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Review Article

Conservative surgical treatment of adenomyosis to improve fertility: Controversial values, indications, complications, and pregnancy outcomes *

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ABSTRACT

Uterine adenomyosis was first reported in the 19th century and early 20th century; von Rokitansky described it in 1860. Since then, the general clinical, pathological, and radiologic findings and potentially useful management methods have been reviewed in many studies. Some authors commented that conservative surgical treatment is impracticable as it is not possible to isolate the adenomyotic tissue adequately; therefore, the authors suggested that hysterectomy is the only rational and complete procedure. There is more evidence supporting the advantages of conservative uterinesparing surgery in providing not only more effective symptom relief, but also longer durable symptom control for symptomatic women with uterine adenomyosis, because the main problem secondary to uterine adenomyosis, dysmenorrhea, can be improved significantly, up to 80%. Menorrhea was also improved in more than two-thirds of patients after type I uterine-sparing surgery, and half of the patients saw benefit in symptom control after type II conservative uterine-sparing surgery. In addition, there was no negative impact on reproductive performance after conservative uterine-sparing surgery, and in fact, reproductive performance seemed to be improved compared with that after medical treatment—not only was there a higher cumulative pregnancy rate, but also a higher cumulative final successful delivery rate. However, there is no doubt that the data supporting the abovementioned benefits for symptomatic women with uterine adenomyosis after conservative uterinesparing surgery are limited, suggesting that the benefit may be moderate. In fact, one of the main indications for surgery is temporary pain relief in women seeking spontaneous conception. However, the effect of surgery on pain is usually only temporarily satisfactory, and the risk of complications varies according to the type of lesion extirpated. In light of this, an extensive review of this topic addressing conservative surgical treatment for adenomyosis to improve fertility, including

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controversial values, indications, complications, and pregnancy outcomes, might be very important, and might help physicians in managing these patients in the future.

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Introduction

Karl Freiherr von Rokitansky [1], in 1860, reported the first pathologic description of adenomyosis—some fibrous tumors in the uterus that contain gland-like structures that resemble endometrial glands, and the tumors appear to have roots deep within the uterine muscle layers, so it is hard to distinguish the border of these tumors within the surrounding myometrial tissues [2]. Adenomyosis is known as "endometriosis (or endometrial glands) of the myometrium in the uterus", and these ectopic endometrial tissues appear to induce hypertrophy and hyperplasia of the surrounding myometrium with resultant diffusely enlarged uterus [3].

Adenomyosis remains an enigmatic disease and a cause of abnormal uterine bleeding and dysmenorrhea, subsequently resulting in chronic pelvic pain and infertility [4]. Adenomyosisassociated morbidity has a significantly negative impact on women's quality of life, and contributes to long-term major health issues. Therefore, a better understanding of adenomyosis might allow less invasive but more accurate diagnostic tests and much more effective treatment. Although we recently reviewed medical treatment and uterine-sparing surgery for adenomyosis [5,6], we wanted to assess whether conservative surgical treatment for adenomyosis can improve fertility through understanding the disease in women undergoing conservative uterine-sparing surgery and by discussing the following issues: controversies, indications, complications, and pregnancy outcome.

Controversy

The need for hysterectomy to diagnose adenomyosis means that it is not easy to diagnose preoperatively. The specificity of a preoperative diagnosis of adenomyosis based on clinical findings is poor, ranging from 2% to 26% [7]. The clinical triad of uterine adenomyosis includes abnormal uterine bleeding (nearly 50%), secondary dysmenorrhea (nearly 30%) and an enlarged, tender uterus [4]. However, many cases of adenomyosis are asymptomatic, and it usually affects multiparous women over the age of 40 years [8]. Clinical diagnoses are suspected after an imaging study or after obtaining an accidental pathological finding when uterine surgery is performed for other indications, suggesting that many cases of adenomyosis go undetected, and this limits our understanding of the prevalence and clinical impact [7]. There have been several pathology-based studies published in which women with adenomyosis found at hysterectomy were often more parous than women in which it was not found [9].

There is a lack of consensus in the literature regarding the relationship between adenomyosis and its associated disease-related clinical problems, such as fertility. This might have resulted from the retrospective nature of the majority of studies and that they mainly included populations undergoing hysterectomy [10]. In addition, these studies used differing criteria for the diagnosis of adenomyosis, and the majority of them did not quantify the severity. The results of retrospective studies showed the absence of a relationship between adenomyosis and the clinical pregnancy rate. In the adenomyosis group, 99 of 206 women had clinical pregnancy, contributing to 48.1% of the clinical pregnancy rate [11].

Compared with the clinical pregnancy rate of 55.1% (383/695) among women without adenomyosis, there was no statistically significant difference between the women with and without adenomyosis [risk ratio (RR) 0.84, 95% confidence interval (CI) 0.67–1.06, p = 0.220] [11]. By contrast, prospective studies showed a significant difference in the clinical pregnancy rate between women with and without adenomyosis. Women with adenomyosis had a significantly lower clinical pregnancy rate (24/98, 24.5%) than women without adenomyosis (245/567, 43.2%), with an RR of 0.55 and a 95% CI ranging from 0.32 to 0.96 [11].

In addition, the use of different diagnostic tools also influenced the results of the studies. Diagnoses made by ultrasound showed absence of a relationship between adenomyosis and clinical pregnancy rate, but diagnoses made by magnetic resonance imaging (MRI) showed a strong association between adenomyosis and clinical pregnancy rate. Of 244 women with ultrasound-diagnosed adenomyosis, 109 finally had a clinical pregnancy (44.7%), relatively similar to the clinical pregnancy rate of 1095 women without adenomyosis (48.3%); there was no statistically significant difference between the two groups (RR 0.84, 95% CI 0.68–1.04). By contrast, diagnoses by MRI showed the significantly negative impact of adenomyosis on the clinical pregnancy rate (RR 0.40, 95% CI 0.25–0.64) [11], suggesting that different study designs contributed to uncertain and/or inconsistent results. Therefore, the potential effect of adenomyosis on fertility continues to be debated.

Furthermore, the presence of a concomitant pathology, for example, leiomyoma (35-55%), endometriosis (6-20%), endometrial polyps (2-3%), endometrial hyperplasia with/without atypia or neoplasms (> 10%), poor ovarian responders (unknown percentage), and others, might have a significant clinical impact on diagnoses, symptoms, and results among women with adenomyosis [12-19].

Finally, the reproductive outcomes of subfertile women with adenomyosis seemed to be varied greatly when different protocol of IVF/ICSI is arranged. Subfertile women with adenomyosis who were treated with a long-protocol of GnRH agonist in the IVF/ICSI cycles, women with and without adenomyosis seemed to have the similar clinical pregnancy rate, with the common RR of clinical pregnancy per patient of 1.05 (95% CI 0.75–1.48) after pooling data from two studies [20,21]. By contrast, the clinical pregnancy rate seemed to be reduced significantly when a short protocol was used in subfertile women with adenomyosis during the IVF/ICSI cycles, with the RR of 0.58 (95% CI 0.38–0.88) in the summarized data of four studies [22–25].

All of them are often overlooked in the study of the relationship between adenomyosis and its clinical observation. Therefore, it is not easy to explore or study the correlation between adenomyosis and fertility problems. We would like to conduct an extensive review of this topic, including recent publications, to highlight the potential influence of adenomyosis on reproduction.

Adenomyosis and fertility

A recent publication by Vercellini et al [11] tried to answer the following question—is adenomyosis associated with assisted reproductive techniques (ART), including *in vitro* fertilization and

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