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Questa è la Versione finale referata (Post print/Accepted manuscript) della seguente pubblicazione:

*Original Citation:*

Ovarian response to Gonadotrophin stimulation in patients with previous endometriotic cystectomy / ME Coccia; F Cammilli; L Ginocchi; F Borruto; F Rizzello.. - ELETTRONICO. - (2006), pp. 95-99. (Intervento presentato al convegno SEGI annual congress tenutosi a Milano nel May 10-13, 2006).

*Availability:*

This version is available at: 2158/782007 since:

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# Ovarian Response to Gonadotrophin Stimulation in Patients with Previous Endometriotic Cystectomy

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## Summary

Aim of this study is to investigate the follicular response of ovaries after laparoscopic ovarian cystectomy for endometriotic cyst. Data from 298 infertile patients with endometriosis referred for IVF-ET/ICSI were reviewed. Forty five women who underwent laparoscopic excision of a monolateral endometriotic ovarian cyst before IVF-ET/ICSI were selected. Follicular responses of postcystectomy ovary and normal ovaries were compared.

The mean ( $\pm$  DS) number of follicles  $> 15$  mm was  $1.5 \pm 1.6$  in postcystectomy ovaries and  $3.6 \pm 2.8$  in the control ovaries ( $P < 0.05$ ). For women  $\geq 35$  years of age, the mean follicular response of normal ovaries and mean number of follicle of  $\geq 15$ mm were reduced significantly when compared to control ovaries in women  $< 35$  years of age ( $4.1 \pm 3.5$  versus  $8.7 \pm 4.4$ ;  $1.9 \pm 1.8$  versus  $5.1 \pm 2.7$ );, while post-surgery ovaries showed a similar reduced response in both age groups.

Postcystectomy ovaries showed reduced follicular response particularly in women  $\geq 35$  years of age. Ovarian surgery in reproductive age, when proposed, should be performed with very cautious technique to preserve normal residual ovarian tissue.

## Introduction

Laparoscopic surgery has become the gold standard for the treatment of ovarian endometriomas (*Canis M et al., 2001*). Endometriotic cysts represent one of the more common ovarian cysts treated by laparoscopic cystectomy also in women who suffered of the concomitant problem of infertility.

It has been proven that cystectomy may induce loss of follicular reserve during IVF, and ovarian cystectomy could provoke loss of normal ovarian tissue either by removing ovarian stroma with oocytes together with the capsule or by thermal damage provoked by coagulation. Studies have shown conflicting results, a detrimental effect or no adverse affect on ovarian response during ovarian stimulation for IVF after laparoscopic cystectomy (*Wong BC et al., 2004*). Loh et al demonstrated that postcystectomy ovaries have reduced follicular response in natural and stimulated cycles (*Loh FH et al., 1999*). Donnez, on the other hand, showed that internal vaporization of endometrioma does not impair IVF outcome (*Donnez J et al., 2001*).

Aim of our study was to evaluate the ovarian response to controlled ovarian hyperstimulation (COH) for ART in patients with a history of endometriomas treated by laparoscopic surgery.

## Material and Methods

Data from 298 infertile patients with endometriosis referred at Department of Gynaecology Perinatology and Human Reproduction, University of Florence were reviewed. Forty-five women who underwent laparoscopic excision of a monolateral endometriotic ovarian cyst before IVF-ET/ICSI were included.

## Patients

The average age of these 45 patients was 33.5 years (range, 24-41 years). 15 (33. %) had moderate disease, whereas 30 (66.7%) had severe disease, patient presented mild disease. All patients had unilateral endometriotic cyst. The mean size of the endometriotic cysts excised was  $5.13 \pm 2.9$  cm.

All patients had transvaginal ultrasound evaluation of the ovaries pre-surgery. Contra lateral normal ovaries of patients with unilateral endometriotic cysts, based on ultrasound findings, were used as controls.

The ovarian response of 45 postcystectomy ovaries and 43 normal ovaries (controls) during monitored cycles was analyzed.

## Ovarian Stimulation and Follicular Monitoring

The IVF-ET protocol used for ovarian stimulation was the long protocol with GnRH analogue plus gonadotropins. GnRHa (Decapeptyl® 0, 1 mg, IPSEN Italy) was injected subcutaneously starting on day 21 of the cycle. After down-regulation (adequate ovarian suppression at pelvic ultrasonography and circulating  $E_2$  below 35 pg/ml), purified urinary FSH (Gonal -F®, 75 IU, sc Sero, Italy), 3 to 4 ampoules (225-300 IU), was administered. Human chorionic gonadotropins (hCG) 10.000 IU (Gonasi® 5000 IU, two ampules; AMSA, Italy) was injected when at least two or more follicles reached a diameter 17-18 mm.

