







International Congress of the Jordanian Society of Obstetricians and Gynecologists

In collaboration with The Jordanian British Society for Obstetrics & Gynecology

Fertility preservation and ovarian endometriosis

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Personal COIs:2019-2022 Editorial Board Involvement
(Reprod Scie, Plos ONE, Scie Rep, Reprod
Biol Endocrinol)
2019: n=1 Consultant as a speaker
2021: n=1 Honorarium as a reviewer
2021-2022: Fee for an academic master

Institutional COIs: 2019-2022: Grants (competitive and noncompetitive) for research activity (Theramex grant 2019, Italian Ministry of Health, 2019)



Plan of the presentation

✤ Why?

Should we do it?

✤ When?



Plan of the presentation

✤ Why?

Should we do it?

✤ When?



Reasons to claim fertility preservation in young age

Level of evidence

Endometriosis affects fertility	+ +
Endometriosis is a recurrent disease	+ +
Ovarian surgery damages ovarian reserve	+ +
Endometriomas damage ovarian reserve	+
Age and ovarian reserve are crucial for preservation	++



Surgery damages ovarian reserve

AMH fluctuations after stripping



-1.13 ng/ml (95%CI: 0.37-1.88) p=0.003

> Raffi et al., JCEM, 2012 Somigliana et al., FS, 2012



Endometrioma damages ovarian reserve

Decrease of AMH in women not operated for endometriosis

FIGURE 1

Endo	Endometriomas		No endometriomas			Mean Difference	Mean Difference	
Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
1.53	1.37	40	2.58	1.58	58	7.8%	-1.05 [-1.64, -0.46]	
2.6	2	23	4.2	2	496	6.1%	-1.60 [-2.44, -0.76]	
1.62	1.09	47	2.06	0.51	12	8.9%	-0.44 [-0.86, -0.02]	
1.92	2.31	26	3.1	2.64	24	3.5%	-1.18 [-2.56, 0.20]	
4.12	2.42	65	6.02	2.29	32	5.2%	-1.90 [-2.89, -0.91]	
2.84	2.98	102	3.61	3.3	198	6.7%	-0.77 [-1.51, -0.03]	
4.3	3.07	59	5.6	4	16	1.9%	-1.30 [-3.41, 0.81]	
5.03	3.07	68	4.84	2.26	32	4.8%	0.19 [-0.88, 1.26]	
2.25	2.14	18	3.31	3.25	36	3.3%	-1.06 [-2.51, 0.39]	
0.97	0.59	65	1.72	0.63	130	10.2%	-0.75 [-0.93, -0.57]	-
3.1	1.9	34	5.7	3.7	33	3.4%	-2.60 [-4.01, -1.19]	
2.27	2.01	122	2.67	2.68	163	8.1%	-0.40 [-0.94, 0.14]	
4	3	77	4.1	3.4	413	6.7%	-0.10 [-0.85, 0.65]	-
2.84	2.47	39	2.33	1.91	38	5.2%	0.51 [-0.47, 1.49]	+
2.81	2.15	30	4.2	2.26	30	4.6%	-1.39 [-2.51, -0.27]	
3.64	1.94	144	3.71	2.09	115	8.4%	-0.07 [-0.57, 0.43]	-
1.5	0.9	9	4.1	2.9	48	5.1%	-2.60 [-3.61, -1.59]	
		968			1874	100.0%	-0.84 [-1.16, -0.52]	•
0.25; Ch	² = 54.	50, df =	16 (P < 0	.00001);	$I^2 = 719$	%		+ + + + +
Z = 5.20	(P < 0.	00001)						-4 -2 0 2 4
	Endor Mean 1.53 2.6 1.62 1.92 4.12 2.84 4.3 5.03 2.25 0.97 3.1 1 2.27 4 2.84 2.81 3.64 1.5 0.25; Ch Z = 5.20	Endometrion Mean SD 1.53 1.37 2.6 2 1.62 1.09 1.92 2.31 4.12 2.42 2.84 2.98 4.33 3.07 5.03 3.07 2.25 2.14 0.97 0.59 3.1 1.9 2.27 2.01 4 3 2.84 2.47 2.81 2.15 3.64 1.94 1.5 0.9 0.25; Chi² = 54.4 2.9 Z = 5.20 (P < 0.1	$\begin{tabular}{ c c c } \hline Endoursetriourset$	$\begin{tabular}{ c c c c c } \hline Endometriomas & No end \\ \hline Mean & SD & Total & Mean \\ \hline 1.53 & 1.37 & 40 & 2.58 \\ \hline 2.6 & 2 & 23 & 4.2 \\ \hline 1.62 & 1.09 & 47 & 2.06 \\ \hline 1.92 & 2.31 & 26 & 3.1 \\ \hline 4.12 & 2.42 & 65 & 6.02 \\ \hline 2.84 & 2.98 & 102 & 3.61 \\ \hline 4.3 & 3.07 & 59 & 5.6 \\ \hline 5.03 & 3.07 & 68 & 4.84 \\ \hline 2.25 & 2.14 & 18 & 3.31 \\ \hline 0.97 & 0.59 & 65 & 1.72 \\ \hline 3.1 & 1.9 & 34 & 5.7 \\ \hline 2.27 & 2.01 & 122 & 2.67 \\ \hline 4 & 3 & 77 & 4.1 \\ \hline 2.84 & 2.47 & 39 & 2.33 \\ \hline 2.81 & 2.15 & 30 & 4.2 \\ \hline 3.64 & 1.94 & 144 & 3.71 \\ \hline 1.5 & 0.9 & 9 & 4.1 \\ \hline \hline $968 \\ \hline 0.25; Chi^2 = 54.50, df = 16 (P < 0 \\ \hline Z = 5.20 (P < 0.00001) \\ \hline \end{tabular}$	Endometriomation No No mean SD Mean SD Total Mean SD 1.53 1.37 40 2.58 1.58 2.6 2 23 4.2 2 1.62 1.09 47 2.06 0.51 1.92 2.31 26 3.1 2.64 4.12 2.42 65 6.02 2.29 2.84 2.98 102 3.61 3.3 4.3 3.07 59 5.6 4 5.03 3.07 68 4.84 2.26 2.25 2.14 18 3.31 3.25 0.97 0.59 65 1.72 0.63 3.1 1.9 34 5.7 3.7 2.27 2.01 122 2.67 2.68 4 3 77 4.1 3.4 2.84 2.47 39 2.33 1.91 2.84 <td>$\begin{tabular}{ c c c c c } \hline Hodometriomulation \$\$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$</td> <td>Endometriomus No endometriomus Mean SD Total Mean SD Total Weight 1.53 1.37 40 2.58 1.58 58 7.8% 2.6 2 23 4.2 2 496 6.1% 1.62 1.09 47 2.06 0.51 12 8.9% 1.92 2.31 26 3.1 2.64 24 3.5% 4.12 2.42 65 6.02 2.29 32 5.2% 2.84 2.98 102 3.61 3.3 198 6.7% 4.3 3.07 59 5.6 4 16 1.9% 5.03 3.07 68 4.84 2.26 32 4.8% 2.25 2.14 18 3.31 3.25 36 3.3% 0.97 0.59 65 1.72 0.63 130 10.2% 3.1 1.9 3.4 5.7 3</td> <td>Endometriomas No endometriomas Mean Difference Mean SD Total Mean SD Total Weight IV, Random, 95% CI 1.53 1.37 40 2.58 1.58 58 7.8% -1.05 [-1.64, -0.46] 2.6 2 23 4.2 2 496 6.1% -1.60 [-2.44, -0.76] 1.62 1.09 47 2.06 0.51 12 8.9% -0.44 [-0.66, -0.20] 1.92 2.31 26 3.1 2.64 24 3.5% -1.18 [-2.56, 0.20] 4.12 2.42 65 6.02 2.29 32 5.2% -1.90 [-2.89, -0.91] 2.84 2.98 102 3.61 3.3 198 6.7% -0.077 [-1.51, -0.03] 4.3 3.07 59 5.6 4 16 1.9% -1.30 [-3.41, 0.81] 5.03 3.07 68 4.84 2.26 32 4.8% 0.19 [-0.88, 1.26] 2.25 2.14 18</td>	$\begin{tabular}{ c c c c c } \hline Hodometriomulation $$ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $	Endometriomus No endometriomus Mean SD Total Mean SD Total Weight 1.53 1.37 40 2.58 1.58 58 7.8% 2.6 2 23 4.2 2 496 6.1% 1.62 1.09 47 2.06 0.51 12 8.9% 1.92 2.31 26 3.1 2.64 24 3.5% 4.12 2.42 65 6.02 2.29 32 5.2% 2.84 2.98 102 3.61 3.3 198 6.7% 4.3 3.07 59 5.6 4 16 1.9% 5.03 3.07 68 4.84 2.26 32 4.8% 2.25 2.14 18 3.31 3.25 36 3.3% 0.97 0.59 65 1.72 0.63 130 10.2% 3.1 1.9 3.4 5.7 3	Endometriomas No endometriomas Mean Difference Mean SD Total Mean SD Total Weight IV, Random, 95% CI 1.53 1.37 40 2.58 1.58 58 7.8% -1.05 [-1.64, -0.46] 2.6 2 23 4.2 2 496 6.1% -1.60 [-2.44, -0.76] 1.62 1.09 47 2.06 0.51 12 8.9% -0.44 [-0.66, -0.20] 1.92 2.31 26 3.1 2.64 24 3.5% -1.18 [-2.56, 0.20] 4.12 2.42 65 6.02 2.29 32 5.2% -1.90 [-2.89, -0.91] 2.84 2.98 102 3.61 3.3 198 6.7% -0.077 [-1.51, -0.03] 4.3 3.07 59 5.6 4 16 1.9% -1.30 [-3.41, 0.81] 5.03 3.07 68 4.84 2.26 32 4.8% 0.19 [-0.88, 1.26] 2.25 2.14 18

