Endometriosis and Uterine Adenomyosis on Fertility**

Superficial, ovarian and deep endometriotic lesions usually coexist (Somigliana et al., 2004; Chapron et al., 2009). Thus, the rationale for removing colorectal endometriosis in infertile women who otherwise would not need intestinal surgery, is that radically excising all pelvic lesions, including deep bowel lesions, significantly increases the likelihood of natural conception compared with removing pelvic lesions other than deep bowel ones. However, no sufficiently robust evidence consistently supports this assumption. Moreover, discriminating the effects of removing different types of lesion seems problematic. In other words, in the absence of a formal RCT, the possibility that postoperative conceptions are due to removal of genital-pelvic lesions independently of the additional removal of deep intestinal lesions cannot be excluded. Even according to proponents of bowel surgery for infertility ‘colorectal endometriosis is often associated with other anatomical lesions, and thus the impact of colorectal endometriosis alone on fertility remains unclear’ (Bendifallah et al., 2017). As gynaecologists practicing bowel surgery, jointly with colorectal surgeons, are generally extremely experienced, pelvic procedures performed by these highly technically capable surgeons may eventually result in higher natural pregnancy rates, compared with procedures performed by less experienced colleagues, independently of removal of deep intestinal endometriotic lesions.

In order to understand whether colorectal endometriosis should be removed in infertile women, a RCT should be conducted with allocation of participants seeking pregnancy via natural attempts to (i) removal of deep bowel lesions via disk excision or segmental resection plus removal of all non-intestinal deep lesions (experimental treatment) or (ii) removal of all non-intestinal deep lesions leaving deep bowel lesions in situ (standard treatment). To assess whether colorectal procedures per se improve IVF outcome, a three-arm trial should be designed, including the two arms described above, but substituting postoperative natural attempts at conception with postoperative IVF, plus a third, control arm, with allocation of participants to first-line IVF without prior surgery. In the two-arm French trial, all non-intestinal deep lesions are removed in the surgery plus postoperative IVF arm. The trials should be multicentre and multinational, as this would accelerate recruitment, increase the generalizability of the observed results and facilitate acceptance of the outcomes, to avoid the possible criticism that surgery only works in a single centre of extraordinary expertise.

The effect of colorectal surgery in women with endometriosis-associated infertility may be limited also by the repeatedly observed strong association between deep endometriosis and uterine adenomyosis. In a surgical series of 292 women, Chapron et al. (2017) detected focal adenomyosis at MRI in 7.5% of patients with superficial peritoneal endometriosis, in 19.3% of those with ovarian endometriomas, and in 66.3% of those with deep endometriotic lesions. The prevalence of adenomyosis in women without endometriosis was 5.3%.

Adenomyosis may impact reproductive outcome, reducing the likelihood of implantation and increasing the risk of miscarriage (Vercellini et al., 2014a; Dueholm, 2017). According to a systematic review among patients who underwent surgical treatment for rectovaginal and colorectal endometriosis including bowel resection, only 11.9% of those who had a preoperative imaging diagnosis of adenomyosis achieved a natural pregnancy, compared with 43.0% of those without adenomyosis. Thus, when adenomyosis is present in addition to deep endometriosis, patients appear to have a particularly poorer prognosis. In this condition, disk excision or segmental resection would have a minor effect on the likelihood of natural conception (Vercellini et al., 2014b). Even if patients undergo postoperative IVF, it is unclear how the detrimental effect of adenomyosis could be overcome by removal of endometriotic bowel lesions (Dueholm, 2017; Vercellini et al., 2014a).
Ethical Issues: How Large Should be the Minimum Worthwhile Effect Size?

The clinical meaning of any medical measure, beyond statistical significance, is also based on the complex relation between the effect size, the risk of harms and the cost (Vercellini et al., 2015, 2017, 2018c). In general, effect sizes have been classified as trivial, small, moderate, large or very large (Sturmberg and Topolski, 2014). In the present case, translating these categories into definite percentages of additional gain in pregnancy rate seems difficult. Several individual variables influence this relation, including the importance of the outcome for a patient (e.g. different women may have different degree of motivation toward getting pregnant), the propensity toward taking risks to personal health, and the severity of the potential harms. Acceptability is another variable to be considered. As an example, some women may find a temporary diverting ileostomy/colostomy (Ledu et al., 2018) unacceptable independent of the risk of harms.

Despite the above considerations, the minimum worthwhile effect size for a low-risk laparoscopy aiming at destroying superficial peritoneal implants, reasonably should differ from that of a technically demanding bowel procedure with opening of the intestinal lumen to excise deep colorectal endometriotic lesions. Therefore, less focus should be given to P values and more consideration should be placed on the effect size of intestinal surgery. According to the results of the systematic review by Darai et al. (2017), the incremental gain associated with bowel surgery in addition to standard surgery for pelvic endometriosis, in terms of the postoperative pregnancy rate, is around 4-5%. If this estimate is confirmed by good-quality studies, it would translate into a number needed to treat of 20, which means that 19 patients would incur additional morbidity and the risk of major complications needlessly.