Ovulation was monitored with transvaginal ultrasound scans. Ovarian follicles were measured in two dimensions and the average diameter was calcu-

lated. The number of follicles with an average diameter  $\geq 15$ mm developed in each ovary just before HCG injection was noted. Follicular responses of postcystectomy ovary and normal ovaries were compared.

### Statistical Analysis

All analyses were performed by using Statistical Package for the Social Science (SPSS for windows, Microsoft, version 13). Data are expressed in percentages or means  $\pm$  SD. Statistical analysis was performed with the *t* test for parametric data or  $\chi^2$  test for categorical data.

Statistical significance was set at  $P < 0.05$ .

### Results

The overall results showed that the mean follicular response of post-cystectomy ovaries was reduced significantly compared with normal ovaries. Specifically, the mean number of follicles was  $3.7 \pm 3$  in the previously operated ovary and  $6.7 \pm 5$  in the control ovary ( $P < 0.001$ ). The number of follicles  $\geq 15$  mm was significantly diminished in the previously operated ovary when compared with control ovary, too ( $1.5 \pm 1.6$  vs  $3.6 \pm 2.8$ ).

Because age is an important determinant in ovarian response and decline in fecundity begin to accelerate after the age of 35 years (Hull MG *et al.*, 1996), the ovarian responses were stratified according to the age groups of  $< 35$  or  $\geq 35$  years (Table 1).

Considering the group of younger women  $< 35$  years of age the mean follicular response, the mean follicular response of postcystectomy ovaries was still reduced significantly compared with normal ovaries. For the older patients  $\geq 35$  years of age, even the normal ovaries showed poor response, and there was no statistically significant difference between the ovarian responses of postcystectomy and normal ovaries.

For women  $\geq 35$  years of age, the mean follicular response of normal ovaries and mean number of follicle of  $\geq 15$ mm were reduced significantly when compared to control ovaries in women  $< 35$  years of age ( $4.1 \pm 3.5$  versus  $8.7 \pm 4.4$ ;  $1.9 \pm 1.8$  versus  $5.1 \pm 2.7$ ), while post-surgery ovaries showed a similar reduced response in both age groups.

Table 1: Mean number of follicles produced by postcystectomy ovaries and normal ovaries, stratified according to age group of patients

	Age of $< 35$ years			Age of $\geq 35$ years		
	Normal ovary	Postcystectomy ovary	<i>P</i>	Normal ovary	Postcystectomy ovary	<i>P</i>
Mean number of follicles $\pm$ SD	8.7 $\pm$ 4.4	4.3 $\pm$ 3.4	$< 0.05$	4.1 $\pm$ 3.5	2.8 $\pm$ 2.1	NS
Mean number of follicles $\geq 15$ mm $\pm$ SD	5.1 $\pm$ 2.7	1.7 $\pm$ 1.9	$< 0.05$	1.9 $\pm$ 1.8	1.3 $\pm$ 1	NS

NS = not significant

## Conclusions

Data literature shows controversy with respect to the surgical intervention for endometriotic cyst of the ovary before IVF-ET.

Excision of the cyst wall of the endometrioma may be removing part of the ovarian tissue and primordial follicles along with it. Ho et al (*Ho HY et al., 2002*) compared ovarian response in women previously treated by surgery for unilateral endometrioma. Diseased ovaries showed a significantly lower number of dominant follicles than normal ovaries.

Loh et al. noted that postcystectomy ovaries showed a reduced follicular response in natural and clomiphene-stimulated cycles, while they observed a response comparable to normal ovaries when stimulated with gonadotropins (*Loh FH et al., 1999*). Canis, in a retrospective cohort study, showed that number of oocytes was not significantly decreased by laparoscopic cystectomy (*Canis M et al., 2001*). In the same way, Marconi confirmed no negative effect of cystectomy (*Marconi G et al., 2002*). In a more recent study Garcia-Velasco demonstrates that laparoscopic cystectomy for endometriomas before commencing an IVF cycles does not compromise the number and quality of oocytes obtained (*Garcia-Velasco JA et al., 2004*), but he asked why perform surgery at all?

In our data, postcystectomy ovaries showed reduced follicular response in younger women. The reduction in response in women  $\leq$  35 years of age seems strictly connected with the age and no statistical significant difference in number of follicles was observed by comparing postcystectomy ovaries in both age groups.

There is still a debate over whether the presence of endometriomas may affect IVF adversely. In symptomatic patients, there is a clear benefit to surgery. On the other hand, the benefit of surgery in asymptomatic patient before controlled ovarian hyperstimulation is still matter of debate.

It is important not to generalize the data to all patients with endometriomas. Ovarian surgery should be proposed in selected cases (based on the size, symptoms) and a very cautious technique is recommended to preserve normal residual ovarian tissue, particularly in younger women.

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