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Fertility-Sparing Treatment of Adenomyosis in Patients With Infertility: A Systematic Review of Current Options

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Abstract

Adenomyosis is a benign gynecological disease observed in women in their reproductive age. Recent studies have shown that adenomyosis might be a relevant factor for infertility, either impairing implantation or leading to early miscarriage. However, conservative treatment of infertility related to adenomyosis is still unclear. This study systematically reviews the literature for the reproductive outcomes of the available conservative treatments for patients with adenomyosis-associated infertility. We conducted a search in PubMed/Medline for studies in English published in the last 7 years and included 16 studies. Six studies evaluated surgical treatments of adenomyosis. When considering only spontaneous pregnancies, the overall clinical pregnancy rate was very low (18.2%). However, when using GnRH analogues for 24 weeks after surgery, the pooled spontaneous pregnancy rate was higher (40.7% vs 15.0%; $P = .002$). No significant difference was observed in the other outcomes. Ten studies evaluated exclusive assisted reproductive techniques for infertility related to adenomyosis and showed that the long stimulation protocol had better outcomes compared to short stimulation protocol in pregnancy rate (43.3% vs 31.8%; $P = .0001$), live birth (43.0% vs 23.1%; $P = .005$), and miscarriage (18.5% vs 31.1%; $P < .0001$).

Keywords

adenomyosis, treatment, infertility, pregnancy

Introduction

Adenomyosis is a benign gynecological disorder frequently observed in women in their reproductive age.[1,2] The diagnosis is classically made by histological analysis of the uterus after hysterectomy but with the development of the imaging tools now it is easily made by transvaginal ultrasound (TVUS) or magnetic resonance imaging (MRI) with good sensitivity and specificity.[3,4] As nowadays, women are more often delaying maternity, it is common to find adenomyosis in patients with infertility, although the relationship of these 2 conditions is still unclear.[5-8] Recently, studies have shown that adenomyosis might be 1 relevant factor for women's infertility, either impairing implantation or leading to early miscarriage, suggesting that such patients may benefit from previous treatment before in vitro fertilization (IVF) or natural pregnancy.[7] The frequent association between adenomyosis and endometriosis is another factor that impairs the analysis of the reproductive outcome of these patients.[9,10]

The definitive treatment of this condition is hysterectomy; however, in patients with associated infertility, a conservative approach is mandatory to preserve the uterus and reproductive capacity. Currently, there are scarce options of conservative treatment for these patients and many of them are still experimental.[11] Literature data about the efficiency of them are few, especially when considering pregnancy rate.[12]

The aim of this study was to perform a systematic review of the current literature to evaluate the reproductive outcomes of the available conservative treatments for patients with adenomyosis-associated infertility.

Methods

Search Strategy

A systematic search of PubMed/Medline database was performed independently by 2 reviewers (T.P.R. and M.P.A.). The

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review was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[13]

We used the search terms "adenomyosis," "treatment," infertility," and "pregnancy" as key words to recover all possible publications on this topic at PubMed database. Strategies for our electronic search at the PubMed database were the following combined MeSH terms with details: ("adenomyosis"[MeSH Terms] OR "adenomyosis"[All Fields]) AND ("therapy"[Subheading] OR "therapy"[All Fields] OR "treatment"[All Fields] OR "therapeutics" [MeSH Terms] OR "therapeutics"[All Fields]) AND ("infertility"[MeSH Terms] OR "infertility"[All Fields]); ("adenomyosis"[MeSH Terms] OR "adenomyosis"[All Fields]) AND ("therapy"[Subheading] OR "therapy"[All Fields] OR "treatment"[All Fields] OR "therapeutics" [MeSH Terms] OR "therapeutics"[All Fields]) AND ("pregnancy"[MeSH Terms] OR "pregnancy"[All Fields]).

Selection Criteria and Eligibility

We included prospective and retrospective studies in English published in the last 7 years (from January 2010 to April 2017) that assessed the treatment of patients with infertility having adenomyosis. We chose to use only articles published in the last 7 years because there were no systematic reviews in the literature about conservative adenomyosis treatment that included publications after 2010. We included studies that evaluated surgical treatments of diffuse adenomyosis (adenomyomectomy); assisted reproductive treatments (ARTs), such as IVF, intracytoplasmic sperm injection (ICSI), or oocyte donation (OD); and medical treatments with gonadotropin releasing hormone analogues (GnRH-a) or GnRH antagonists.

