

ART EFFICIENCY IN AGED WOMEN AFTER SURGERY

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Abstract.

The aim of this research was to study the effect of previous surgery on ovarian response to stimulation in subsequent IVF (In vitro fertilisation) / IVF + ICSI (Intra Cytoplasmic Sperm Injection) protocols in women of older reproductive age.

Key words: senior reproductive age, ovarian stimulation, IVF, surgery, oocytes, ovarian puncture

I. INTRODUCTION

Nowadays patients of older reproductive age are more likely to be met in ART clinics, which is associated with the women's postponing of their reproductive plans. It is in this age group of patients that the effectiveness of the IVF protocol is much lower than in patients under 35 years of age. In this age group of patients, concomitant gynecological diseases and surgical interventions on the pelvic organs are more common. The ovaries of women from their birth are already endowed with a certain number of oocytes, on average about 1 million. The maximum peak is also observed in utero at 18-20 weeks - about 7 million. Upon reaching puberty, the number of oocytes is 300,000 [1], steadily decreasing every month; by the time of menopause, the ovarian supply is almost completely exhausted. Thus, it was determined that by the age of 30, only 12% of oocytes is preserved in the ovaries, and by the age of 40, only 3% of the antral follicles, laid before its birth. It was also noted that the number of antral follicles depended mainly on the age of the woman (95%) and the remaining 5% was due to the influence of smoking, BMI, and the stress during labor [2]. This change in the ovaries is explained by the involvement of the pool of follicles in the process of folliculogenesis, dominant growth and atresia of the others, also by apoptosis.

It was noted that after 35 years, the physiological decrease in ovarian reserve is proceeding more rapidly. With various kinds of surgical interventions on the pelvic organs, a decrease in the ovarian reserve was also detected, especially during operations on the ovary itself, in particular with cysts, endometriosis, etc.

Purpose of study.

To study the effect of surgical interventions on the pelvic organs on the response of the ovaries during stimulation in IVF / ICSI protocols in women of older reproductive age.

II. MATERIALS AND METHODS

We studied 124 women of advanced reproductive age entering the IVF / IVF + ICSI protocol. An analysis of the anamnesis was carried out, in particular, the presence in the anamnesis of surgical interventions and their effect on the number of oocytes obtained during the puncture.

Clinical examination of patients included a medical history, initial examination, gynecological examination, ultrasound examination of the pelvic organs using a vaginal probe.

The study analyzed the following indicators of ovarian stimulation in IVF cycles:

- course dose of gonadotropins;
- duration of ovarian stimulation;
- number of growing follicles;
- frequency of ovarian puncture;
- average number of oocytes obtained by puncture;
- frequency of ovarian punctures in which oocytes were not obtained;
- frequency of cancellation of ovarian stimulation due to lack of follicular growth.

On average, 8 out of ten women with infertility underwent one or another gynecological operation to the older reproductive age (table). Moreover, laparoscopy, as a less traumatic approach, was used more often (table). There was a repeated laparoscopy in more than a third of women (table).

Every second woman had intrauterine interventions. Hysteroscopy had a history of every third patient (table).

Table

Types of surgical interventions on the organs of the reproductive system in patients of the examined groups

Laparoscopy	single	69,4
	repeated	23,1
Laparotomy	single	21,7
	repeated	4,4
Hysteroscopy	total	32,2
	diagnostic	16,1
	resectoscopy	16,1
	repeated	1,1

Of the operations on the uterus, coagulation of foci of endometriosis on the uterus was most often encountered. Myomectomy was performed in 12% (15) of women. A caesarean section was a history of 0.3% (4) patients.

Table

Types of surgical operations on the uterus in patients of the examined groups

Types of surgical operations on the uterus		
Caesarean section	n	4
	%	0,3
Myomectomy	n	15
	%	12

Cactosalpinx was revealed in the history of 10.9% (10) patients from the main group and 12.5% (4) from the comparison group.

Bilateral removal of the fallopian tubes was performed for every fifth patient (21.7% -20; 21.9% -7).

