



## CONTEMPORARY CLINICAL CONSIDERATIONS OF INFERTILITY DUE TO ENDOMETRIOSIS

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***Annotation.** The development of organ-preserving approaches to the treatment of uterine fibroids began in parallel with the introduction of radical surgical methods. However, for many years, conservative strategies lagged behind and had relatively few advocates. In recent decades, organ-preserving interventions have moved into the forefront of gynecological practice. This shift is both logical and expected, being driven by advancements in medical technologies as well as the increasing demand among women for solutions that safeguard reproductive potential. Several factors explain this trend. On the one hand, there is a steady rise in pregnancies occurring at later reproductive ages. On the other hand, uterine fibroids are being diagnosed more frequently in young, nulliparous women. Another contributing factor is the influence of mass media and the Internet, which have begun to pay greater attention to health-related topics, including coverage of innovative medical technologies. Successful organ-preserving management of uterine fibroids requires a thorough understanding of the nature of the disease itself. The term “uterine fibroids” encompasses a heterogeneous group of pathological changes within the uterus. A clinician may describe fibroids as a single, asymptomatic 1 cm intramural nodule, or, conversely, as multiple large formations equivalent in size to a 25-week pregnancy, accompanied by profuse bleeding and compression of adjacent pelvic organs.*

*Consequently, treatment strategies are largely determined by the accuracy of the clinical classification applied.*

*The existing classifications—histological and localization-based—are of limited practical value, as they do not provide sufficient guidance for clinical decision-making. In practice, current indications for hysterectomy allow conservative management only up to fibroid sizes equivalent to 12 weeks of gestation, which effectively promotes a passive approach in patients with smaller lesions. Therefore, there is a pressing need for a clinically oriented classification system that integrates such parameters as fibroid size, number of nodules, anatomical location, and the patient's reproductive plans. Such a system would enable clinicians to determine treatment tactics more precisely and personalize therapeutic strategies in line with reproductive goals.*

**Key words:** *uterine fibroids, mifepristone, uterine artery embolization, proliferating uterine fibroids.*

**Relevance.** Uterine fibroids rank second in the overall structure of gynecological morbidity. Epidemiological studies indicate that signs of this condition can be detected in up to 77% of women. Over the past decade, there has been a marked trend toward a “rejuvenation” of the disease: in Russia, the prevalence of fibroids in women under 30 years of age has increased from 2% to 12.5%, while in the United States the incidence in women aged 18–30 years reaches 43–57%. Fibroids have a significant negative impact on both reproductive function and women's general health; however, to date, a clear pathogenetic mechanism that directly explains their effect on fertility has not been fully established.

The management of patients with uterine fibroids continues to attract considerable attention from gynecologists worldwide. The

recurrence rate following organ-preserving surgery ranges from 15% to 45%, while repeat surgical intervention is associated with increased trauma, a higher risk of intraoperative bleeding, and the likelihood of postoperative adhesion formation. This highlights the importance of developing new strategies aimed at reducing the necessity for repeated surgical procedures. Furthermore, postoperative anti-relapse therapy is essential, since the surgical removal of fibroid nodules does not address the underlying causes of their development, and intraoperative damage to the myometrium itself predisposes patients to recurrence. Consequently, enhancing the effectiveness of both conservative surgical techniques and pharmacological prevention of relapse remains a pressing clinical challenge.

The use of anti-relapse drug therapy raises a number of controversial and debated issues. These include the development of specific complications related to hormonal and metabolic disturbances, the short duration of therapy, the recurrence of disease after drug discontinuation, and—most importantly—the limitations of using such treatments in young women. Gonadotropin-releasing hormone agonists (GnRH agonists) are among the most widely employed pharmacological agents in the management of uterine fibroids, yet their application is restricted due to the induction of hypoestrogenic states, disturbances of mineral metabolism, short-term therapeutic efficacy, and high recurrence rates after withdrawal. At the same time, many researchers emphasize the promise of antigestagens, with mifepristone being the first representative of this class, which opens up new possibilities in the pharmacological treatment of uterine fibroids.

**The aim of the research.** The primary aim of the study was to improve reproductive outcomes following surgical treatment of uterine fibroids and to prolong the period of remission of the disease.

**Materials and Methods.** The investigation was carried out in the gynecology department of the multidisciplinary clinic of Samara State Medical University. A prospective comparative cohort study included 90 women who had undergone organ-preserving surgical treatment for uterine fibroids between 2012 and 2023. The inclusion criteria were: age 25–45 years (mean age  $33 \pm 5.5$  years) and previous organ-preserving surgery for fibroids. Exclusion criteria comprised: allergic reactions or contraindications to mifepristone, severe somatic comorbidities, liver disease, as well as concurrent hyperplastic uterine conditions (adenomyosis, endometrial hyperplasia). Patients were stratified into groups depending on the type of surgical intervention received.

