

THE NICHE IN THE UTERINE CESAREAN SCAR: A NEW PROBLEM OF WOMEN'S REPRODUCTIVE HEALTH

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■ **Hypothesis/aims of study.** In the recent decades, the quality of uterine suture repair after a cesarean section is widely discussed, as local thinning of the myometrium forming uterine scar defects, or the so-called scar niche, are relatively common after the operation. The aim of this study was to identify the causes of local thinning of the uterine scar after cesarean section, to determine the effectiveness of existing methods for assessing the uterine scar in non-pregnant women, and to develop a method for surgical correction of this pathology.

Study design, materials and methods. Over 4 years, 175 non-pregnant women with a uterine scar were examined. The 50 of them were diagnosed with the uterine scar niche, with a laparoscopic metroplasty performed in these patients. The effectiveness of the operation was evaluated in the long-term postoperative period.

Results. Performing cesarean section because of weakness of labor activity and a complicated course of the postpartum period are significant factors in the formation of a uterine scar niche ($p < 0.05$). Ultrasound examination and magnetic resonance imaging of the pelvic organs can be used to detect local thinning of the myometrium with a sensitivity of 82% and 96%, and a specificity of 85% and 90%, respectively.

Conclusion. Metroplasty for patients with a diagnosed scar niche can significantly increase the thickness of the myometrium ($p < 0.05$) and reduce the frequency of complaints of such menstrual irregularities as postmenstrual vaginal bleeding, dysmenorrhea, and hypermenorrhea ($p < 0.05$).

■ **Keywords:** cesarean section; uterine scar; niche; metroplasty.

НИША РУБЦА НА МАТКЕ ПОСЛЕ КЕСАРЕВА СЕЧЕНИЯ — НОВАЯ ПРОБЛЕМА РЕПРОДУКТИВНОГО ЗДОРОВЬЯ ЖЕНЩИНЫ

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■ **Актуальность.** В последние десятилетия широко обсуждается тема качества репарации шва на матке после операции кесарева сечения, при нарушении которой развивается локальное истончение миометрия с формированием так называемой ниши рубца.

Цель — выявить причины возникновения локального истончения маточного рубца после кесарева сечения, определить эффективность существующих методов оценки состояния рубца на матке вне беременности и разработать методику хирургической коррекции данной патологии.

Материалы и методы исследования. За 4 года обследовано 175 небеременных пациенток с рубцом на матке. У 50 из них диагностирована ниша рубца и выполнена лапароскопическая метропластика. Эффективность операции оценена в отдаленном послеоперационном периоде.

Результаты исследования. Кесарево сечение, проведенное в связи с развитием слабости родовой деятельности, а также осложненное течение послеродового периода являются значимыми факторами при формировании

ниши рубца ($p < 0,05$). Ультразвуковое исследование и магнитно-резонансная томография органов малого таза могут быть использованы для выявления локального истончения миометрия с чувствительностью 82 и 96 %, специфичностью 85 и 90 % соответственно.

Выводы. Выполнение метропластики пациенткам с диагностированной нишей рубца позволяет значимо увеличить толщину миометрия ($p < 0,05$), а также способствует нормализации менструального цикла, уменьшению выраженности таких симптомов, как постменструальные кровянистые выделения из половых путей, дисменорея, гиперменорея ($p < 0,05$).

■ **Ключевые слова:** кесарево сечение; рубец на матке; ниша рубца; метропластика.

Introduction

Scarring on the uterus after a cesarean section (C-section) remains an issue in obstetrics and gynecology. The frequency of C-section is constantly increasing and has reached 29.3% in Russia [1] because of multifactorial etiologies. However, the diverse problems in maternal and child health have not yet been resolved.

Thus, researchers in the last decades have focused on the long-term complications of C-section surgery caused by scarring on the uterus (placenta accretion or presentation, pregnancy in the scar, uterine ruptures, and so on). The increased frequency of complications is associated with the increased proportion of abdominal delivery [2, 3].