We excluded reviews, case reports, animal studies, duplicates, studies on hysterectomy, insertion of intrauterine devices, and endometrial ablation. Articles that included patients with endometriosis, even if the results were not separated, were included because we found very few studies that excluded these patients.

Data Extraction

One reviewer (T.P.R.) abstracted the data into tables, and another author (M.P.A.) reviewed the data independently. The tables included the following data: first author, publication year, study design, sample size, inclusion of patients with endometriosis, number of women included, age, diagnostic method for adenomyosis, treatment, follow-up, clinical pregnancy rate, miscarriage rate, live birth rate, and ongoing pregnancy rate.

For data extraction, clinical pregnancy was defined as the presence of intrauterine gestational sac at ultrasound and miscarriage as pregnancy loss before 20 weeks of gestational age. Ongoing pregnancy rate was defined as 12-week viable pregnancy at ultrasound.

From the articles that compared outcomes of patients with and without adenomyosis, we only extracted the data of women with the disease.

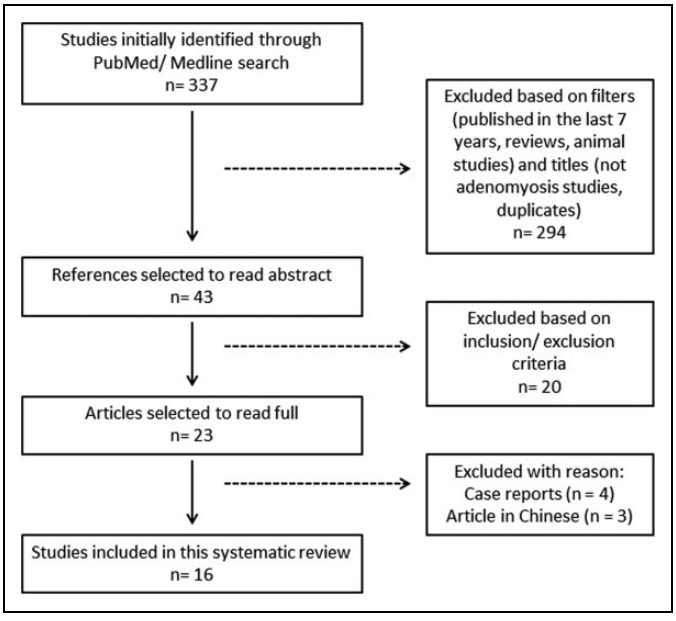

Figure 1. Flow diagram of systematic search of literature.

Statistical Analysis

The data extracted were divided in categorical and continuous variables. Categorical variables were analyzed by description and compared by χ^2 test. Continuous variables were used to calculate absolute and relative frequencies. We considered statistically significant $P < .05$.

Results

Study Selection

We found 337 studies through the initial search with the MeSH terms described, 176 of them published in the last 7 years. Thus, after excluding reviews, animal studies, not adenomyosis studies and duplicates by title, we selected 43 to read the abstract. After applying the inclusion and exclusion criteria, 23 articles were chosen to be read in full. Finally, 7 publications were excluded for being in Chinese language (n = 3) and case reports (n = 4), retrieving 16 articles included in this systematic review for qualitative analysis (Figure 1 and Table 1).

Surgical Treatment

Our search identified 6 articles[14-19] on surgical treatment of adenomyosis, with a total of 353 patients, 5 of them being retrospective[14-18] and 1 being prospective.[19] The surgical techniques for diffuse adenomyosis used were adenomyomectomy with unilateral salpingectomy,[14] microsurgical adenomyomectomy,[15,17] adenomyomectomy using triple-flap method,[16] adenomyomectomy with continuous horizontal mattress technique,[19] and laparoscopic adenomyomectomy with laser.[18] Only 1 article[15] described spontaneous pregnancies after surgical treatment, the other 5 studies reported both spontaneous and

Table 1. Summary of Articles Included in the Systematic Review on Adenomyosis-Related Infertility.