Unilateral tubectomy occurred with a frequency of 10.9% in the main group, 6.3% in the comparison group. 11.9% of women in the main group and 15.6% of women in the comparison group underwent the surgery of restoring the patency of the tubes.

In the study groups, tubes were passable in every fifth patient of the main group (22.8%) and in every third patient of the comparison group (31.3%). Separation of fusion of the pelvic organs was performed in more than half of those examined with one or another surgical intervention. In the main group, salpingo-ovariolysis occurred in 44.6% (41) of the women; in the comparison group, 65.6% (21) of the women.

Table

Types of surgical operations on the fallopian tubes in patients of the examined groups

Type of operation		Main group	Comparison group	p
One-sided tubectomy	n	10	2	
	%	10,9	6,3	
Double-sided tubectomy	n	20	7	
	%	21,7	21,9	

Salpingo-ovariolysis	n	41	21	
	%	44,6	65,6	

Every fourth patient in the main group and every third patient in the comparison group underwent ovarian surgery (25%; 34.4%, respectively). Most often, in the main group, a resection of one ovary was used - 7.6% (in the comparison group - 9.4%), in one patient a second ovarian resection was performed. In the comparison group, ovarian cystectomy was used more often - 15.6% (in the main group - 6.5%).

Unilateral ovariectomy occurred with the same frequency in both groups (3.3%; 3.1%, respectively).

Table

Types of ovarian surgery in patients of the examined groups

Surgical and combined methods of treatment of external genital endometriosis were found with almost the same frequency in the main group (7.6% and 8.7%), in the comparison group the combined treatment of external genital endometriosis was more common (18.8%; surgical - 9.4%).

Type of operation		Main group	Comparison group	p
Total ovarian surgery	n	23	11	
	%	25	34,4	
Ovarian cauterization	n	6	4	
	%	6,5	12,5	
Cystectomy	n	6	5	

	%	6,5	15,6	
Single ovarian resection	n	7	3	
	%	7,6	9,4	
Resection of both ovaries	n	0	2	
	%	0	6,3	
Ovariectomy unilateral	n	3	1	
	%	3,3	3,1	
Ovarian resection	n	1	0	
	%	1,1	0	

Table

History of external genital endometriosis in patients of the examined groups

Type of treatment for external genital endometriosis		Main group	Comparison group	p
Surgical	n	7	3	
	%	7,6	9,4	
Combined	n	8	6	
	%	8,7	18,8	

We found that in the case of a history of ovarian surgery and removal of an ovarian cyst, the number of oocytes obtained during ovarian puncture was significantly less (4.6 ± 0.7 oocytes) than in the absence of a history of surgical interventions (6.8 ± 0.5 ; $p < 0.05$) (Fig.).