Myometrial, vascular, and nerve ending cells are damaged during surgery; therefore, questions regarding the quality of uterine repair after C-section [4–7] and complications associated with an imbalance of this process are becoming increasingly relevant. One of these complications is local myometrial thinning with scar niche formation [8–10], the symptoms of which appear in the remote postoperative period [11–13]. Interest in this topic is steadily growing, as confirmed by a large number of publications (i.e., 105 articles and one monograph) [14].

The purpose of our study is to identify the causes of local thinning of the uterine scar after C-section to determine the effectiveness of existing methods for assessing the state of the scar on the uterus outside of the pregnancy and to develop a surgical correction method for this pathology.

Material and methods

From 2015 to 2018, we examined 175 non-pregnant patients with a uterine scar after C-section surgery in the lower segment of the uterus at full-term gestation (single pregnancy). Fifty patients included in the study underwent metroplasty.

The anamnesis data of the patients were collected, and patients' menstrual and reproductive functions were further elucidated (including indications for the last C-section, the course of postpartum period, etc.).

All patients underwent transvaginal ultrasound (US) examination of the pelvic organs (PO) ($n = 175$) [14], followed by the magnetic resonance imaging (MRI) of the PO for those patients whose US data revealed a myometrial depression of at least 2 mm on the endometrium side, the so-called "scar niche" ($n = 50$), as well as 20 patients without signs of scar thinning. On the basis of noninvasive instrumental study data (US and MRI), the patients were divided into two groups. The first (main) group included patients ($n = 50$) whose US and/or MRI data revealed local myometrial thinning in the form of a niche with a residual thickness of the myometrium (PO) less than or equal to 5.0 mm. The second (control) group consisted of patients ($n = 125$) whose myometrium thickness was more than 5.0 mm. Then, diagnostic hysteroscopy was performed. Furthermore, if local myometrial thinning was detected in the form of a niche, we performed laparoscopy and metroplasty. After excision of the scar tissue, the tissue sample was collected and sent for histological examination to evaluate the contents of the muscle, fibrous tissue, and adipose tissue; the presence of foci of endometriosis in the structure of scar-smooth muscle actin- α , %; the degree of vascularization — CD31 (antigen that marks endothelial cells), %; and the severity of inflammation — CD45 (total leukocyte antigen), %. A uterine scar biopsy was performed in the control group by using a needle for a Bard-Monortu puncture biopsy to obtain histological material.

The effectiveness of treatment was evaluated in the course of prospective monitoring for patients of the main group, which included repeated questionnaires and examination, US and MRI of

the PO after 3–6 and 7–12 months, respectively, and a study of reproductive function.

Statistical processing of the obtained data was performed using SAS 9.4. Statistical data obtained during the immunological study were analyzed using AtteStat 12.1.7.

Research result

The average age of the patients was 33.49 ± 3.49 years. There were no significant inter-patient differences ($p > 0.05$) with regard to the number of pregnancies (2.21 ± 1.49 ; 2.06 ± 1.22 in the main group and 2.26 ± 1.59 in the control group), births (1.53 ± 0.79 ; 1.36 ± 0.69 in the main group and 1.60 ± 0.81 in the control group), and C-section (1.30 ± 0.61 ; 1.28 ± 0.57 in the main group and 1.30 ± 0.63 in the control group).

Indications for C-section to determine their effect on scar formation were divided into the following groups [1, 15]:

1) placenta previa (complete or incomplete with bleeding);

- 2) premature detachment of normally located placenta;
- 3) previous surgeries on the uterus (two or more C-section, one C-section in combination with other relative indications, myomectomy (except for the submucous location of the myomatous node and the subserous node on a thin base), or a surgery for a history of abnormalities in the uterine development (removal of the rudimentary uterine horn));
- 4) incorrect position and presentation of the fetus (oblique position, pelvic presentation with an estimated fetal weight of ≥ 3600 g, or pelvic presentation in combination with other relative indications);
- 5) pregnancy duration of ≥ 41 weeks in the absence of the effects of childbirth preparation;
- 6) fetal–pelvic disproportion (clinically narrow pelvis, fetal–pelvic disproportion with a large fetus, or deformity of the pelvic bones);
- 7) anatomical obstacles to childbirth through the natural birth canal (scarring of the cervix and