The diagnostic program incorporated standard clinical, laboratory, and morphological methods. Before the initiation of therapy, data were collected to confirm patient eligibility, including adherence to inclusion/exclusion criteria, anthropometric characteristics, lifestyle habits (smoking, alcohol consumption), reproductive and medical history, comorbidities, physical examination, gynecological status, ultrasound with Doppler, general laboratory testing, and the type of organ-preserving surgery performed. Clinical-anamnestic evaluation focused on gynecological history, duration and course of the disease, while somatic status was assessed through clinical examination.

Laboratory tests included a complete blood count, urinalysis, biochemical profile, coagulation panel, blood group and Rh factor determination, and bacterioscopic examination of cervical canal

discharge. Instrumental studies involved transvaginal and transabdominal pelvic ultrasound with Doppler assessment. Material for morphological evaluation was obtained through invasive diagnostic procedures, including endometrial aspiration biopsy.

**Results.** The mean age of patients was  $33 \pm 5.5$  years (range 25–45). Analysis of clinical and social characteristics revealed no statistically significant differences between groups in terms of age at menarche, onset of sexual activity, body mass index, disease duration, or comorbid gynecological and somatic conditions. Anamnesis showed that uterine fibroids were asymptomatic in 40% of women, while 60% reported pain, 50% had menstrual irregularities (predominantly menorrhagia), and 45% experienced a combination of these complaints. Overall, 81 of 136 patients presented with pain of varying severity.

Pain intensity was evaluated using the Verbal Rating Scale (VRS), Numerical Rating Scale (NRS), and Wong–Baker facial pain scale. According to these assessments, 36 patients rated their pain as mild (VRS) and scored 2 points on the NRS (not interfering with daily activities); 27 patients experienced moderate pain (VRS), 4–5 points on the NRS (interfering with daily activities); and 18 patients reported severe pain (VRS), 7 points on the NRS (interfering with basic needs). Ultrasound revealed uterine sizes corresponding to 6–16 weeks of gestation (mean  $10 \pm 3.1$  weeks), with 1–10 fibroid nodules per patient (mean  $3.4 \pm 1.4$ ). The size of the nodes ranged from 2 to 10 cm (mean  $5.5 \pm 2.4$  cm).

Based on symptomatology, fibroid size, number, localization (according to the 2011 FIGO classification), and the patient's reproductive intentions, various types of organ-preserving surgeries were

performed. Laparoscopic myomectomy was performed in 48 patients with subserosal-intramural fibroids (FIGO class 5–7), vaginal myomectomy in 8 patients (class 6–7), laparotomy myomectomy in 24 women with intramural fibroids (class 3–4), and hysteroscopic myomectomy in 16 women with submucosal fibroids (class 0–1). In addition, 40 patients who did not wish to preserve fertility and had submucosal-intramural fibroids (class 2–4) underwent uterine artery embolization (UAE). No intraoperative or postoperative complications were observed, and the menstrual cycle was restored within 14–21 days in all cases.

Among patients who underwent myomectomy without adjuvant therapy, pregnancy occurred in 4 cases (25%), with only one resulting in spontaneous delivery. In contrast, after surgery followed by three months of anti-relapse therapy with Ginestril, pregnancy was achieved in 37 patients (46%), 34 of whom (91%) delivered at term. In the UAE group treated with Ginestril, pregnancy was recorded in 3 women (10%), all of which resulted in live births.

Pregnant women with a history of surgical treatment for fibroids were classified as high risk for obstetric and perinatal complications. The most frequent complication across all groups was threatened miscarriage, observed in 19 women (51%) after myomectomy and in all patients of the control group (100%). Threatened preterm labor required hospitalization in every fourth case. Other pregnancy complications included anemia (27%), preeclampsia (16%), and fetoplacental insufficiency (8%). The incidence of pregnancy complications did not significantly differ depending on the surgical technique used. Overall, 34 of 37 women (91%) who conceived after treatment and adjuvant therapy

carried pregnancies to term, underscoring the favorable impact of Ginestril on reproductive outcomes.

**Conclusion.** Long-term follow-up demonstrated that the use of Ginestril in the postoperative period in women who underwent organ-preserving surgery for proliferating fibroids effectively prevented recurrences for up to 24 months after discontinuation. Adjunctive therapy with Ginestril following UAE also contributed to a reduction in postoperative recurrence rates. A combined treatment strategy—surgical myomectomy followed by Ginestril—enabled the realization of reproductive potential in 46% of patients. Vaginal delivery occurred in 24% of women who received adjuvant therapy after myomectomy, while the overall incidence of obstetric complications did not depend on the surgical method employed.

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