



**OOCYTE FREEZING IN
ENDOMETRIOSIS PATIENTS:
OOCYTE QUALITY AND QUANTITY**



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CONFLICTS OF INTERESTS

❖ **COIs with Industry**

Personal: None

Institutional : Grants for research received during the
last three years from *Ferring* and *Merck-Serono*

❖ **Other COIs**

Clinical : Poorly engaged in surgery (mainly ART)

Revenue-related : Mixed (public 65% - private 35%)

Patency: None



PLAN OF THE PRESENTATION

- ❖ Endometriosis and oocyte quality & quantity
 - Biological evidence
 - Clinical evidence
 - The role of surgery
- ❖ Data on fertility preservation
- ❖ Conclusions

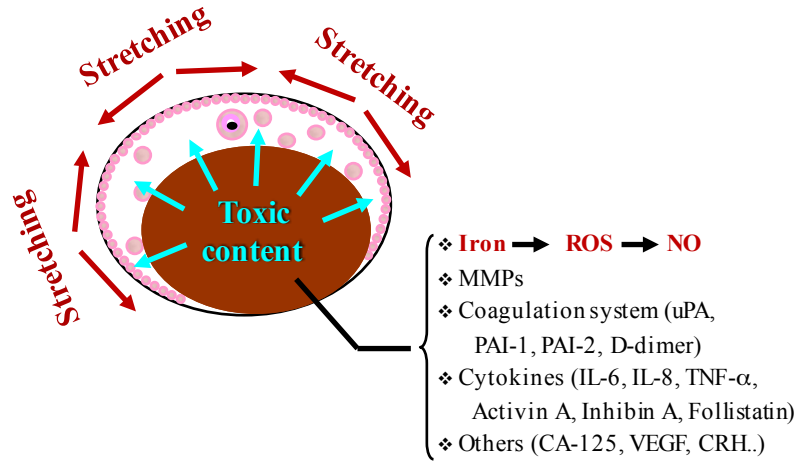


PLAN OF THE PRESENTATION

- ❖ **Endometriosis and oocyte quality & quantity**
 - Biological evidence**
 - Clinical evidence
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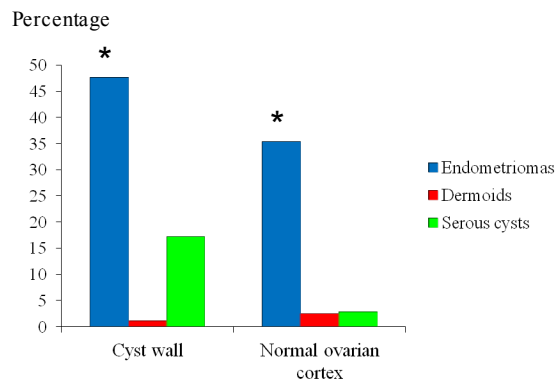
ENDOMETRIOMAS



Sanchez et al., 2014; Sanchez et al., 2016; Giacomini et al., 2016; Sanchez et al., 2017

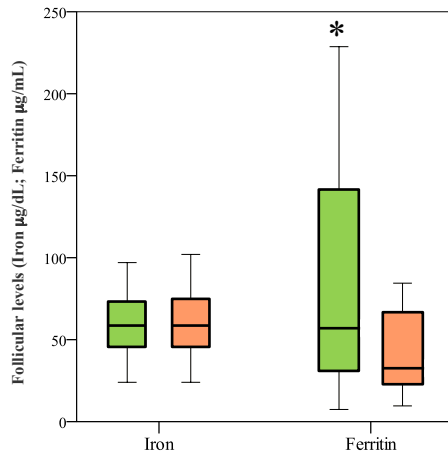
IRON AND ROS

Percentage of immunostained nuclear surface for 8-hydroxydeoxyguanosine.