Meta-analysis. Weighted mean difference in AMH in patients with ovarian endometriomas compared to patients without ovarian endometriomas.

Muzii. AMH is reduced with endometriomas. Fertil Steril 2018.

Muzii et al. 2018



Reasons to claim fertility preservation in young age

Level of evidence

Endometriosis affects fertility	+ +
Endometriosis is a recurrent disease	+ +
Ovarian surgery damages ovarian reserve	+ +
Endometriomas damage ovarian reserve	+
Age and ovarian reserve are crucial for preservation	++



Plan of the presentation

✤ Why?

Should we do it?

✤ When?



Evidence of effectiveness

Study	N. cases	Frozen materia
Elizur <i>et al.,</i> 2009	1	Oocytes
Garcia-Velasco <i>et al.,</i> 2013	38	Oocytes
Raad <i>et al.,</i> 2018	49	Oocytes
Cobo <i>et al.,</i> 2020	1,044	Oocytes
Kim <i>et al.,</i> 2020	34	Oocytes
Mathieu d'Argent et al., 2020) 108	Oocytes



Incremental benefit



Mean time between freezing and thawing:

→ 1.6 years

Among women who failed to become

pregnant, 58 came again to perform

fresh cycles:

→ 24 conceived (**41%**)

Cobo et al., Fertil Steril, 2020



'the vitrification of oocytes was performed as adjuvant option within the treatment of endometriosis-related infertility' *Cobo et al., Fertil Steril, 2020*

This may overestimate the benefit of fertility preservation



Incremental benefit Pregnancy *Hormonal therapies* Surgeries seeking Never seek pregnancy Natural pregnancy **IVF** pregnancy **Failed IVF**



Incremental benefit



Number needed to be treated (NNT)



Somigliana et al., 2009: Smith et al., 2015



Plan of the presentation

✤ Why?

Should we do it?

When?



Possible clinical situations in endometriosis

- 1. Unilateral cyst
- 2. Bilateral cysts
- 3. Deep endometriosis no cyst
- 4. Previous unilateral cystectomy no recurrence
- 5. Previous bilateral cystectomy no recurrence
- 6. Previous unilateral cystectomy omolateral recurrence
- 7. Previous unilateral cystectomy contralateral recurrence
- 8. Previous bilateral cystectomy unilateral recurrence
- 9. Previous bilateral cystectomy bilateral recurrence





1.

2.

3.

4.

5.

Unilateral cyst

Bilateral cysts

Deep endometriosis - no cyst

When?



- Previous unilateral cystectomy omolateral recurrence 6.
- 7. Previous unilateral cystectomy - contralateral recurrence
- 8. Previous bilateral cystectomy - unilateral recurrence
- 9. Previous bilateral cystectomy - bilateral recurrence



1.

2.

3.

4.

5

Unilateral cyst

Bilateral cysts

Deep endometriosis - no cyst

When?



•••		-		-	-
6.	Previous unilateral cystectomy - omolateral recurrence	4	6	4	6
7.	Previous unilateral cystectomy - contralateral recurrence	7	2	3	2
8.	Previous bilateral cystectomy - unilateral recurrence	8	4	2	4
9.	Previous bilateral cystectomy - bilateral recurrence	9	3	1	5

Severe and recurrent ovarian endometriosis

When?