Author Year	Study Design	Adenomyosis Diagnosis	n (patient/ cycle)	Age (Mean)	Adenomyosis Treatment	Endometriosis Included (n)
Mijatovic et al 2010	Retrospective cohort	TVUS	20	33.0	IVF/ICSI	Yes (20)
Nishida et al 2010	Retrospective	MRI + biopsy	44	37.1	Surgery	Yes (3)
Youm et al 2011	Case–control	TVUS	81	33.6	IVF	Yes (18)
Martínez-Conejero et al 2011	Retrospective cohort	TVUS	152/328	40.5	IVF + OD	Yes (23)
Costello et al 2011	Retrospective cohort	TVUS	37	39.0	IVF/ ICSI	Yes (5)
Osada et al 2011	Retrospective	TVUS + MRI + biopsy	104	37.6	Surgery	Unclear
Al Jama 2011	Retrospective cohort	TVUS + MRI + biopsy	18	38.1	Surgery	Unclear
Thalluri & Tremellen 2012	Retrospective cohort	TVUS	38	35.0	IVF	Yes (1)
Salim et al 2012	Retrospective cohort	TVUS	18	34.0	IVF/ ICSI	Yes (1)
Huang et al 2012	Retrospective	TVUS	9	34.2	Surgery	Unclear
Niu et al 2013	Retrospective cohort	TVUS	194	32.1	IVF/ ICSI	Yes (15)
Niu et al 2013	Retrospective cohort	TVUS	145	31.5	IVF/ICSI	Yes (10)
Benaglia et al 2014	Prospective cohort	TVUS	49	35.0	IVF/ ICSI	Yes (21)
Yan et al 2014	Retrospective cohort	TVUS	77	34.2	IVF/ ICSI	Yes (21)
Saremi et al 2014	Prospective	TVUS	103	37.5	Surgery	No
Kishi et al 2014	Retrospective cohort	MRI	75	36.0	Surgery	Yes (54)
Park et al 2016	Retrospective cohort	TVUS	116/ 147	36.1	IVF	Unclear
Park et al 2016	Retrospective cohort	TVUS	87/ 105	35.2	IVF	Unclear
Park et al 2016	Retrospective cohort	TVUS	38/43	34.9	IVF	Unclear

Abbreviations: IVF, in vitro fertilization; ICSI, intracytoplasmic sperm injection; MRI, magnetic resonance imaging; OD, oocyte donation; TVUS, transvaginal ultrasound.

Table 2. Surgical Treatment for Adenomyosis and Fertility Outcomes.

Author Year	Surgical Technique	n	Clinical PR n (%)	Live Birth Rate, n (%)	Spontaneous PR, n (%)	IVF PR, n (%)	Miscarriage, n (%)
Nishida et al 2010	Adenomyomectomy with unilateral salpingectomy	44	2/16 (12.5)	1/16 (6.2)	1/16 (6.2)	1/16 (6.2)	1/2 (50.0)
Osada et al 2011	Adenomyomectomy with triple flap method	104	16/26 (61.5)	14/26 (53.8)	4/26 (15.4)	12/26 (46.1)	2/16 (12.4)
Kishi et al 2014	Laparoscopic adenomyomectomy with laser	102	31/75 (41.3)	26/75 (34.7)	16/75 (21.3)	15/75 (20)	5/31 (16.1)
Saremi et al 2014	Adenomyomectomy with continuous horizontal mattress technique	103	21/70 (30.0)	16/70 (22.8)	7/70 (10.0)	14/70 (20)	4/21 (19.0)
Pooled without GnRH-a		353	70/187 (37.4)	57/187 (30.5)	28/187 (15.0)[a]	42/187 (22.5)	12/70 (17.1)
Al Jama 2011	Microsurgical adenomyomectomy + GnRH-a 24 weeks	18	8/18 (44.4)	6/18 (33.3)	8/18 (44.4)	0	2/8 (25)
Huang et al 2012	Microsurgical adenomyomectomy + GnRH-a 24 weeks	9	5/9 (55.5)	2/9 (22.2)	3/9 (33.3)	2/9 (22.2)	NA
Pooled with GnRH-a		27	13/27 (48.1)	8/27 (29.6)	11/27 (40.7)[a]	2/9 (22.2)	2/8 (25)
Pooled overall		380	83/214 (38.8)	65/214 (30.4)	39/214 (18.2)	44/196 (22.4)	14/78 (17.9)

Abbreviations: GnRH-a, gonadotropin-releasing hormone agonist; IVF, *in vitro* fertilization; NA, data not available; PR, pregnancy rate.
[a]Chi-square test, $P = .002$.

