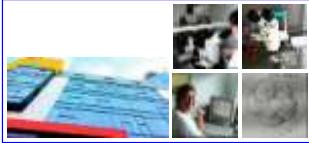


Assisted Reproduction in Endometriosis

Infertility Center Dortmund
Associates Dieterle , Neuer and Greb
Accredited Endometriosis Center (Level I)

www.ivf-dortmund.de




Robert Greb

ESHRE guidelines for the diagnosis and treatment of endometriosis
ESHRE Campus 2010
Budapest Hungary, 26. February 2010



Assisted Reproduction in Endometriosis

Assisted Reproduction in ENDOMETRIOSIS - Anything different ? -



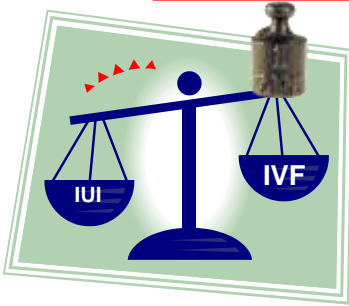
⊛ **Mechanisms of endometriosis-associated infertility ?**

- ▶ Tubal function impaired (mechanical)
- ▶ Immunologic factors ?
- ▶ Uterine dysperistalsis ?
- ▶ Ovarian dysfunction (oocytes, endocrine) ?
- ▶ Impaired embryo implantation (uterine) ?
- ▶ Dyspareunia ?

Budapest
26. February 2010



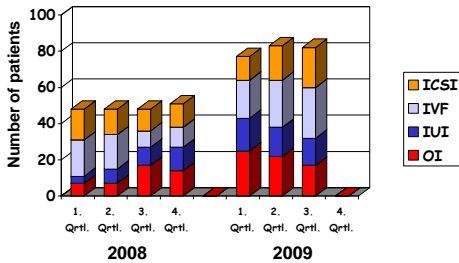
- Duration of infertility
- Women's age
- Male factor
- „Severity“ of endometriosis





Endometriosis Center Dortmund

Infertility treatments
(in patients with endometriosis)






IUI (Insemination)

▲ Treatment with intra-uterine insemination (IUI) improves fertility in nonendometriosis; IUI with ovarian stimulation is effective but the role of unstimulated IUI is uncertain (Tomson et al., 1997). Evidence: Level II.

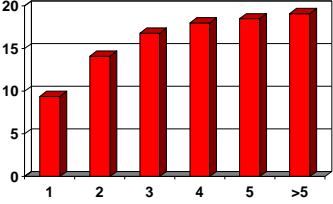
- ~ 3-fold increase in live birth rate
- Other studies often include combination of different types of infertility
- Systematic reviews indicate:
Endometriosis reduces treatment efficiency (compared to unexplained infertility)

Assisted Reproduction in Endometriosis

IUI results (German registry)



n = 76.169 cycles
1996 - 2006



Number of attempts	Pregnancy rate %
1	~10
2	~14
3	~17
4	~18
5	~19
>5	~19.5

Schill T. personal communication

pregnancy rate %

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IVF

- **IVF: Treatment of choice if**
 - ▶ Tubal function compromised
 - ▶ Male factor
 - ▶ Failure of other treatments



- **Why are pregnancy rates lower, compared to tubal factor (w/o endometriosis) ??**

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Endometriosis and IVF

● **Egg OR Uterus**

Leyendecker et al. (2006)

- **Evidence from oocyte donation cycles suggests „egg“ factor**

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Assisted Reproduction in Endometriosis

Assisted Reproduction in Endometriosis

Boston Reproduction Unit, No Page 1789-1794, 2009
© Elsevier B.V. All rights reserved. © 2009

The methodological quality of clinical guidelines of the European Society of Human Reproduction and Embryology (ESHRE)

W.L.D.M. Nelen¹*, B.H. van der Pijker², H.P.M.G. Hermans³, C. Brough⁴, P. de Sutter⁵, K.G. Nöcker⁶, A.M.M. Wetzels⁷, H.P.T.M. Grob⁸ and J.A.M. Kremer¹

AGREE **Score (0-100)**


(Appraisal of Guidelines for Research and Evaluation)

► Scope and purpose	81
► Stakeholder involvement	56
► Rigour of development	73
► Clarity and presentation	83
► Applicability	6
► Editorial independence	63

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Assisted Reproduction in Endometriosis

Assisted Reproduction in Endometriosis



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Assisted Reproduction in Endometriosis


Assisted Reproduction in Endometriosis

Case report 29707

- Endometriosis and Infertility -



- 27-year old patient
- 3 years infertility
- Primary dysmenorrhoea
- Laparoscopy:
right tube patent
left tube compromised
- Endometriosis III (rASRM)
ovarian, peritoneal,
bladder, adhesions
- ICSI cycle: no pregnancy
- NOW:** slight dysuria,
dyspareunia



- 47-year old partner
- Severe OAT

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Case report - Endometriosis and infertility -

- IVF/ICSI in severe endometriosis:
Clinical questions:



- Repeat surgery before IVF ?
- Hormonal treatment before IVF ?
- Ovarian stimulation protocol ?
- Increased risk for recurrence after IVF ?

