eshre
SCIENCE MOVING
PEOPLE
MOVING SCIENCE

Is there any place for reproductive surgery in the era of ART

Special Interest Group Reproductive Surgery

8

1 July 2012
Istanbul, Turkey

Is there any place for reproductive surgery in the era of ART?

Istanbul, Turkey
1 July 2012

Organised by
the Special Interest Group Reproductive Surgery

Contents

Course coordinators

Marco Gergolet (Italy), Vassilios Tanos (Cyprus), Grigoris Grimbizis (Greece), TC Li (United Kingdom), Stephan Gordts (Belgium), Nataša Kenda Šuster (Slovenia)

Course description

Aim of the course is to assess a consensus on the limits and the indication to reproductive surgery related to the outcome, costs and negative side effects of ART. The course will be interactive and the participiants will be asked to express their opinion on the management of the patients before and after hearing the lecture. After each topic an effort to reach consensus will be done.

Target audience

Specialist physicians and surgeons, nurse specialists and clinical scientists

Scientific programme

Can infertility be defined and treated without endoscopy?
Chairman: George Pados (Greece)

09.00 - 09.15	Case presentation
09.15 - 09.40	Pro – **Recai Pabuçcu (Turkey)**
09.40 - 10.05	Contra – **Vassilios Tanos (Cyprus)**
10.05 - 10.15	Discussion
10.15 - 10.30	Consensus conclusions
10.30 - 11.00	Coffee break

Proximal and distal tubal pathology
Chairman: Stephan Gordts (Belgium)

11.00 - 11.15	Case presentation
11.15 - 11.40	Surgery – **Tin-Chiu Li (United Kingdom**)
11.40 - 12.05	ART – **Anna Pia Ferraretti (Italy)**
12.05 - 12.15	Discussion
12.15 - 12.30	Consensus conclusions
12.30 - 13.30	Lunch

Myometrial pathology and implantation: borders of treatment
Chairman: Tin Chiu Li (United Kingdom)

13.30 - 13.45	Case presentation
13.45 - 14.10	Is there any sense to treat myomas before ART? – **Stephan Gordts (Belgium)**
14.10 - 14.35	How to handle patients with adenomyosis before ART – **Grigoris Grimbizis (Greece)**
14.35 - 14.45	Discussion
14.45 - 15.00	Consensus conclusions
15.00 - 15.30	Coffee break

Uterine cavity
Chairman: Marco Gergolet (Italy)

15.30 - 15.45	Case presentation
15.45 - 16.10	Imaging techniques in the exploration of the uterine cavity – **Pietro Gambadauro (Sweden)**
16.10 - 16.35	Hysteroscopy: added value? **– Rudi Campo (Belgium)**
16.35 - 16.45	Discussion
16.45 - 17.00	Consensus conclusions

ESHRE PRECONGRESS COURSE
July 1, 2012
Istanbul

Case Presentation

Recai PABUÇCU, MD,
Professor and Head,
Ufuk University Department of Obstetrics &Gynecology

Can infertility be defined & treated without endoscopy?

Case presentation

- **36 years old, 3 years of primary infertility**
- **Normal menstrual cycles**
- **No previous history of PID and endometriosis**
- **HSG ⇒ Normal**
- **Chlamydia antibody ⇒ Normal**
- **Semen analysis ⇒ Normal**
- **Hormone profile ⇒ Normal**

UNEXPLAINED INFERTILITY

Should we start treatment with:

- **3 cycles of IUI than IVF or L/S & H/S in order to exclude periadnexial adhesion and minimal to mild endometriosis ?**
- **If the first option is adopted, after 3 failed IUI cycles should we suggest IVF or L/S & H/S?**

Infertility

- **Definition:** Unable to conceive despite unprotected intercourse of 1 year
- **Unexplained Infertility:** Unable to conceive without any identifiable cause (30%)

Practice Committee of the ASRM

failure to achieve pregnancy..

- after 12 months of attempting conception despite a thorough evaluation
- after six months in women 35 and older

Fertil Steril, 2008

Unexplained Infertility How to Define?

The initial diagnostic tests should be

- **Midluteal progesterone**
- **Semen analysis**
- **Hysterosalpingography**

Eshre Capri Workshop Group, Human Reproduction, 2000

- **L/S if indicated**

ASRM 1992

The Role of L/S??

- Strong suspicion of endometriosis
- Pelvic and adnexal adhesions
- Significant tubal disease

⇒ L/S

ASRM 2006

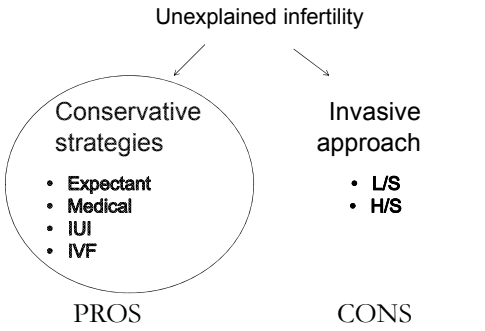
Otherwise ??

- Women thought to have co-morbidities should be offered laparoscopy
- tubal and other pelvic pathology can be assessed at the same time

Grade B

NICE Guideline Fertility 2004

First Line Options



Treatment Options

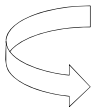
- Expectant management
- Ovulation Induction
- IUI
- IVF

Expectant Management

- 3.8 % average cycle fecundity in the untreated group (Guzick et al 1998)
- 27.4% of cumulative pregnancy rate after 12 months in untreated subfertile population (Snick et al 1997)
- Spontaneous pregnancy rate of 19.9% after 12 months of observation (Gleicher et al 1996)

Expectant Management

- 27% vs 23% OPR compared with COH-IUI group (Steures et al 2006 Lancet)
- ***Empirical CC*** and ***natural IUI*** *cycles* do not offer superior live birth rates than expectant management (Wordsworth 2011)



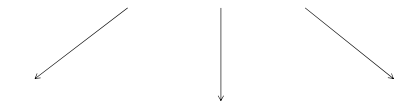
Chance of spontaneous pregnancy is low but NOT ZERO!

Therefore, expectant management DOES play an important role where limited resources are available..

Treatment Options

- Expectant management
- Ovulation Induction
- IUI
- IVF

Ovulation Induction



CC

Gonadotrophins

Aromatase Inhibitors

Ovulation Induction-CC

- Clomiphene Citrate: commonly used agent
- *3 (level 1) RCT* and *1 case control study* revealed that: no of cycles needed for one additional pregnancy with CC was **40** (95% CI)

ASRM Practice Comitee 2000

- Latest RCT showed no better rates with CC than expectant management..

(14% vs 17% LBR) Bhattacharya 2008

Unexplained infertility: an update and review of practice

compared	*pregnancy/woman*		
CC versus expectant management	1.03 (0.64–166)	0.79 (0.45–1.38) (Bhattacharya *et al.*, 2008)	Fisch *et al.* (1989); Bhattacharya *et al.* (2008)
CC + IUI versus placebo + IUI	2.40 (0.70–8.19)	NA	Melis *et al.* (1987); Deaton *et al.* (1990)
CC with HCG without IUI versus placebo	1.66 (0.58–4.80)	NA	Harrison and O'Moore (1983); Fisch *et al.* (1989)
CC + IUI versus HMG + IUI	0.54 (0.21–1.37)	0.51 (0.18–1.47)	Echochard *et al.* (2000); Karlström *et al.* (1993)
CC versus recombinant FSH	NA	NA	NA
CC versus high-purity urinary	0.22 (0.04–1.20)	NA	Balasch *et al.* (1994)

No evidence that CC was more effective than no treatment or placebo for LBR

Hughes 2010 Cochrane

Ovulation Induction Gonadotrophins

- CC vs hMG: no significant difference in LBR/couple (OR 0.51)
- CC vs hMG: significantly higher CPR with hMG (OR 0.44)
- No studies have compared CC vs recFSH
- Gonadotophins only vs IUI: in favor of IUI (OR 1.68)

Ataullah et al 2009 Cochrane Database

- Insufficient evidence to suggest that oral agents are inferior or superior to injectable agents in the treatment of unexplained subfertility

Ataullah et al 2009 Cochrane Database

Gonadotrophins in Unexplained infertility

Gonadotrophins versus expectant management	–	NA	NA
CC versus HMG	0.54 (0.21–1.37)	0.51 (0.18–1.47)	Karlström et al. (1993); Echochard et al. (2000)
CC versus high-purity urinary gonadotrophins(follitropin α)	0.22 (0.04–1.20)	NA	Balasch et al. (1994)
CC versus recombinant FSH	NA	NA	NA
Gonadotrophins versus IUI	1.68 (1.03–2.75)	NA	Karlström et al. (1993); Chung et al. (1995); Melis et al. (1995); Janko et al. (1998)
Gonadotrophins versus IVF	NA	NA	NA

Ovulation Induction Aromatase Inhibitors (AI)

- Supress estrogen production without antiestrogenic effects
- No trials comparing AI with plasebo..
- Meta analysis and systematic review by Polyzos et al (2008) showed NO DIFFERENCE between CC according to pregnancy rates (OR 0.87)
- Large RCT needed evolving AI

Treatment Options

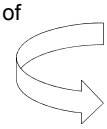
- Expectant management
- Ovulation Induction
- IUI
- IVF

IUI

- Rationale

Increasing the number of gametes at the site of fertilization

Inseminating motile and morphologically good sperms



High probability of pregnancy

IUI

The standart treatment in couples with:

- **unexpalined infertility**
- **mild male factor**
- **cervical factor**

Cohrane 2007

Question Marks of IUI

- Stimulated or natural?
- 3 cycles or more (6 cycles)?
- Single IUI or double IUI?

. Pregnancy rates following treatment for unexplained infertility.

Treatment	Monthly fecundity (%)
No treatment	3
IUI	4
Clomiphene	6
Clomiphene plus IUI	7
Gonadotrophin	8
Gonadotrophin plus IUI	18
IVF	23
GIFT	26

- Gonadotrophins increase the monthly fecundity rate 10-15 % in IUI cycles in unexplained group

Adamson, 2003

Cochrane Database Syst Rev.

Intra-uterine insemination for unexplained subfertility

Verhulst SM, 2006

- **IUI vs Timed intercourse (both in stimulated cycles)**

  Increased chance of pregnancy with IUI (OR 1,68)

- **COH+IUI vs Natural cycle IUI**

  (OR 2.33) favoring COH+IUI

Verhulst, Cochrane Database, 2006

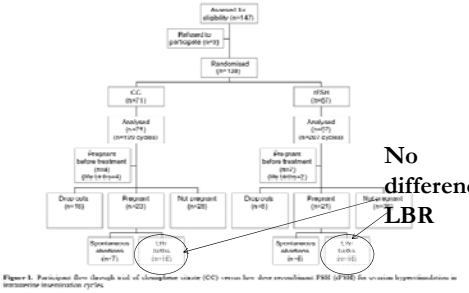
Pregnancy rates per cycle

	%
Expectant	1.3
IUI	3.8
CC	5.6
CC + IUI	8.3
HMG	7.7
HMG + IUI	**17.1**
IVF/ICSI	**20.7**

Similar

Guzick et al, 1998

CC-IUI vs low dose recFSH-IUI in unexplained infertility



No difference in LBR

Dankert et al Hum Reprod 2007

Table 3. Aggregate pregnancy rates in trials of IUI with and without ovarian stimulation for unexplained infertility.

Ovarian stimulation	No. (%) of pregnancies per cycle IUI	TI	OR (95% CI)
No stimulation	61/1102 (6)	25/963 (3)	2.09 (1.35–3.22)
FSH	90/625 (14)	21/331 (6)	2.19 (1.45–3.32)

Adapted from the ESHRE Capri Workshop Group (1996).

Pregnancy rate per cycle;

- **3 % with observaion & timed intercourse**
- **6 % in FSH cycles**
- **14 % in FSH+IUI cycles**

ESHRE Capri Workshop, 1996

Table 4. Aggregate data for alternative treatments for unexplained infertility.

Treatment	No. of studies	No. (%) of pregnancies per initiated cycle	Percentage of quality adjusted pregnancies per initiated cycle
Control groups	11	64/3539 (1.8)	1.3
Control groups, randomized studies	6	23/597 (3.9)	4.1
IUI	9	15/378 (4.0)	3.8
FSH	13	139/1806 (7.7)	7.7
FSH + IUI	14	207/1153 (18.3)	17.1

Adapted from Guzick et al. (1998).

- **Pregnancy rates were increased from 8% to 18 % when IUI was added to gonadotrophins**

Guzick, 1998

Table 5. Aggregate pregnancy rates of 20 randomized controlled trials comparing alternative treatments for unexplained infertility. Figures in parentheses are percentages.

Comparison	No. (%) of pregnancies per cycle	OR (95% CI)
FSH + IUI versus FSH + TI	170/929 (18) versus 76/711 (11)	1.71 (1.28–2.28)
FSH + IUI versus IUI	107/478 (22) versus 59/466 (13)	1.77 (1.26–2.49)
FSH + IUI versus FSH + cervical insemination	127/476 (27) versus 74/517 (14)	1.86 (1.36–2.54)

Adapted from Aboulghar et al. (2003).

- **Pregnancy rates in the OI+IUI group was significantly higher than IUI alone group**

Aboulghar, 2003

Single or double IUI ?

Double versus single intrauterine insemination for unexplained infertility: a meta-analysis of randomized trials

Nikolaos P. Polyzos, M.D.,[a] Spyridon Tziveras, M.D., Ph.D.,[a] Davide Mauri, M.D., Ph.D.,[a] and Athina Tatsioni, M.D., Ph.D.[b]

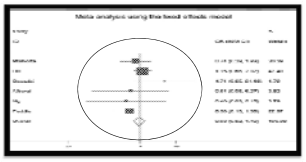
Fertil Steril, 2010

Single or double?

- 6 randomised trials, 829 women with unexplained infertility

Clinical pregnancy:

- Double IUI ⇨ 14.4 %
- Single IUI ⇨ 13,6 %



No difference…

Single or double?

- **No superiority of** double IUI **to** single IUI

Cochrane 2003,
Cantineau 2003,
Zeyneloğlu 2004
Nikolaos, 2009
Bagist, 2010

Optimal cycle number?

Controlled ovarian hyperstimulation and intrauterine insemination for treatment of unexplained infertility should be limited to a maximum of three trials

Mohamed Aboulghar, M.D., Ragab Mansour, M.D., Gamal Serour, M.D., Ashraf Abdalla, M.D., Yehia Amin, M.D., and Catherine Rhodes, M.R.C.O.G.

Cyclic fecundity rate in first 3 trials 16.4%

4-6 trials 5.6%

3 failed COH+ IUI ⇨ **IVF**

Aboulgar 2001

It seems that:

- OI with gonadotrophins significantly improves the probability of conception when associated with IUI (COH-IUI better)
- No difference between single and double IUI
- IVF is much more reasonable after 3 failed COH-IUI

Treatment Options

- Expectant management
- Ovulation Induction
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Treatment Options

- Expectant management
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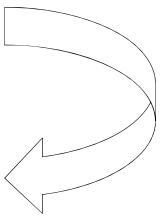


WHEN?

IVF

- **Expensive, invasive but considered as the most effective method**
- **Average success rates are..**

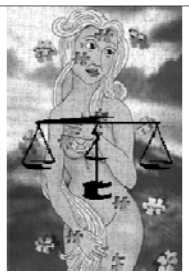
< 35 years old ⇨ 28,2 %
35-37 years old ⇨ 23,6 %
38-39 years old ⇨ 18,3 %
(Human Fertilisation Embryology Authority, UK)

- **But increased success rate comes with the price of high multiple pregnacy rate**

Unexplained infertility

First choice ???

KOH+IUI
Goverde,2000
Homburg, 2003
Homburg and Insler, 2002
Collins, 2003



IVF
Gleicher, 2000
Gleicher and Karande, 2000

IVF for unexplained subfertility

- Higher pregnancy rates than expectant management (OR 3,24)
- Live Birth Rate /women with a single cycle of IVF significantly higher than expectant management (OR 22.0)

Pandian, Cochrane Database, 2005

Is IVF more effective than stimulated intrauterine insemination as a first-line therapy for subfertility?

A cohort analysis

Chambers, Aust N Z J Obstet Gynaecol, 2010

- **Unexplained, mild male & female infertile couples**

272 ⇒ **2 cycles of IUI/COH**
176 ⇒ **1 cycle of IVF**

	IVF	COH + IUI
Cumulative live birth rate	39,2 %	27,6 %
Mean time to pregnancy	44 days	69 days
Cost	⇧	
Multiple delivery rate	10,1 %	13,3 %

Results

- 1 cycle of IVF was more effective but expensive than 2 cycles of COH+IUI
- With IVF, higher success rates, shorter times to pregnancy & a trend to less higher order multiple pregnancy

Couples with unexplained subfertility and unfavorable prognosis: a randomized pilot trial comparing the effectiveness of in vitro fertilization with elective single embryo transfer versus intrauterine insemination with controlled ovarian stimulation

Inge M. Custers, M.D.,[a] Tamar E. König, M.D.,[b] Frank J. Broekmans, M.D., Ph.D.,[c] Peter G. A. Hompes, Prof.,[b] Eugenie Kaaijk, M.D., Ph.D.,[d] Jur Oosterhuis, M.D., Ph.D.,[e] Monique H. Mochtar, M.D.,[a] Sjoerd Repping, Prof.,[a] Madelon van Wely, Ph.D.,[a] Pieternel Steures, M.D., Ph.D.,[a] Fulco van der Veen, Prof.,[a] and Ben W. J. Mol, Prof[a,f]

- **116 couple randomised to one cycle of IVF-Single embryo transfer (SET) (n=58) and 3 cycles of IUI-COS (n=58)**

TABLE 2

Pregnancy outcomes at 4 months from randomization.

Outcome measure	IVF-eSET (n = 58)	IUI-COH (n = 58)	RR (95% CI)
Clinical pregnancies	15	14	1.07 (0.57–2.01)
Ongoing pregnancies	14 (24)[a]	12 (21)[b]	1.17 (0.60–2.30)
Multiple pregnancies	2 (14)	3 (25)	
Twin	2	2	
Triplet	0	1	
Live births	13[c] (22)	12 (21)	1.08 (0.55–2.16)
Miscarriage	1 (2)	2 (3)	
Ectopic pregnancy	0	1 (2)	

Note: Values are number (percentage).
[a] One spontaneous pregnancy (IVF-eSET).
[b] Two spontaneous pregnancies (IUI-COH).
[c] One couple was lost to follow-up.

Custers. IVF-SET vs IUI-COS in unexplained subfertility. Trial Sem 2011

- Ongoing pregnancy rates;
  - IVF-SET 24%
  - IUI-COS 21%

Multiple gestation; IVF-SET 14%, IUI-COS 25%

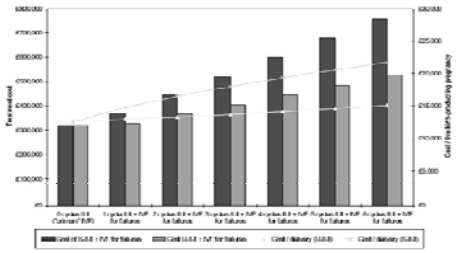
One cycle of IVF-eSET transfer might be as effective as 3 cycles of IUI+COS as primary treatment

BMC Health Services Research

Cost-effectiveness of primary offer of IVF vs. primary offer of IUI followed by IVF (for IUI failures) in couples with unexplained or mild male factor subfertility

Nora Pashayan[*1], Georgios Lyratzopoulos[2] and Raj Mathur[3]

- Mathematical modelling was used to estimate the comperative and clinical cost effectiveness of either primary IVF or IVF following IUI failures



- **Cost-effectiveness ratios for IVF, Unstimulated IUI (U-IUI) & Stimulated IUI (S-IUI) are £12,600, £ 13,100 & £ 15,100 per live birth producing pregnancy**

Results

- **For couples with unexplained subfertility, primary offer of a full IVF cycle is less costly and more cost effective than providing IUI followed by IVF**

A randomized clinical trial to evaluate optimal treatment for unexplained infertility: the fast track and standard treatment (FASTT) trial

Richard H. Reindollar, M.D.,[a] Meredith M. Regan, Sc.D.,[b] Peter J. Neumann, Sc.D.,[c] Bat-Sheva Levine, M.D.,[c] Kim L. Thornton, M.D.,[d] Michael M. Alper, M.D.,[d] and Marlene B. Goldman, Sc.D.[e]

Patient(s): Couples with unexplained infertility.
Intervention(s): Couples were randomized to receive either conventional treatment (n = 247) with three cycles of clomiphene citrate (CC)/IUI, three cycles of FSH/IUI, and up to six cycles of IVF or an accelerated treatment (n = 256) that omitted the three cycles of FSH/IUI.
Main Outcome Measure(s): The time it took to establish a pregnancy that led to a live birth and cost-effectiveness, defined as the ratio of the sum of all health insurance charges between randomization and delivery divided by the number of couples delivering at least one live-born baby.
Result(s): An increased rate of pregnancy was observed in the accelerated arm (hazard ratio [HR], 1.25; 95% confidence interval [CI], 1.00–1.56) compared with the conventional arm. Median time to pregnancy was 8 and 11 months in the accelerated and conventional arms, respectively. Per cycle pregnancy rates for CC/IUI, FSH/IUI, and IVF were 7.6%, 9.8%, and 30.7%, respectively. Average charges per delivery were $9,800 lower (95% CI, $25,100 lower to $3,900 higher) in the accelerated arm compared to conventional treatment. The observed incremental difference was a savings of $2,624 per couple for accelerated treatment and 0.06 more deliveries.