ART pregnancies rates. The follow-up time ranged from 12 to 83 months (Table 2).

The overall pooled clinical pregnancy rate after surgical resection of adenomyosis was 38.8%, ranging from 12.5% to 61.5%. The pooled miscarriage rate was 17.9%, and pooled live birth rate was 30.4%. When considering only spontaneous pregnancies, the overall clinical pregnancy rate was very low (18.2%). However, when using GnRH-a for 24 weeks after surgery,[15,17] the pooled spontaneous pregnancy rate was higher than not using adjuvant GnRH (40.7% vs 15.0%; $P = .002$; Figure 2). There was no significant difference between pooled results with or without GnRH-a after adenomyomectomy for pregnancy rate ($P = .39$), live birth rate ($P = .89$), IVF pregnancy rate ($P = .69$), or miscarriage rate ($P = .95$).

Nishida et al[14] included 44 patients with symptomatic adenomyosis that expressed a desire to preserve the uterus, with 16 of them having primary infertility. They used an adenomyomectomy technique with unilateral salpingectomy and

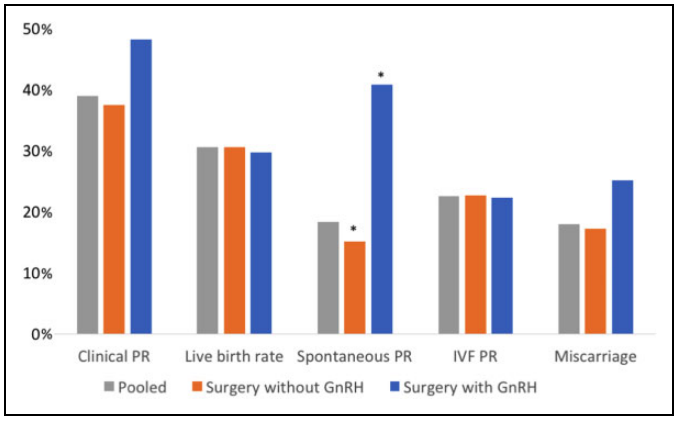

Figure 2. Surgical treatment for adenomyosis and fertility outcomes.

observed a very low pregnancy rate (12.5%). Authors attributed the pregnancy rate (PR) to the reduced uterine volume and weakness of uterine muscle after surgery. Also, follow-up time was short (12 months), and the number of patients trying to achieve pregnancy after surgery was not clear.

Osada et al,[16] evaluated 104 patients with severe adenomyosis diagnosed by MRI and confirmed by histological evaluation, 26 of them wishing to conceive. Patients were submitted to a radical myometrial resection, and the uterine wall was reconstructed with a novel technique described as "triple-flap method". After 24 months, they observed a pregnancy rate and live birth rate of 61.5% and 53.8%, respectively, with 75% of these pregnancies being achieved by IVF. There were no cases of uterine rupture during pregnancy. Saremi et al[19] performed classic adenomyomectomy in 103 patients, 70 of them attempting pregnancy, and had a clinical pregnancy rate of 30% in 24 months. Similarly, the majority of pregnancies (66.7%) were achieved by IVF.

Two studies[15,17] used a microsurgical technique followed by GnRH-a treatment. The first one[15] was a retrospective cohort that compared patients submitted to adenomyomectomy followed by GnRH-a for 24 weeks (n = 18) with those who received only GnRH-a for 6 months (n = 22). They found a better spontaneous pregnancy rate (44.4% vs 13.6%; P = .0393) and live birth rate (33.3% vs 4.5%; P = .0328) in the surgery group. No patient was submitted to ART, and all pregnancies were spontaneous. The second study[17] evaluated 9 patients with adenomyosis diagnosed by TVUS and unexplained infertility. They were submitted to adenomyomectomy followed by GnRH-a for 24 weeks. They observed a similar pregnancy rate to the first study (55.5%), 60% of them achieved by IVF, with a low live birth rate (22.2%). Miscarriage rate was not reported.