When considering surgery for superficial peritoneal and ovarian endometriosis, effectiveness (does the intervention work in practice?) and efficiency (is the effect of the intervention worth the resources it consumes?) are the main issues, whereas safety is generally not the central concern (Vercellini et al., 2017). The opposite seems true for colorectal surgery. How large should the anticipated effect size be to compensate for such a risk of harms? Even supporters of colorectal surgery for infertility acknowledge ‘it should be underlined, nevertheless, that the expected benefit must be weighed against surgery-associated morbidity. Indeed, this option exposes women to major postoperative complications including neurogenic bladder, rectovaginal fistulae and anastomotic dehiscence, or pelvic abscesses’ (Bendifallah et al., 2017). Of relevance here, non-randomized studies are often conservative in estimating absolute risks of harms (Papanikolau et al., 2006).

Treatment of colorectal endometriosis before IVF is promoted by Roman and co-workers also for the prevention of complications after ovarian stimulation or during pregnancy (Roman, 2015; Darwish et al., 2018). In fact, several cases of bowel occlusions, ureteral stenosis and obstetrical problems have been reported in women undergoing IVF without prior removal of colorectal endometriotic lesions (Setúbal et al., 2014; Roman et al., 2015; Seyer-Hansen et al., 2018; Touleimat et al., 2018). This is a serious issue that merits utmost consideration independent of improvement of IVF outcome, also because it is not possible to exclude that these complications are under-reported.

Women with colorectal endometriosis should be referred to tertiary-care centres of expertise in order to undergo in-depth evaluation to exclude already existing bowel stenosis or hydroureteronephrosis. When these conditions are reliably excluded, it is not likely to incur major lesion progression during IVF and pregnancy (Benaglia et al., 2011; Santulli et al., 2016). Complications at both vaginal and abdominal delivery are also frequent in this population, but the risk does not seem to be reduced by previous radical surgery (Thomin et al., 2016).

Undoubtedly, more data are urgently needed on these scarcely known aspects of endometriosis management in infertile women. In this case, the study objective would be to assess the incidence and severity of complications during pregnancy and delivery in women with or without previous resection of bowel endometriotic lesions. Given the low incidence of events, the RCT may not be the best study design to investigate this outcome. In any case, the association seems to be with deep endometriosis in general and not specifically with colorectal endometriosis (Vigano et al., 2015; Leone Roberti Maggiore et al., 2017; Zullo et al., 2017).

Prospectus: Patient Engagement, Shared Decision-Making and Therapeutic Equipoise

Many infertile patients would do almost anything to have a baby. This should induce physicians to raise the ethical bar even more than usual during information and counselling (McCullough and Jones, 2009). It is one thing to resect the rectosigmoid colon because of sub-occlusion or other severe bowel symptoms, but it is another thing to perform the procedure solely for the purpose of increasing the likelihood of conception in women who could otherwise avoid bowel surgery. When pain compromises health-related quality of life and the patient seeks a natural pregnancy and refuses IVF, surgery is indicated as it has been demonstrated to relieve symptoms (Abrão et al., 2015, 2017; Roman et al., 2016, 2018; Darai et al., 2017; Donnez and Roman, 2017; Nezhat et al., 2017). If this is not the case, the caring gynaecologist must describe the uncertainties regarding the causal relation between different endometriotic lesions and infertility, and the potential benefits and harms of removing or leaving colorectal endometriotic lesions in diverse clinical conditions. Endometriosis, even when severe, is not a cancer and, as long as there is no robust evidence of a benefit, should not be treated as such. Furthermore, surgery is not indicated to prevent disease aggravation or impairing deep lesion progression, as the available data do not support this position (Fedele et al., 2004). These aspects are crucial also from a medico-legal perspective.

The information must be expressed quantitatively and in an easily comprehensible manner, using absolute numbers (e.g. crude percentages with a consistent denominator, such as 100 treated), and avoiding the use of estimates such as relative risks. Wording is important, and the negative rather than the positive side of different options should be brought to the attention of the patient (Thornton, 2009). Women must be informed that data supporting the efficacy of colorectal surgery as a measure to improve fertility are mostly derived from non-comparative observational studies, and that the strength of this type of evidence is limited. They should also know that major
bowel surgery is associated with potentially severe complications in 5–10% of cases (Vercellini et al., 2009a; De Cicco et al., 2011; Bouaziz and Soriano, 2017; Iversen et al., 2017). The types of complications together with incidence estimates derived from systematic reviews should be listed. It must be explained that the decision to create a diverting colostomy or ileostomy cannot always be anticipated and sometimes is taken only in the operating room.