Fertil Steril, 2010

TABLE 2

Number of couples initiating treatment cycles, total number of cycles initiated, and pregnancy rates by treatment group as of April 30, 2006.

	Treatment type and randomization strategy								
	CC/IUI			FSH/ IUI	IVF			Total	
	Conventional	Fast track	All	Conventional	Conventional	Fast track	All	Conventional	Fast track
No. couples initiating	233	242	475	169	111	172	283	247	256
No. of cycles initiated	640	640	1294	439	201[a]	301[a]	622	1340	1009
No. of pregnancies									
Total[b]	55	68	123	50	96	145	240	200	213
Losses	10	15	25	7	22	27	49	39	42
Ongoing (≥ 20 wks)	4	2	6	6	16	18	33	38[c]	28[c]
Live birth	41	51	92	37	58	100	158	150[c]	171[c]
Pregnancy rates (live birth + ongoing)									
Per initiated cycle	7.0 (4.8 10.0)	8.2 (5.8 11.4)	7.6 (6.2 9.2)	9.8 (6.8 14.0)	28.0 (21.8 35.2)	32.7 (27.0 38.9)	30.7 (27.1 34.5)		
Per couple	[illegible] (14.5-25.0)	[illegible] (16.9-27.7)	[illegible] (17.1-24.6)	25.4 (19.1-32.7)	[illegible] (58.9-74.5)	[illegible] (61.1-75.5)	[illegible] (61.7-72.9)	[illegible] (69.0-80.2)	77.7 (72.1-82.7)

Note: CC = clomiphene citrate; IUI = intrauterine insemination; FSH = gonadotropin.
[a] For IVF, 32 of the conventional and nine of the fast track cycles used cryopreserved embryos that had been collected in an earlier IVF cycle and frozen for later use. These cycles, called thaw cycles, are included in the calculation of the pregnancy rates per initiated cycle.
[b] Total pregnancies include all ultrasound confirmed pregnancies, including spontaneous abortions.
[c] Of these, there were 18 ongoing pregnancies (10 in conventional and 8 in fast track) and 31 live births (11 in conventional and 20 in fast track) that occurred outside of treatment cycles.

- **Per cycle pregnancy rates are 7.6 %, 9,8 % and 30,7 % for CC+IUI, FSH/IUI and IVF respectively**

Accelerated arm;

- ⇧ **rate of pregnancy**
- ⇩ **median time to pregnancy (8 vs 11 months)**
- **Average charge/delivery $9,800 lower**

Results

- FSH/IUI treatment was of no added value
- Accelerated approach to IVF results in a shorter time to pregnancy

Even if..

- The patient had minimal-mild endometriosis???

Endometriosis and Subfertility

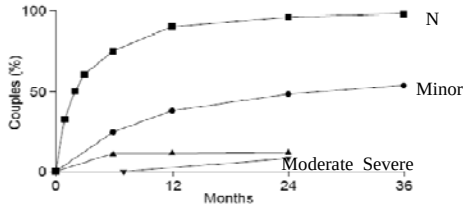
Fecundity rate

- Endometriosis; %2-10
- Fertil population; %15-20

The Practice Committee of the American Society for Reproductive Medicine, 2006

FECUNDITY IN WOMEN WITH ENDOMETRIOSIS

Cumulative conception rates with untreated endometriosis related to disease grading, compared with normal conception rate



Kevin D. Jones, 2002

Laparoscopic surgery & restoration of fertility

Can laparoscopic resection of lesions of Stage I & II Endometriosis restore fertility alone?

Human Reproduction vol.14 no.5 pp.1332–1334, 1999

Ablation of lesions or no treatment in minimal–mild endometriosis in infertile women: a randomized trial

Gruppo Italiano per lo Studio dell'Endometriosi*
Correspondence to: Dr Fabio Parazzini, Istituto di Ricerche Farmacologiche 'Mario Negri', via Eritrea, 62–20157 Milano, Italy

- **Patients with Stage I&II endometriosis**
  - **54 ⇨ assigned to resection or ablation**
  - **47 ⇨ assigned to diagnostic laparoscopy only**

Gruppo Italiano per lo Studio dell'Endometriosi, Human Reprod Update, 1999

- **1 year follow up birth rates**
  - **Resection & Ablataion ⇨ 19.6%**
  - **Diagnostic L/S only ⇨ 22.2%**

There is no significant difference..

Surgery for peritoneal disease (ASRM stage I–II)

Table 7 Comparison of Two Randomized Controlled Trials[36,73] Evaluating Fertility Outcome in Women with Minimal-Mild Endometriosis after Surgical Excision of Endometriosis (Excision Group) and after Diagnostic Laparoscopy (Control Group)

Parameter	Endocan, 1997	CISE Italy, 1999
N patients included	341	91 (54 excision, 47 control)
Duration infertility	2 years	4 years
Postoperative GnRH analogs	No	Yes, *n* = 41 (18 excision, 23 control)
MFR control group	2.4%	No data
MFR excision group	4.7%	No data
Rate ratio comparing MFR between groups	1.9 (95% CI, 1.2–3.1)	No data
CPR control group	17.7%	No data
CPR excision group	30.7%	No data
P value comparing CPR between groups	*P* = 0.006	No data
Live birth per patient (control group)	No data	22%
Live birth per patient (excision group)	No data	20%
P value comparing live birth per patient between groups	No data	NS

MFR, monthly fecundity rate; CPR, cumulative pregnancy rate.

Hum Reprod 2005

ESHRE guideline for the diagnosis and treatment of endometriosis

Clinical condition	Recommendation ESHRE 2005
Minimal-mild endometriosis (stage I–II (ASRM))	Limited benefit; surgery recommended (Review)

Assisted reproduction i

Intrauterine insemination

(ASRM stage I–II)

A Treatment with intrauterine insemination (IUI) improves fertility in minimal–mild endometriosis. IUI with ovarian stimulation is effective but the role of unstimulated IUI is uncertain (Tummon *et al.*, 1997).

Stephen Kennedy[1,10], Agneta Bergqvist[2], Charles Chapron[3], Thomas D'Hooghe[4], Gerard Dunselman[5], Robert Greb[6], Lone Hummelshoj[7], Andrew Prentice[8] and Ertan Saridogan[9] on behalf of the ESHRE Special Interest Group for Endometriosis and Endometrium Guideline Development Group*

ENDOMETRIOSIS

Why COH + IUI?

64

Why COH + IUI?

FERTILITY AND STERILITY
The Official Journal of the American Society for Reproductive Medicine

Randomized controlled trial of superovulation and insemination for infertility associated with minimal or mild endometriosis*

Ian S. Tummon, M.D.†‡
Linda J. Asher, R.N.A.C.†
James D. B. Martin, M.D.†§
Togas Tulandi, M.D.‡

The University of Western Ontario, London, Ontario, and McGill University, Montreal, Quebec, Canada

Patient(s): Three hundred eleven cycles in 103 couples in whom minimal or mild endometriosis was the sole identified subfertility factor.
Intervention(s): Superovulation with FSH and IUI.
Main Outcome Measure(s): Live birth.

FORUM: guideline for the diagnosis and treatment of endometriosis

Tummon IS, Fertil Steril, 1997

Minimal-Mild Endometriosis-COH + IUI

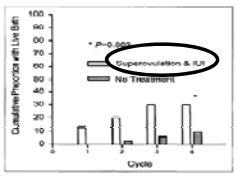


Figure 1 Cumulative proportion of patients with live birth.

Table 2 Cycles and Live Births

	Superovulation and IUI		No treatment	
Cycle	No.	Live births	No.	Live births
1	53	7	50	0
2	39	3	48	1
3	27	4	44	1
4	8	0	42	2

10 **Tummon et al.** *Superovulation / IUI for endometriosis*

Result(s): Live birth followed 14 of 127 (11%) superovulation and IUI cycles and 4 of 184 (2%) no-treatment cycles. The odds ratio was 5.6 (95% confidence interval 1.8 to 17.4) in favor of superovulation and IUI.
Conclusion(s): Treatment with superovulation and IUI was associated with superior outcome both by crude live-birth rates and proportional hazard analysis. (Fertil Steril® 1997;68:8–12. © 1997 by American Society for Reproductive Medicine.)

Tummon IS.,Fertil Steril 1997

Why COH + IUI?

FECUNDITY IN WOMEN WITH ENDOMETRIOSIS

Cycle fecundity in women with stage I or II endometriosis, according to treatment.

Group	Unexplained infertility	Endometriosis-associated infertility			
Treatment	Guzick et al. (27)	Deaton et al. (28)	Chatman et al. (29)	Fedele et al. (30)	Kemmann et al. (31)
No treatment or intracervical insemination	0.02	0.033	—	0.045	0.020
IUI	0.05[a]	—	—	—	—
Clomiphene	—	—	—	—	0.066
Clomiphene/IUI	—	0.095[a]	—	—	—
Gonadotropins	0.04[a]	—	0.066	—	0.073[a]
Gonadotropin/IUI	0.09[a]	—	0.129[a]	0.15[a]	—
IVF	—	—	—	—	0.222[a]

The Practice Committee of the American Society for Reproductive Medicine, 2006

Subfertility guidelines in Europe: the quantity and quality of intrauterine insemination guidelines

Human Reproduction Vol.21, No.9 pp. 2103–2109, 2006

E.C.Haagen[1,2], R.P.M.G.Hermens[2], W.L.D.M.Nelen[1,2], D.D.M.Braat[1], R.P.T.M.Grol[2] and J.A.M.Kremer[1,3]

Table IV. Comparison of recommendations of the intrauterine insemination (IUI) guideline from England and Wales (n = 8) with recommendations of IUI guidelines from Denmark, France and the Netherlands

Recommendations topics	Denmark	England and Wales	France	Netherlands
Indications for (un)stimulated IUI[a]				
Male-factor subfertility	Stimulated IUI	Unstimulated IUI	Stimulated IUI	Stimulated IUI in mild male-factor subfertility[b] Unstimulated IUI in severe male factor subfertility[c]
Unexplained subfertility	Stimulated IUI	Unstimulated IUI	Stimulated IUI	Stimulated IUI
Minimal to mild endometriosis	Stimulated IUI	Unstimulated IUI	Stimulated IUI	Not mentioned

- Does the stage of endometriosis change the success rates in COH + IUI?
- IVF-ET or COH + IUI cycle?

Cycle fecundity in women with stage I or II endometriosis, according to treatment.

Group / Treatment	Unexplained infertility: Guzick et al. (27)	Endometriosis-associated infertility: Deaton et al. (28)	Chaffkin et al. (29)	Fedele et al. (30)	Kennmann et al. (31)
No treatment or intracervical insemination	0.02	0.033	—	0.045	0.028
IUI	0.05[a]	—	—	—	—
Clomiphene	—	—	—	—	0.066
Clomiphene/IUI	—	0.095[a]	—	—	—
Gonadotropins	0.04[a]	—	0.066	—	0.073[a]
Gonadotropin/IUI	0.09[a]	—	0.129[a]	0.15[a]	—
IVF	—	—	—	—	0.222[a]

Int J Fertil Menopausal Stud 1993;38:16-21.

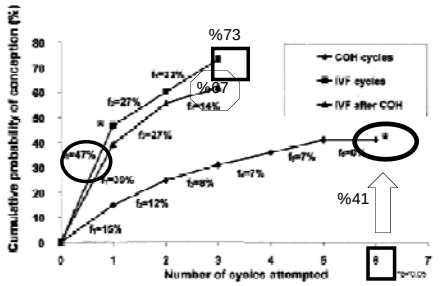
Cycle-specific and cumulative fecundity in patients with endometriosis who are undergoing controlled ovarian hyperstimulation–intrauterine insemination or in vitro fertilization–embryo transfer

W. Paul Dmowski, M.D., Ph.D., Michelle Pry, M.S.N., Jianchi Ding, Ph.D., and Nasir Rana, M.D., M.P.H.

FERTILITY AND STERILITY

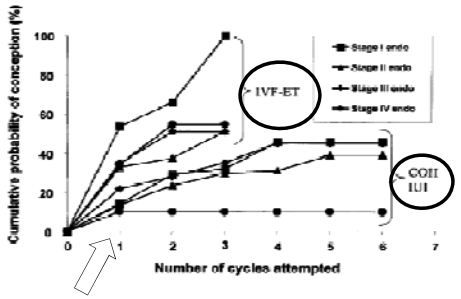
Dmowski et al. Fertil Steril 2002

Cycle and cumulative fecundity in women with endometriosis undergoing COH-IUI, IVF-ET, or IVF-ET after failed COH-IUI.



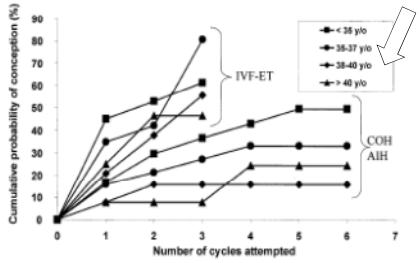
Dmowski et al. Fertil Steril 2002

Effect of COH-IUI or IVF-ET on fecundity according to the stage of endometriosis.



Dmowski et al. Fertil Steril 2002

Effect of COH-IUI or IVF-ET on fecundity according to the age of the women with endometriosis.



Dmowski et al. Fertil Steril 2002

Pregnancy rates and outcome according to treatment.

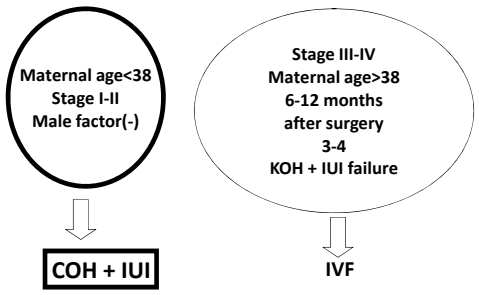
Treatment group	No. patients	No. cycles	No. (%) pregnant	No. embryos transferred (mean)	Implantation rate (%)	% Multiple gestation	No. SAB (%)
COH-IUI	202	648	69 (11)	N/A	N/A	10	18 (26)
IVF-ET	111	139	65 (47)[a]	2.9	27[a]	26	13 (20)
IVF after COH	56	68	30 (44)[a]	3.1	23[a]	27	3 (17)
IVF-ET + FUET	111	139	71 (51)[a]	2.8	28[a]	25	13 (18)
Excluding significant male factor							
COH-IUI	172	534	58 (11)	N/A	N/A	8	16 (27)
IVF-ET	85	94	48 (51)[a]	2.9	29[a]	26	7 (14)

[a] Significantly different than the corresponding COH-IUI group at $P < .05$.
SAB = spontaneous abortion; FUET = cryopreserved embryo transfer.
Dmowski. Fecundity with COH or IUI in endometriosis. Fertil Steril 2002.

Treatment group	No. patients	No. cycles	No (%) pregnant
COH-IUI	202	648	69 (11)
IVF-ET	111	139	65 (47)[a]
IVF after COH	56	68	30 (44)[a]

Dmowski et al. Fertil Steril 2002

When COH + IUI ?



Dmowski et al. Fertil Steril 2002

Endometriosis

- **Surgery increases fecundity rates.**
- **But COH + IUI have better results than surgery.**
- **COH+IUI is effective in endometriosis associated infertility in Stege I&II but data is not sufficient for Stage III&IV**

Laparoscopy in unexplained infertility?

- **There is still a considerable debate regarding the place of laparoscopy for cases of unexplained infertility**

Skipping L/S ?

- **There is a growing tendency for by-passing diagnostic laparoscopy in unexplained infertility**
- **Both Efficient & cost effective protocol**

(Balash,2000; Fatum 2002; Badawy 2008)

Accuracy of diagnostic laparoscopy in the infertility work-up before intrauterine insemination

- **495 patients (cervical, unexplained & mild male factor)**
- **L/S performed to all before IUI**
- **124 patients (124/495, %25) positive pelvic & peritoneal pathology**
- **If minimal and mild endometriosis is excluded, %8 additional pathology**
- **No need of L/S before IUI**

Tanahatoe, 2003

Human Reproduction Vol.18, No.11 pp. 2235–2239, 2003 doi:10.1093/humrep/deg201
Advance Access publication July 8, 2003

The role of laparoscopy in intrauterine insemination: a prospective randomized reallocation study

S.J.Tanahatoe, C.B.Lambalk[1] and P.G.A.Hompes

- **Diagnostic Laparoscopy First Group (DLSF): 77 patient (L/S than IUI)**
- **IUI First Group : 77 patient (6 cycle IUI followed by L/S)**

Results

- Number of abnormal findings resulted in laparoscopic intervention in DLSF is not significantly different from IUIF group (48% vs 56%)
- Ongoing pregnancy rate 44% vs 49 % (not significant)

Results

- **Impact of the detection and laparoscopic treatment of observed pelvic pathology prior to IUI seems negligible in terms of IUI outcome**

Benefit of diagnostic laparoscopy for patients with unexplained infertility and normal hysterosalpingography findings

- **57 infertile patient with normal HSG findings underwent diagnostic laparoscopy**

Tohoku 2009

Findings surgery	N (%)
Normal	11 (19.3%)
Abnormal	46 (80.7%)
Endometriosis	36 (63.2%)
I stage	14 (24.6%)
II stage	7 (12.3%)
III stage	8 (14.0%)
IV stage	7 (12.3%)
Peritubal/peritumbrial adhesions	5 (8.8%)
Tubel occlusion	3 (5.3%)
Myoma uteri	6 (10.5%)
Ovarian cyst	1 (1.8%)

- But **NOT** all abnormal findings led to changes in treatment plan
- **only in 14% of patients !**

The position of diagnostic laparoscopy in current fertility practice

Jan Bosteels[1,5], Bruno Van Herendael[2], Steven Weyers[3] and Thomas D'Hooghe[4]

- The position and timing of laparoscopy in ovulation induction treatment is difficult to establish due to the lack of randomised controlled trials.

Human Reproduction Update, Vol.13, No.5 pp. 477–485, 2007

The position of diagnostic laparoscopy in current fertility practice

Jan Bosteels[1,5], Bruno Van Herendael[2], Steven Weyers[3] and Thomas D'Hooghe[4]

- laparoscopy can be avoided in all cases where the available evidence indicates that IVF is the most appropriate and successful treatment
- selected adnexal pathology, such as hydrosalpinx and ovarian endometriotic cysts, still have to be treated by laparoscopic surgery prior to IVF.

Human Reproduction Update, Vol.13, No.5 pp. 477–485, 2007

Conclusion

- Except in selected cases such as hydrosalpinx, endometrioma >5 cm, myoma, septus, polyp there is no need L/S-H/S
- Under age 38, first line treatment option is IUI up to 3 cycles
- After 3 failed IUI cycles, IVF is the best option
- Although HSG is the best diagnostic tool to detect tubal pathology than L/S, more RCT are needed

Can infertility be defined and treated without Endoscopy ?