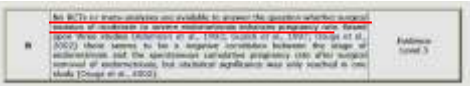


Surgery in severe endometriosis for infertility?





Surgery in severe endometriosis for infertility?




- → uncertain, whether surgery
improves infertility (B).

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Case report
- Endometriosis and Infertility -

- IVF/ICSI in severe endometriosis:
Clinical questions:




- Repeat surgery before IVF ? **Not because of infertility**
- Hormonal treatment before IVF?
- Ovarian stimulation protocol?
- Increased risk for recurrence after IVF?

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Case report
- Endometriosis and Infertility -

- IVF/ICSI in severe endometriosis:
Clinical questions:

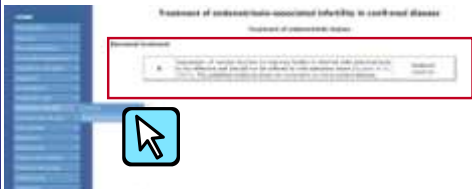


- Repeat surgery before IVF ? **Not because of infertility**
- Hormonal treatment before IVF?
- Ovarian stimulation protocol?
- Increased risk for recurrence after IVF?

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Hormonal treatment for endometriosis and infertility?



- → **Suppression of ovarian function ineffective to improve fertility (A).**

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Hormonal treatment for endometriosis and infertility?

Assisted reproduction in endometriosis

→ Consider GnRH-Agonist for 3-6 months before IVF/ICSI (A).

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Assisted Reproduction in Endometriosis

Ovarian stimulation for IVF in endometriosis?

Ultralong protocol

2-7 Months

Gonadotropin stimulation

GnRH-a

36 h

48-72 h

Follicular puncture

Embryo transfer

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17

Endometriosis (A)

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Assisted Reproduction in Endometriosis

<http://guidelines.endometriosis.org>

Guidelines for the use of GnRH-agonists in assisted reproduction in endometriosis

1. GnRH-agonist treatment should be considered for 3-6 months before IVF/ICSI in women with endometriosis. The duration of treatment should be individualized based on the clinical response to the treatment. The use of GnRH-agonist treatment should be based on the results of a randomized study and called for further research, particularly on the mechanism of action (Lorenzi et al., 2015).

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<http://guidelines.endometriosis.org>

1 Endometriosis is a chronic condition for which there is no cure. It is characterized by the presence of endometrial tissue outside the uterus, which can lead to pain, inflammation, and infertility. The exact mechanism of endometriosis is not fully understood, but it is believed to be related to retrograde menstruation and metaplasia. The condition can affect women of any age, but it is most commonly diagnosed in women in their 30s and 40s. Endometriosis is a leading cause of infertility, and it can also lead to other complications, such as pelvic pain and anemia.

2 The management of endometriosis is based on the patient's symptoms and the extent of the disease. Treatment options include hormonal therapy, pain management, and surgery. The goal of treatment is to reduce symptoms, improve quality of life, and preserve fertility. The choice of treatment depends on the patient's individual needs and preferences.

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Assisted Reproduction in Endometriosis

<http://guidelines.endometriosis.org>

The Cochrane Library

1 Endometriosis is a chronic condition for which there is no cure. It is characterized by the presence of endometrial tissue outside the uterus, which can lead to pain, inflammation, and infertility. The exact mechanism of endometriosis is not fully understood, but it is believed to be related to retrograde menstruation and metaplasia. The condition can affect women of any age, but it is most commonly diagnosed in women in their 30s and 40s. Endometriosis is a leading cause of infertility, and it can also lead to other complications, such as pelvic pain and anemia.


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Assisted Reproduction in Endometriosis

Case report
- Endometriosis and Infertility -

- **IVF/ICSI in severe endometriosis: Clinical questions:**



- **Repeat surgery before IVF? Not because of infertility**
- **Hormonal therapy before IVF? NO**
- **Ovarian stimulation protocol? Ultralong p.**
- **Increased risk for recurrence after IVF?**

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Case report - Endometriosis and Infertility -

- IVF/ICSI in severe endometriosis:
Clinical questions:



- Reoperation vor IVF ? **Nicht aufgrund Sterilität**
- Hormonal therapy before IVF? **NO**
- Ovarian stimulation protocol? **Ultralong p.**
- Increased risk for recurrence after IVF?



