HOW CAN SURGERY INCREASE THE SUCCESS RATE OF ART

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How can Surgery improve the results of ART

- Intra-uterine pathology
- Structural uterine anomalies
- Distal tubal disease
- Endometrial scratch

HYSTEROSCOPY

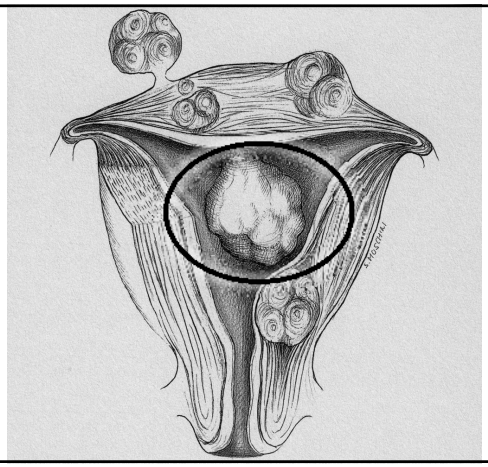
- RCT by Demirol & Gurgan (2004)
- 421 women with 2 or more IVF failures
- 56 out of 210 (26%) women with normal HSG had intrauterine leisons detected by office hysteroscopy, and treated
- The subsequent pregnancy rate in the treated group (30.4%) and the group with normal hysteroscopy (32.5%) was significantly higher than the group who did not undergo hysteroscopy (21.6%)

A

Will Hysteroscopy Improve Outcome of Recurrent Implantation Failure?

Bosteels, J. et al. Hum Reprod Update 2010
Systematic Review and meta-analysis

- Effects of *office hysteroscopy* (in the preceding menstrual cycle) on outcome of further IVF after two failed attempts



UTERINE FIBROIDS

Fibroids and infertility: an updated systematic review of the evidence

Elizabeth A. Pritts, M.D.,[a] William H. Parker, M.D.,[b] and David L. Olive, M.D.[a]

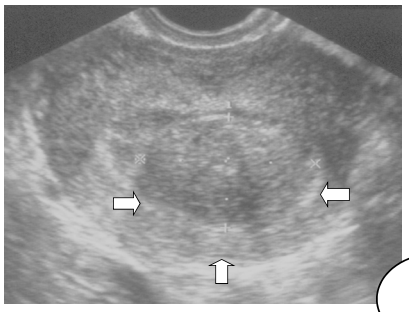
TABLE 3

Effect of fibroids on fertility: submucous fibroids.

Outcome	Number of studies/ substudies	Relative risk	95% confidence interval	Significance
Clinical pregnancy rate	4	0.363	0.179–0.737	$P=.005$
Implantation rate	2	0.283	0.123–0.649	$P=.003$
Ongoing pregnancy/live birth rate	2	0.318	0.119–0.850	$P<.001$
Spontaneous abortion rate	2	1.678	1.373–2.051	$P=.022$
Preterm delivery rate	0	–	–	–

Pritts. Fibroids and infertility. Fertil Steril 2009.

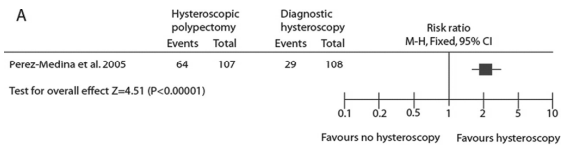
SUBMUCOUS FIBROID



B

Polypectomy in Subfertile Patients with Polyps Undergoing IUI

Outcome: Clinical pregnancy



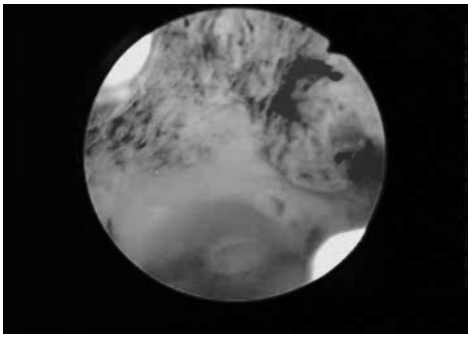
RR = 2.3; 95% CI: 1.6-3.2

Bosteels, J. et al. Hum Reprod Update 2010 16:1-11

Human Reproduction Update

Summary

Hysteroscopic polypectomy doubles CPR in women undergoing IUI



Intrauterine adhesiolysis (scissors)

How can Surgery improve the results of ART

- Intra-uterine pathology
- Structural uterine anomalies
- Distal tubal disease
- Endometrial scratch