Definition of infertility of this case
Chlamydial antibodies characteristics and limitation
HSG versus 4D US / TVU
Use of Hydrosonography / 4D US
Polonged sperm liquefaction
Induction of Ovulation cc / HMG+/- IUI
Endoscopy infertility diagnosis
Alternative to standard Laparoscopy
The importance of "one stop clinic"

ESHRE SIG Reproductive Surgery

1 - 4 July 2012
28th Annual Meeting
Pre-Congress Course 8

Istanbul Congress Center

Vasilios Tanos, MD, PhD.
Professor in Obstetrics and Gynaecology
ARETAEION HOSPITAL University of Cyprus

Facts of the case

- 36 y old, free history of PID, endometriosis
- Prolactin, Thyroid, Progesterone all normal
- 1 y before normal HSG + Chlamydial Ab neg
- 18m/ml sperm, Liquefaction 60'- prolonged

- Treatment consideration
- IUI +/- cc or HMGs x 3 courses Vs Lpy / Hpy
- IVF Vs Lpy / TVE

Causes of Infertility -Risks and Statistics

- Tubal and pelvic Pathology 30 - 40%
- Ovulatory dysfunction 15 - 40%
- Unexplained infertility 10%
- Unusual problems 10%

- Ovulatory dysfunction mainly in younger couples
- Tubal, unexplained and male factors in older couples
- Infertility duration correlates to more severe and multiple problems

(Am.Soc.ReprMed A Practice Com Report 2000)

Age limitations and Fertility potential

- At the age of 32 patient has to be aware about aging and quality of oocytes
- Her family planning will partly direct our plan of action
- The pace and extent of evaluation are based on couple's urgency to have a child and
- couple's, age, duration of infertility and any medical history and/or clinical examination diagnosis

Chlamydia main characteristics

- Frequently asymptomatic
- Rate of perinatal transmission 60 - 70%
- Sensitive to ligase chain reaction assay from first stream urine catch is approximately 95%
- A,B, Ba and C Binding trachoma
- D through K NGU, PID, cervicitis, epididymitis, proctitis and conjuctivitis
- Diagnosed by microimmunoflorescence

(JE Turentine Clin Protoc in ObGyn 2008)

Chlamydia and infertility

- Chlamydia Ab test as accurate as HSG in detecting tubal pathology (Rowland AS et al Epidemiology 2002) (Mol BW ASRM Birmingham, AL 2001)
- Chlamydia antibody tests: Immunoflorescence, Microimunoflorescence ELISA Immunoperoxidase
- Source of antigen: Genus –specific major outer membrane proteins Inactivated organism, Whole cell inclusion

Some methods are highly specific for the chlamydia species do not distinguish antibodies between C trachom., C pneumonia or C psirlaci

(Jones CS et al J Clin Pathol 2003) (Land JA et al Hum Reprod 1998)

Chlamydia diagnostic test in infertility has practical serious limitations

- The PPV of any diagnostic test depends on prevalence of the disease in the population
- Very high prevalence disease is common
- Very low prevalence test has little or no value
- So the diagnostic value is important when the disease prevalence is between the extremes
- So the Chlamydia test is validated according to chlamydia prevalence in each specific population

(Even JLH et al Sem Reprod Med 2003)

Chlamydia test as a selective criteria to send patients for endoscopic surgery

- Select patients likely to benefited most by laparoscopy
- If applied as screening test tool early in a evaluation a positive chlamydia antibody test might alert one to the possibility of tubal factors although it may be unjustified for all infertile patients

(Johnson NP et al BJOG 2000)

- May be recommended for unexplained infertility, with normal HSG, those suspected to have tubal factor

Frequency of pathologies causing female infertility

- Prevalence of polyps in infertile women is 3 -5% **(Hourvitz A et al Reprod Biomed Online 2002)**
- Risk of subsequent tubal infertility after PID is 10 -12% after 1 episode
- 23 -35% after 2 episodes
- 54 -75% after 3 episodes

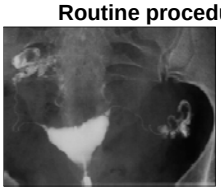
(Westrom LV et al Sex Transm Diseas 1994)

- Mucosal subtle adhesions value has not yet fully validated by prospective studies and it is difficult to interpret and compare

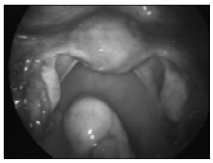
(Al-Inany H Acta Obs Gynec Scand 2001)

Infertility risk due to female genital tract pathology is 15 - 20%
Endometrial anomalies and infertility 4 - 8%
Endometrial anomalies & Recurrent Spont Abort is 15 - 25%

Routine procedures have limitations



HSG
Not sufficient
Radiology Dpt
Radiation



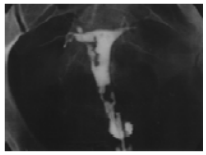
Laparoscopy
Frequently postponed
To invasive / OR
To expensive

Hysterosalpingogram – HSG Diagnostic accuracy !!

Glatstein Fertl Steril 1997 – American Reproductive Endocrinologists: basic tests as the cornerstone of the daily practice for infertility evaluation were Semen analysis, HSG., PCT and ovulation assessment

- Diagnosis for endometrial abnormalities
  - Sensitivity = 80% - 95%.
  - Specificity =70% - 79%.
  - False positive =11,7% - 15.6%
  - False negative =13,3% - 35%

Prevedourakis et al, Hum Reprod, 1994
Wang et al JAAGL 1996, Campo R 1999



The majority of Gynecologists the last 40ys use HSG as their 1st line infertility diagnosis… Medical Conservatism ?!

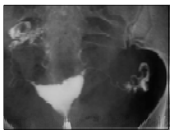
HSG and intrauterine pathology

- Detecting intrauterine pathology varied widely overall and for specific abnormalities

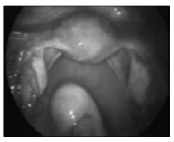
- HSG versus hysteroscopy in 300 cases
- HSG 98% sensitivity and 35 % specificity
- PPV 70% and NPV 8% overall
- For uterine anomalies further evaluation is needed by 4D US, MRI, hysteroscopy

(Homer HA et al Fertil Steril 2000)
(Preutthipan S et al J Obst Gyn Res 2003)

HSG has serious limitations in diagnosis of tubal patency



- **TUBAL PATENCY**
  - **Sensitivity: 65% (95% CI: 50 - 78)**
  - **Specificity: 83% (95% CI: 77 - 88)**



- **PERITUBAL ADHESIONS**
  - **Sensitivity: 62% (range: 0 - 83)**
  - **Specificity: 67% (range: 50 - 99)**

Swart, et al. Fertil Steril 1995; 64:486

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Substantial variability in interpretation of HSG

- When HSG reveals obstruction there is a 60% chance that the tube is open
- When HSG demonstrates patency there is a 5% chance the tube to be occluded

(Glatstein JZ et al Fertil Steril 1997)

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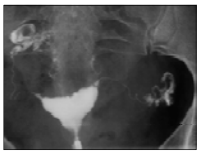
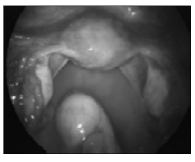
HSG has limitations



HSG two-sided abnormality



Laparoscopy was normal in 42% of the patients

Mol B, 2002 Hum Reprod

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HSG sensitivity

- HSG chance for tubal pathology diagnosis
- Bilateral tubal patency 60-75%
- Unilateral or bilateral tubal occlusion 15 -25%

(Mol BW et al Hum Reprod 1999)

- False negative occlusion are more often than the false negative patency
- Peritubal adhesions, partial phymosis and hydrosalpinx are usually misintepreted

4D US – Hydrosonography Detection of intrauterine pathology

- 4DUS+contrast has better sensitivity than HSG
- Observation of fluid accumulation in the PoD as an indication of tubal patency
- Contrast media with surfactant producing mirobubles when injecting into the tube can detect tubal patency

(Prefumo F et al Ultrasound Obst Gynecol 2002)

(Watrelot A et al Best Pract Res Clin Obst Gynecol 2003)

HSG versus 4D US / Hydrosography

- Sonohysterography /4DUS+NS= cavity contours and intrauterine lesions
- Interface of the 2 layers endometrium is better visualized during the late proliferative phase
- During proliferative phase endometrium is relatively hypoechoic and grows in thickness and a prominent “triple line” is visible
- Uterine artery flow velocity and pulsatility index correlated to implantation has inconclusive results
- US better accuracy then HSG is detecting shape of uterine cavity and fundal contour
- In septated or bicornuated uterus can measure the midline cleft which is of varying depth

(Tan SL et al Obst Gynecol1996), (Breitkopf D et al Obst Gyn 2003)
(Sylvestre C et al Fertil Steril 2003)

Sperm liquefaction

- So the possible diagnosis of this patient is unexplained infertility we have to justify and explained to the couple why we suggest the specific treatment
- Ovulation induction and IUI
- IVF … fast train
- What is our most probable diagnosis … unexplained infertility ??

Unexplained Infertility

- Incidence 10 -30 % among infertile women 513 depending on diagnostic criteria
- The necessity of diagnostic endoscopy with unexplained infertility has been controversial **(Crosignani PG Hum Reprod 1993)**
- Canadian study **(Marcoux S et al NEJM 1997)**
- Multicenter study, randomized infertile women with minimal and mild endometriosis
- Resection/ablation Vs expectant management
- Outcome after 36 weeks of surgery PR was
- 29% operated Vs 17% expectant management

Unexplained infertility and fecundity rate

- The average cycle fecundity in untreated with unexplained infertility is about 2 - 4 % as compared to 20 -25% in normal fertile couples. **(Collins JA Fertil Steril 1995)** **(Guzick DS et al Fertil Steril 70:207, 1999)**
- After 3 ys of infertility the chance for spontan. pregnancy falls about 40%
- After 4ys falls to 20% **(Evers JL Lancet 2002)**

Efficacy of treatment for unexplained infertility

- No treatment 1.3 - 4.1%
- IUI 3.8%
- Clomiphene citrate 5.6%
- Clomiphene & IUI 8.3%
- HMGs 7.7%
- HMGs + IUI 17.1%
- IVF 20.7%

(Guzick DS et al Fertil Steril 70:207, 1999)

Current challenges in infertility work-up

The current conservative approach to explore the infertile couple with HSG is time-consuming, frequently costly and paradoxically may lead to over-treatment as well as under treatment

Management Approach
is a critical decision for Infertility Investigation
Most important is "Efficacy and Timing"

Logistics

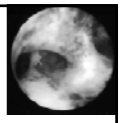
Accurate diagnosis and accurate treatment
First treatment should ideally offer a Pregnancy & take home baby

Ambulatory GYN endoscopy offers Diagnosis and Treatment
·Restores fertility, Improves chances for spont. conception and/or ART
Minimize medication and dosage administration

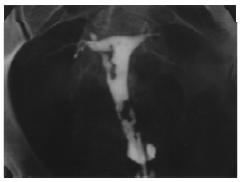
The ONE STOP fertility Clinic offers an Efficient and integrated approach

… as all the other health problems…deserves complete diagnosis and then treatment

Diagnosis of IUA / Septum



- Hysteroscopy is the gold standard method for accurate detection and diagnosis. Hpy can diagnose even minimal adhesions that are not apparent on a hysterogram
- HSG is an insufficient diagnostic method because the filling defects of the endometrial cavity or obliteration of the tubes are not conclusive for the exact condition in the endometrial cavity




ARETAEION HOSPITAL University of Cyprus


SCIENTIFIC PAPER *JSLS* 2006

Diagnostic Hysteroscopy as a Primary Tool in a Basic Infertility Workup

Moty Pansky, MD, Michal Feingold, MD, Ron Sagi, MD, Arie Herman, MD, David Schneider, MD, Reuvit Halperin, PhD, MD

ABSTRACT

Objective: To assess the value of diagnostic hysteroscopy in a primary workup of infertility.

Methods: We performed a retrospective analysis (Canadian Task Force Classification II-2) of 221 infertile patients referred to the Outpatient Center for Uterine Cavity Evaluation and the Tel-Aviv University affiliated Assaf Harofe Medical Center for evaluation of the uterine cavity. Patients underwent a diagnostic office hysteroscopy.

Results: Hysteroscopy revealed an abnormal uterine cavity in 30% of women evaluated for either primary or secondary infertility. No significance was found regarding the total number of intrauterine pathologies when comparing the groups of primary versus secondary infertility.

Conclusion: Routine diagnostic hysteroscopy should be part of an infertility workup in primary and secondary infertility.

INTRODUCTION

It is widely accepted that a complete infertility workup should include an evaluation of the uterine cavity. Uterine abnormalities, congenital or acquired, are implicated as one of the causes of infertility. In fact, infertility related to uterine cavity abnormalities has been estimated to be the causal factor in as many as 10% to 15% of couples seeking treatment. Moreover, abnormal uterine findings have been found in 5.6% to 62% of infertile women.[1]

Today, hysteroscopy is considered the gold standard for evaluating the uterine cavity, and due to improved endoscopic developments, can be performed reliably and safely as an office procedure.[2,3] Direct view of the uterine cavity offers a significant advantage over other blind or indirect diagnostic methods.[4] Although Fayez reported hysterosalpingography (HSG) to be as accurate as hysteroscopy in the diagnosis of normal and abnormal cavities, the nature of the intrauterine filling defects is more accu-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European Journal of Obstetrics & Gynecology and Reproductive Biology
www.elsevier.com/locate/ejogrb

Compliance and diagnostic efficacy of mini-hysteroscopy versus traditional hysteroscopy in infertility investigation

Giuseppe De Placido, Roberto Clarizia *, Camillo Cadente, Gennaro Castaldo, Carmine Romano, Antonio Mollo, Carlo Alviggi, Salvatore Conforti

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Received 19 July 2006; received in revised form 23 November 2006; accepted 19 February 2007

Abstract

Objective: The aim of this study was to compare traditional hysteroscopy with mini-hysteroscopy in terms of compliance, side effects and diagnostic efficacy.
Study design: We prospectively considered 950 female candidates for an IVF programme. All women underwent outpatient hysteroscopy; in 602 cases (Group A) a mini-hysteroscope was employed; in 348 women (Group B) a 5-mm hysteroscope was adopted.
Results: Cavity findings were similar in both groups. Endometrial polyps and uterine septum seem to be more frequent in our infertile patients than in the general population. No significant differences in terms of side effects were found between the groups. Mean visual analogue pain scale score was significantly lower in the patients of Group A than in those of Group B ($p < 0.001$).
Conclusions: Office mini-hysteroscopy is a very effective diagnostic tool in an infertility work-up and is more widely accepted than traditional hysteroscopy. Routine use of the technique should be considered.


ARETAEION HOSPITAL University of Cyprus


Gynecological Endocrinology, August 2008; 24(8): 465–469

HYSTEROSCOPY

[Kremer et al., 2000; Soriano et al., 2000; Unfried et al., 2001; De Angelis et al., 2003; Guida et al., 2003; Litta et al., 2003; Pellicano et al., 2003; Marsh et al., 2004; Shankar et al., 2004; Campo et al., 2005; Sharma et al., 2005; Garbin et al., 2006; Guida et al., 2006; Isaje et al., 2006; De Placido et al., 2007; Kalfi and Tulandi, 2008,).

Office hysteroscopy in an *in vitro* fertilization program

FILOMENAMILA LORUSSO, ORONZO CECI, STEFANO BETTOCCHI, GIUSEPPINA LAMANNA, ALFREDO COSTANTINO, GIUSEPPE SERRATÌ, & RAFFAELLA DEPALO

Department of Gynecology, Obstetrics and Neonatology, Gynecology and Obstetric Section 'A', University of Bari, Bari, Italy

Conclusions. This study suggests that hysteroscopy as a routine infertility examination should be performed in all patients, owing to the elevated incidence of hysteroscopic pathological findings (59.4%); hysteroscopy also seems to be the best way to repair the uterine cavity when pathological conditions are present. However, performing OH before IVF-embryo transfer is of no significant value in improving pregnancy outcomes.

Gynecological Endocrinology, October 2005; 21(4): 235–237

ASSISTED REPRODUCTIVE TECHNOLOGY

Pathologic findings in hysteroscopy before *in vitro* fertilization–embryo transfer (IVF–ET)

NICOLA DOLDI, PAOLA PERSICO, FRANCESCA DI SEBASTIANO, ELENA MARSIGLIO, LUCIA DE SANTIS, ELISA RABELLOTTI, FRANCESCO FUSI, CLAUDIO BRIGANTE, & AUGUSTO FERRARI

IVF Unit, Obstetric Gynecology Department, Vita-Salute University, H San Raffaele, Milan, Italy

Table I. Findings of hysteroscopies.

Total no. of hysteroscopies	300
Normal hysteroscopy	180 (60%)
Abnormal hysteroscopy	120 (40%)
Endometrial polyps	18 (65%)
Endometrial hyperplasia	20 (17%)
Endometrial hypotrophia	16 (13%)
Others (endometritis, adhesions, etc.)	6 (5%)

Table IV. Differences in pregnancy rate with and without hysteroscopy.

	Pregnancy rate (%)
Hysteroscopy group	38% (114)
No hysteroscopy group	18% (54)
	$p = 0.02$

Hysteroscopic findings in patients with repeated IVF failure and normal HSG

Normal	**30**
Abnormal	**25 (45%)**
SUBMUCOUS LEYOMYOMA	**2**
POLYPS	**10**
ADHESIONS	**6**
ENDOMETRITIS	**7**

Oliveira et al. Fertil Steril, 80, 2004

Laparoscopic Treatment of Distal Tubal Pathology

after Lysis of adhesions 50% PR

Distal Tubal obstruction treatment of

- Mild disease 80% PR
- Moderate Disease 30% PR
- Severe disease 15% PR

(Schlaff WD et al Fertil Steril 1990)

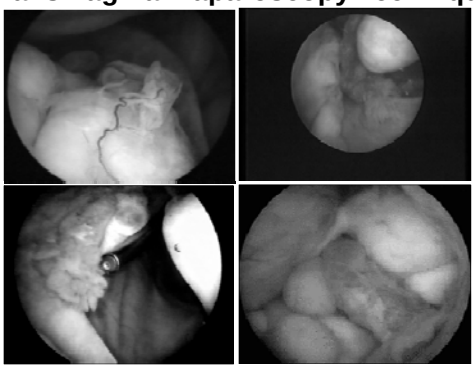
Gynaecological Endoscopy
Trans Vaginal Laparoscopy & Hysteroscopy

A valid alternative
As early as a HSG
As accurate as Laparoscopy

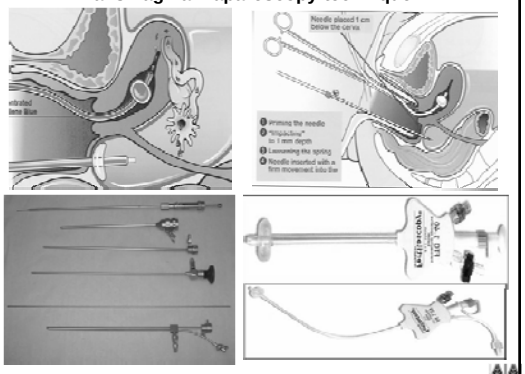
Prospective multi-centre randomized clinical trial, GRADE A EVIDENCE - By reducing the diameter of the hysteroscope the effects of patient parity and also surgeon's experience are no longer important !!!

Campo R, Molinas CR et al, Hum Reprod *2005*

Trans Vaginal Laparoscopy Technique



Trans Vaginal Laparoscopy technique



TRANSVAGINAL LAPAROSCOPY Vs HSG

	normal HSG	abnormal TVL
Moore (2001)	9	5 (56%)
Dechaud (2001)	23	9 (39%)
Durai (2000)	54	14 (26%)
Watrelot (1999)	155	79 (51%)
Total	241	106(44%)

TVL Diagnostic Accuracy

Salpingoscopy and Patency test easily performed

Inter observer disagreement is greater at Standard Laparoscopy

	unexplained infertility
Standard laparoscopy	0%
Transvaginal laparoscopy	45%

Campo R. et al. Fert. Steril. 1999

TVL Diagnostic Accuracy

Transvaginal Ultrasound has a very low sensitivity for detection of small endometrioma

Endometriomas less than 1.5cm are missed by US

Size	TVU pos	TVE pos	Sensitivity TVU
< 1.5 cm	5	11	5/11 (45%)
> 1.5 cm	11	11	11/11 (100%)
Total	16	22	16/22 (72.7%)

TVL Diagnostic & Therapeutic Potential

magnification effect on diagnosis

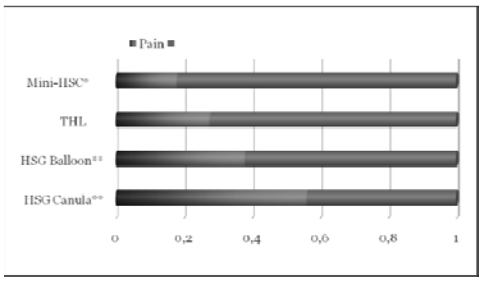
effect of hydroflotation on diagnosis

- **Subtle lesions**
- **Endometriosis**
- **Ovarian drilling**
- **Adhesions**

Curr Opin Obstet Gynecol 11: 371-7,

J Am Assoc GynecLaparosc 7:45-9,2000 **•Fertil Steril 75: 1009-1012, 2001**

TVL, HPY Vs HSG: Compliance



****Tur-Kaspa, et al. Hum Reprod 1998** ***Campo, et al.* Hum Reprod 2005**

Hysteroscopy and TVL Diagnostic Accuracy

Higher potential to exclude unexplained infertility at least 50-60% of those with false HSG

Unexplained infertility is highly frustrating for doctors and patients

The wrong interpretation of "no cause" for their sub-fertility and hence no effective treatment can lead to wrong decisions and adverse psychological, social problems and rising health costs

Conclusion

TVE - ONE STOP Fertility Diagnosis and Treatment

Hysteroscopy and TVL can provide essential anatomical and functional information about fertility potential in an accurate, fast, painless and economical way in one session. In addition treatment can be provided concomitantly to diagnosis.

Our results and the review of the literature document the feasibility, acceptability and safety of Hysteroscopy and TVL (TVE) in an ambulatory setting to replace the traditional approach of HSG and laparoscopy

Tubal Surgery

Prof T C LI
Professor of Reproductive Medicine & Surgery
Sheffield, England

Istanbul, 2012

IVF or tubal surgery ?

Why not IVF?

1. The successful rate of IVF treatment is ever increasing

Why bother about surgery?

Why not IVF?

2. IVF usually produces a result (baby) quicker than surgery

Other things being equal, IVF has an advantage

Why not IVF?

3. IVF is fashionable

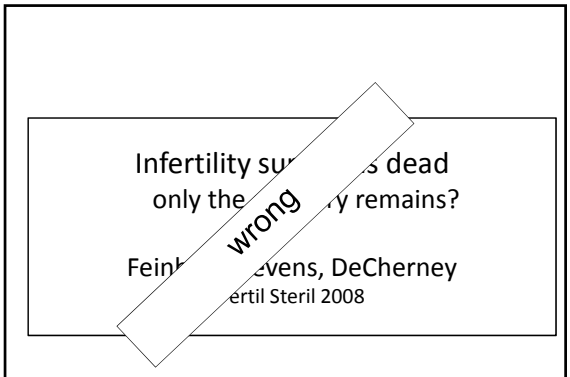
Why not IVF?