Matsuzaki and Schubert, 2010

IRON AND ROS

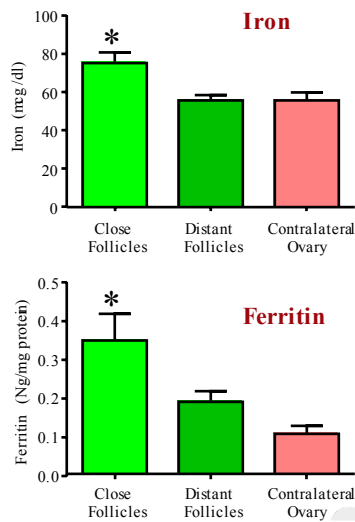


- ❖ 39 women with monolateral endometriomas
- ❖ Pick-up
- ❖ Comparison between the affected and the contralateral intact gonad

■ Ovary with the endometrioma
■ Intact ovary

Benaglia et al., 2015

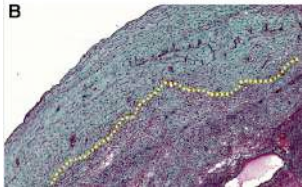
IRON AND ROS



- ❖ 13 women with monolateral endometriomas
- ❖ Pick-up
- ❖ Comparison between close follicles, distant follicles and contralateral follicles

Sanchez et al., 2014

PRIMORDIAL FOLLICLES

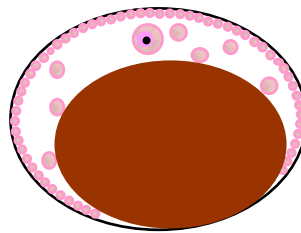
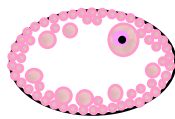


	Affected ovary	Intact ovary	p
Foll. density	6.3 ± 4.1	25.1 ± 15.0	<0.001
Fibrosis	80%	27%	0.007

Kuroda et al., 2012
Pavone et al., 2014
Kitajima et al., 2014

Katajima et al., 2011

PRIMORDIAL FOLLICLES



Endometrioma

Ovarian surface (cortex)