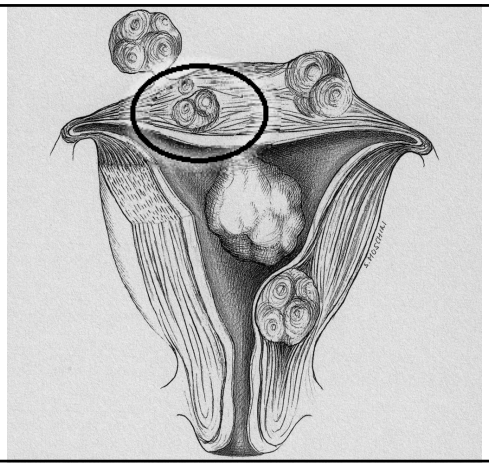
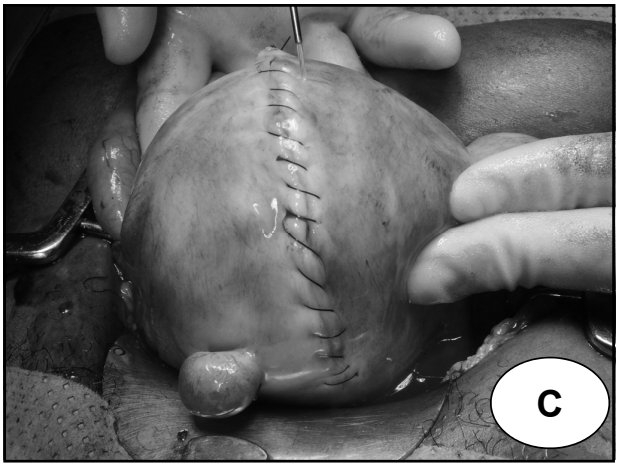


TABLE 5

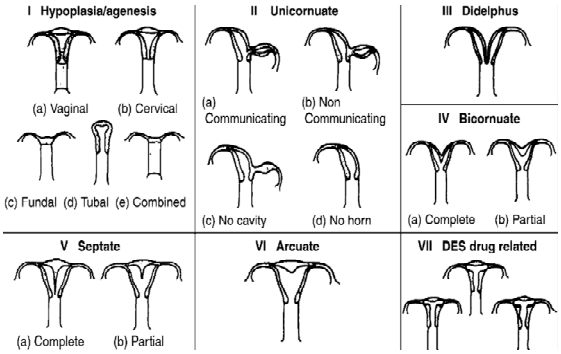
Effect of fibroids on fertility: intramural fibroids.

Outcome	Number of studies/ substudies	Relative risk	95% confidence interval	Significance
A. All studies				
Clinical pregnancy rate	12	0.810	0.696–0.941	$P=.006$
Implantation rate	7	0.684	0.587–0.796	$P<.001$
Ongoing pregnancy/live birth rate	8	0.703	0.583–0.848	$P<.001$
Spontaneous abortion rate	8	1.747	1.226–2.489	$P=.002$
Preterm delivery rate	1	6.000	0.309–116.606	Not significant
B. Prospective studies				
Clinical pregnancy rate	3	0.708	0.437–1.146	Not significant
Implantation rate	2	0.552	0.391–0.781	$P=.001$
Ongoing pregnancy/live birth rate	2	0.465	0.291–0.744	$P=.019$
Spontaneous abortion rate	2	2.384	1.110–5.122	$P=.002$
Preterm delivery rate	0	—	—	—
C. Studies using hysteroscopy in all subjects				
Clinical pregnancy rate	2	0.845	0.666–1.071	Not significant
Implantation rate	1	0.714	0.547–0.931	$P=0.013$
Ongoing pregnancy/live birth rate	2	0.733	0.383–1.405	Not significant
Spontaneous abortion rate	2	1.215	0.391–3.774	Not significant
Preterm delivery rate	1	6.000	0.309–116.606	Not significant

Pritts. Fibroids and infertility. Fertil Steril 2009.

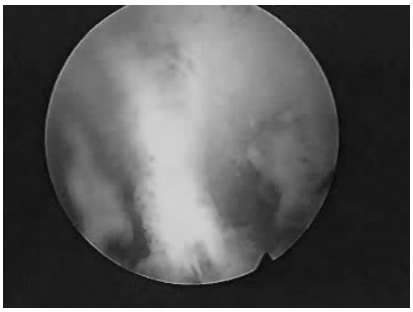


Classification of congenital uterine anomalies



American Fertility Society. *Fertil Steril* 1988;49:944–955.

What is the abnormality?



SEPTUM TRANSECTION

C

Retrospective Control Study

The outcome of singleton pregnancies after IVF/ICSI in women before and after hysteroscopic resection of a uterine septum compared to normal controls

Ban-Frangez et al, European J Obstet Gynae & Reprod Biol 2009

	Miscarriage rate	Miscarriage rate in matched controls	P value
Large septum, not removed	83.3%	16.7%	<0.001
Small septum, not removed	78.9%	23.7%	<0.001
Large septum removed	30.6%	20.4%	NS
Small septum removed	28.1%	19.3%	NS

How can Surgery improve the results of ART

- Intra-uterine pathology
- Structural uterine anomalies
- Distal tubal disease
- Endometrial scratch

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

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

- Hydrosalpingeal fluid is embryo toxic
- Hydrosalpingeal fluid contains inhibitors of implantation, thereby impairing endometrial receptivity

Hydrosalpinges and Leukaemia inhibitory factor (LIF) expression in the endometrium