<http://guidelines.endometriosis.org>

World Guidelines for the Diagnosis and Treatment of Endometriosis

Assisted reproduction in endometriosis

Key advice Statement

Statement	Strength
1. In women with severe endometriosis, IVF/ICSI is recommended as the first-line treatment for achieving pregnancy.	Strong
2. In women with severe endometriosis, IVF/ICSI is recommended as the first-line treatment for achieving pregnancy.	Strong
3. In women with severe endometriosis, IVF/ICSI is recommended as the first-line treatment for achieving pregnancy.	Strong

The endometriosis data suggest as a guideline recommendation for the pathologic condition that endometriosis does not increase the risk for recurrence after IVF/ICSI.

Statement	Strength
1. In women with severe endometriosis, IVF/ICSI is recommended as the first-line treatment for achieving pregnancy.	Strong
2. In women with severe endometriosis, IVF/ICSI is recommended as the first-line treatment for achieving pregnancy.	Strong
3. In women with severe endometriosis, IVF/ICSI is recommended as the first-line treatment for achieving pregnancy.	Strong



<http://guidelines.endometriosis.org>

● Risk for recurrence is not increased in women with severe endometriosis after surgery for endometriosis stage III or IV with cumulative endometriosis excystic resection (EMR) are not increased after ovarian hyperstimulation for IVF (IVF) (strong) or IVF (strong) (strong)




Risk for recurrence **NOT** increased
after ovarian hyperstimulation for
IVF

Assisted Reproduction in Endometriosis

Case report
- Endometriosis and Infertility -

- IVF/ICSI in severe endometriosis: Clinical questions:





- Repeat surgery before IVF? **Not because of infertility**
- Hormonal therapy before IVF? **NO**
- Ovarian stimulation protocol? **Ultralong p.**
- Increased risk for recurrence after IVF? **NO**

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26. February 2010

Assisted Reproduction in Endometriosis

Case report
- Endometriosis and Infertility -

- 27 year old patient
- Prolonged downregulation (Nafarelin, 8 weeks before start with gonadotropin)
- Stimulation with rFSH 150 – 100 IE/day
- 10 oocytes, 9 fertilized (ICSI)
- 2 embryos, 4 pronucleus stage oocytes cryopreserved
- Birth of twins
- 47-year old partner
- Severe OAT

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26. February 2010

Assisted Reproduction in Endometriosis

IVF and endometrioma

Careful consideration: surgery really necessary? Especially in recurrence situation!

The effect of surgical treatment for endometriosis on in vitro fertilization outcomes: a systematic review and meta-analysis

Abstract
Background: Endometriosis is a common gynecological condition that can affect fertility. The aim of this study was to evaluate the effect of surgical treatment for endometriosis on in vitro fertilization (IVF) outcomes. Methods: A systematic review and meta-analysis of randomized controlled trials (RCTs) and observational studies was conducted. Results: The analysis included 10 studies with a total of 1,234 IVF attempts. Surgical treatment for endometriosis was associated with a significantly higher number of IVF attempts (OR 1.45, 95% CI 1.15-1.80) and a higher number of IVF pregnancies (OR 1.35, 95% CI 1.05-1.75) compared to medical treatment. Conclusion: Surgical treatment for endometriosis may improve IVF outcomes. However, the quality of the evidence is low, and further research is needed.

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26. February 2010

Ovarian Failure due to Endometriosis

- Fertility preservation (oocyte cryopreservation)

CASE REPORT

Oocyte cryopreservation in a young woman with severe and symptomatic endometriosis: a new indication for fertility preservation

Paul F. Elias, M.D., Ph.D., David C. Olson, Ph.D., Steven E. Li, Bruce A. Miller, David C. Olson, M.D.,

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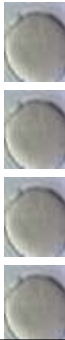
© 2010 Society for Assisted Reproductive Technology (SART)

Objective: To report a case of oocyte cryopreservation in a young woman with severe and symptomatic endometriosis.

Case: A 28-year-old woman with severe and symptomatic endometriosis underwent oocyte cryopreservation.

Discussion: Oocyte cryopreservation is a new indication for fertility preservation in young women with severe and symptomatic endometriosis.

Key Words: Oocyte cryopreservation, endometriosis, fertility preservation, assisted reproductive technology



- Oocyte donation

Take home and Discussion

- IUI possible
- IVF most effective option (but success rates compromised)
- Consider prolonged GnRH-induced downregulation
- Endometrioma: Surgery not compulsory
- Risk for recurrence not increased by IVF
- Oocyte cryopreservation ?