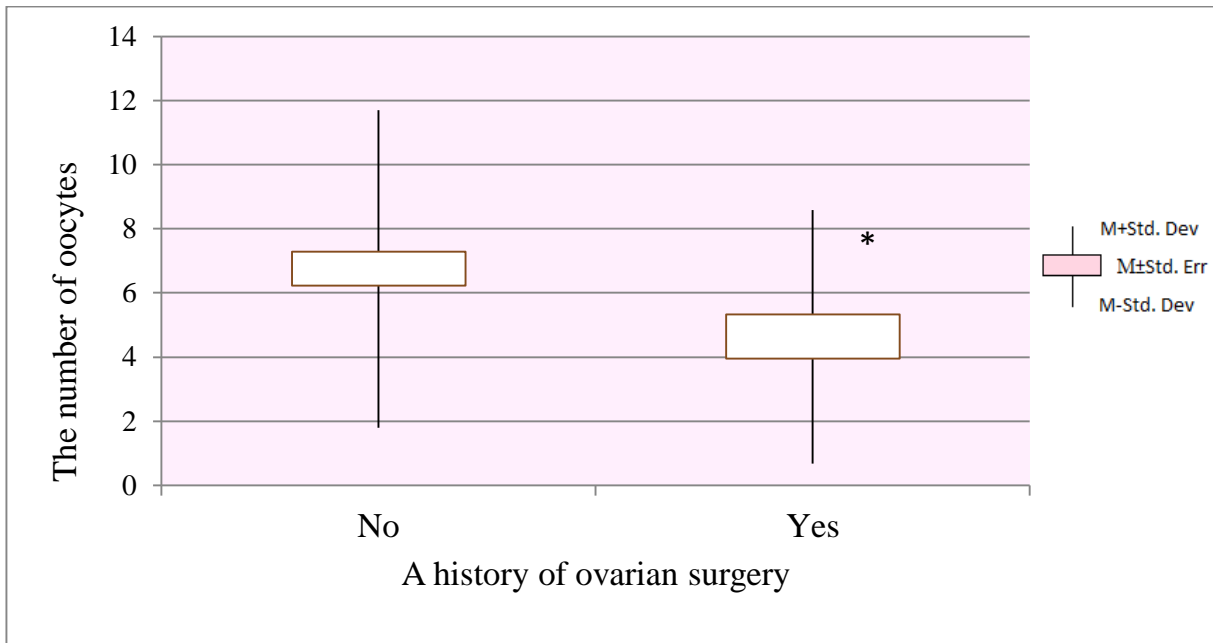


Fig. The lower (-95%) and upper (+ 95%) boundaries of the confidence interval of the number of oocytes obtained in the presence or absence of a history of surgery on the ovaries.

* - $p < 0.05$ when compared with patients without a history of ovarian surgery

In the presence of a history of removal of the ovarian cyst, the number of oocytes was 3.3 ± 0.7 , in the absence of this intervention, 6.5 ± 0.5 ($p < 0.05$).

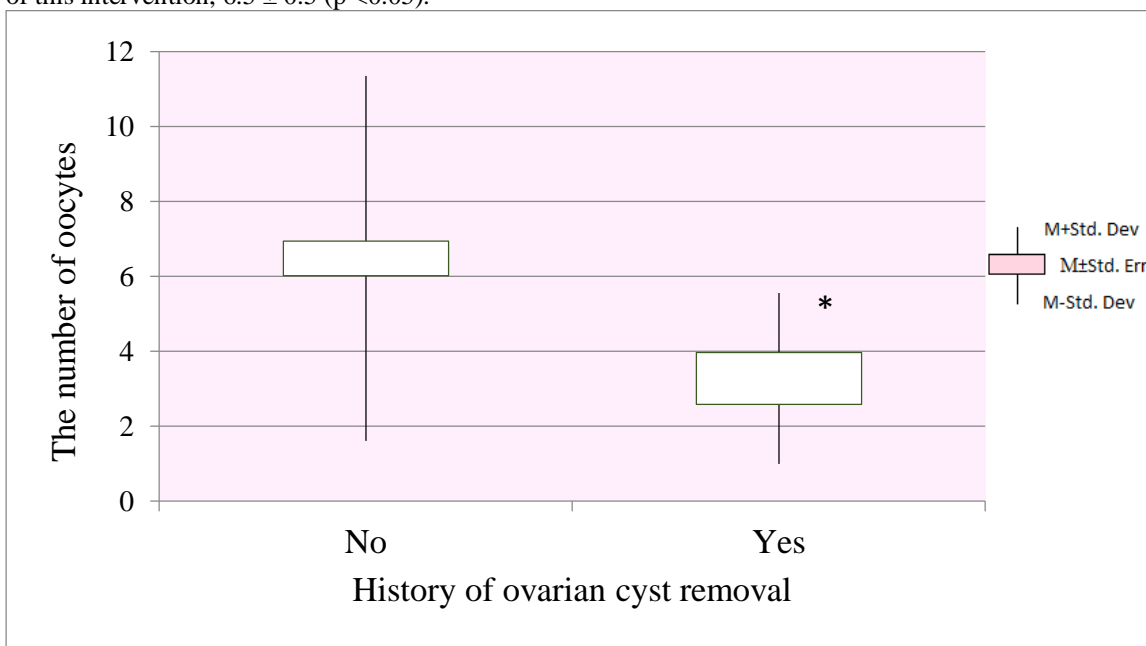


Fig. The lower (-95%) and upper (+ 95%) boundaries of the confidence interval of the number of oocytes obtained in the presence or absence of a history of ovarian cysts.