4. Surgery is an admission that medical treatment has failed or not possible

It seems logical to advice IVF first

Infertility surgery is dead
only the obituary remains?

Feinberg, Levens, DeCherney
Fertil Steril 2008



Why surgery?

Tubal surgery is justified
only if it produces a better result

Why Surgery?

1. Surgery produces comparable results to that of IVF

Distal Tubal Disease

MICROSURGICAL SALPINGOSTOMY: SHEFFIELD SERIES

Live birth rate 28/97 (29%)

IU pregnancy rate 33/97 (34%)

Singhal, Li and Cooke
BJOG, 1991

MICROSURGICAL SALPINGOSTOMY

Tubal score	*Term pregnancy*
Stage I	**22/56 (39%)**
Stage II	**20/99 (20%)**
Stage III/IV	**6/75 (8%)**

Winston and Magara
BJOG 1991

PATIENT SELECTION

Everything in surgery is patient selection –
the chief determinant of results

SALPINGOSTOMY: GOOD PROGNOSTIC FEATURES

- small hydrosalpinx
- no/minimal peri-tubal adhesions
- normal mucosa
- normal/thin wall
- partial occlusion

SURGICAL TIPS

Proximal Tubal Disease

REVERSAL OF STERILISATION SHEFFIELD SERIES

- Pregnancy rate = 81% in women who had:
  - –Filshie clip sterilisation
  - –reversal with microsurgical techniques

Wahab, Li & Cooke,1997

Proximal Tubal Disease

REVERSAL OF STERILISATION
SHEFFIELD SERIES - 132 CASES

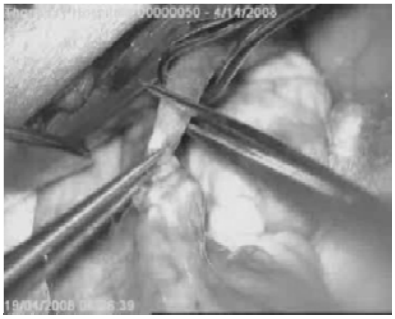
- Microsurgical reversal techniques produces results 20% higher than the conventional techniques

Wahab, Li & Cooke
JOG, 1997

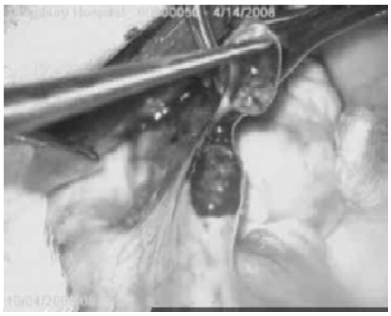
Microsurgery

1. Remove clip

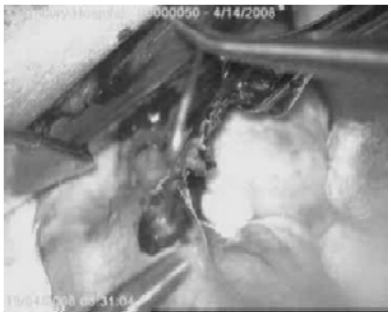
2. Trim edges



3. Remove redundant tissue



4. Insert stent



5. Irrigation & micro-surgical techniques throughout

6. Micro-suture in two layers

Why Surgery?

1. Surgery produces comparable results to that of IVF
2. Surgery can improve the results of IVF

Hydrosalpinges and IVF

- The live birth rate of patients with hydrosalpinges undergoing IVF is only one-half that of women who do not have hydrosalpinges

Hydrosalpinx and IVF outcome : a prospective randomized multicentre trial in Scandinavia on salpingectomy prior to IVF

Strandell et al 1999 Human Reprod 14:2762

First IVF cycle, regardless of whether or not hydrosalpinges demonstrable by USS

Group	Patient	PR	miscarriage	Live birth
Salpingectomy	112	36.6%	16.2%	28.6%
No salpingectomy	92	23.9%	26.3%	16.3%

PR, p=0.067 LB, p=0.045

Hydrosalpinges and IVF

- Salpingectomy prior to IVF in women with hydrosalpinges improves pregnancy, implantation and live birth rates

Why does the presence of hydrosalpinges adversely affect IVF pregnancy rate ?

- Hydrosalpingeal fluid is embryo toxic
- Mechanical effect – wash out of embryos
- Impaired endometrial receptivity

Why Surgery?

1. Surgery produces comparable results to that of IVF
2. Surgery can improve the results of IVF
3. Surgery can reduce the miscarriage rate

Case History

- 33 year old woman
- one miscarriage at 7 weeks
- Infertility for 15 months
- Conceived spontaneously, but miscarried again at 8 week gestation
- Investigation – L tube normal. R hydrosalpinx, grossly dilated, intraluminal adhesions, salpingectomy.
- Three months later, spontaneously conception, term delivery

Hydrosalpinx and IVF outcome : a prospective randomized multicentre trial in Scandinavia on salpingectomy prior to IVF

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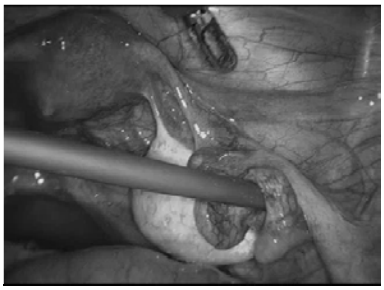
Why Surgery?

1. Surgery produces comparable results to that of IVF
2. Surgery can improve the results of IVF
3. Surgery can reduce the miscarriage rate
4. Surgery can reduce the ectopic pregnancy rate

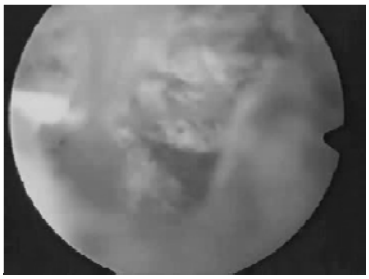
Salpingotomy

Why Surgery?

1. Surgery produces comparable results to that of IVF
2. Surgery can improve the results of IVF
3. Surgery can reduce the miscarriage rate
4. Surgery can reduce the ectopic pregnancy rate
5. Surgery may be simpler than what you think



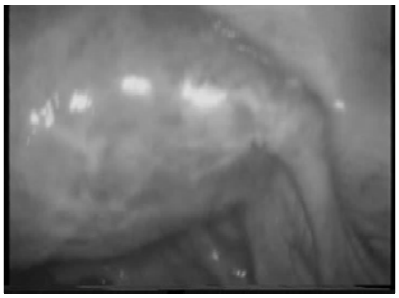
TUBAL CANNULATION



NICE Guidelines

- For women with proximal tubal obstruction selective salpingography plus tubal catheterisation, or hysteroscopic tubal cannulation, may be treatment options because these treatments improve the chance of pregnancy

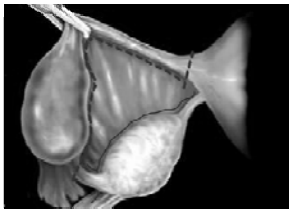
Proximal block, and ….



….Distal block too

Salpingectomy

Devascularization of the ovary is rare if the operation is carried out properly and carefully by keeping as close to the tube and as far away from the ovary as possible



Infertility su… dead
only the o… remains?

Feinb… evens, DeCherney
…ertil Steril 2008

wrong

Patient's choice

– It is the responsibility of a doctor to carefully explain the various treatment options … the patient should be involved in the decision making process

General Medical Council

Diversity

Not Mono-therapy

IVF vs TUBAL SURGERY

- Tubal surgery and IVF complementary, not competitive …together have improved the outlook of couples suffering from tubal infertility

Gomel and Taylor
J Asst Reprod Gen, 1992

Tubal Surgery – Two Safeguards

- Careful selection of cases – don't operate indiscriminately
- Proper techniques and training – don't ask the cowboys to do it

email

- From: xxxxxxxxxx (Obstetrics & Gynaecology)
- Sent: 13 January 2012 13:31
- To: Li, Tin (Obstetrics & Gynaecology)
- Subject: Reversal sterilisation

TC I did a 4th CS and sterilisation on a pt (Mea…….) you did a reversal after 2 children. I felt it such a shame to undo what was beautiful workmanship by you! One really could hardly tell that she had had tubal surgery.

xxxxxxx

THANK YOU

Proximal and distal tubal pathology

ART

A.P. Ferraretti, C.M. Magli, L. Gianaroli

S.I.S.ME.R. Reproductive Medicine Unit - Via Mazzini, 12 - 40138 Bologna

iiarg www.iiarg.com www.sismer.it SISMER

Disclosure

- No commercial relationships
- No potential conflicts of interest

SISMER

Learning Objectives

- *In clinical practice, is the decision between IVF or surgery based on EBM , on patient's choice or doctor's experience ?*
- *Factors that must be considered when deciding between IVF and surgical repair : the pros and cons of the IVF option*
- *ART in tubal infertility : EBM on efficacy and side effects*

SISMER

	WHO	Collins	Royal College
Female factor	35%	54%	46.7%
- ovulatory		*27%*	
- tubal		*22%*	
- endometriosis		*5%*	
Semen abnormality	15%	25%	19%
Unexplained	15%	17%	11.2%
Female + male	30%		18.2%
Other (genetic,…)	5%	4%	5%

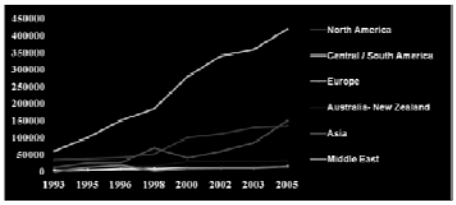
Infertile population

- ***Sterile subjects***
  Impossibility to conceive (is not spontaneously reversible)
  Azospermia
  Bilateral tubal blockage
  POF
- ***Subfertile couples***
  Diminished capacity to conceive (is not an irreversible state)

Potential fecundity of the female partner

ART World collaborative report (ICMART)

Cycle/ year



ART in 2008

	N. of ART of cycles	Diagnosis of tubal disease only
USA	104 673	8792 (8.4%)
Australia	53 696	2334 (4.3%)
Europe	405 726	NA
Italy	44 065	4563 (12.4%)
Germany	40 354	2886 (7.1%)

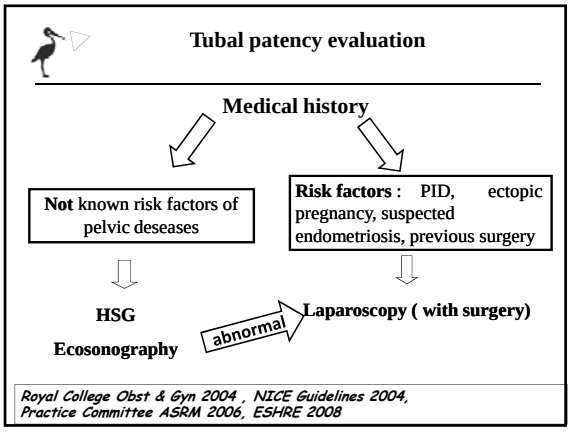
IVF vs Surgery
Cochrane Review 2008 (Pandian et al)
Practice Committee of ASRM (2012)

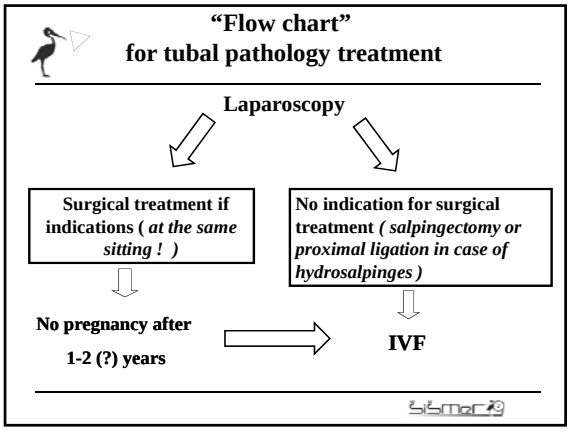
At present there are no adequate trials to determinate the effectiveness, or othrewise, of tubal surgery vs IVF .

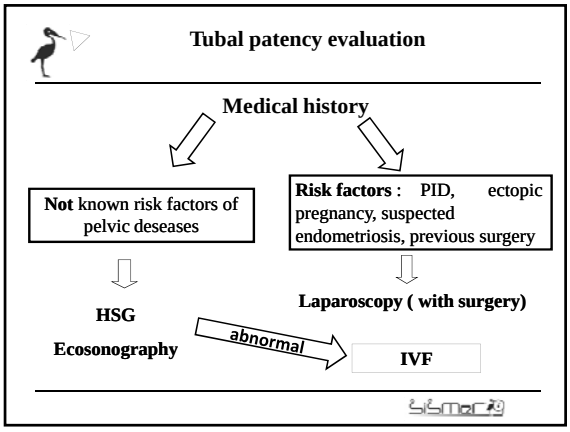
More research is needed, including information about adverse outcome and costs

General considerations

- **The most important factor for choosing the best treatment is an "accurate "diagnosis .**
- **Laparoscopy is considered the "gold standard" technique to assess tubal function, but today there is a tendency to leave out this procedure during the infertility workshop**


Tubal patency evaluation
Medical history
Not known risk factors of pelvic deseases
Risk factors : PID, ectopic pregnancy, suspected endometriosis, previous surgery
HSG
Ecosonography
abnormal
Laparoscopy (with surgery)
Royal College Obst & Gyn 2004 , NICE Guidelines 2004,
Practice Committee ASRM 2006, ESHRE 2008


"Flow chart"
for tubal pathology treatment
Laparoscopy
Surgical treatment if indications (at the same sitting !)
No indication for surgical treatment (salpingectomy or proximal ligation in case of hydrosalpinges)
No pregnancy after
1-2 (?) years
IVF


Tubal patency evaluation
Medical history
Not known risk factors of pelvic deseases
Risk factors : PID, ectopic pregnancy, suspected endometriosis, previous surgery
HSG
Ecosonography
abnormal
Laparoscopy (with surgery)
IVF

General considerations

- **Most patients proceed to ART without laparoscopy (incompletely evaluated patients ?) :**
- **in case of normal HSG it is hard (patient ' s option and guide lines) to propose an invasive procedure . Therefore, 20-40% of pelvic diseases are no diagnosed and treated)**
- **in case of altered HSG , clinicians often beleive that turning directely to IVF is appropriate and patients often prefer to have the treatment with the highest PR per cycle (IVF)**

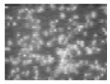
Learning Objectives

- *In clinical practice, is the decision between IVF or surgery based on EBM , on patient's choice or doctor's experience ?*
- ***Factors that must be considered when deciding between IVF and surgical repair : the pros and cons of the IVF option***
- ART in tubal infertility : EBM on efficacy and side effects

Factors to be considered when couseling patients with tubal infertility regarding surgery or IVF

- ***Presence of other infertily factors***
- ***Number and quality of sperm in the ejaculate***

Conventional Sperm Evaluation



Volume	min 2mL→ 1.5mL
Sperm concentration	>20 x 10^6/mL → 15 x 10^6/mL
Motility	>50%, → > 32%,
Sperm morphology	>14% → 4%
Vitality	75% → 59%

criteria recommended by WHO (2010)

SISMAR

Regional and world- wide variation of semen parameters

- Within USA, New York had highest concentrations (134 x 10^6/mL)
  Iowa had lowest concentrations (48 x 10^6/mL)
  cf Thailand (52 x 10^6/mL)
- In Japan, fertile men had lower semen quality, similar to Norway (20% < WHO)
- In Europe, Finland and Denmark's fertile men have markedly different semen profiles

Fisch et al, 1996, Swan, 2006; Jorgensen et al, 2006; Iwamoto et al, 2006

SISMAR

Sperm DNA damage

Male Infertility

Occupation
Plastics and resins, solvents, wood processing, metal industry, Automobile, truck and aircraft mechanics
Sedentary or stressful job

Environment
Endocrine disruptors
xenoestrogens
Anti-androgens
Toxic compounds

Genetic Inheritance
CABVD
Robertsonian translocations
Y-chromosome deletions
Paternal Age

Lifestyle
diet
smoking
alcohol
recreational drugs
STIs
injury
infection

SISMAR

Trends in sperm concentrations

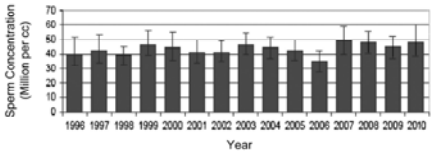


FIGURE. Sperm concentrations for Danish military draftees from 1996 to 2010 based on information from the Danish monitoring program (Department for Growth and Reproduction, Rigshospitalet, Copenhagen, Denmark). This figure was first presented in March 2011 on a government agency website by the Danish National Board of Health.[7]

Bonde et al. *Trends in Sperm Counts The Saga Continues* Epidemiology • Volume 22, Number 5, September 2011

iiarg

Factors to be considered when couseling patients with tubal infertility regarding surgery or IVF

- *Presence of other infertily factors*
- *Number and quality of sperm in the ejaculate*
- ***The site and extend of tubal disease***

IVF vs Surgery
Cochrane Review 2008 (Pandian et al)
Practice Committee of ASRM (2012)

The evidence is " fair" to recommand :

- ***tubal canulation for proximal tubal obstruction***
- ***fimbryoplasty or neosalpingostomy for mild hydrosalpinges***

in young women with no other significant infertility factors

Factors to be considered when couseling patients with tubal infertility regarding surgery or IVF

- *Presence of other infertily factors*
- *Number and quality of sperm in the ejaculate*
- *The site and extend of tubal disease*
- ***Age and ovarian reserve***

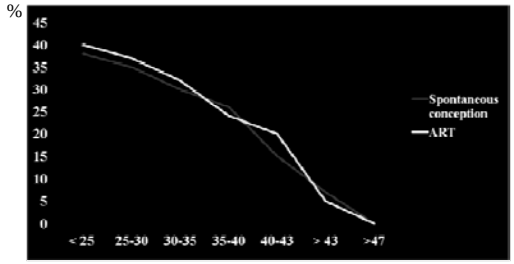
At which age surgery should be recommanded ?

- Which age limit ? < 35? , < 38?, < 40?
- When" loosing" time in not affecting subsequent IVF outcome ?

AGING

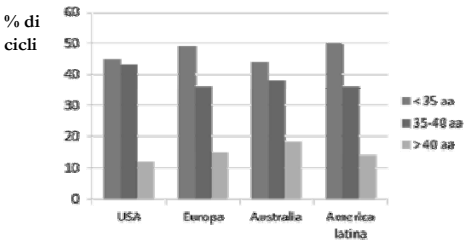
Age is the most important single fsctor determining fecundity in female

In vivo and in vitro *fecundity*
(pregnancy rate in one cycle)
depending on age

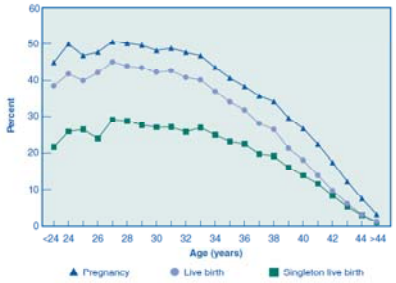


Age (years)

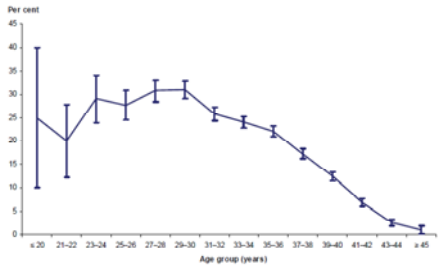
ART - female age
(International ART register - 2006)



Percentages of ART Cycles Using Fresh Nondonor Eggs or Embryos That Resulted in Pregnancies, Live Births, and Singleton Live Births, by Age of Woman,* 2008



SART Register



Note: The bars on the graph represent the 95% confidence intervals of the live delivery rates, with the narrower bars representing more reliable estimates.

Figure 2: Live delivery rate per initiated autologous fresh cycle and 95% CI by women's age group, Australia and New Zealand, 2007

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Ovarian Reserve and tubal pathology management

- **The role of the *ovarian reserve* tests (ORTs) in the decision- making process between IVF and Surgery**

?????

Factors to be considered when couseling patients with tubal infertility regarding surgery or IVF

- *Presence of other infertily factors*
- *Number and quality of sperm in the ejaculate*
- *The site and extend of tubal disease*

- *Age and ovarian reserve*
- ***The efficacy*** *?*

IVF vs Surgery
Cochrane Review 2008 (Pandian et al)
Practice Committee of ASRM (2012)

At present there are no adequate trials to determinate the effectiveness, or othrewise, of tubal surgery vs IVF .

