

Is fertility preservation a necessity before endometriosis surgical treatment?

Abstract

Endometriosis is a common cause of infertility. Personalized counselling regarding fertility preservation should be offered particularly to young women with high risk of recurrence of endometriosis or to those with bilateral endometriomas. The surgical treatment of ovarian endometriosis consists in cystectomy. The methods used for preserving fertility in women with endometriosis are oocyte or embryo cryopreservation. In this study, we reviewed the literature in order to investigate if fertility preservation is necessary before the surgical treatment of endometriomas. We concluded that more clinical data and economic analyses are needed in order to recommend fertility preservation as a routine procedure for all women before undergoing surgical treatment for endometriosis.

Keywords: fertility preservation, endometriosis, oocyte cryopreservation, embryo cryopreservation

Rezumat

Endometrioza este o cauză frecventă a infertilității. Consilierea personalizată privind conservarea fertilității ar trebui prezentată în special femeilor tinere cu risc crescut de recurență a endometriozei sau celor cu endometrioame bilaterale. Tratamentul chirurgical al endometriozei ovariene constă în chistectomie. Metodele utilizate pentru conservarea fertilității la femeile cu endometrioză sunt reprezentate de crioconservarea de ovocite sau embrioni. În acest articol, am realizat revizuirea literaturii cu privire la conservarea fertilității preoperatoriu în cazul chirurgiei pentru endometrioame. Concluziile arată că sunt necesare mai multe date clinice și analize economice pentru a recomanda conservarea fertilității ca procedură de rutină înaintea intervenției chirurgicale pentru endometrioză.

Cuvinte-cheie: prezervarea fertilității, endometrioză, crioconservare de ovocite, crioconservare embrioni

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Introduction

Endometriosis is defined by the presence of endometrial glands and stroma outside the uterus, and is mostly found on the pelvic peritoneum, ovaries, rectovaginal septum and ureters. Endometrial implants rarely appear in the bladder, pericardium or pleura⁽¹⁾. Endometriosis affects about 10% of women of reproductive age⁽²⁾. Thus, infertility is common in women with endometriosis and has two leading causes: the disease itself and iatrogenicity due to reduced ovarian reserve after surgical treatment^(3,4).

Women with endometriosis – especially young women with high risk of recurrence of endometriosis or those with bilateral endometriomas – should be counselled regarding fertility preservation⁽³⁾.

Originally, methods for preserving fertility were proposed to women who undergo gonadotoxic treatments such as oncologic treatment and consists of: oocyte cryopreservation, embryo cryopreservation or ovarian tissue cryopreservation⁽⁵⁾.

In this article, we will investigate if fertility preservation is necessary before the surgical treatment for endometriosis, and if it is necessary, in which patients.

A narrative literature review was conducted in the PubMed database, in order to select full-length articles published in peer-reviewed journals up to the 14th of September 2020. The keywords along with respective combinations included in the search strategy were: fertility preservation, severe endometriosis, surgical treatment.

We found a total number of 139 relevant articles, published between 1984 and 2020. We selected only full-text articles, with studies including population of adult females, published in this period in the literature.

Preoperative fertility preservation

It is well known that the surgical treatment for stage I or II endometriosis improves fertility, *in vitro* fertilization (IVF) and intracytoplasmic sperm injection (ICSI) outcome^(6,7).

There are no randomized control trials to prove the same outcome in moderate or severe endometriosis. Literature data show that it is recommended to remove large endometriomas prior to attempting spontaneous conception, as part of the treatment of ovarian endometriosis⁽⁸⁾.

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The surgical technique used for endometriomas is cystectomy⁽⁸⁾. It is usually preferred due to the lower risk of recurrence of the disease, but recent studies show that CO₂ laser and plasma energy produce less thermal injury and improve ovarian reserve when compared to ablation using electrosurgery or even cystectomy⁽⁹⁻¹²⁾.

Prior to the surgical treatment, a clear assessment of ovarian lesions is required. Ovarian sparing surgical techniques are mandatory, and these interventions should be performed by skilled gynecologists. All of these measures are taken to prevent further damage to the ovary either by excess excision of healthy ovarian tissue or by deep coagulation that might lower the circulation from the hilum and, therefore, lower the ovarian reserve^(4,13).

During cystectomy, a consistent amount of ovarian tissues is removed and the number of ovarian follicles decreases due to ovarian vascularization damage by electrosurgical coagulation for haemostasis purposes^(14,15).

Anti-Müllerian hormone (AMH) levels are the best current available measure to estimate ovarian reserve⁽¹⁶⁾. Studies have shown that AMH levels decrease up to 30% after excision of unilateral endometrioma and up to 44% after bilateral endometriomas^(17,18). However, AMH is a poor predictor of spontaneous fertility⁽¹⁹⁾.

Antral follicle counting (AFC) is another marker of ovarian reserve and it correlates with AMH levels. AFC can be difficult to determine in the presence of endometriomas and is less reproducible than AMH^(20,21).