Kishi et al[18] compared pregnancy outcomes of 102 women with adenomyosis with desire to conceive submitted to laparoscopic adenomyomectomy using laser. They observed a lower clinical pregnancy rate in women aged ≥40 years compared to those youngers (3.7% vs 41.3%; P = .0006). In the group of women aged <39 years, the spontaneous pregnancy rate was 21.3%, and the IVF pregnancy rate was 60%. In the multivariable analysis, the authors found a lower clinical pregnancy rate in patients with history of previous IVF failure (P = .002) and in those with posterior wall involvement by adenomyosis (P = .004), which was attributed to extrinsic adenomyosis coexisting with pelvic endometriosis.

Assisted Reproduction Treatment

We identified 10 studies about ART for the treatment of adenomyosis-related infertility[20-29]: 7 retrospective cohorts,[20-22,25,26,28,29] 2 prospective cohorts,[24,27] and 1 case–control study.[23] All articles used clinical pregnancy rate as primary outcome; however, only 5[21-23,27,28] described live birth rate (Table 3).

In our pooled analysis, we found an overall clinical pregnancy rate of 36.1%, an overall miscarriage rate of 25.9%, and an overall live birth/ongoing pregnancy rate of 29.9%. When comparing the long and short stimulation protocol of ART in patients with adenomyosis and infertility, a higher pooled clinical pregnancy rate (43.3% vs 31.8%, respectively; P = .0001), a higher live birth/ongoing pregnancy rate (43% vs 23.1%; P = .005), and a lower frequency of miscarriage (18.5% vs 31.1%; P < .0001; Figure 3) were observed.

Most of the studies[20-22,24,25,27,28] compared reproductive outcomes of patients with and without adenomyosis. Four authors[22-25] used a short protocol of ovarian stimulation with a total of 289 patients. For controlled ovarian stimulation, GnRH agonist with Follicle-stimulating hormone (FSH),[23,24] GnRH-a with FSH/Luteinizing hormone (LH),[25] and OD without GnRH-a before embryo transfer were used.[22] Youm et al[23] compared patients with adenomyosis having different myometrial thickness in TVUS and reported a lower clinical pregnancy (56.4% vs 31.5%; P = .02), live birth rate (46.9% vs 15.1%; P < .001), and higher miscarriage rate (12.9% vs 52.2%; P < .001) in women with myometrial thickness higher than 2.5 cm using short protocol stimulation. Other authors also found higher miscarriage rate,[22,24] lower term pregnancy rate,[22] lower clinical pregnancy rate,[24,25] and lower ongoing pregnancy rate[24] in patients with adenomyosis submitted to ART compared to controls.

Two authors[20,21] included a total of 57 patients with infertility and 218 without adenomyosis submitted to IVF/ICSI with GnRH-a long protocol. No difference was observed in implantation rate (31% vs 28.2%; P = .999),[20] clinical pregnancy rate (35.1% vs 31.1%; P = .634),[21] live birth rate (29.7% vs 26.1%; P = .652),[21] ongoing pregnancy rate (35% vs 30%; P = .999),[20] and miscarriage rate (19% vs 26.1%; P = .743 and 15.4% vs 27.1%; P = .376)[20,21] between patients with and without the disease, respectively.

Two authors compared patients with and without adenomyosis.[27,28] Benaglia et al[27] included 49 women with adenomyosis. They found no difference in implantation rate, clinical pregnancy rate, and live birth rate between adenomyosis and control groups or between the type of adenomyosis (focal and difuse). Controversially, Yan et al[28] included 77 patients with

Table 3. Assisted Reproduction Techniques for the Treatment of Adenomyosis-Related Infertility.