Table 1 / Таблица 1

Differences in indications for cesarean section between the main and control groups

Различия показаний к кесареву сечению между основной и контрольной группами

Indications for a C-section	Group 1		Group 2		Total		p
	quantity	frequency, %	quantity	frequency, %	quantity	frequency, %	
Placental previa	1	2	7	5.6	8	4.6	0.44
PDNLP	3	6	6	4.8	9	5.2	0.71
Previous operations on the uterus	9	18	25	20	34	19.4	0.83
Incorrect position and presentation of the fetus	9	18	14	11.2	23	13.2	0.22
Pregnancy for 41 weeks and more in the absence of the effect of preparing for childbirth	1	2	0	0	1	0.6	0.28
Fetal–pelvic disproportion	7	14	15	12	22	12.6	0.8
Anatomical obstacles to childbirth	0	0	5	4	5	2.8	0.32
Threatening rupture of the uterus	0	0	5	4	5	2.8	0.32
Preeclampsia severe	1	2	11	8.8	12	6.8	0.18
Somatic diseases that require the exclusion of attempts	2	4	10	8	12	6.8	0.51
Fetal stress	6	12	22	17.6	28	16	0.49
Abnormalities of contractile activity of the uterus	11	22	5	4	16	9.2	<0.05
Total	50	100	125	100	175	100	–

Note. PDNLP — premature detachment of the normally located placenta.

Table 2 / Таблица 2

Characterization of the postpartum complications in the study groups

Характеристика осложнений послеродового периода в обеих группах

Group of complications	Group 1		Group 2		Total		p
	n	%	n	%	n	%	
Pyo-inflammatory	9	66.7	3	25	12	50	<0.001
Related to pathological blood loss	3	33.3	2	16.7	5	20.8	0.10
Subinvolution of uterus	0	0	4	33.3	4	16.6	0.25
Other (renal colic, thrombophlebitis)	0	0	3	25	3	12.6	0.27
Total	12	100	12	100	24	100	–

vagina after suture of a third-degree perineal tear in previous births);

- 8) threatening rupture of the uterus;
- 9) severe preeclampsia;
- 10) somatic diseases requiring the exclusion of attempts (severe neurological pathology or syndrome of the operated spine);
- 11) fetal distress (acute fetal hypoxia in childbirth or decompensated forms of placental insufficiency);
- 12) abnormalities of a contractile activity of the uterus (weakness of labor, resisting to a medication).

A C-section made in connection with the development of abnormalities of contractile activity of the uterus (weakness of labor activity) significantly influenced the local myometrial thinning ($p < 0.05$) (Table 1).

Various complications in the postpartum period were registered for 13.7% of the examined patients. The percentage was 24% ($n = 12$) in the first group and 9.6% ($n = 12$) in the second, showing a significant difference ($p = 0.012$). A tendency to a predominance of the frequency of complications was found in the postpartum period for patients who underwent C-section because of the development of a fetal–pelvic disproportion ($p = 0.08$) and abnormalities of labor (primary weakness of labor) ($p = 0.09$).

The number of patients with local myometrial thinning and whose postpartum period was complicated by the development of purulent–septic disease significantly increased (Table 2).

Menstrual disorders (MDs; postmenstrual discharge from the genital tract, hypermenorrhea, and dysmenorrhea) were observed for 46.3%

($n = 81$) of all women examined and their percentages were 56% ($n = 28$) in the main group and 42.4% ($n = 53$) in the control group. No significant differences were found between the groups ($p = 0.10$). In addition, the number of women with menstrual cycle disorders in the form of postmenstrual bleeding from the genital tract was significantly greater in the first group than the control group ($p < 0.05$).