Llarena et al. presented in a study the benefits of the surgical treatment of endometriomas. They consist in facilitating oocyte retrieval and prevention of spillage of endometrioma contents into oocyte⁽²²⁾.

In 2015, Hamdan et al. published a meta-analysis of the surgical treatment for endometriomas prior to IVF and concluded that untreated patients had a higher rate of cycle cancellation and a lower mean number of oocytes retrieved⁽²³⁾. Furthermore, two other meta-analyses could not demonstrate a statistical difference in pregnancy rate when comparing surgically untreated and treated endometriomas prior to IVF^(24,25).

However, there are some studies that reveal a major impairment in the ovarian reserve especially after the surgical treatment of bilateral endometriomas⁽²⁶⁻²⁸⁾.

In 2015, a study conducted by Rizk et al. concluded that surgery is recommended as first-line treatment in women affected with minimal or mild endometriosis, as well as for patients with moderate and severe endometriosis⁽²⁹⁾.

Another retrospective study, with the same outcome, compared pregnancy rates in women with advanced endometriosis who underwent repeat surgery versus IVF. It showed a cumulative pregnancy rate of 70% after two IVF cycles, compared to 24% in 9 months of spontaneous trial after repeat surgery⁽³⁰⁾. In a similar way, an additional decrease of AMH levels and AFC was observed after the surgical treatment for recurrent endometriomas rather than after the initial surgery^(31,32).

To minimize the negative effects of surgery on the ovarian reserve, some authors suggested a combined

treatment for endometriomas: laparoscopic cyst drainage and biopsy to confirm the diagnosis of endometriosis, followed by a 12-week treatment with a gonadotropin receptor hormone (GnRH) agonist – this being used to reduce the cyst volume and its mitotic activity, followed by laparoscopic ablation of the cyst wall using CO₂ laser⁽³³⁾. A major disadvantage of this approach is the need for multiple laparoscopies. Despite this disadvantage, a randomized controlled study was conducted by Tsolakidis et al. and reported a significant decrease in postoperative AMH decline with this three-stage approach⁽³⁴⁾.

A series of studies were conducted in order to evaluate pregnancy rate after laparoscopic cystectomy versus combined excision/ablation⁽³⁵⁾.

According to ESHRE guidelines, in women with ovarian endometrioma receiving surgery for infertility, the standard surgical management is excision, because it is proven that it increases the rate of spontaneous postoperative pregnancy^(36,37).

The American Society for Reproductive Medicine suggests that for a 4 cm or larger endometrioma, surgery can be used for histological diagnosis, to ease the access to follicles during oocyte retrieval and to improve ovarian response⁽³⁸⁾.

Fertility preservation (FP) procedures should be taken into consideration for women with endometriosis. It is well known that infertility is commonly found in women suffering from endometriosis, particularly in patients with unoperated bilateral endometriomas and in those who already had surgery for unilateral endometriomas and require surgical treatment for contralateral recurrence⁽³⁹⁾. However, to improve pregnancy rates, surgical and medical treatment for endometriosis should be done before assisted reproduction technology^(5,41).

Bedoschi et al. recommended that women at reproductive age with risk of severe endometriosis or even surgery should be counselled regarding fertility preservation⁽⁵⁾. If oocyte cryopreservation becomes widely used in women with endometriosis, more studies will be needed in this population. More so, the reproductive potential of the ovarian tissue must be assessed, as it might be compromised due to endometriomas^(4,42).

Some reports have demonstrated that ovarian tissue cryopreservation aiming future transplantation and ovarian tissue fresh transplantation are valuable techniques⁽⁴³⁻⁴⁵⁾. Age, history or planned surgeries, the success rates of fertility preservation technologies, as well as ovarian reserve are all factors to be considered when counselling patients regarding fertility preservation. Thus, this approach should be highly individualized^(4,22,39).

The quality of banked oocytes is likely higher in younger women and the risk of endometriosis recurrence is also higher^(39,46). Studies demonstrate that age influences the live birth rate per warmed vitrified oocyte⁽⁴⁷⁾. Doyle et al. proved in their study that the estimated efficiencies per warmed oocyte by age group were as follows: 7.4% for women aged <30 years old at the time

of oocyte cryopreservation; 7% for women aged 30-34 years old; 6.5% for women aged 35-37 years old; and 5.2% for women aged ≥ 38 years old⁽⁴⁷⁾. With this piece of information as a basis, Streuli et al. recommend preserving 15-20 oocytes if the patient is younger than 38 years old, or 25-30 oocytes for the 38-40 years old range⁽⁴⁸⁾.

Conclusions

Firstly, fertility preservation should be an option to be taken into consideration before the surgical treatment in women with bilateral endometriomas, in women with

unilateral endometrioma with history of surgery for contralateral endometrioma, history of multiple surgeries or at risk for multiple surgeries.

Secondly, age is also a criterion. Women older than 37 years of age with any stage of endometriosis should consider fertility preservation.

Thirdly, for patients with endometriosis, oocyte or embryo cryopreservation are the preferred methods. ■

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