Author Year	ART	Protocol	N	Clinical PR, n (%)	Live Birth/Ongoing Pregnancy, n (%)	Miscarriage Rate, n (%)
Youm et al 2011	IVF	GnRH agonist short protocol + fresh ET	81	24/81 (29.6)[a]	11/81 (13.6)	13/24 (54.2)
Martínez-Conejero et al 2011	IVF + OD	OD + fresh ET	152/328	131/ 328 (40)[a]	88/ 328 (26.8)	43/131 (32.8)
Thalluri & Tremellen 2012	IVF	GnRH antagonist short protocol + fresh/ frozen ET	38	9/38 (23.6)	NA	3/9 (33.3)
Salim et al 2012	IVF/ ICSI	GnRH agonist short protocol + fresh ET	18	4/18 (22.2)	2/18 (11.1)	2/4 (50.0)
Niu et al 2013	IVF/ICSI	Frozen ET	145	36/145 (24.8)	31/145 (21.4)	5/36 (13.9)
Park et al 2016	IVF	GnRH antagonist short protocol + fresh ET	116/147	37/147 (25.2)[a]	NA	9/37 (24.3)
Pooled short protocol				241/757 (31.82232)[b]	132/572 (23.1)[c]	75/241 (31.1)[d]
Mijatovic et al 2010	IVF/ ICSI	GnRH agonist 3 months + fresh ET	20	11/20 (55)	7/20 (35.0)	4/11 (36.4)
Costello et al 2011	IVF/ ICSI	GnRH agonist long protocol + fresh ET	37	13/37 (35.1)	11/37 (29.7)	2/13 (15.4)
Niu et al 2013	IVF/ ICSI	GnRH agonist 1 month + frozen ET	194	100/194 (51.3)	90/194 (46.4)	10/100 (10.0)
Park et al 2016	IVF	GnRH agonist 2-3 months + fresh ET	87/105	32/105 (30.5%)[a]	NA	10/32 (31.2)
Park et al 2016	IVF	GnRH agonist 2-3 months + frozen ET	38/43	17/43 (39.5)[a]	NA	6/17 (35.3)
Pooled long protocol				173/399 (43.3)[b]	108/251 (43.0)[c]	32/173 (18.5)[d]
Benaglia et al 2014	IVF/ ICSI	long (26) short (11) other (12) + fresh ET	49	21/49 (43.0)	17/49 (34.7)	4/21 (19.0)
Yan et al 2014	IVF/ ICSI	long (57) short (17) other (3) + fresh ET	77	28/77 (36.4)	19/77 (24.7)	9/28 (32.1)
Pooled overall				463/1282 (36.1)	276/949 (29.1)	120/463 (25.9)

Abbreviations: ART, assisted reproduction treatment; ET, embryo transfer; GnRH, gonadotropin-releasing hormone; IVF, in vitro fertilization; ICSI, intracytoplasmic sperm injection; NA, data not available; OD, oocyte donation; PR, pregnancy rate.
[a]χ^2 test per cycle.
[b]$P = .0001$.
[c]$P < .0001$.
[d]$P = .005$.

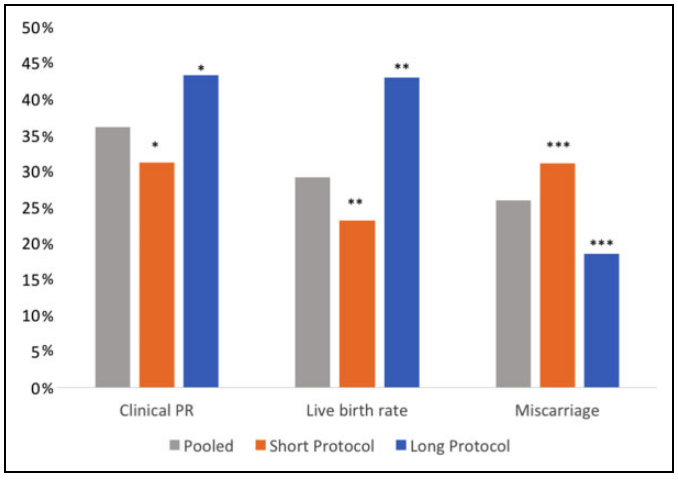

Figure 3. Assisted reproduction techniques using short and long protocol of stimulation with GnRH-a for the treatment of adenomyosis-related infertility.

adenomyosis submitted to ART and observed a lower live birth rate (24.8% vs 33.3%; $P = .022$) compared to control group.