Diameter 20 mm → Increased 3.4 folds

Diameter 40 mm → Increased 12.3 folds

Diameter 60 mm → Increased 27.3 folds

PLAN OF THE PRESENTATION

❖ Endometriosis and oocyte quality & quantity

Biological evidence

Clinical evidence

The role of surgery

❖ Data on fertility preservation

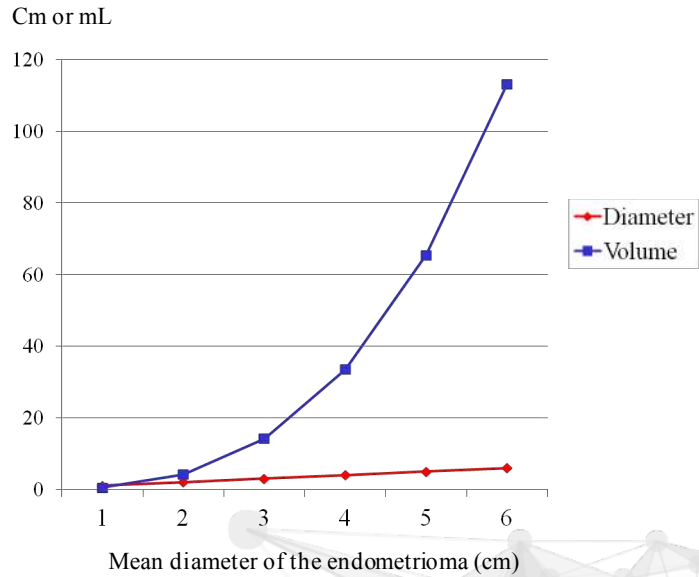
❖ Conclusions

OVARIAN RESPONSIVENESS

Ovarian responsiveness (IVF) in **unoperated women with unilateral cysts**

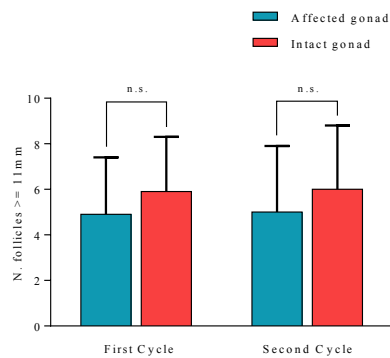
Study	N. cases	Affected ovary	Intact ovary	p
Somigliana <i>et al.</i> , 2006	36	3.2 ± 2.0	4.1 ± 2.2	n.s.
Benaglia <i>et al.</i> , 2011	84	5.3 ± 2.8	5.6 ± 3.5	n.s.
Almog <i>et al.</i> , 2011	81	6.0 ± 0.4	6.1 ± 0.5	n.s.
Esinler <i>et al.</i> , 2012	19	5.9 ± 4.3	5.4 ± 3.8	n.s.
Ashrafi <i>et al.</i> , 2014	37	7.0 ± 6.9	6.6 ± 5.8	n.s.
Filippi <i>et al.</i> , 2014	29	3.7 ± 2.4	4.1 ± 1.7	n.s.
Coccia <i>et al.</i> , 2014	64	5.1 ± 3.2	5.7 ± 3.3	n.s.
Lima <i>et al.</i> , 2015	37	3.1 ± 3.4	3.0 ± 3.6	n.s.
Ferrero <i>et al.</i> , 2017	29	2.0 ± 1.2	4.2 ± 1.7	<0.001

THE ROLE OF THE DIMENSION



THE ROLE OF TIME

Repeated IVF in 29 women with *monolateral endometriomas*
 > 6 months, median 11 months, IQR=8-14 months



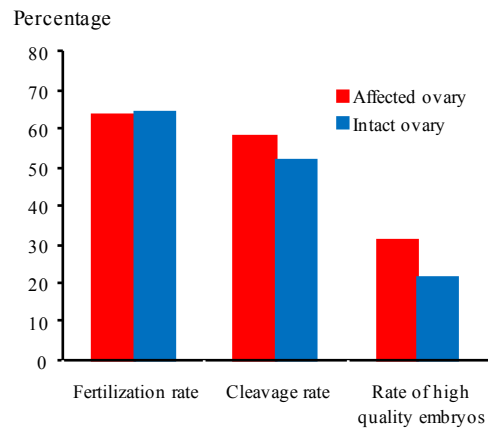
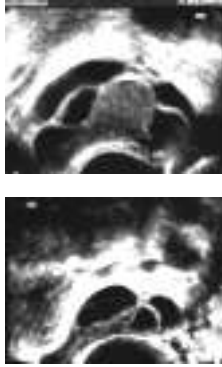
Proportion (IQR) of follicles
 in the affected ovary:

1° cycle: 44% (31-58%)
 2° cycle: 44% (35-55%) } p=ns

Benaglia et al., 2017

OOCYTE QUALITY

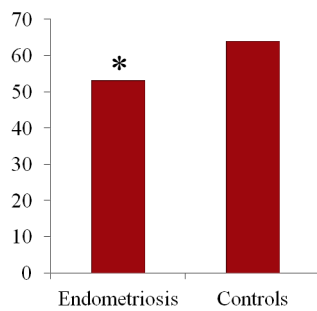
37 monolateral
endometriomas



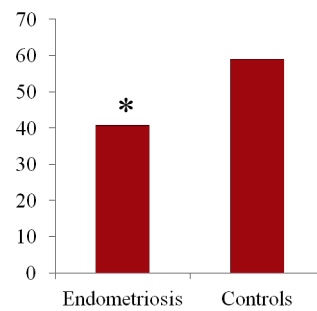
Filippi et al., 2014

OOCYTE QUALITY

Rate of *normal*
oocytes (%)



Rate of *normal*
oocytes (%)