About 13.7% ($n = 24$) of the examined patients were affected by secondary infertility. The duration of infertility was 36 (24; 78) months. Problems with pregnancy were significantly more frequent ($p < 0.05$) among the overweight women of the first group (32%; $n = 16$) compared with patients from the second group (6.4%; $n = 8$).

Miscarriage after C-section occurred in 10.9% of cases, 16% ($n = 8$) in the first group and 8.8% in the second group ($n = 11$), with no significant differences between the groups ($p = 0.16$) (Fig. 1).

In general, reproductive disorders in the form of infertility or miscarriage were observed in 24 patients (48%) of the first group and 19 (15.2%) of the second group ($p < 0.05$).

The US study ($n = 175$) revealed no significant differences in scar thickness between the groups ($p < 0.05$). Thus, the median value of the uterine scar thickness of the main group patients (OTM) was 3.0 mm (2.00; 3.66) and that of the control group was 6.0 mm (5.60; 6.60) (Fig. 2).

Statistical analysis confirmed significant differences in the scar thickness between the examined groups, as revealed by US ($p = 0.01$). MRI data showed that the median value of PO was 2.55 mm (2.0; 3.3) in the main group and 5.4 mm (5.3; 5.95) in the control group.

US revealed local myometrial thinning in the form of a niche for 41 out of 50 patients (82%), and 17 out of 20 women (85%) were classified as patients without local myometrial thinning.

The MRI result of PO revealed local myometrial thinning in the form of a niche in 48 out of 50 patients (96%), and 18 out of 20 women (90%) were correctly classified as patients without local myometrial thinning.

Hysteroscopy was performed in 70 women to verify the diagnosis of local myometrial thinning in the presence of a scar niche.

On the 4th to 7th days of the menstrual cycle, laparoscopic metroplasty coupled with intraoperative hysteroscopy was performed.

External genital endometriosis (EGE) was intraoperatively detected in 17 (34%) patients (I and III degree EGE was detected in 14 and 3 patients, respectively), and endometrioid heterotopias were excised.

EGE significantly influenced the frequency of the secondary infertility ($p < 0.05$) but not the incidence of dysmenorrhea ($p > 0.05$) and miscarriage ($p > 0.05$) in patients with local myometrial thinning and scar niche formation.

The average duration of the surgery was 101.20 ± 30.36 min. The duration of hospital stay was 5.73 ± 1.84 bed days. For rehabilitation after the laparoscopic metroplasty of the lower segment of the uterus and for contraception, monophasic combined oral contraceptives were prescribed for 6 months.

Repeated questionnaires were made to assess the condition of patients in the long-term postoperative period and determine the effectiveness of the surgery in relation to gynecological symptoms of the niche, such as postmenstrual bleeding from the genital tract, dysmenorrhea, and hypermenorrhea. The survey was conducted no earlier than a month after the end of hormonal contraceptives. Complaints about MD remained only in 13.6% ($n = 7$) of the respondents ($p < 0.001$). Hyperpolymenorrhea was detected in 10% ($n = 5$) ($p = 0.01$), postmenstrual bleeding from the genital tract was observed in 4% ($n = 2$) ($p < 0.001$), and dysmenorrhea was detected in 4% ($n = 2$) of the women after a surgery ($p < 0.001$) (Fig. 3).

The thickness of the scar in 3–6 months after the operation according to ultrasound data was 6.4 (2.2) mm, in 7–12 months was 6.38 (1.9) mm,