More research is needed, including information about adverse outcome and costs

Good evidence for recommending surgery for tubal ligation reversal, at any age

IVF vs Surgery : results

	Surgery	IVF
Evaluation of success	***PR per patient in a certain period of time***	***PR per cycle***
Drop –out from treatment	**Impossible !!**	**Very high or patient distress (" incomplete" treatment)**

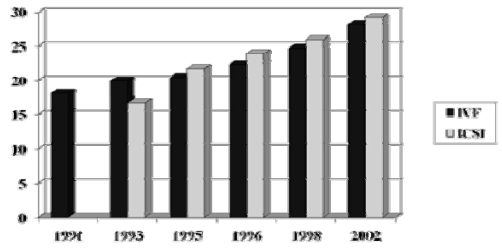
In Vitro Fertility (3 IVF cycles) compared to *in vivo* fertility

AGE group	Cumulative LBR in 3 IVF cycles in tubal infertiltiy	% conceiving within one year
20-24	81%	86%
25-29	72%	78%
30-34	59%	63%
35-39	42%	52%
40 – 42	20%	43%

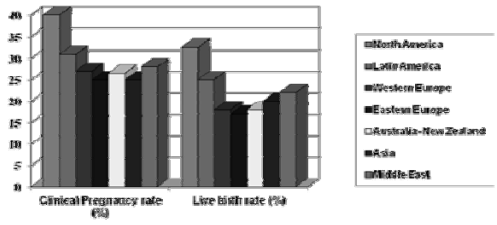
IVF vs Surgery : results

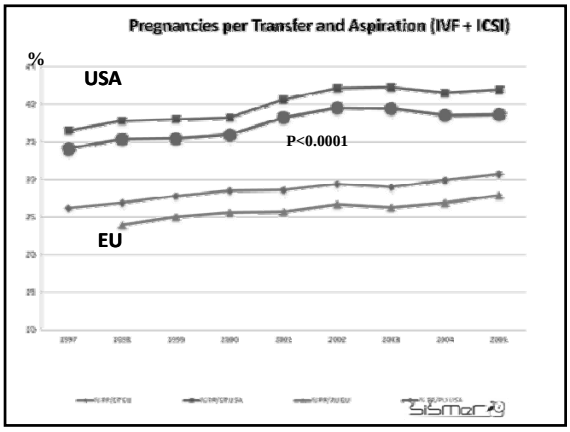
	Surgery	IVF
Evaluation of success	*PR per patient over a given period of time*	*PR per cycle*
Drop –out from treatment	Impossible !!	Very high for patient distress (“ incomplete” treatment)
Report of Results	Data reported in the literature from the surgeons with the greatest expertice	Very well documented in national , regional and world Registers
Reproducibility	Difficult because the skill of the surgeons can be very different ?	Easy because IVF is a standarized procedure ?

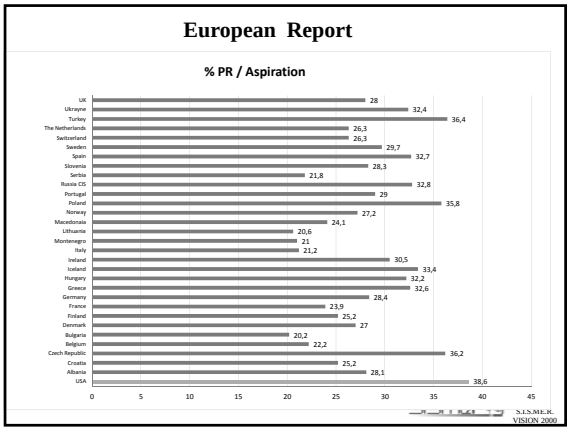
Pregnancy Rates (%) per OPU
World reports



Success Rates per OPU (%) by Region
World Report 2002







ART in 2008

	n. of cycles	Diagnosis of Tubal disease only	LBR per started cycle (total)	LBR per started cycle in tubal infertility
USA	104 673	8792 (8.4%)	30.0%	31.6%
Australia	53 696	2334 (4.3%)	18.8%	17.1%
Europe	405 726	NA	28% PR per aspiration	NA

No data available regarding ART in tubal surgery failure

Factors to be considered when couseling patients with tubal infertility regarding surgery or IVF

- *Presence of other infertily factors*
- *Number and quality of sperm in the ejaculate*
- *The site and extend of tubal disease*

- *Age and ovarian reserve*
- ***Efficacy ?*** ⟹ ***The experience of the surgeon and the success rate of the IVF program***
- ***Risks and Costs***

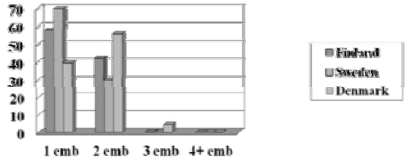
Risks
IVF vs Surgery

	Surgery	IVF
Risks related to the surgical procedure	More frequent and more severe	Less frequent and less severe
Ectopic pregnancy	7-15%	< 5%
OHSS	0%	1-2%
Triplets deliveries	In vivo incidence (1/6400)	<1-3.5/100(embryo reduction)
Twins deliveries	In vivo incidence (1/80)	20-30/100
Obstetric complications	No data available compared to the general population	Higher incidence compared to the general population
Adverse perinatal outcome	No data compared to the general population	Higher incidence compared to the general population (also in singletons) ?

IVF vs Surgery (Risks)

- **Some complication of IVF can be reduced :**
  - OHSS : mild stimulation and GnRH agonist trigger of ovulation
  - multiple pregnancies :sDET and sSET

Number of embryos transferred after IVF and ICSI, 2007
The Nordic countries - SET policy



The "optimal end-points". The cumulative delivery rates after fresh and FER. Deliveries/ aspiration

	Initiated cycles IVF and ICSI	Deliveries, "fresh" cycles IVF and ICSI	Multiple Deliveries fresh	FER cycles (thawings)	Deliveries FER	Multiple deliveries FER	Deliveries fresh	Cumulative Deliveries, Fresh and FER	All multiples
Finland	4589	977	110	3475	556	55	21.3%	33.4%	10.8%
Sweden	9511	2246	106	4500	776	53	23.6%	31.8%	5.3%

IVF vs Surgery : the "*core*" difference

	Surgery	IVF
Pregnancy	***In vivo***	***In vitro***

Infertility treatments

Programma riproduttivo per ogni singola coppia

To choose the most successful treatment ?

No EBM in favour of IVF for tubal infertility but in practice IVF seems the preferred choice (both for patients and clinicians ?)

To restore spontaneous fertility whatever possible ?

Surgery should be considered as first choice in tubal infertility even in case of lower PRs comapred to IVF

"Traditional" flow chart for tubal pathology treatment

Laparoscopy

Surgical treatment(*at the same sitting !)* if indications and young age

No pregnancy after 1-2 (?) years

No indication for surgical treatment *(salpingectomy or proximal ligation in case of hydrosalpinges)*

IVF

Lite IVF in good prognosis patients

Treatment including 3 low cost cycles with a fixed (mild stimulation) protocol

GnRH antagonist

HCG (or GnRHa)

Clomiphene citrate (100 mg)

FSH (150 IU)

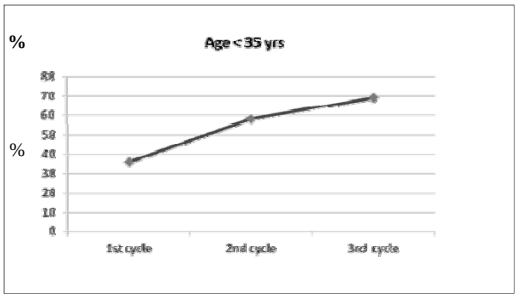
Cycle day

1 2 3 4 5 6 7 8 9 10 11 12

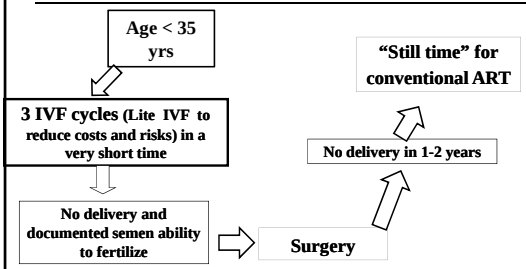
Cycle days

US and E2 monitoring

Cumulative ongoing PR per patient in 12 months (Lite IVF approach)



"Challenge" flow chart for tubal pathology treatment



In Vivo and *in Vitro* Fertility

AGE group	% conceiving within one year	Cumulative LBR in 3 IVF cycles in tubal infertiltiy
20-24	86%	81%
25-29	78%	72%
30-34	63%	59%
35-39	52%	42%
40-42	**43%**	**20%**

"Challenge" flow chart for tubal pathology treatment

Age 35-40

⇩

IVF (?)

Age > 40 yrs

⇦

Surgery and IVF in a short time

to maximize the "residual" fertility potential

Conclusions

In the absence of EBM on the effectiveness of IVF vs surgery , the decision is mainly based on doctor's experience, patients preference , risks and costs.

However, the option between surgery and IVF should not be regarded as competitive (in term of results) but rather complimentary in order to achieve the highest probability of pregnancy

and in the shortest time *(time in crucial in infertility)*

Is there any sense to treat myoma before ART?

Stephan Gordts
Coordinator SIG Reproductive Surgery ESGE

ESHRE Annual Meeting Istanbul
S. GORDTS
PCC Tuesday 1 July 2012
Tuesday 1 July 2012

DISCLOSURE

Consultant

Karl Storz, Germany

LEARNING OBJECTIVES

- To evaluate the correlation between reproduction and myoma
- Possible mechanism of interference
- To judge the benefit or necessity of performing a myomectomy – best available evidence
- To debate the necessity of a more accurate classification

EPIDEMIOLOGY

- **20-40% of women in reproductive age are affected by leiomyomas**
- **Myomas directly or indirectly associated with 5-10% of cases of infertility**

Size **Location** **Number** **Type**

20 – 50% with symptoms

Menorrhagia **Dysmenorrhoea** **Infertility**

American Fertility Society. Guidelines for practice: myomas and reproductive dysfunction. 1992

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Reproductive Outcome

Is difficult to asses the direct impact of leiomyomas in infertility:

- Myomas ⇧ Age
- Fertility ⇩ Age
- Women with myomas conceive
- Association with other factors
- Size / Number / Localization

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Infertility and myoma

More common in IVF patients

because of the delay of childbearing when fibroids are more common

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IS THERE ANY RELATION?

Impact of myoma on fertility: Review

Donnez et al ,2004

	Distorting cavity		No distortion		Control	
	PR %	N	PR %	N	PR %	N
Elder Geva 1998	10	1/10	16.4	9/55	30	38/318
Stoval 1998	37	34/91	53	48/91		
Farhi 1997	9	5/55	29	25/88	25	32/127
Ramzy 1998	39	15/39	34	123/367		
Surrey 2001	50.7	37/73	58.4	191/327		
Jun 2001	30.5	46/141	41.6	169/406	40.4	661/1636

Myomectomy efficacy: allows pregnancy in 60% of the patients with unexplained infertility in the first year following surgery

Vercellini P.1998 Hum.Reprod.

Proposal of Classification

- ***Submucosal (JZ) fibroid***
  - **type 0, I, II (ESH-criteria, 1994)**
  - **type III : abutting the endometrium**
- ***"Outer myometrium" fibroid***
  - **type IV: intramural**
  - **type V, VI: subserosal, pedunculated**

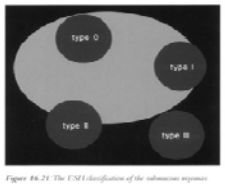

Figure 16.21 The ESH classification of the submucous myomas

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Effects of the position of fibroids on fertility
Casini et al.Gynecol Endocrinol. 2006.

Prospective controlled study : n= 181

	SM	IM	SM-IM	IM-SS
Myomectomy	**43.3%**	**56.6%**	**40%**	**35%**
Controls	**27.2%**	**41%**	**15%**	**21%**

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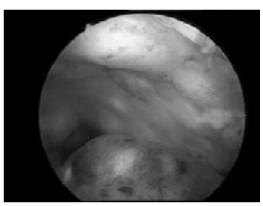
Submucosal myoma



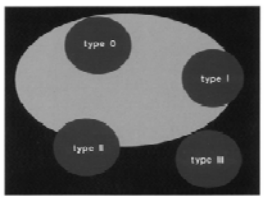


Figure 16.21 The ESH classification of the submucous myomas

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Reproductive outcome following hysteroscopic myomectomy in patients with infertility and recurrent abortions

Roy KK et al. Arch Gynecol Obstet. 2010

	Before myomect	After myomect	P value
Infertile patients	44%	12.9%	0.024
Miscarriage<12w	69.1%	23.3%	0.021
Miscarriage>12w	11.7%	1.29%	0.001
Live birth	16.2%	74.02%	0.001

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Submucous myomas and their implications in the pregnancy rates of patients with otherwise unexplained primary infertility undergoing hysteroscopic myomectomy: a randomized matched control study
Shokeir T et al. Fertil Steril. 2010

	Number	Pregn. %
Myomectomy	101	63.4%
Observation	103	28.2%

RR= 2.1 95% CI 1.5-2.9

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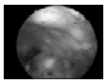
Submucosal myoma

Fibroids and reproductive outcome
(Klatsky et al Am J Obst Gynecol 2008)



	Implantation rate	Clinical pregn. rate	Spontaneous abortion rate
Submucous	3%	14 %	46.7 %
Control	11.5 %	30.4 %	21.9 %

Summary of the data of the IVF model shows that patients with fibroid distorting the endometrial cavity have impaired implantation and pregnancy rates
(Somigliana E. et al Hum reprod Update2007,13)

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Myoma and Infertility: Review

(Pritts EA 2009 Fertil Steril 91, 4:1215-1223)

Conclusions

- ✓Subserosal fibroids do not affect fertiltiy or spontaneous abortion rates
- ✓Submucosal fibroids lowers fertility rates and myomectomy enhances rates of conception and live births
- ✓Intramural myoma with or without distortion of the uterine cavity may cause a detrimental effect on conception and reaching viability with pregnancy.
  Effect of myomectomy is unclear.

Impact of Intramural Myomas on In Vitro Fertilization

The decision to proceed with myomectomy in an asymptomatic patient with unexplained infertility remains controversial. Current data suggest surgical treatment for patients who have uterine cavity distortion.

Sachev and Seifer. Infert. and Reprod. Clin, North Am. 2002

Intramural Leiomyoma

Pregnancy Rate after IVF

	Subjects	PR	Controls	PR
Hart	**106**	**23%***	**322**	**34%**
Stovall (cycles)	**91**	**37%***	**91**	**53%**
Eldar-Garcia	**46**	**16%***	**249**	**30%**
Khalaf Y	**122**	**24%***	**322**	**33%**

Intramural Leiomyoma

Pregnancy Rate after IVF

	Subjects	PR	Controls	PR
Surrey	73	51%	316	60%
Check	61	34%	61	48%
Ramzy	39	38%	367	34%
Oliviera	130	48%	245	45%
Klatsky	94	47%	275	54%

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Intramural Leiomyoma

Miscarriage Rate After IVF

	Subjects	MR	Controls	MR
Eldar-Garcia	46	33%	249	30%
Check	61	34%	61	20%
Ramzy	39	20%	367	15%
Oliveira	130	27%	245	29%
Gianaroli	129	40%*	129	19%*

Effect of intramural myoma & IVF

Intramural fibroids negatively affects IVF results
- Hart R et al 2001 Hum reprod 11: 2411-2417
- Khalaf Y et al2006 Hum Reprod 10: 2640-2644

Intramural fibroids do not affect IVF results
- Ng EH, Ha PC, 2002,Hum Reprod 3: 765-770
- Oliveira Fg et al. 2004 Fertil Steril 81: 582-587
- Klatsky Pc et al. 2007, Hum Reprod 2: 521-526

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Effect of large intramural fibroids (>5 cm)
Hart R et al Hum Reprod 2001 16(11): 2411

Results of IVF where all significantly reduced:

Implantation rate	dropped from	20.2 to 11.9 % (p=0.018)
Pregnancy rate	dropped from	34.1 % to 23.3 % (p=0.016)
Ongoing pregnancy rate	dropped from	28.3 to 15.1 % (p=0.003)

Large intramural myoma negatively affects pregnancy outcome after IVF
Large intramural myomas should be removed before IVF

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Intramural fibroids smaller than 5 cm
THE GREY ZONE

Should they be disregarded?

Should we operate before IVF?

Should we operate after IVF failure?

and so yes after how many failures?

Should we operate before any infertiltiy treatment?

Should the decision be influenced according to the cost of IVF in different countries?

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Influence of small intramural fibroids: *cumulative* outcome
(Khalaf et al Hum Reprod 2002)

	Pregnancy rate	Ongoing PR	Live birth rate
Intramural < 5 cm	23.6 %	18.8 %	14.8 %
Control	32.9 %	28.5 %	24 %

($p < 0.05$)

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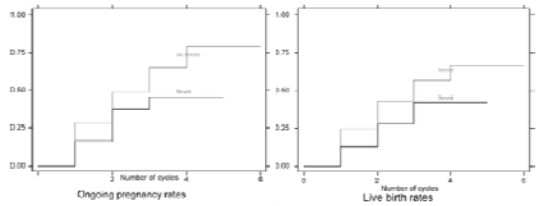
Intramural fibroids and cumulative outcome assisted conception



40 % reduction of success rate in each cycle

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The effect of intramural fibroids without uterine cavity involvement on the outcome of IVF treatment: a systematic review and meta-analysis

Sesh Kamal Sunkara1, Mohammed Khairy, Tarek El-Toukhy,Yacoub Khalaf, and Arri Coomarasamy

Human Reproduction, Vol.25, No.2 pp. 418–429, 2010

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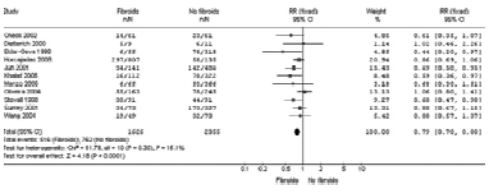
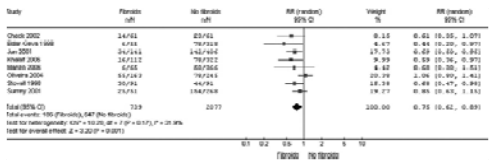
Forest plot of studies of non-cavity-distorting intramural fibroids versus no fibroids in women undergoing IVF treatment for outcome of live birth rates.



Sunkara S K et al. Hum. Reprod. 2010;25:418-429

human reproduction

Forest plot of studies of non-cavity-distorting intramural fibroids versus no fibroids in women <37 years undergoing IVF treatment for outcome of live birth rates.

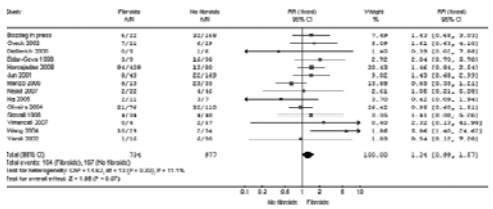


18% - 25% reduction in the clinical PR

Sunkara S K et al. Hum. Reprod. 2010;25:418-429

human reproduction

Forest plot of studies of non-cavity-distorting intramural fibroids versus no fibroids in women undergoing IVF treatment for outcome of miscarriage rates.



Sunkara S K et al. Hum. Reprod. 2010;25:418-429

human reproduction

Conclusion

This systematic review, which included 6087 IVF cycles, found that the presence of non-cavity distorting intramural fibroids on average reduces the live birth rate by 21% and the clinical PR by 15% per IVF cycle compared with no fibroids.

Sunkara S K et al. Hum. Reprod. 2010;25:418-421

Intramural fibroids smaller than 5 cm

Metwally et al. (RBM online) meta-analysis: no hard data to support the negative effect of intramural myoma upon pregnancy rates.

Uterine leiomyomas reduce the efficacy of assisted reproduction cycles: results of a matched follow-up study
Stovall et al. Hum reprod 1998, 13.

	Fibroids	Controls	RR	CI	
Nb	91	91			
Impl. rate	13.8%	19.7%			
Clin Pr	34.3%	52.7%	0.71	95%	0.51-0.98
LBR	33%	48.4%	0.68	95%	0.47-0.98

No cavity deformation, no submucosal fibroids

Infertility and myoma controversial because

- difficult to prove causal relation
- reviews of previous (70-80) studies indicates a pregnancy rate of 50 % after myomectomy in infertile patients
- no well controlled randomized studies
- no clear description of size, numbers and location
- no standardization of diagnostic methods
- different outcome parameters
- results varying between 10- 70 % (Donnez et al.)

POSSIBLE UNDERLYING MECHANISM?

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Impact of Uterine Myomas on Fertility

Mechanical factors

Greater distance for sperm travel ?
Encroachment on tubal ostium: occlusion
Distortion of uterine cavity

Hunt J. 1974 Clin.Obstet.Gynecol.
Iosif C. 1983 Acta Obstet.Gynecol.Scand
Vercellini, P. 1992 Fertil Steril
Verkauf B fertil Steril 1992
Wallach, E.E. 1995 Obstet.Gynecol.Clin.N.Am.

Impact of Uterine Myomas on Fertility

Greater distance for sperm travel
Encroachment on tubal ostium. occlusion
Distortion of uterine cavity

Interfere normal rhythmic uterine contractions
Vascular changes

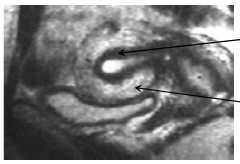
Impaired implantation
Abnormal endometrial maturation
Alteration on oxytocinase activity

Hunt J. 1974 Clin.Obstet.Gynecol.
Iosif C. 1983 Acta Obstet.Gynecol.Scand
Vercellini, P. 1992 Fertil Steril
Verkauf B fertil Steril 1992
Wallach, E.E. 1995 Obstet.Gynecol.Clin.N.Am.