In collaboration with The Jordanian British Society for Obstetrics & Gynecology

REVIEW ARTICLE

Edward W. Campion, M.D., Editor

Fertility Preservation in Women

Jacques Donnez, M.D., Ph.D., and Marie-Madeleine Dolmans, M.D., Ph.D.

Table 1. Indications for Fertility Preservation. Malignant diseases requiring gonadotoxic chemotherapy, radiotherapy, or bone marrow transplantation Hematologic diseases (leukemia, Hodgkin's lymphoma, non-Hodgkin's lymphoma) Breast cancer Sarcoma Some pelvic cancers Nonmalignant conditions "Severe and recurrent ovarian endometriosis" Systemic diseases requiring chemotherapy, radiotherapy, or bone marrow transplantation Ovarian diseases Bilateral benign ovarian tumors Severe and recurrent ovarian endometrios Possible ovarian torsion Risk of premature ovarian insufficiency Family history Turner's syndrome Personal reasons Age Childbearing postponed until later in life



Prevention: Estroprogestins



OR=0.12 (95%IC: 0.05-0.29)

The risk of recurrence is reduced with the use of estroprogestins



Conclusions

Fertility preservation may be considered in women with endometriosis.

However, the indication remains **EXPERIMENTAL**. The **incremental benefit** is uncertain.

Oocyte cryopreservation seems to be more valid in women with **endometriomas in both ovaries**

Prevention is routinely recommended



THANKS FOR THE ATTENTION



Oocyte cryopreservation



When?



Llarena et al 2019

Fertility preservation: LBR per oocyte correlated with age

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15

20

38.8 (32.0-45.6

49.6 (40.7-58.4)

69.8 (57.4-82.2)

77.6 (64.4-90.9)

94.4 (84.3-100.4)

Kaplan-Meier plotting of the cumulative live birth rates (CLBR) of at least one baby, depending on the total number of consumed oocytes and categorized by age (\leq 35 y and \geq 36 y)

Cobo	et	al.,	2018	
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15

20

24

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Fertility preservation: Outcomes related age

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TABLE 2

In vitro fertilization data and clinical outcome according to age in years.

Parameters	≤35	>35	P value
No. of patients	260	225	NA
Mean age (y)	32.3 ± 2.6	38.3 ± 1.9	<.001
No. of OS cycles	$422(1.7 \pm 1.0)$	$409(1.7 \pm 1.1)$.991
No. of ICSI procedures	$288(1.1 \pm 0.1)$	$241(1.0 \pm 0.2)$.990
Antral follicular count	13.5 ± 8.7	8.8 ± 5.8	<.001
No. of retrieved oocytes/cycle	8.4 ± 7.3	6.0 ± 5.4	<.001
No. of retrieved oocytes/patient	13.5 ± 9.4	10.4 ± 6.3	<.001
No. of MII oocytes/cycle	6.6 ± 5.9	4.6 ± 4.3	<.001
No. of MII oocytes/patient	10.7 ± 7.9	8.0 ± 4.9	<.001
Survival rate (%)	85.1	80.8	.033
Embryo score (%)			<.001
A	14.9	9.8	
В	38.5	19.4	
C	15.0	31.0	
D	26.3	28.9	
E	5.3	10.9	
Clinical pregnancy rate (%)	49.2	41.4	<.001
Ongoing pregnancy rate (%)	40.9	29.6	.022
CLBR/patient (%)	161 (61.9)	64 (28.4)	<.001
Note: Unless otherwise indicated, numbers are mean \pm star	ndard deviation. CLBR = cumulative live-birth rate; ICSI	= intracytoplasmic sperm injection; MII = metaphase	ll; OS = ovarian stimulation.

Cobo. FP can help patients with endometriosis. Fertil Steril 2019.



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Fertility preservation in women affected by endometriosis:

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Llarena et al 2019





When?

Level of evidence

- Oocyte cryopreservation is influenced by age +++
- Oocyte cryopreservation is influenced by ovarian reserve + + +
- Ovarian reserve decreases with age
 + + +
- A previous ovariectomy does not reduce IVF success rate + + +
- More than 1 cycle of oocyte cryopreservation is possible
- ✤ A second line surgery is of limited efficacy on fertility + +
- Estroprogestins prevent endometrioma occurrence