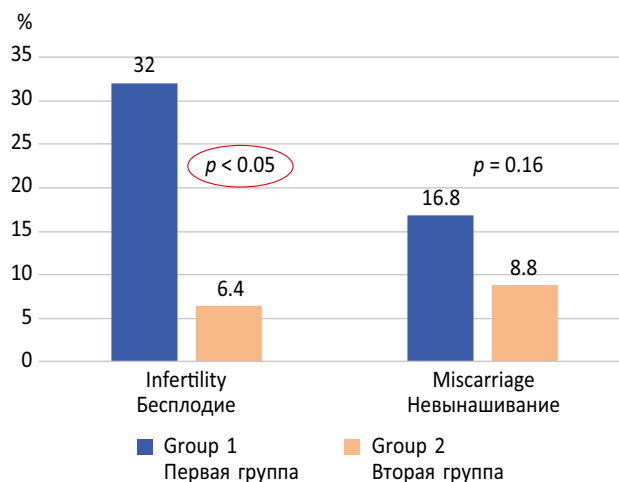


Fig. 1. Frequency of complaints of secondary infertility and miscarriage in patients in the study groups

Рис. 1. Частота жалоб на вторичное бесплодие и невынашивание беременности у пациенток обследованных групп

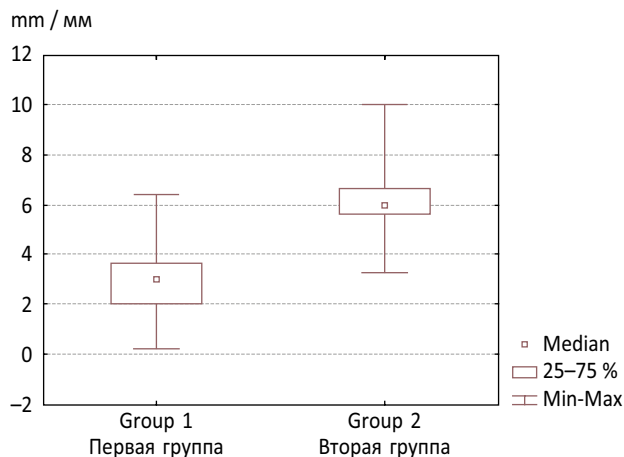


Fig. 2. Pelvic ultrasound evaluation of the uterine scar thickness in patients in the study groups

Рис. 2. Диапазон значений толщины рубца у пациенток обследованных групп по данным ультразвукового исследования органов малого таза

according to MRI data was 6.09 (1.8) and 6.09 (1.9) mm, respectively ($p < 0.05$) (Fig. 4, 5).

Among the 16 women who suffered from the secondary infertility before a surgery (32%), 3 became pregnant (20%) 10 \pm 2 months after a metroplasty ($p = 0.08$). In two cases, EGE foci were detected intraoperatively; in one case, no random intraoperative findings were found. In addition, 76.9% of cases ($n = 10$) from the remaining 13 patients had an intraoperative detection of other gynecological diseases associated with infertility: 61.5% ($n = 8$) with EGE foci, 7.7% ($n = 1$) with polycystic ovaries (after further examination,

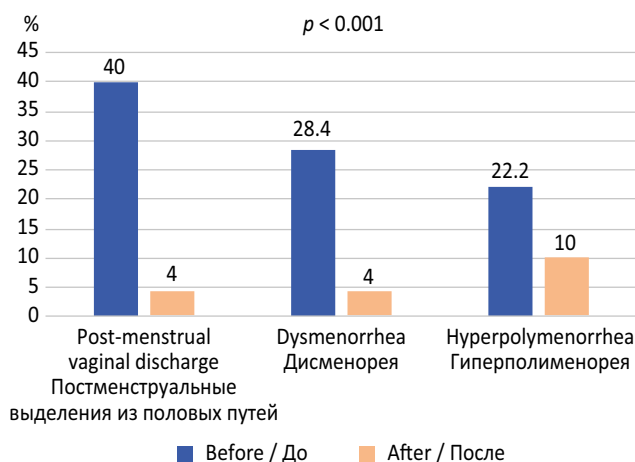


Fig. 3. Dynamics of patient complaints of menstrual disorders after metroplasty

Рис. 3. Динамика жалоб пациенток на нарушения менструального цикла после метропластики

polycystic ovarian syndrome was established), and 7.7% ($n = 1$) with hydrosalpinx of a single tube, for which tubectomy was made (in the future, the patient refused to use assisted reproductive technologies). No intraoperative pathology was detected in 23% ($n = 3$) (Fig. 6). Thus, laparoscopic metroplasty allows not only to eliminate the niche of the scar but also to identify a concomitant pathology, the elimination of which increases the possibility of a pregnancy.