The Myometrial Junctional zone

MRI
clinical significance of the myometrial architecture

Myometrium has 2 structural and functional different entities



Junctional zone
small central zone of increased density
IMPORTANT IN REPRODUCTION

Outer myometrium
Larger outer hypodenser zone

Adenomyosis
B.E.
Endometriosis

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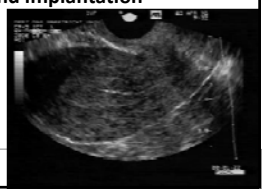
Junctional Zone Myometrium

Functional important entity in reproduction

- **Ontogenetically related to endometrium**
- **Cyclic changes in SSH receptors**
- **Role in gamete transport and implantation**



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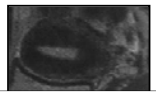
Junctional Zone Myometrium Important role in Reproduction

Functional important entity in reproduction

- **Early changes from time of implantation**
- **Decidualization and trophoblast invasion**
- **Defective transformation of JZ spiral arteries in spectrum of pregnancy complications**
- **Preterm rupture membranes**
- **Preterm delivery**



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The Myometrial Junctional zone

JZ myometrium is a distinct uterine structure

More akin to the endometrium than outer myometrium

Like the endometrium, the JZ is of Müllerian origin, while the outer myometrium is of non-müllerian, mesenchymal origin (Noe et al. 1999)

The JZ but not outer myometrium undergoes cycle-dependent changes

Uterine peristaltic activity originates exclusively from the JZ while the outer myometrium remains quiescent throughout the cycle

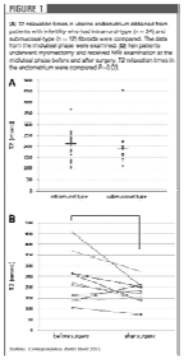
Adenomyosis
B.E.
Endometriosis

Functions of the peristaltic activity of the stratum subvasculare (Archimyometrium) during the early process of reproduction

- Directed rapid and sustained sperm transport
- High fundal "ipsilateral" implantation of the embryo
- Retrograde menstruation

- Kunz et al., 1996, 1998, 2006, 2007

Myometrial T2 relaxation time before and after myomectomy
Yoshino et al. Fertil Steril 2011



Decreased pregnancy rate is linked to abnormal Uterine peristalsis caused by intramural fibroids

O. Yoshino, T. Hayashi et al. Hum Reprod 2010, 25: 3475-79.

Methods:

- ✓ presence intramural fibroids, exclusion submucosal
- ✓ no other fertility factors except endometriosis
- ✓ regular menstrual cycles
- ✓ cine MRI in luteal phase

Nb = 51

evaluation uterine peristalsis:

low peristalsis: 0 - 1 time /3min

high peristalsis: ⩾ 2 times /3min

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Decreased pregnancy rate is linked to abnormal Uterine peristalsis caused by intramural fibroids

O. Yoshino, T. Hayashi et al. Hum Reprod 2010, 25: 3475-79.

	Low peristalsis	High peristalsis
Number	29 (57%)	22 (43%)
No endometriosis	22	16
Yes endometriosis	7	6
Nb fibroids	2.8 (2.8)	3.5 (+ 3.0)
Max. diam.	53 (17)	58 (21)
Deformation cav.	15	10
No deformation cav.	14	12

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Myomectomy decreases abnormal uterine peristalsis And increases pregnancy rates.

O. Yoshino, Osamy Nishii et al.JMIG 2012, 19.

Methods:

presence of intramural myoma
infertility 24 months
menoragia & infertility 12 months
no other fertility impairing factors
MRI before and after myomectomy

Number: 15
high peristalsis: > 2/ 3 min

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Myomectomy decreases abnormal uterine peristalsis
And increases pregnancy rates.
O. Yoshino, Osamy Nishii et al.JMIG 2012, 19.

After myomectomy (n=15)

peristalsis: normalisation in 14 patients

pregnancy: 6/15 40% (p<0.0012)

Increased aromatase expression in uterine myomas
Bulun et al. 2005.

Increased aromatase expression

↓

elevated tissue estrogen concentrations

↓

increased uterine peristalsis

Mechanism of impaired fertility in case of intramural-submucosal myoma

Richards et al.(Hum Reprod Upd;1998,4)

- the numbers of *caveolae* in host myometrium and fibromyomata are conceivably *decreased* compared to normal myometra.
- This specific structural abnormality may affect calcium metabolism by causing a decrease in defect calcium extrusion and thus *raising the intracellular calcium* .
- *Increased* intracellular calcium produces *myometrial irritability* and hyperactivity.
- Resulting in disruption of the rhythmical contraction process of the JZ.

Effect of intramural myoma

A plausibel mechanism for intramural fibroids not distorting the cavity has been seen in a possible *disruption of the junctional zone* within the myometrial layer at the intial stages of embryo invasion and placentation.

(Horne AW, Critchley HO, Semin reprod Med, 2007,25: 483)

Differential infiltration of macrophages and prostaglandin production by different uterine leiomyomas

Seiyou Miura et al. Hum reprod 2006, 21

(i) Besides cavity deformity, SMM nodules may also cause a strong and diffuse inflammatory reaction in the autologous endometrium.
(ii) (ii) Even when there is no cavity deformity, the presence of IMM nodule may also create an inflamed endo- metrium.
(iii) (iii) Endometria of control women and women with SSM display a minimal inflammatory change and may not have impaired fertility outcome. (iv) Surgical or medical treat- ments should be considered in infertile women who have sub- mucosal and/or intramural fibroids before resorting to ART.

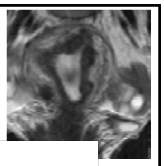
Effect of submucous myoma

Rackow, B, Taylor H (*Fertil Steril,2008)* found that submucous leyomyoma have a global decrease in endometrial Hox gene expression, a molecular marker of endometrial receptivity.

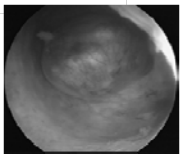
Leiomyomas may impair fertility through several mechanism:

- ✓ mechanical factor (cavity deformation)
- ✓ disturbed uterine peristalsis
- ✓ alterations of the endometrium
  - inflammation
  - subcellular and molecular defects

PERFORMING MYOMECTOMY?



Despite the lack of randomized studies the sharp decline in pregnancy rates in case of *submucous myoma* is quite convincing and myomectomy should be performed in subfertile patients & before ART



Intramural myoma:

more controversial ; lack of homgeneous opinion

decreased fertility

effect of myomectomy ?

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Intramural myoma:

Best available evidence

intramural myoma > 5cm
advice to operate before ART
(mostly distorting cavity?)

intramural < 5 cm?
reported outcome varies between no differences and significant decreased cumulative pregnancy rates?

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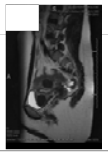
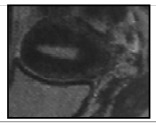
Is intramural fibroid a misnomer?

The intramural fibroid should be classified as either
outer myometrium or JZ fibroid.





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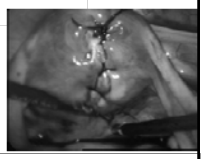
Risks of Myomectomy

Morbidity: infection, blood transfusion

Complications : laparotomy and /or laparoscopy

Postoperative adhesion formation



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Myomectomy Risks

Adhesions

Fertility Outcome

Uterine Rupture

Obstetrics Outcome

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MYOMECTOMY AND INFERTILITY

Laparotomy Myomectomy

Adhesions Rate formation : ⇧ 90 %

Butram VC Jr, Reiter RC. *Uterine leiomyomata: etiology, symptomatology and*

Laparoscopy Myomectomy

Tulandi T, Murray C, Guralnick M. *Adhesion formation and reproductive outcome after myomectomy and second-look laparoscopy.* Obstet Gynecol 1993; 82:213-215.

Significantly reduced adhesions

Luciano A, Maiet O, Koch E, et al. *A comparative study of post operative adhesions following laser surgery by laparoscopic vs laparotomy in the rabbit model.* Obstet Gynecol 1989; 74:220-224.

Lundorf P, Hahlin M, Kallfelt B, et al. *Adhesion formation after laparoscopic surgery in tubal preganancy: a randomized trial vs laparotomy.* Fertil Steril 1991; 55:911-915.

MYOMECTOMY AND INFERTILITY

AUTHOR	(n)	ADHESIONS	ADNEXAL ADHESIONS
Laparoscopy			
Hasson (92)	24	67 %	NR
Mais (95)	50	64 %	36%
Bulletti (96)	14	28.6 %	NR
Dubuisson (98)	45	35.6 %	24.4 %
Total	133	51.1 %	30.5 %
Laparotomy			
Starks (88)	20	100 %	NR
Tulandi (93)	26	100 %	76.9 %
Mamsg (95)	27	92.6 %	NR
Bulletti (96)	14	71.4 %	NR
Ugur (96)	48	83.3 %	64.6 %
Total	135	89.6 %	68.9 %

NR: no report

Dubuisson et al, Hum Reprod Update, 2000.

Uterine Rupture during Pregnancy

Inadequate suturing

Haematoma formation

Wide use of electrosurgery

Dubuisson JB, Fauconnier A, Deffarges JV, et al. ***Pregnancy outcome and deliveries following laparoscopic myomectomy.*** **Hum Reprod 2000; 15:869-873.**

Seinera P, Farina C, Todros T. ***Laparoscopic myomectomy and subsequent pregnancy: results in 54 patients.*** **Hum Reprod 2000; 15:1993-1996.**

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Uterine Myoma and Pregnancy

Washington State Birth Records

- **Abruptio placentae OR: 3.87 95% CI: 1.63, 9.17**
- **First trim. Bleeding OR: 1.82 95% CI: 1.05, 3.20**
- **Dysfunctional labor OR: 1.85 95% CI: 1.26, 2.27**
- **Breech presentation OR: 3.98 95% CI: 3.07, 5.16**
- **Caesarean delivery OR: 6.39 95% CI:5.46, 7.50**

Coronado et al. 2000

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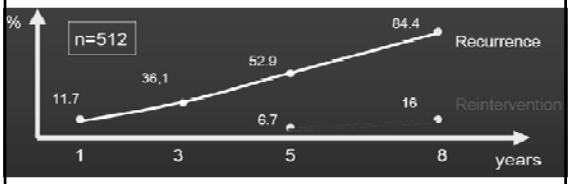
Risk of recurrence



✓ Age >35 years
✓Number of myomas > 2
✓ Uterus size > 13 wks
✓Childbirth after surgery

⇧ Risk of recurrence

Yoo EH, Journal of Minimal Invasive Gynecology 2007

Conclusions III

Controversies in final conclusion are probably due to :

- differences in investigation between the different studies
- lack of properly performed investigation: need for standardization
- evaluation related to distance to and/or involvement of junctional zone – uterine peristalsis?
- need for randomized studies

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How to handle patients with adenomyosis before ART? – Grigoris Grimbizis

Contribution not submitted by speaker

Imaging techniques in the exploration of the uterine cavity

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no conflict of interest to declare

AKADEMISKA SJUKHUSET
UPPSALA UNIVERSITY HOSPITAL

Outline

- background
- imaging techniques
- reproducibility
- defining our goals: morphology or function?
- conclusions

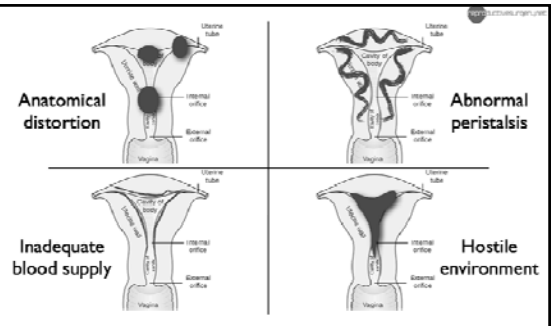
Background

the uterus and fertility

- The uterus is the **natural incubator**, and its integrity plays one of the most crucial roles in fertility and assisted reproduction.
- It plays a fundamental role in the establishment of successful pregnancies, and its impairment by **several gynecological conditions may cause subfertility and limit ART success**.
- **Repeated ART failures** may be due to **unrecognized uterine pathology**.

Uterine factors

- mullerian anomalies
- polyps
- fibroids
- adenomyosis
- adhesions, thin endometrium, and metaplasia
- endometritis



uterine factor | Gambadauro P. 2012

- Chapter 5 Investigation of fertility problems and management strategies
  - 5.1 Semen analysis
  - 5.2 Assessing ovulation
  - 5.3 Screening for Chlamydia trachomatis
  - 5.4 Assessing tubal damage
  - **5.5 Assessing uterine abnormalities**
  - 5.6 Postcoital testing of cervical mucus

Fertility assessment and treatment for people with fertility problems
RCOG-NICE Clinical Guideline

- 5.5 Assessing uterine abnormalities
  - *Women should not be offered hysteroscopy on its own as part of the initial investigation unless clinically indicated because the effectiveness of surgical treatment of uterine abnormalities on improving pregnancy rates has not been established.*

Fertility assessment and treatment for people with fertility problems
RCOG-NICE Clinical Guideline

Exploring the uterine cavity

- Hysterosalpingography
- Transvaginal ultrasound (± contrast)
- Magnetic resonance imaging
- 3D ultrasound
- Hysteroscopy

Imaging techniques

Hysterosalpingography

hysterosalpingography

- allows indirect evaluation of tubal patency and uterine cavity
- it is not commonly performed by gynaecologists
- not an office based exploration

http://knol.google.com/k/-/-iy3nX1p4o/yvHEAJHSG1.jpg

hysterosalpingography

- relative discomfort, especially for nulliparae
- not all the patients need a tubal patency assessment (e.g. male factor indicating IVF)
- seldom used in non-fertility patients (operator experience?)

http://knol.google.com/k/i-i/y3nX1p4oJyvf/EiA/HSG2.jpg

hysterosalpingography

- When compared with hysteroscopy, it has been found to have:
  - sensitivity of 81%
  - specificity of 80%
  - false-negative rate of 9%
  - false-positive rate of 22%
- *"still a useful screening test for the evaluation of the uterine cavity in the study of primary or secondary infertility"*

Roma, Dalló A, Ubeda B, Ubeda A. et al.: Diagnostic value of hysterosalpingography in the detection of intrauterine abnormalities: a comparison with hysteroscopy.AJR Am J Roentgenol. 2004;183(5):1405-9.

hysterosalpingography

- But other authors also found:
  - sensitivity 21.56%
  - specificity 83.76%
  - positive predictive value 55.26%
  - negative predictive value 70.75%.
  - false-negative rate 78.43%
  - false-positive rate 16.23%.
- Overall agreement between the HSG and hysteroscopy is 68.9%.

Taşkın et al. Comparison of hysterosalpingography and hysteroscopy in the evaluation of the uterine cavity in patients undergoing assisted reproductive techniques. Fertil Steril 2011;96:349–52.

hysterosalpingography

- The differential diagnosis of intrauterine filling defects:
  - polyp?
  - endometrial hyperplasia?
  - submucosal fibroids?
  - intrauterine adhesions?
  - uterine septa?
- 10–35% of women undergoing fertility investigations, who have a normal cavity at HSG, have been reported to have abnormal hysteroscopic findings.

Gaglione R et al.Int. J. Gynaecol. Obstet. 52(2), 131–133 (1996).

Golan A et al.Acta. Obstet. Gynecol. Scand. 75(7), 651–656 (1996).

hysterosalpingography

- Associated with relatively high false-positive and false-negative rates and a low positive predictive value.
- Its diagnostic value for the cavity is **unconvincing** or at least **controversial**

Pandit J, El Toukhy T. Womens Health (Lond Engl). 2010;6(6):841–7

Taskin et al. Fertil Steril 2011;96:349–52.

Transvaginal Ultrasound

ultrasound

- Office transvaginal ultrasound is the most common way to assess uterine pathology.
- It allows evaluation of the myometrial layer, the endometrial lining and the uterine cavity.

ultrasound

- simple, established and well tolerated
- low requirements and high availability
- global exploration, including ovaries and tubal patency (with contrast)
- it is integrated in most fertility treatments (ie: it is not an "extra" procedure)

ultrasound

- In comparison with hysteroscopy:
  - 84.5% sensitivity
  - 98.7% specificity
  - 98% positive predictive value
  - 89.2% negative predictive value.

Ayida G, Chamberlain P, Barlow D et al.: Uterine cavity assessment prior to in vitro fertilization: comparison of transvaginal scanning, saline contrast hysterosonography and hysteroscopy. Ultrasound Obstet. Gynecol. 1997;10(1), 59-62.

ultrasound

- But other authors found that TVS, although cheap and very easily available:
  - produces a high number of equivocal findings
  - is the least effective technique
  - and misses polyps

Dueholm M et al. Fertil Steril 2001;76:150–7.

Dueholm M, et al. Acta Obstet Gynecol Scand 1999;78:150–4.

Cicinelli E et al. Gynecol Obstet Invest 1994;38:266–71.

- Solution? Ultrasound + Contrast!
  - Sonohysterography
  - Contrast sonography
  - Hystero(salpingo)sonography

Hysterosonography

- It is clearly superior to TVUS alone for the diagnosis of intrauterine lesions.
- For polypoid lesions, it has the **same diagnostic accuracy of hysteroscopy**, while TVUS only a sensitivity of 50%.

Soares SR, Barbosa dos Reis MM, Camargos AF. Diagnostic accuracy of sonohysterography, transvaginal sonography, and hysterosalpingography in patients with uterine cavity diseases. Fertil Steril. 2000;73:406–411.

Hysterosonography

- Ultrasound
  - sensitivity 69%
  - specificity 83%
  - PPV 71%
  - NPV 82%
- Hysterosonography
  - sensitivity 83%
  - specificity 90%
  - PPV 85%
  - NPV 89%

Duelholm M et. al. Magnetic resonance imaging, transvaginal sonography, hysterosonographic examination and diagnostic hysteroscopy in evaluation of the uterine cavity. Fertil Steril 2001;76:350-7.

Hysterosonography

- Hysterosonography
  - sensitivity 83%
  - specificity 90%
  - PPV 85%
  - NPV 89%
- Hysteroscopy
  - sensitivity 84%
  - specificity 88%
  - PPV 80%
  - NPV 91%

Duelholm M et. al. Magnetic resonance imaging, transvaginal sonography, hysterosonographic examination and diagnostic hysteroscopy in evaluation of the uterine cavity. Fertil Steril 2001;76:350-7.

Hysterosonography

- Bingol et al. recently compared the accuracy of transvaginal sonography (TVS), saline infusion sonohysterography (SIS) and hysteroscopy (HS) for uterine pathologies among **infertile** women.
- 346 patients selected for operative hysteroscopy, following SIS after TVS.
- Sensitivity, specificity, positive and negative predictive values (PPV, NPV) were calculated to compare accuracy.
- SIS showed a sensitivity of 87%, specificity of 100% and PPV of 100% for endometrial hyperplasia, and a sensitivity and NPV of 100% for polypoid lesions. For submucosal myoma SIS showed a sensitivity of 99% with PPV of 96%.
- Hysteroscopy had a sensitivity, specificity, PPV and NPV of 98%, 83%, 96% and 91%, respectively for overall uterine pathologies.
- **Finally, SIS seems to be superior to TVS, for uterine pathologies, with respect to hysteroscopy as the gold standard.**

Bingol B et al. Comparison of diagnostic accuracy of saline infusion sonohysterography, transvaginal sonography and hysteroscopy. J Obstet Gynaecol. 2011;31(1):54-8.

Bingol et al. J Obstet Gynaecol. 2011;31(1):54-8.		sensitivity	specificity	PPV	NPV
Hyperplasia	TVS	0.62 (0.51–0.73)	0.95 (0.91–0.98)	0.84 (0.72–0.92)	0.87 (0.82–0.91)
	SIS	0.87 (0.77–0.93)	1.00 (0.98–1.00)	1.00 (0.95–1.00)	0.95 (0.91–0.98)
	HSC	1.00 (0.96–1.00)	1.00 (0.98–1.00)	1.00 (0.96–1.00)	1.00 (0.98–1.00)
Polyps	TVS	0.87 (0.79–0.93)	0.80 (0.74–0.86)	0.73 (0.64–0.80)	0.91 (0.86–0.95)
	SIS	1.00 (0.97–1.00)	0.93 (0.89–0.97)	0.90 (0.83–0.95)	1.00 (0.98–1.00)
	HSC	1.00 (0.97–1.00)	1.00 (0.98–1.00)	1.00 (0.97–1.00)	1.00 (0.98–1.00)
SM fibroids	TVS	0.95 (0.89–0.98)	0.96 (0.92–0.98)	0.92 (0.85–0.97)	0.97 (0.94–0.99)
	SIS	0.99 (0.94–1.00)	0.98 (0.95–0.99)	0.96 (0.90–0.99)	0.99 (0.97–1.00)
	HSC	1.00 (0.96–1.00)	0.98 (0.95–0.99)	0.96 (0.90–0.99)	1.00 (0.98–1.00)
overall accuracy	TVS	0.93 (0.89–0.96)	0.60 (0.49–0.71)	0.87 (0.83–0.91)	0.74 (0.62–0.83)
	SIS	0.98 (0.96–0.99)	0.83 (0.71–91)	0.96 (0.93–0.98)	0.91 (0.81–0.97)
	HSC	0.98 (0.96–0.99)	0.83 (0.71–0.91)	0.96 (0.93–0.98)	0.91 (0.81–0.97)

sonohysterography

- Grimbizis et al. compared the accuracy of TVS, SIS and hysteroscopy after receiver operating analysis.
- Saline infusion sonohysterography is significantly more accurate than TVS for the diagnosis of **intracavitary masses** (P=.010).
- Saline infusion sonohysterography is significantly more accurate for the diagnosis of **intracavitary myomas** and **endometrial polyps** compared with TVS (P=.003 and P=.005, respectively).
- For **structural abnormalities**, when ROC curves were compared, **no method (TVS, SIS or hysteroscopy) is better** than the others.