Two studies evaluated the outcomes of different ART protocols in patients with adenomyosis.[26,29] Niu et al[26] compared 339 frozen embryo transfer cycles with or without previous GnRH-a treatment for 1 month. They observed a higher clinical pregnancy rate (51.3% vs 24.8%; $P = .04$) and ongoing pregnancy rate (48.9% vs 21.3%; $P = .02$) in those who received GnRH-a. Park et al[29] in a retrospective cohort compared 3 groups of different ART on infertility patients with adenomyosis: (i) fresh embryo transfer after short protocol stimulation (n = 147 cycles), (ii) fresh embryo transfer after long protocol stimulation (n = 105 cycles), and (iii) frozen embryo transfer after downregulation with GnRH-a for 2 to 3 months (n = 43 cycles). No difference was observed per cycle between groups in clinical pregnancy rate (25.2%, 30.5%, and 39.5%, respectively; $P > .05$) and miscarriage rate (6.1%, 9.5%, and 13.9%, respectively; $P > .05$).

Discussion

Recently, several publications have reinforced the possibility that adenomyosis negatively impair on pregnancy outcomes.[7,8,10] Two meta-analysis by Vercellini et al[7,10] observed a 28% reduction in the likelihood of clinical pregnancy in women with infertility having adenomyosis who underwent IVF/ICSI[7] and a 68% reduction in spontaneous pregnancy in patients with coexisting adenomyosis and endometriosis submitted to surgery for rectovaginal and colorectal endometriosis.[10] Since 1995, de Souza et al[30] reported an incidence of 54% myometrial junctional zone hyperplasia in subfertile patients complaining of menorrhagia or dysmenorrhea. A case–control study on baboons also observed a strong association between lifelong infertility and adenomyosis (odds ratio = 20.6, 95% confidence interval: 2.7-89.7), even after excluding cases with coexisting endometriosis.[31] The possible mechanisms involved in infertility associated with adenomyosis are anatomical distortion of uterine cavity, disturbed uterine peristalsis, abnormal endometrial steroid metabolism, and expression of estrogen and progesterone receptors, abnormal inflammatory response, altered uterine oxidative stress environment, and impaired implantation.[8,32]

Treatment of infertility related to adenomyosis may include assisted reproductive techniques; however, there is no consensus on the best stimulation protocol. This review showed that the long stimulation protocol with GnRH-a before embryo transfer had better outcomes compared to short stimulation protocol, although there are few comparative studies with a high level of heterogeneity between them. Similar results were described by Vercellini et al in their meta-analysis in 2014.[7]

Surgical treatment is a conservative therapeutic option for the treatment of infertility in patients with adenomyosis. Few studies on surgical treatment of adenomyosis with a small number of patients were conducted, most of them being retrospective, and include different surgical techniques, such as adenomyomectomy with unilateral salpingectomy,[14] microsurgical adenomyomectomy,[15,17] adenomyomectomy using triple-flap method,[16] adenomyomectomy with continuous horizontal mattress technique,[19] and laparoscopic adenomyomectomy with laser.[18] However, there is no consensus of which is the best approach, how significant is the impact on fertility, and which are the consequences to a future pregnancy.[33] In the present study, we observed a low-pooled spontaneous pregnancy rate after surgery (18.2%). However, when surgery was followed by GnRH-a, a higher spontaneous pregnancy rate was observed (40.7% vs 15.0%; $P = .002$). Also, when the procedure was followed by ART, the pooled pregnancy rate was 38.8%. The use of GnRH-a seems to have benefic effects in the results of surgery and ART, probably because of its effects on reducing adenomyosis foci in the uterus.

New conservative treatment techniques are being studied, such as high-intensity-focused ultrasound. Some authors observed a significant improvement of dysmenorrhea and abnormal uterine bleeding with good tolerability, although reproductive outcomes have not been described yet.[34,35]

Limitations of this study are the absence of controlled well-designed trials on conservative treatment of adenomyosis, the small number of patients enrolled in the included papers, and the inclusion of women with prior history of IVF failure. Also, most of included studies do not exclude patients with concurrent endometriosis, a disease that might also compromise reproductive outcomes.

In conclusion, adenomyomectomy alone has low impact on infertility treatment, with low spontaneous pregnancy rates, and should be followed by ART or medical therapy with GnRH agonists. Assisted reproductive treatments have good pregnancy rates in women with adenomyosis, and data suggest that long stimulation protocol is superior to short protocol. Further randomized controlled trials are necessary to define the best strategy for patients with adenomyosis who want to conceive; thus, this condition remains a challenge in clinical practice.

Declaration of Conflicting Interests

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