The study also found that 28.5% of the patients ($n = 2$) became pregnant after a metroplasty with the threat of termination.

Nine deliveries occurred during the study (one patient had two deliveries), and two women

were currently pregnant. All women in the early stages of the pregnancy were assessed the place of attachment of the fetal egg to exclude the pregnancy in the rumen. Monitoring of the course of such pregnancy was carried out in accordance with the order of the Ministry of Health of the Russian Federation No. 572n. The area of the lower segment of the uterus was examined at 34 weeks of pregnancy. In consideration of the presence of a reconstructive plastic surgery on the uterus, all patients were offered a delivery by the planned C-section. All women were delivered at the term with live full-term babies by the planned C-section at 38/39 weeks of a gestation. During the pregnancy, data for a threatening rupture of the uterus were not received. Intraoperatively, the thickness of the scar throughout the entire length was established to be more than 2 mm. The postpartum period was uneventful.

Morphological and immunohistochemical studies of the histological material revealed differences in the structure of the scar for patients of the examined groups. Thus, in addition to increasing the content of fibrous tissue in the scar, namely, 5.0% (43.0; 65.0) in the first group and 42.0% (28.0; 52.0) in the second group ($p = 0.08$), the scar tissue of the patients with local myometrial thinning was significantly more vascularized than that of the patients without local thinning (CD31 (%) of 1.15% (0.7; 1.3) in the first group and 1.9% (1.5; 3.3) in the second group ($p = 0.003$)). Scar and adipose tissue

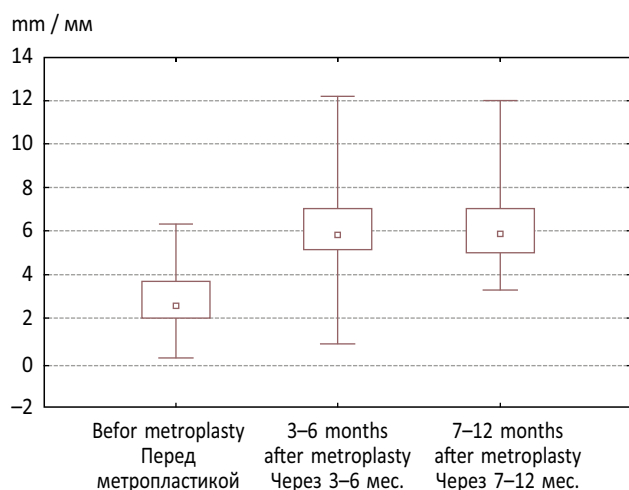


Fig. 4. Dynamics of the uterine scar thickness measured by ultrasound

Рис. 4. Динамика изменения толщины рубца по данным ультразвукового исследования

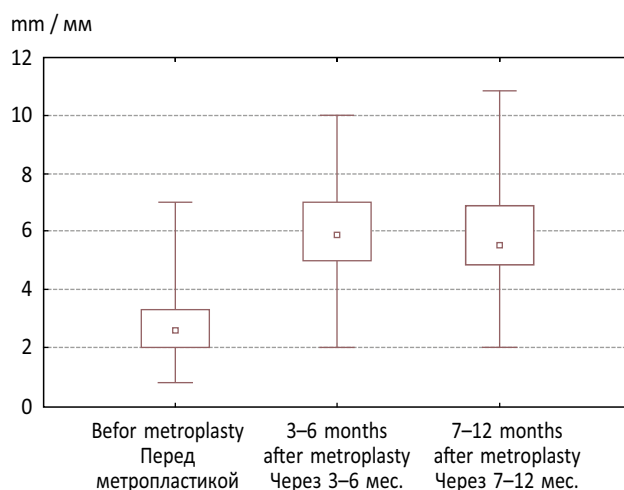


Fig. 5. Dynamics of the uterine scar thickness measured by magnetic resonance imaging