* $p < 0.001$

Shebl et al., 2017; Kasapoglu et al., 2017

PLAN OF THE PRESENTATION

❖ Endometriosis and oocyte quality & quantity

Biological evidence

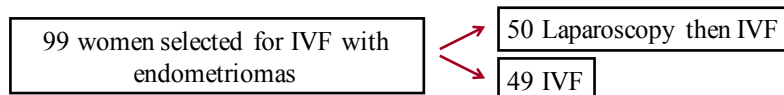
Clinical evidence

The role of surgery

❖ Data on fertility preservation

❖ Conclusions

SURGICAL INJURY



Characteristics	Surgery	Controls	p
Duration of stimulation	14.0 ± 2.5	10.8 ± 2.6	0.001
Dose FSH (IU)	4575 ± 530	3675 ± 792	0.001
E2 (pg/ml)	1170 ± 417	1680 ± 429	0.001
N. oocytes	7.8 ± 3.1	8.6 ± 2.8	0.032
Fertilization rate	86%	88%	n.s.
Pregnancy rate	34%	38%	n.s.

SURGICAL INJURY

Ovarian responsiveness in women operated for monolateral endometriomas

Study	N. cases	Operated ovary	Intact ovary	p
Loh <i>et al.</i> , 1999	12	4.6	3.6	n.s.
Ho <i>et al.</i> , 2002	38	1.9 ± 1.5	3.3 ± 2.1	<0.001
Somigliana <i>et al.</i> , 2003	46	2.0 ± 1.5	4.2 ± 2.5	<0.001
Ragni <i>et al.</i> , 2005	38	1.8 ± 1.8	4.5 ± 2.0	<0.001
Duru <i>et al.</i> , 2007	28	3.1 ± 1.8	4.4 ± 1.4	<0.05
Alborzi <i>et al.</i> , 2007	70	3.2 ± 1.1	3.2 ± 1.7	n.s.
Almogh <i>et al.</i> , 2010	81	4.7 ± 3.9	7.5 ± 4.7	<0.001
Benaglia <i>et al.</i> , 2010	93	3.4 ± 2.4	5.7 ± 3.0	<0.001
Tang <i>et al.</i> , 2013 (< 4 cm)	51	2.6 ± 2.2	3.4 ± 2.3	0.05
Tang <i>et al.</i> , 2013 (> 4 cm)	63	2.1 ± 2.2	4.0 ± 2.7	<0.001

Somigliana et al., 2015

OVARIAN FAILURE



93 women operated for monolateral endometriomas who underwent IVF:
Absence of follicular growth in 12 cases

13% (95%CI: 7-21%)



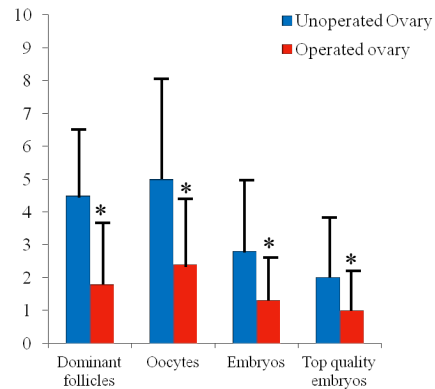
➔ $(13\%)^2 = 1.7\%$

POF after surgery for bilateral endometriomas:

3/126 cases (**2.4%**, 95%CI: 0.5-6.8%)

Busacca et al., 2006; Benaglia et al., 2010

OOCYTE QUALITY



38 women *previously operated*
for *unilateral* ovarian endometrioma

	Unoperated	Operated	p
Fertilization	61% (50-83%)	55% (33-76%)	0.50
Top quality embryos	47% (9-51%)	33% (0-75%)	0.99

Ragni et al., 2005

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FERTILITY PRESERVATION FOR ENDOMETRIOSIS

Level of evidence

❖ Endometriosis affects fertility	++
❖ Endometriosis is a recurrent disease	++
❖ Endometriomas damage ovarian reserve	+
❖ Ovarian surgery damages ovarian reserve	++