Outcomes of complex surgery are strictly operator-dependent, and published data may not be generalizable as surgeons publishing their results may not be representative of all surgeons (Johnson et al., 2008). Women should know that the likelihood of favourable surgical outcomes may be inferior to published figures in case the procedure is carried out in hospitals not specializing in the treatment of severe endometriosis. If the caring gynaecologist is not specifically experienced in removal of bowel endometriotic lesions and is unwilling to refer the patient to tertiary-care centres of expertise, she/he has the ethical obligation of describing the type of surgical activity performed in her/his division including the number of major bowel procedures for colorectal endometriosis per year and the relative outcome. This is already current practice in UK centres accredited by the British Society for Gynaecological Endoscopy and in the endometriosis centres in German speaking countries.

Women should be informed about the risk of complications during pregnancy and at delivery associated with IVF without prior removal of deep pelvic endometriotic lesions including rectovaginal plaques and bowel nodules (Vercellini et al., 2018d). They should also know that there is no robust demonstration that prophylactic surgery decreases the risk of such complications substantially (Somigliana and Garcia-Velasco, 2015; Leone Roberti Maggiore et al., 2016; Somigliana et al., 2017). Couples should not be pushed to undergo IVF, especially when they are willing to continue expectant management. Factors such as the age of the woman, the degree of her ovarian reserve, tubal patency status, presence of large endometriomas and quality of semen must be taken into consideration (Cohen et al., 2016; Abrão et al., 2017). The active participation of the patient should be fostered, promoting the expression of her priorities (Novel, 2017). On these bases, a shared decision should be taken on whether undergoing surgery with or without disk excision/segmental resection or direct IVF. In case of proven tubal patency and normal semen analysis, surgery and IVF are not mutually exclusive and the choice of the sequence of interventions should be left to the woman based on her preferences. When adequately informed and empowered, different women may choose differently, especially when the quality of the evidence in favour of surgery is weak (Johnson et al., 2008).

Patient decision aids according to the International Decision Aid Standards minimum qualifying and certifying criteria (http://ipdas.ohri.ca/using.html. Accessed on 28 December 2017) should be developed (Drug and Therapeutics Bulletin, 2013; Joseph-Williams et al., 2014). Visual decision aids should address the risk of intra- and postoperative major complications, the likelihood of postoperative conception and the pregnancy rate after IVF, with or without removal of deep bowel endometriotic lesions.

Prasad et al. (2012) believe that investigators often conduct studies of modest incremental value without knowing whether the basic standards of care promoted over the years and based on pathophysiological considerations are appropriate. From a research perspective, those practices that have been implemented without prior RCTs demonstrating their effect should be tested first because, in case of uncertainty, the principle of equipoise is fully satisfied and randomization is indicated (Prasad et al., 2012). In order to limit potential investigator bias (e.g. surgeons cannot be blinded), academic ‘rivals’ should be invited to collaborate in designing future RCTs on bowel surgery for colorectal endometriosis (adversarial collaboration), and data should be analysed also by other independent research groups (Leichsenring and Steiner, 2017).

Finally, we suggest that journal editors require that submitted manuscripts reporting the results of observational studies on bowel surgery for colorectal endometriosis performed with the sole intent of improving the chances of conception include the step-by-step description of the shared decision-making process adopted, the text of the information leaflet/brochure for patients, and copies of the informed consent form for both, the scheduled procedure and participation in the study. This supplemental material should be provided online to readers in case of eventual publication of the manuscript. This should apply also to IVF, given the complex nature of the intervention, the limited likelihood of success and the frequent pressure for repeated cycles.

In conclusion, radical removal of bowel endometriotic lesions in infertile women appears to have taken the slippery slope of implementation of a novel surgical approach without prior adequate evaluation. In general, large treatment effects are initially observed in small studies at high risk of bias, but when additional, better-quality trials are conducted, the effect sizes typically become much smaller (Pereira et al., 2012). This appears to be the case also for some surgical procedures for endometriosis-associated infertility as, historically, accrual of better-quality data has led to downsizing of the initially reported effect. When the potential benefit in terms of likelihood of conception is uncertain and the risk of harms is not marginal, there seems to be no alternative to RCTs. Indeed, bowel surgery for colorectal endometriosis appears to be the riskiest procedure to enhance fertility ever performed in the reproductive medicine field. Therefore, before suggesting it, we all have the duty, toward patients, practising clinicians and the scientific community, of providing a sufficiently robust demonstration that the incremental gain of this medical intervention is worth the risk of harms the women take to their health.

Authors’ roles

P.V. conceived and drafted the original version of the article; M.P.F. and A.B. searched the literature, retrieved articles on the topic and extracted data; and P.Vi. and E.S. participated in the conception of the article. All the authors revised critically the article for important intellectual content and approved the final version of the article to be published.

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Conflict of interest

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