Рис. 5. Динамика изменения толщины рубца по данным магнитно-резонансной томографии

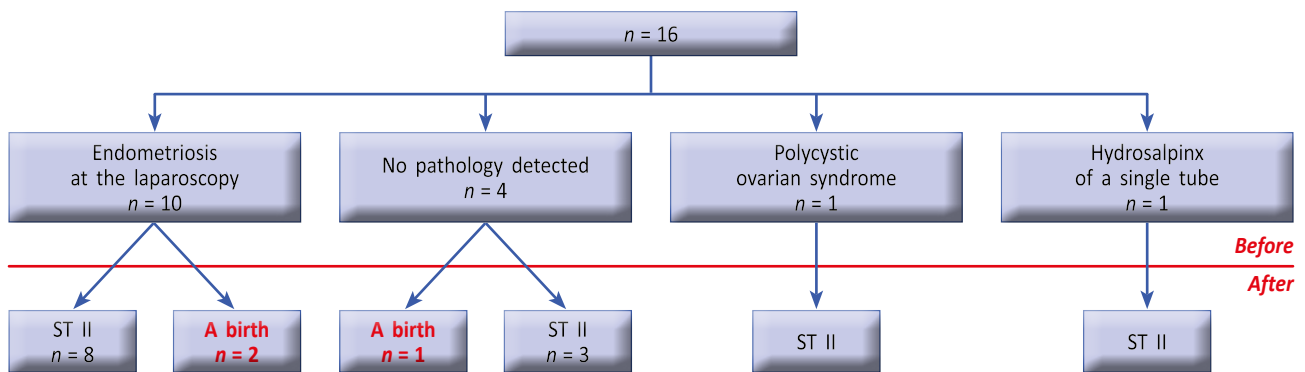


Fig. 6. Characterization of patients with secondary infertility before and after metroplasty. ST II — secondary infertility

Рис. 6. Характеристика пациенток с вторичным бесплодием до и после метропластики. ST II (от лат. sterilitas) — вторичное бесплодие

endometriosis showed no significant effect on the scar niche formation ($p > 0.05$).

Thus, the results of morphological research confirmed the fundamental ideas about the course of reparative processes in wound healing and the link between the nature of the reparative process developing in the scar zone and the intensity of angiogenesis.

Discussion

The pathophysiology of myometrial repair that leads to niche formation is widely discussed in the scientific community. A large number of factors affect scar healing on the uterus after C-section. Analysis of modern literature allows us to divide factors that disrupt scar repair on the uterus into four main groups [16].

1. Factors related to suturing.

Two randomized studies on short-term outcomes after the use of various C-section techniques have been published: CAESAR trial (2010) [17] and CORONIS trial (2007) [18]. Various methods of suturing the layers of the uterine wall and the effect of a suture material on the healing process in more than 3000 patients (CAESAR) and more than 15,000 patients (CORONIS) were evaluated. No significant differences in outcomes were found either for the mother or for the fetus. These results indicate that the surgeon could independently choose the C-section technique.

The lack of analysis of the impact of C-section on long-term results in our work cannot be considered a significant drawback because C-section does not significantly influence reproductive function.

2. Factors associated with changes in the lower segment of the uterus (gestation period, deli-

very period) or the level of the uterine incision [19, 20].

C-section performed by fully opening the fallopian pharynx did not significantly influence the formation of a thinned scar ($p = 0.8$). However, this result may be due to the small number of patients ($n = 22$). Thus, further research with a large number of examined patients for should be conducted to understand the effect of incision level on the uterus.

3. A surgical technique that can induce the formation of adhesions between the scar on the uterus and the abdominal wall and cause deterioration in wound healing.