Grimbizis G et al. Fertil Steril 2010;94:2720–5.

sonohysterography

- Van Dongen et al. compared **patient discomfort** during saline infusion sonography (SIS) and office vaginoscopic hysteroscopy in a randomised controlled trial.
- 100 women were randomly allocated to either SIS or vaginoscopic office hysteroscopy.
  - Pain scores on both the VAS and the PPI (present pain intensity) scales were lower for SIS when compared with hysteroscopy (P<.05).
  - The success rate, (adequate inspection of the cervical canal and uterine cavity), was 94% for SIS compared with 92% for office hysteroscopy (P = 0.633).
  - SIS, multiparity, shorter procedure time and anteverted uterus decreased pain scores.
- Both SIS and office hysteroscopy are successful procedures but **SIS induces significantly less discomfort** and should therefore be considered the **method of choice**.

van Dongen H, de Kroon CD, van den Tillaart SA, Louwé LA, Trimbos-Kemper GC, Jansen FW. A randomised comparison of vaginoscopic office hysteroscopy and saline infusion sonography: a patient compliance study. BJOG. 2008 Sep;115(10):1232-7.

Saline or Gel?

- Werbrouck et al. conducted a prospective cohort study where two consecutive cohorts of patients underwent SIS or GIS.
- INTERVENTION(S): Vaginal ultrasound (n=804) followed by SIS (n=402) or GIS (n=402); office hysteroscopy in 685 patients, and endometrium sampling in 487 patients; surgery in 274 women: operative hysteroscopy (n=230) or hysterectomy (n=44).
- The authors evaluated patients' characteristics, technical failure rates, and final diagnosis.

Werbrouck E et al. Detection of endometrial pathology using saline infusion sonography versus gel instillation sonography: a prospective cohort study. Fertil Steril. 2011;95(1):285-8.

Saline or Gel?

Werbrouck et al. Fertil Steril 2011	SIS	GIS	difference between proportions and CI or significance
technical failure rate	5.0%	1.8%	3.21 (0.69-5.95)
failure due to inadequate distention	1.5%	0.3%	1.25 (-0.16-2.99)
diagnosis of pathology	49%	40.2%	8.88 (1.69-15.95)
sensitivity	77.8%	85.0%	ns
NPV	79.1%	88.6%	9.54 (2.17-16.89)

"Gel instillation sonography is a feasible, accurate alternative for SIS in the evaluation of women with abnormal bleeding, and has fewer technical failures."

Magnetic Resonance

MRI

- expensive and non-office based
- cannot be considered a routine, screening method
- unspecific findings by MRI in the presence of various endometrial abnormalities makes MRI an unrealistic diagnostic tool for diagnosis of endometrial abnormalities

Ducholm M et al. Magnetic resonance imaging, transvaginal sonography, hysterosonographic examination and diagnostic hysteroscopy in evaluation of the uterine cavity. Fertil Steril 2001;76:350–7.

MRI

- Inadequate accuracy for exclusion of intracavitary abnormalities, mainly because it fails to diagnose **polyps.**
- However, it is very precise for evaluation of submucous **fibroids** and their in-growth. Thus, it might be useful **preoperatively** when advanced surgery of fibroids is planned.

Ducholm M et al. Magnetic resonance imaging, transvaginal sonography, hysterosonographic examination and diagnostic hysteroscopy in evaluation of the uterine cavity. Fertil Steril 2001;76:350–7.

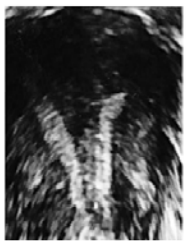
3D Ultrasound

3D Ultrasound

- Transvaginal 3D ultrasonography is highly accurate for the diagnosis of congenital uterine anomalies.

3D Ultrasound

- MRI diagnosis was correct in 24/31 patients.
- **Concordance between 3D-US and operative hysteroscopy or laparoscopy in all 31 cases.** (29 septum, 2 bicornuate)
- 3D-US appears to be extremely accurate for the diagnosis and classification of congenital uterine anomalies.
- It may conveniently become the only mandatory step in the assessment of the uterine cavity in patients with a suspected septate or bicornuate uterus.
- Faivre E et al. J Minim Invasive Gynecol. 2011 Oct 19.



3D hysterosonography

- **3D hysterosonography** compared prospectively with diagnostic hysteroscopy:
  - sensitivity of 91.9%
  - specificity of 98.8%
  - positive predictive value of 97.1%
  - negative predictive value of 96.5%

Makris N et al. Three-dimensional hysterosonography versus hysteroscopy for the detection of intracavitary uterine abnormalities. Int J Gynaecol Obstet 2007;97:6-9.

3D hysterosonography

- 3D with contrast to plan surgery?
- 3D saline sonohysterography was used to examine the potential value of various ultrasound variables for the prediction of successful submucous fibroid resection.
- Submucous fibroid protrusion ratio, fibroid diameter and size of the fibroid's intramural component are significantly associated with the likelihood of successful fibroid resection.
- A logistic regression model can calculate individual probability of complete resection and may improve preoperative counseling of patients.

Harrelos D, Naftalin J, Hoo W, Ben-Nagi J, Holland T, Jurkovic D. Preoperative assessment of submucous fibroids by three-dimensional saline contrast sonohysterography. Ultrasound Obstet Gynecol. 2011;38:350–4.

Reproducibility

Reproducibility of TVUS

- Transvaginal ultrasound findings of 235 patients with abnormal uterine bleeding were recorded systematically on videotape.
- Recordings were reviewed by three observers who had different levels of experience.
- Reproducibility was expressed by the observed rates of interobserver agreement and by kappa statistics.
  - Endometrium/uterine cavity: agreement 0.85–0.89; k 0.70–0.78
  - Myometrium: agreement rates 0.86–0.91; kappa values 0.67–0.80.
- TVUS of the uterus in patients with aub has a good reproducibility.
- Observations of the endometrium/uterine cavity with a normal appearance were the most highly reproducible, with the smallest effect of observer experience.
- This may reduce the need for invasive diagnostic procedures in patients with aub.

Emanuel MH et al. The reproducibility of the results of transvaginal sonography of the uterus in patients with abnormal uterine bleeding. Ultrasound Obstet Gynecol. 1996;8:316–9.

Reproducibility of contrast US

- Inter- and intra-observer agreement for video recordings of SCSH procedures according to different levels of experience.
- METHODS: SCSH examinations by an experienced operator were recorded on video. Video material was scored by observers allocated to different groups according to experience.
- RESULTS: Significant difference in kappa values for inter-observer agreement between the most experienced group and the less experienced observers.
  - High experience: k 0.62 (95% CI, 0.56-0.67)
  - Low experience: k 0.38 (95% CI, 0.33-0.43)
  - No experience: k 0.47 (95% CI, 0.43-0.52).
- The inter-observer agreement in Group A was significantly higher than that in Groups B and C ($P < 0.001$ and $P = 0.023$, respectively), and Group C performed better than Group B ($P = 0.024$).
- Intraobserver agreement was good, with a mean kappa of 0.66 (Group A, 0.63; Group C, 0.71).

Beemsterboer SN et al. Reproducibility of saline contrast sonohysterography for the detection of intracavitary abnormalities in women with abnormal uterine bleeding. Ultrasound Obstet Gynecol. 2008;31:445-9.

Reproducibility of contrast US

- CONCLUSIONS: Interobserver agreement in interpretation of video recordings of SCSH by inexperienced sonographers is poor, whereas the intraobserver agreement is good.
- This findings might depend on non-uniform diagnostic criteria.

Beemsterboer SN et al. Reproducibility of saline contrast sonohysterography for the detection of intracavitary abnormalities in women with abnormal uterine bleeding. Ultrasound Obstet Gynecol. 2008;31:445-9.

Is hysteroscopy reproducible?

- The **intra-observer** agreement of the one hysteroscopy performer for the assessment of a normal versus abnormal uterine cavity was substantial. The k value was 0.71 and perfect agreement was found in 93.5% of the cases.
- The **inter-observer** agreement between three gynecologists for the assessment of the cavity to be normal or abnormal was found to be **moderate**, with an ICC (as equivalent of the overall k) of 0.49.

Kasius JC et al. Observer agreement in the evaluation of the uterine cavity by hysteroscopy prior to in vitro fertilization. Hum Reprod. 2011;26:801-7.

Reproducibility

- Dueholm et al. compared the inter-observer reproducibility by:
  - magnetic resonance imaging (MRI)
  - transvaginal ultrasonography (TVS)
  - hysterosonographic examination (HSE)
  - hysteroscopy (HY).
- Different observers consecutively evaluated MRI, TVS, HSE and HY independently in 51 pre-menopausal women, who underwent hysterectomy for benign diseases.

Dueholm M et al. Reproducibility of evaluation of the uterus by transvaginal sonography, hysterosonographic examination, hysteroscopy and magnetic resonance imaging.Hum Reprod. 2002;17:195-200.

Dueholm et al Hum Reprod 2002	anomalies exclusion	submucous fibroids	polyps	intramural fibroids	adenomyosis
tvs	k 0.68	k 0.59	k 0.48	k 0.74	k 0.38
hse	k 0.48	k 0.6	k 0.35		
mri	k 0.97	k 0.97	k 0.49	k 0.97	k 0.73
hysteroscopy	k 0.63	k 0.67	k 0.5		

Reproducibility

- High level of **inter-observer disagreement** by TVS, HSE and hysteroscopy
- Inter-observer disagreement reached substantial levels **for exclusion** of uterine cavity benign abnormalities by HY, TVS and HSE.
- Agreement on evaluation of abnormalities in the uterine cavity, submucous myomas, number of myomas and adenomyosis was **significantly greater by MRI** than by any of the other techniques.
- **Better** agreement among the most **experienced** observers.

Dueholm M et al. Reproducibility of evaluation of the uterus by transvaginal sonography, hysterosonographic examination, hysteroscopy and magnetic resonance imaging.Hum Reprod. 2002;17(1):195-200.

Reproducibility

- The accuracy and inter-observer reproducibility of ultrasound and hysteroscopy seems to be operator dependent.

Loffer. 1989; Emanuel et al. 1996; Widrich et al. 1996; Schwarzler et al. 1998; Dueholm et al. 2002

- Still, both techniques are widespread and essential.
- Strategies are needed to increase their diagnostic power and minimize inter-observer variability.

Reproducibility

- Possible strategies to reduce observer variability:
  - decentralized organization with **referral** to specialized staff
  - systematic standardized **training** of all gynaecologists in us and hysteroscopy
- *otherwise MRI, that is more costly and less available, will replace a considerable part of gynaecological imaging techniques in the future*

Dueholm M et al. Reproducibility of evaluation of the uterus by transvaginal sonography, hysterosonographic examination, hysteroscopy and magnetic resonance imaging. Hum Reprod. 2002;17(1):195-200.

Morphology or Function?

a normal cavity does not mean a functional uterus

- endometrial receptivity
- beyond the endometrium
- are all patients the same?

Endometrial receptivity

- we now focus on pathology rather than function
- with new tests on endometrial receptivity we might broaden up our investigation in order to assess what we most need in reproductive medicine, ie the chances for conception, the ability of the endometrium to do its job

Beyond the endometrium

- Uterine fertility factors can be found "beyond" the endometrium (e.g. intramural fibroids or adenomyosis)
- abnormal peristalsis of the myometrium and pathology of the uterine junctional zone have been linked to subfertility
- Both ultrasonography and MRI explore the subendometrium and the junctional zone
- This is certainly an advantage of this imaging techniques

Are all patients the same?

- When choosing a diagnostic plan for our patients we cannot loose our clinical mind/ vision
- We always need to provide individualized care
- And keep our goal in focus
  - screening?
  - diagnosis?

- Ideally we should be able to identify:
  - **low risk** patients where ultrasound with contrast is enough
  - **high risk** patients (such as those with repeated failures or an unclear ultrasound) where referral for second opinion US or more invasive techniques might be necessary.

Conclusions

Conclusions

- The **integrity** and **functionality** of the uterine cavity is extremely important in reproductive medicine.
- Assessing the uterine cavity on each fertility patient, **regardless of the indication** (eg tubal or male factor), is equivalent to **screen a population**.
- Therefore our tools must have the characteristics of **screening** tools and have a good balance between **accuracy, costs** and **patient-friendliness**.

Conclusions

- On the contrary, many of the available studies are on **symptomatic patients** (eg. bleeding). Can we extrapolate the results to the general infertile population?
- And all the techniques, except MRI, show **poor interobserver agreement**, especially among less experienced performers.
- Moreover, the evaluation of the uterine cavity in reproductive medicine is (and must be) **dynamic**, we virtually perform it every time we meet a patient.
- Many of the abnormalities are **diagnosed during the treatment**, not at the beginning of it.

Conclusions

- **Ultrasound** is **cheap, patient-friendly** and **repeatable**.
- It can be performed virtually at **every visit**.
- US, **with saline or gel contrast**, is the **key** to the **evaluation of the uterine cavity**.
- **Moreover**, it gives useful information on the **myometrium**, **ovaries** and **tubal patency**.
- It is very **easy to switch** from a common US **to a contrast US**.
- In addition, **3D ultrasound** seems to be the **best method** to assess **uterine anomalies**.

Conclusions

- Both **imaging** techniques and **hysteroscopy** show **poor reproducibility**. Inter-observer agreement is **inadequate**.
- More **experienced** operators have a stronger agreement.
- Reproducibility should be improved by setting **standards** for **diagnosis** and **training.**
- In any case, **identifying high risk** cases to refer to further testing is extremely important
- It would be useful to have knowledge of other prognostic factors that, together with a basal ultrasound, might help identifying the patients who require further testing.

Thank you!

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- [illegible]
- Kasius JC et al. Observer agreement in the evaluation of the uterine cavity by hysteroscopy prior to in vitro fertilization. Hum Reprod 2011;26:801-7.
- Dueholm M et al. Reproducibility of evaluation of the uterus by transvaginal sonography, hysterosonographic examination, hysteroscopy and magnetic resonance imaging Hum Reprod 2002;17:195-200.

ADDED VALUE OF HYSTEROSCOPY ?

European theAcademy of Gynaecological Surgery

Rudi Campo, MD
Leuven Institute for Fertility and Embryology
LIFE
Leuven - Belgium

Modern Hysteroscopy

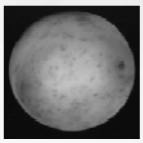
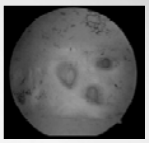
Important tool to evaluate the cervical - uterine pathway and validate the shape and form of the uterine cavity

Gold standard to examine the endometrium.

Novel tool to explore the junctional myometrial area

Hystroscopy gold standard to evaluate the endometrium and uterine cavity.

Feasibility ???

Modern Hysteroscopy

GRADE A EVIDENCE

By reducing the diameter of the hysteroscope and using the atraumatic vagino-cervical approach with a low viscosity fluid at the lowest needed distention pressure, diagnostic hysteroscopy can successfully be performed by any trained gynecologist in over 97 % of the patients.

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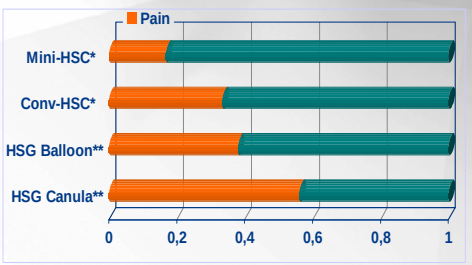
Campo R, Molinas CR et al, Hum Reprod *2005*

PAIN SCORE HSC - HSG



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**Campo, et al. Prospective randomised trial (474 pat.) p<0.0001*
***Tur-Kaspa, et al. Hum Reprod 1998;13:75*

Visualization Scores

theAcademy

Campo R, Molinas CR et al, Hum Reprod *2005*

New generation of hysteroscopes

Because infertility patients are often challenging and based on the available scientific evidence a new Hysteroscope was developed for the ambulatory procedures.

The hysteroscope is named after the ESHRE – ESGE multicentre

"Trial of Outpatient Hysteroscopy" **TROPHY**

All study participants valued the scope extremely high, providing essential benefits to any other current hysteroscope

theAcademy

El-Toukhy T, Campo R et al.
Trial of Outpatient Hysteroscopy – (TROPHY) in IVF. Reprod Health. 2009 Dec 3;6:20.

Trophy hysteroscope

Single flow, compact hysteroscope of 2,9 mm total diameter which does not require assembling.

The advantages are

- Smooth passage through cervical canal
- No sticking of tissue to the optic
- Comfortable instrument length and handling
- Innovative gliding mechanism for accessory sheets
- Progressive and atraumatic dilatation possible.
- Compatible with high level fast disinfection procedure.

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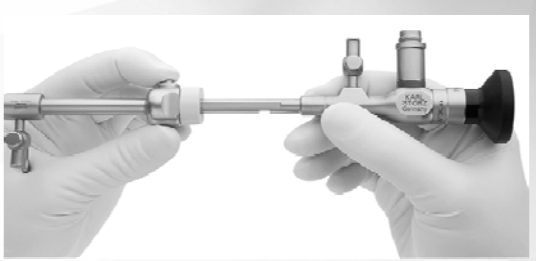
Trophy Scope : Fast reuse of instrument possible

For the ambulatory use the compatibility of this instrument with a biodegradable high level disinfection agent like Tristel Fuse ® offers the possibility to reuse the Trophy hysteroscope within 10 minutes and improves the efficiency and cost benefit of the ambulatory surgery.

theAcademy

Trophy hysteroscope : Accessory sheets



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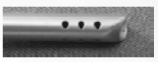
Trophy Hysteroscope
Diagnostic accessory sheet

In active position

Atraumatic cervical dilatation up to 3.7 mm under visual control

Creating double flow and blocking the cervix in case of passive outflow



Passive

In free position

Suction device for endometrial sampling

Guide for ultrasound guided intrauterine procedures like post hysteroscopic D&C, positioning Embryo transfer catheter or for Spirotome endomyometrial biopsy

Guide for Active

Free

theAcademy

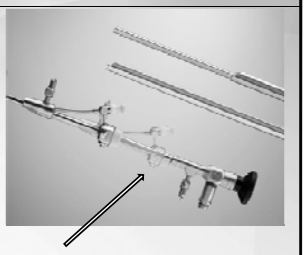
Trophy Scope
Operative accessory sheet

In passive position

Operative sheet does not interfere the diagnostic phase (2,9mm).

In active position

Atraumatic cervical dilatation under visual control , creating double flow, access for 5 French instruments and blocking the cervix up to 4,4 mm



Activation with a simple push on the bottom

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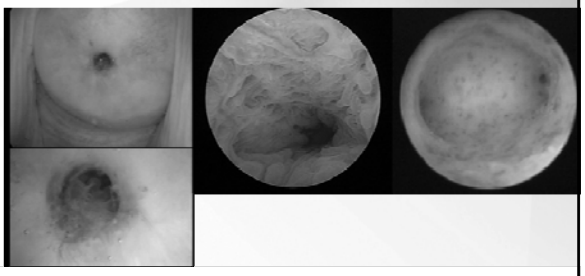
Modern Hysteroscopy

Gold standard for intra uterine diagnosis and treatment



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How to organise a one stop uterine diagnostic unit.

Ambulatory or office endoscopic unit with US facilities

Watery (Saline) distension medium

Trophy hysteroscope compatible with fast disinfection procedure

Mechanical and Bipolar Surgery with atraumatic technique

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Watery distension medium

Grade A evidence
Less painful than CO_2

Hydro-flotation
subtle lesions !!

Saline for bipolar surgery

theAcademy

Optimal Fluid administration

- Pressure and flow controlled pump system with continuous control of fluid balance to work at minimal necessary pressure

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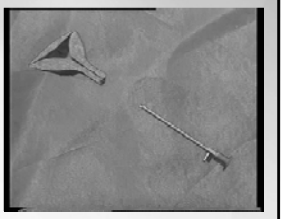
Atraumatic insertion technique

No speculum
No tenaculum
No cervical dilatation
No anaesthesia, no analgesia
Atraumatic and sight controlled insertion of the hysteroscope.



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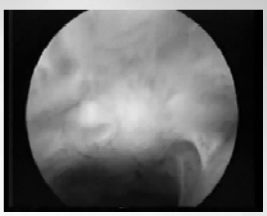
Atraumatic insertion technique



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Atraumatic insertion technique

Learning curve is very acceptable.

Every resident in ZOL Genk, Belgium reaches full proficiency to perform a diagnostic hysteroscopy with the Trophy hysteroscope during their 3 month stay in the IVF unit .