* - $p < 0.05$ when compared with patients without a history of ovarian cysts

In the presence of a history of tubectomy, the number of obtained oocytes was 6.1 ± 0.5 , in the absence of 9.3 ± 1.8 oocytes ($p < 0.05$).

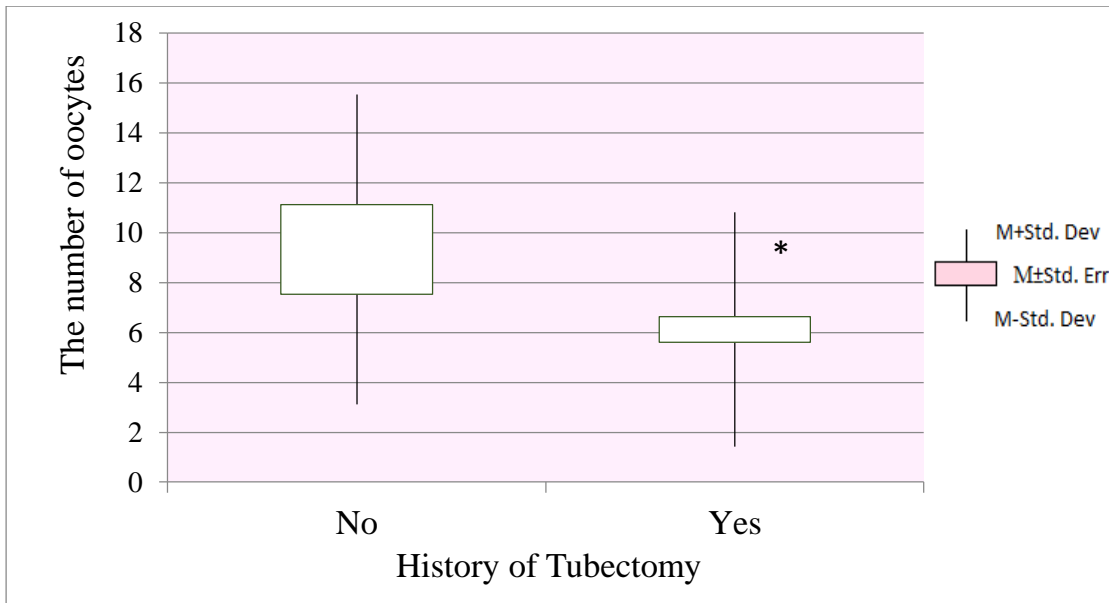


Fig. The lower (-95%) and upper (+ 95%) boundaries of the confidence interval of the number of received oocytes in the presence or absence of a history of tubectomy.

* - $p < 0.05$ when compared with patients without a history of tubectomy

The table shows a significant difference in the course dose of spent gonadotropins in patients with a history of myomectomy and without it. So, with a history of myomectomy, an average of 2437.7 ± 241.2 IU of gonadotropins is spent on stimulation. And with stimulation of patients not operated for fibroids- 1953.6 ± 80.4 IU.

Index	History of myomectomy	Value	ANOVA	p
Course dose of gonadotropins	Yes	$2437,7 \pm 241,2$	0,04	<0,05
	No	$1953,6 \pm 80,4$		

Indices of ovarian stimulation with gonadotropins in patients with a history of myomectomy and without it ($M \pm m$).

When patients with a history of myomectomy were punctured, 3 out of 15 patients had no history of oocytes (20%), in the group without myomectomy, in 5 of 109 patients (4.5%; $p < 0.05$).

Table

Characterization of ovarian puncture in the absence or presence of a history of myomectomy

Oocytes	History of myomectomy		p
	Yes	No	
Not received	5	3	<0,05
	4,5%	20%	
Received 1 or more oocytes	98	12	<0,05

The surgical interventions on the organs of the reproductive systems have a negative effect on the stimulation of the ovaries with gonadotropins (recombinant and urinary). Surgical interventions in history lead to an average decrease of 1.5 times the number of oocytes obtained by ovarian puncture;

A significant inverse correlation dependence of the number of oocytes obtained during puncture was revealed on the dose spent on ovarian stimulation of gonadotropins ($R = -0.228$, $p < 0.05$), on the presence in the history of coagulation of foci of endometriosis ($R_s = -0.192$, $p < 0.05$).