A study found a predominance of large scar defects of women in the retroflexia of the uterus [10]. However, we were unable to confirm this hypothesis. In 93% of the women examined, the uterus was in the position of antelexia.

Factors such as inadequate hemostasis, infectious inflammation, and tissue hypoxia can cause the formation of adhesions. V.I. Kulakov et al. (1997) noted that even a minimal inflammatory reaction leads to the resorption of collagen fibers of a connective tissue and, thus, to the weakening of the scar on the uterus after C-section [7, 21]. The present research confirmed that inflammation in the postpartum period can significantly affect local myometrial thinning ($p = 0.01$).

4. Factors possibly related to scar healing.

Statistical analysis showed that the patients of the examined groups were comparable in the number of pregnancies, abortions, births, and the number of C-section. All the women were delivered with live full-term babies. Consequently, these

factors do not significantly disrupt scar formation ($p > 0.05$). The same applies to the pathological intraoperative blood loss ($p = 0.01$). However, the lack of a statistically significant effect of this factor on scar formation may be due to the small number of patients ($n = 8$).

The question of the preferred method for diagnosing the scar niche remains unresolved. PO US is the most accessible from the possible ways to visualize scar [13]. Examining the scar using US in 3–12 months, 1–5 years, or 5–10 years after C-section, the appearance of the scar, as a rule, does not change [22]. Thus, despite significant differences in the timing of the examination of patients after C-section in our study ($p < 0.05$), we believe that the research methodology does not affect the results. The sensitivity and specificity of the US method in detecting local thinning of the scar on the uterus with niche formation were 82% and 85%, respectively.

In the Russian literature, the frequency of detecting a scar niche using MRI is not reported. This research gap may be due to the fact that MRI in our country is not routinely used to determine the causes of abnormal uterine bleeding or infertility, unlike in some western countries [23].

In the present study, PO MRI was performed for 70 women. The sensitivity of the method in detecting the scar niche was 82%, and the specificity was 85%.

Thus, another controversial issue is the need for metroplasty for women planning pregnancy.

As a result, the scar tissue of patients with local myometrial thinning significantly differs from the scar tissue of patients without local thinning not only in scar thickness but also in morphological structure. Data from the immunohistochemical study allowed objectification of the morphological study results and proved that the scar tissue of the main group of patients was significantly more vascularized than that of the control group ($p = 0.003$). In addition, a high content of connective tissue was found in the scar ($p = 0.08$).

Thus, the scar niche formed because of an imbalance of reparative processes in the area of a surgery, which largely depend on the nature of angiogenesis [24]. The revealed changes in the scar structure indicate its functional inferiority and the need for its surgical correction.

Conclusions

1. The leading etiological risk factors for the development of local myometrial thinning are C-section in connection with the development of abnormalities of a contractile activity of the uterus (primary weakness of labor) ($p < 0.05$), as well as complicated course of the postpartum period (purulent-inflammatory diseases) ($p = 0.01$). The number of births, abortions, and C-section does not significantly affect scar formation ($p > 0.05$).
2. The niche of the scar on the uterus affects the reproductive system. Indeed, complaints on MD in the form of postmenstrual spotting from the genital tract ($p < 0.05$) and secondary infertility ($p < 0.05$) of women with local myometrial thinning significantly predominate. However, data on a significant effect on the frequency of miscarriage are lacking ($p = 0.16$).
3. The scar thickness on the uterus during US (82% sensitivity, 85% specificity) and MRI (96% sensitivity, 90% specificity) can be used to identify women with local myometrial thinning in the area of the scar on the uterus after C-section in the form of a niche.
4. Laparoscopy allows detecting gynecological diseases in 38% of cases ($n = 19$) and individualizing treatment tactics. Metroplasty can restore the anatomical and functional consistency of the uterus of women with local myometrial thinning in 92% of cases and significantly increase scar thickness ($p < 0.05$), which will reduce the severity of complaints about MDs, such as postmenstrual bleeding from the genital tract, dysmenorrhea, and hypermenorrhea ($p < 0.001$).

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