Somigliana et al., 2015

EXPERIENCES OF FERTILITY PRESERVATION

Cryopreservation of oocytes in a young woman with severe and symptomatic endometriosis: a new indication for fertility preservation

*Shai E. Elizur, M.D., Ri-Cheng Chian, Ph.D., Hananel E. G. Holzer, M.D., Yariv Gidoni, M.D.,
Togas Tulandi, M.D., M.H.C.M., and Seang Lin Tan, M.D., M.B.A.*

- ❖ 25 years
- ❖ Four interventions for endometriosis: right ovarian cystectomy,
right oophorectomy, right salpingectomy, adhesiolysis
- ❖ Oocytes vitrification cycles
 1. Long protocol + 600 IU daily FSH 4
 2. Long protocol + 600 IU daily FSH 4
 3. GnRh antagonists + 600 IU daily FSH 13

Total N. frozen eggs	21

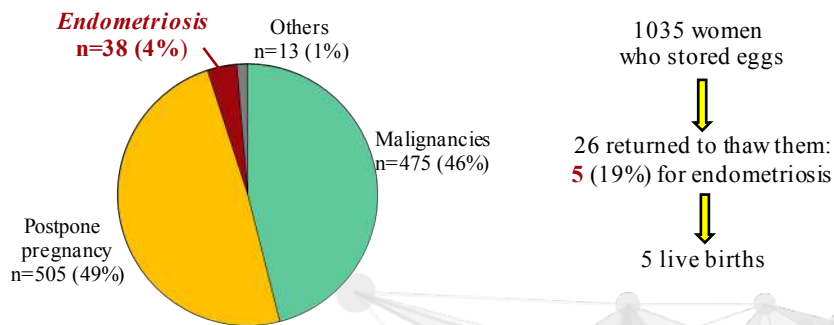
Elizur et al., 2009

EXPERIENCES OF FERTILITY PRESERVATION

Five years' experience using oocyte vitrification to preserve fertility for medical and nonmedical indications

Juan A. Garcia-Velasco, M.D.,^{1,2} Javier Domingo, M.D.,³ Ana Cobo, Ph.D.,⁴ Maria Martinez, M.D.,⁵ Luis Carmona, M.D.,⁶ and Antonio Pellicer, M.D.⁷

¹IVI-Madrid, Madrid; ²IVI Las Palmas, Las Palmas; ³IVI Valencia, Valencia; and ⁴Rey Juan Carlos University, Madrid, Spain

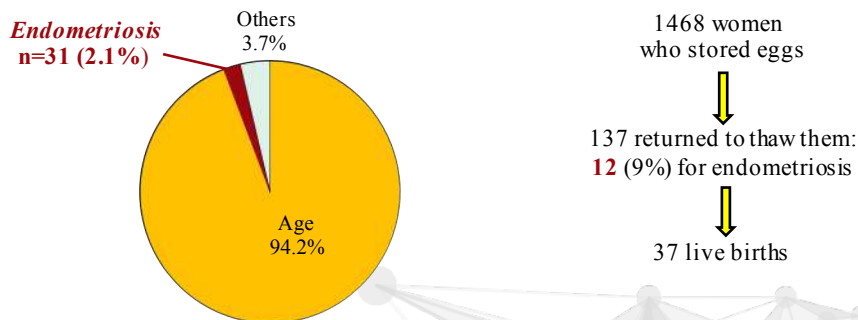


Garcia-Velasco et al., 2013

EXPERIENCES OF FERTILITY PRESERVATION

Oocytes vitrification as an efficient option for elective fertility preservation

Ana Cobo, Ph.D.,¹ Juan A. Garcia-Velasco, M.D.,² Aila Coello, Ph.D.,³ Javier Domingo, M.D.,⁴ Antonio Pellicer, M.D.,⁵ and José Remohí, M.D.⁶



Cobo et al., 2016

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REVIEWS ON FERTILITY PRESERVATION

Barnett R, Banks N, Decherney AH. *Endometriosis and Fertility Preservation*. Clin Obstet Gynecol. 2017 Sep;60(3):517-523.