Table

The odds ratio (OR) of factors, which is significant for predicting a negative outcome in IVF / IVF + ICSI protocols in women of older reproductive age

Parameters	OR	p
History of unilateral tubectomy	2,6	<0,05

The frequency of clinical pregnancy when considering individual factors is shown in the table.

Table

Clinical pregnancy rate when considering individual factors

Index	No clinical pregnancy	Have a clinical pregnancy	OR	CI	P	
History of Tubectomy	No	10	1			
		90,9%	9,1%			
	single sided	58	15	2,586	0,43-21,79	<0,05
		79,5%	20,6%			
	Double sided	11	9	8,181	0,94-76,63	<0,05
		55,0%	45,0%			

Table

The peculiarity of the response of the ovaries to stimulation with gonadotropins in the IVF / IVF + ICSI protocol depending on the obstetric and gynecological history of the patient

Parameter	"Weak answer" of the ovaries		Received 4 or more oocytes	P	
Uterine fibroids	No	n	29	65*	
		%	30,9	69,2	
	Yes	n	16	13*	*<0,05
		%	55,2	44,8	
History of ovarian surgery	Yes	n	18	15*	
		%	54,6	45,5	
	No	n	27	63*	*<0,05
		%			

		%	30	70	
Cystectomy	No	n	37	75*	
		%	33	66,9	
	Yes	n	8	3*	*<0,05

		%	72,7	27,3	
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The risk (OR) of a negative result in the IVF / IVF + ICSI protocols in women of older reproductive age, depending on the clinical and anamnestic factors

History of unilateral tubectomy	2,6	<0,05
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Table

Correlation of oocyte count with a history of tubectomy

	The number of oocytes M ± m	N	p
There was no history of tubectomy	6,12±0,51	84	
History of Tubectomy *	9,33±1,79	12	<0,05

Table

Correlation of oocyte count with a history of ovarian surgery

	The number of oocytes M ± m	N	p
There was no history of ovarian surgery	4,63±0,68	33	
A history of ovarian surgery *	6,75±0,5	90	<0,05

Table

Correlation of oocyte count with history of ovarian cyst removal

	The number of oocytes M ± m	N	p
There was no history of ovarian cyst removal	6,47±0,46	112	
History of ovarian cyst removal*	3,27±0,68	11	<0,05

III. Conclusion

Thus, the analysis of the anamnestic data of patients of older reproductive age, who applied to the ART (Assisted Reproductive Technology) department, showed that surgical operations on organs of the reproductive systems have a negative effect on stimulation of the ovaries with gonadotropins (recombinant and urinary). Surgical interventions in history lead to an average decrease of 1.5 times the number of oocytes obtained by an ovarian puncture; that previous surgical interventions on the pelvic organs reduce the ovarian reserve of patients, in particular, if there was a history of ovarian operations and removal of the ovarian cyst, the number of oocytes obtained by ovarian puncture significantly reduced the number of oocytes obtained by puncture (p <0.05). The number of obtained oocytes decreases with a history of tubectomy, the number of obtained oocytes was 6.1 ± 0.5, in the absence of 9.3 ± 1.8 oocytes (p <0.05).

The course dose of spent gonadotropins in patients with a history of myomectomy is significantly higher than that without myomectomy (2437.7 ± 241.2 IU and 1953.6 ± 80.4 IU, respectively). Also, the presence of a history of myomectomy affects the abolition of protocols due to the absence of follicle growth (20% and 4.5%; p <0.05, respectively).

A significant inverse correlation dependence of the number of oocytes obtained during puncture was revealed on the dose spent on ovarian stimulation of gonadotropins (R = -0.228, p <0.05), on the presence in the history of coagulation of foci of endometriosis (Rs = -0.192, p <0.05).

The frequency of clinical pregnancy when considering individual factors is shown in the table.

What affects the response of the ovaries during ovarian stimulation during IVF reduces the number of oocytes received during puncture.

IV. Reference

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