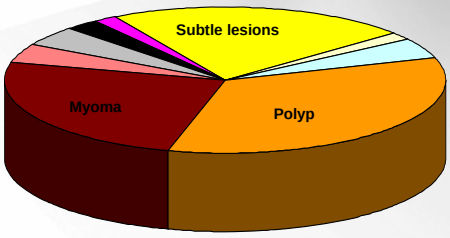
Findings

Prospective multi-centre randomized clinical trial

Different pathology in infertile versus AUB patients

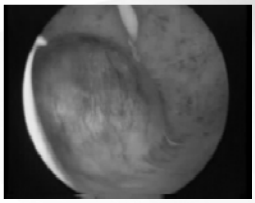
Molinas CR, Campo R et al
Best Pract Res Clin Obstet Gynaecol. 2006

Abnormal findings in AUB patients

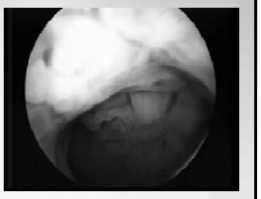


Molinas CR, Campo R et al Best Pract Res Clin Obstet Gynaecol. 2006

Myoma - Polyp



MYOMA



POLYP

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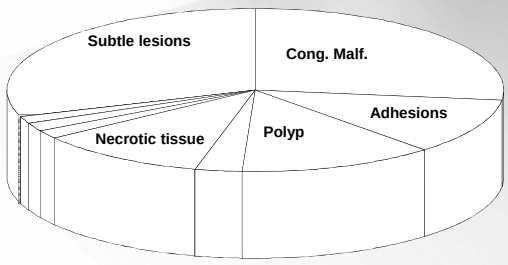
Abnormal findings in the infertile patient



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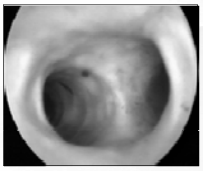
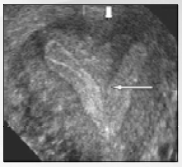
Molinas CR, Campo R et al Best Pract Res Clin Obstet Gynaecol. 2006

Congenital malformation





In the diagnosis of a uterine congenital malformation hysteroscopy is only an accessory tool to the ultrasonographic and MRI possibilities

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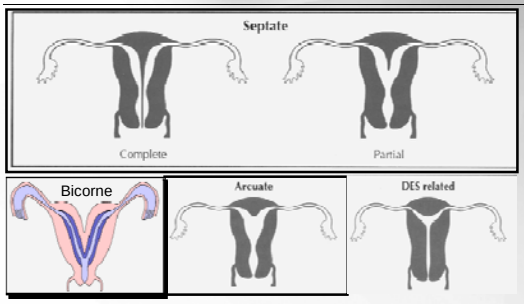
Diagnostic Challenge



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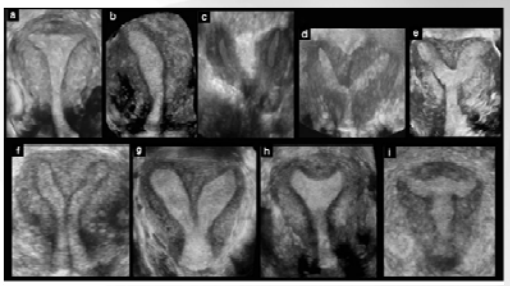
3 D ultrasound in the diagnosis of Mullerian duct anomalies.



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C. BERMEJO , Ultrasound Obstet Gynecol 2010; 35: 593–601

Modern diagnosis uterine congenital malformations

One stop uterine screening

2D Ultrasound – Fluid Mini-Hysteroscopy – 2D Kontrast sonography.

In case of malformation : 3 D Ultrasound

3D obtains in a systematical way the coronal vision, the relationship between cavity and fundus becomes evident and it is possible to make exact measurements such as length and thickness of a septum and volume of the cavity

In case of complex anomalies : MRI – Laparoscopy/HSC

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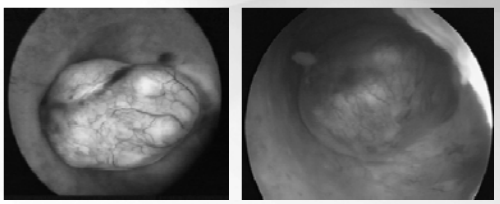
Polyp - Myoma



Typ 0 : Polyp - Myoma

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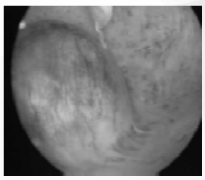
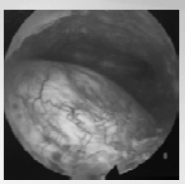
Myoma



Typ 1 Myoma



Typ 2 Myoma

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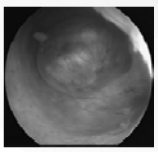
Scientific evidence Myoma – IVF outcome

If a myoma protrudes in the uterine cavity it is likely to interfere with the reproductive outcome

Conservative resection of submucosal myoma is recommended prior to any ART procedure.



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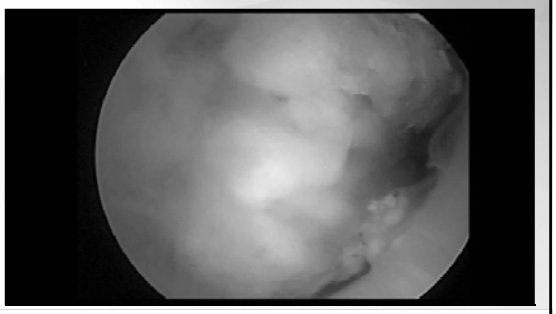
Necrotic tissue



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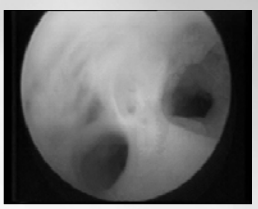
Intra-uterine Adhesions



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Post cesarean section scar pathology

Hysteroscopy provides the standard tool to evaluate the access to the uterine cavity after a cesarean section in case of planned ART.

Also the not yet fully recognized secondary infertility problems due to the cesarean section scar implants and secretions can easily be visualized and treated by hysteroscopy.

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Added value hysteroscopy (1)

In the infertile patient, hysteroscopy remains the gold standard to validated the pathway to and the absence of pathology in the uterine cavity.

Ultrasound (2-3 D) should be performed simultaneous to any hysteroscopic procedure to increase the diagnostic and therapeutic capacities.

Modern Hysteroscopy

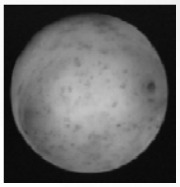
Important tool to evaluate the cervical uterine pathway and validate the shape and form of the uterine cavity

Gold standard to examine the endometrium.

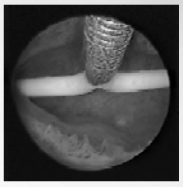
Novel tool to explore the junctional myometrial area

Gold standard to examine the endometrium

What is the significance on the reproductive capacity of minimal endometrial changes ?

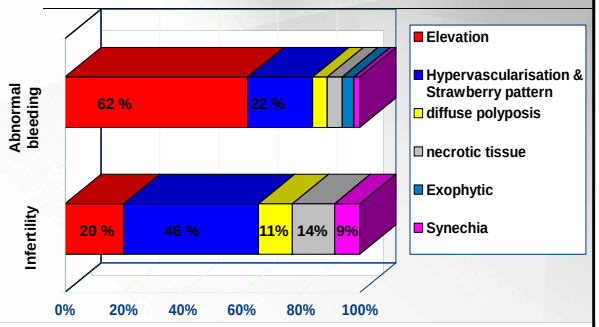


Normal - atrophic



IUD - hypervascularisation

Subtle endometrial changes



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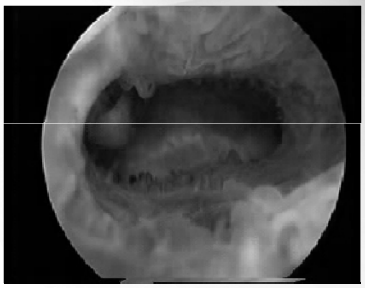
Molinas CR, Campo R et al Best Pract Res Clin Obstet Gynaecol. 2006

Diffuse polyposis



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Strawberry pattern

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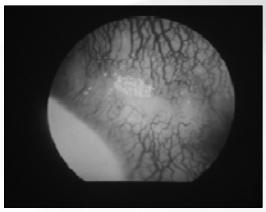
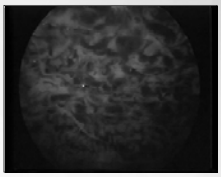
Hypervascularisation





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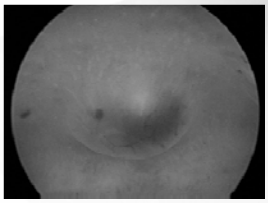
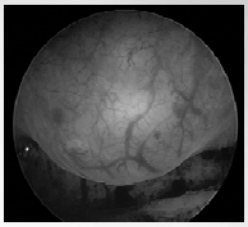
Mucosal elevation





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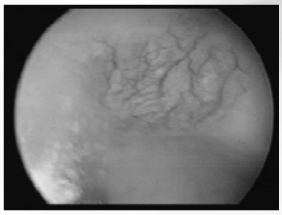
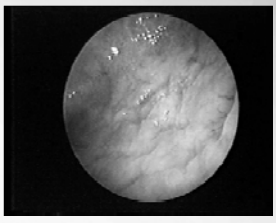
marked localised vascular pattern





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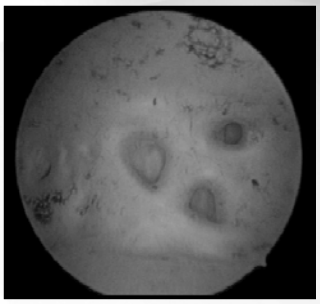
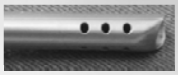
Endometrial defects



Novel tools to sample the endometrium and sub endometrial myometrium

Trophy Scope (acc. to Campo)

Guide for D&C suction device for endometrial sampling
Guide for embryo transfer catheter
Spirotome for endo - myometrial biopsy



Access for 5 French instruments for intrauterine surgical procedures.

Modern Hysteroscopy

Important tool to evaluate the cervical uterine pathway and validate the shape and form of the uterine cavity

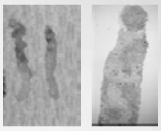
Gold standard to examine the endometrium.

Novel tool to explore the junctional myometrial area

Novel tools to explore the junctional myometrial area

Spirotome acc. to Gordts

A device built on the pioneering concept of a cutting helix on a cutting cannula to harvest high quality samples from soft tissues.



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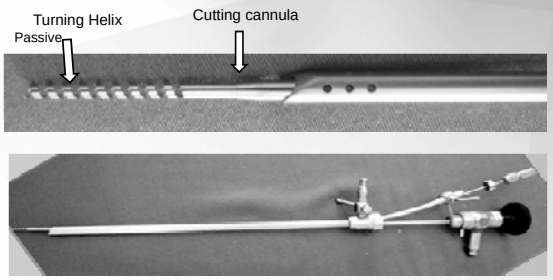
Novel tools to explore the junctional myometrial area



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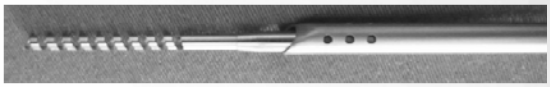
Spirotome use through diagnostic sheet

The Throphy hysteroscope can be removed leaving the continuous flow in place , sampling of endometrium or application of special probe for myometrial biopsy can be done.



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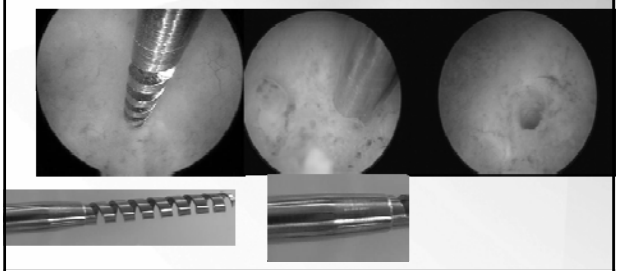
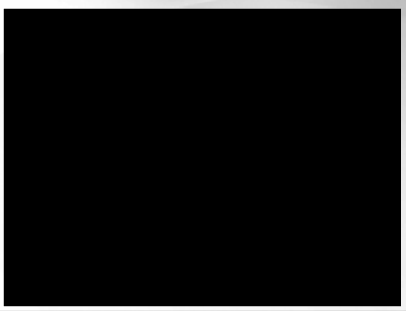
Trophy Scope – Spirotome - Ultrasound

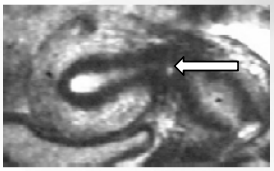
Spirotome use through Trophy operative accessory sheet



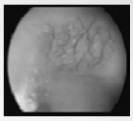
Spirotome use through Trophy operative accessory sheet

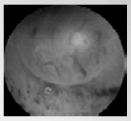


Hysteroscopy
Natural access to JZ myometrium

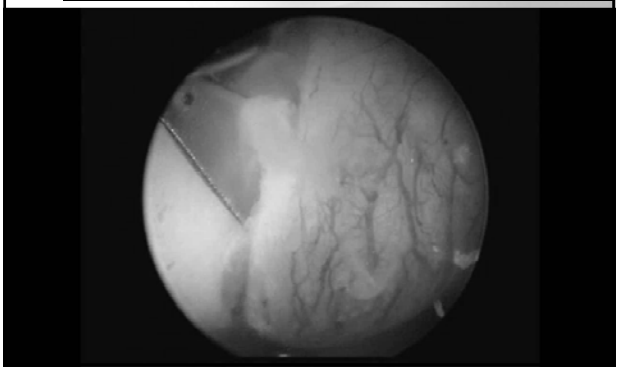


Endometrial changes sign of JZ pathology ?



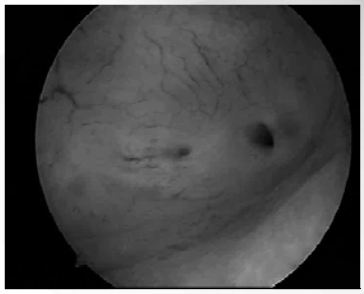


Exploration of focal hypervascularisation



Exploration of focal hypervascularisation

Endometrial defect – focal hypervascularisation



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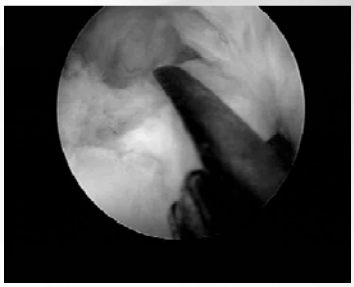
Resection of cystic laesion



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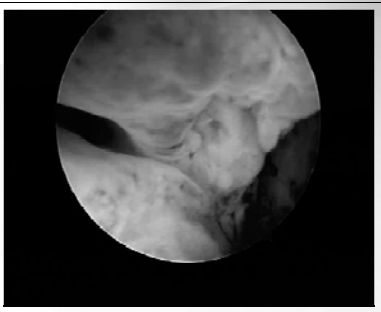
Result after resection



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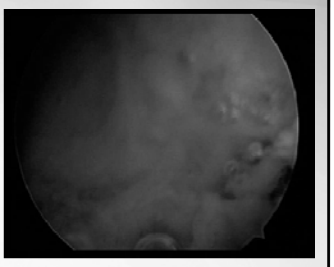
Bipolar coagulation of cystic laesion



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Comparison of postoperative result

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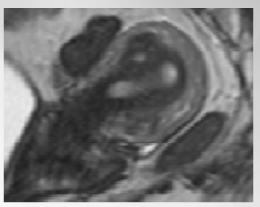
Exploration for DD Myoma Typ 2 - Adenomyoma



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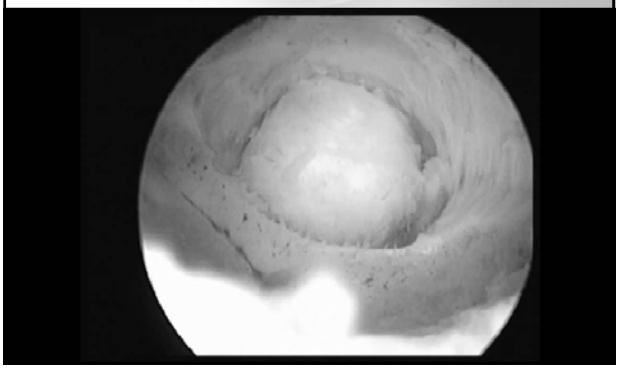
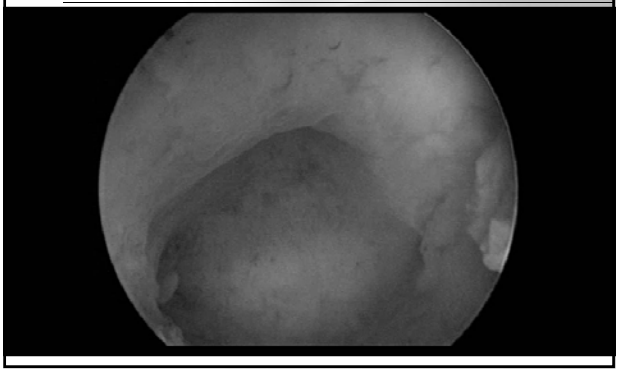
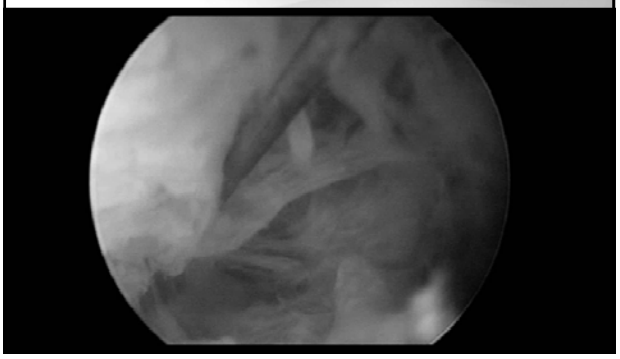
Exploration and resection intramural myoma



Exploration JZ myometrium : Adenomyoma



Resection adenomyoma



Hysteroscopy prior to IVF cycle improves pregnancy Outcome

A systematic review and meta analysis of two randomized (n = 941) and three non-randomized studies (n = 750). (1691 participants)

Evidence of benefit from Office Hysteroscopy in increasing the chance of pregnancy in the subsequent IVF cycle.

Pooled RR = 1.75, 95% CI 1.51–2.03, *P < 0.00001*
number needed to treat (NNT) to achieve an additional pregnancy was 6 (95% CI 5–8).

Meta analysis of 2 Randomised and 3 Non Randomised studies

Table 3. Patient characteristics and hysteroscopy details in the included studies.

Reference	*Type of infertility*	*Previous investigations*	*IVF history*	*Timing of hysteroscopy*	*Distension medium*	*Abnormal findings (%)*	
Demirol and Gurgan, 2004	Primary	HSG	≥2 failed cycles	In follicular phase	Normal saline	26	**R**
Raju *et al.*, 2006	Primary	HSG	≥2 failed cycles	In follicular phase	Glycine	37	
Mooney and Milki, 2003	Not reported	TVS	First or subsequent cycle	In an OCP cycle	Normal saline	56	**NR**
Dadi *et al.*, 2005	73% primary	HSG	First or subsequent cycle	In follicular phase	Normal saline	40	
Chung *et al.*, 2006	Not reported	HSG	≥2 failed cycles	Not reported	Not reported	25	

HSG = hysterosalpingogram, OCP = oral contraceptive pill, TVS = transvaginal sonography.

Hysteroscopy prior to IVF cycle improves pregnancy Outcome

Also in case of a normal uterine cavity ?

There remained a significant improvement in the outcome of the normal hysteroscopy subgroup compared with controls.

RR= 1.63, 95% CI 1.35–1.98, *P < 0.001*
NNT of 7 (95% CI 5–11).

Added value hysteroscopy (2)

Hysteroscopy is the gold standard to explore the endometrium with currently optimal facilities to sample tissue for histological examination.

There is sufficient scientific evidence that with the small hysteroscopes the examination is accessible for any Gynaecologist in the majority of patients.

Hysteroscopy should be performed in the first line exploration of an infertile patient and the novel exploration possibilities of the JZ myometrium looks very promising to improve our IVF outcome.

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11 – 14 September 2012

Leuven Institute for Fertility & Embryology

Rudi Campo
Stephan Gordts
Patrick Puttemans
Roger Molinas
Sylvie Gordts
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Endoscopy Courses 2008

More info on the special training programs in endoscopic surgery

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Mark your calendar for the upcoming ESHRE Campus events

- Basic Semen Analysis Course in Greek Language
  4-7 September 2012 - Athens, Greece
- Basic Genetics for ART practitioners
  7 September 2012 - Rome, Italy
- Regulation of quality and safety in ART – the EU Tissues and Cells Directive perspective
  14-15 September 2012 - Dublin, Ireland
- Basic Semen Analysis Course in Spanish language
  18-21 September 2012 - Galdakano,Vizcaya
- GnRH-antagonists in ovarian stimulation
  28 September 2012 - Hamburg, Germany
- The best sperm for the best oocyte
  6-7 October 2012 - Athens, Greece
- Basic Semen Analysis Course in Italian language
  8-11 October 2012 - Rome, Italy
- Accreditation of a preimplantation genetic diagnosis laboratory
  11-12 October 2012 - Istanbul, Turkey
- Endoscopy in reproductive medicine
  21-23 November 2012 - Leuven, Belgium
- Evidence based early pregnancy care
  29-30 November 2012 - Amsterdam, The Netherlands

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