Carrillo L, Seidman DS, Cittadini E, Meirou D. *The role of fertility preservation in patients with endometriosis*. J Assist Reprod Genet. 2016 Mar;33(3):317-323.

Grynberg M, Benard J. *Fertility preservation and endometriosis: When medical borders on social*. Gynecol Obstet Fertil. 2015 Dec;43(12):759-60.

Sönmezer M, Taşkın S. *Fertility preservation in women with ovarian endometriosis*. Womens Health. 2015 Aug;11(5):625-31.

Somigliana E, Viganò P, Filippi F, Papaleo E, Benaglia L, Candiani M, Vercellini P. *Fertility preservation in women with endometriosis: for all, for some, for none?* Hum Reprod. 2015 Jun;30(6):1280-6.

Bedoschi G, Turan V, Oktay K. *Fertility preservation options in women with endometriosis*. Minerva Ginecol. 2013 Apr;65(2):99-103.

Donnez J, Squifflet J, Jadoul P, Lousse JC, Dolmans MM, Donnez O. *Fertility preservation in women with ovarian endometriosis*. Front Biosci. 2012 Jan 1;4:1654-62.

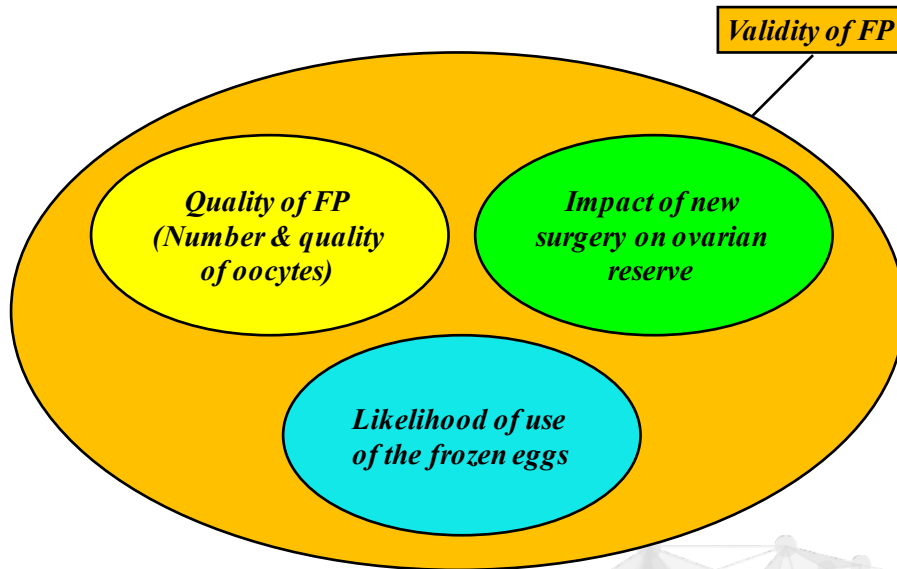


CONCLUSIONS

**Fertility preservation in women
with endometriosis is *experimental*.**



FERTILITY PRESERVATION



Somigliana et al., 2015

FERTILITY PRESERVATION

1. Bilateral OMAs
2. Previous unilateral excision of OMAs – contralateral recurrence
3. Previous bilateral excision of OMAs – no recurrence
4. Previous bilateral excision of OMAs – unilateral recurrence
5. Previous bilateral excision of OMAs – bilateral recurrence
6. Previous unilateral excision of OMAs – ipsilateral recurrence
7. Unilateral OMAs
8. Deep endometriosis – no OMAs
9. Previous unilateral excision of OMAs – no recurrence

Validity of FP

Somigliana et al., 2015