- LIF expression in the mid-luteal phase endometrium of infertile women (n=10) with hydrosalpinges was significantly lower than control fertile subjects
- Salpingectomy resulted in increase of LIF expression in 8/10 subjects with hydrosalpinges

Seli et al 2005
Human Reprod 20:3012

Hydrosalpinges and integrin expression (αvβ3) in the endometrium

- Integrin (αvβ3) expression in the mid-luteal phase endometrium of women with hydrosalpinges was significantly lower than control subjects
- Salpingectomy resulted in increase of integrin (αvβ3) expression

Meyer et al 1997
Human Reprod 12:1393

Bildirici et al 2001
Human Reprod 16:2422

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, in women with USS visible hydrosalpinges

Group	Patient	PR	Live birth
Salpingectomy	35	45.7%	40%
No salpingectomy	40	22.5%	17.5%

PR, p=0.029 LB, p=0.038

Hydrosalpinges and IVF

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

Is it cost-effective to routinely remove all hydrosalpinges prior to IVF ?

Cost-effectiveness of salpingectomy prior to IVF, based on a RCT

Strandell et al 2005 Human Reprod 20:3284

Up to three IVF cycles, in women with hydrosalpinges demonstrable by USS

Group	Patient	Cost per LB
Salpingectomy	51	Euro 22823
No salpingectomy	44	Euro 29517

Cost-effectiveness of salpingectomy prior to IVF, based on a RCT

Strandell et al 2005 Human Reprod 20:3284

Up to three IVF cycles, in women with hydrosalpinges demonstrable by USS

Group	Patient	Cost per LB
Salpingectomy	51	Euro 22823
No salpingectomy	44	Euro 29517

More cost-effective

1. Is it still worth doing surgery if the hydrosalpinx is not visible by ultrasound?

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

2. Is it still necessary to consider surgery in unilateral tubal disease?

Unilateral Hydrosalpinx with a Contra-lateral Patent Tube

McComb & Taylor 2001 Fertil Steril 76:1279

- 23 women with unilateral hydrosalpinx underwent salpingostomy
- IU pregnancy rate 43.5%
- Conclusion – unilateral salpingostomy in women with a contra-lateral patent tube improves fertility

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

3. Is ultrasound guided aspiration of the fluid just as effective?

Surgical Drainage of Hydrosalpinx Retrospective Analysis

Sowter et al 1997 Human Reprod 12:2147

	Hydrosalpinx Not seen	**Hydrosalpinx Not drained**	**Hydrosalpinx drained**
Implantation	23/239 (9.6%)	4/53 (7.5%)	7/85 (8.2%)
Live birth per embryo transferred	19/239 (7.9%)	4/53 (7.5%)	5/85 (5.9%)

Ultrasound-guided hydrosalpinx aspiration, RCT

Hammadien et al, Human Reprod 2008

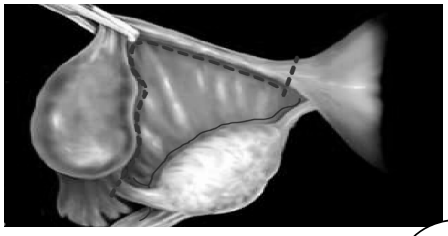
	Aspiration	No aspiration	P value
Biochemical pregnancy	14/32 (43.8%)	7/34 (20.6%)	0.04
Clinical pregnancy	10/32 (31.3%)	6/34 (17.6%)	0.2

Disadvantages of transvaginal aspiration of hydrosalpinges

- **Fluid rapidly re-accumulate**
- **Underlying pathology not altered**
- **Risk of infection**
- **Efficacy not proven**

Which type of tubal surgery for hydrosalpinges?

Salpingectomy



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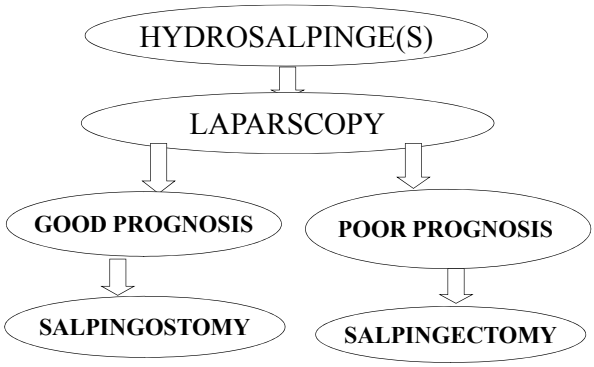
A case of salpingectomy

- Large hydrosalpinx visible on ultrasound
- One failed IVF treatment
- Laparoscopic surgery
- Dense adhesions between L tube and bowel and pelvic side wall
- 2 hour operation, salpingectomy
- Day 3, sepsis, bowel leak
- Colostomy, ITU for 1 weeks



Which type of tubal surgery for hydrosalpinges?

- Salpingostomy
- Salpingectomy
- Proximal tubal occlusion / ligation

Gelbaya et al Fertil Steril 2006, 85;1464

- Retrospective study involving 40 women who had salpingectomy and 25 women who had proximal tubal division
- Prophylactic salpingectomy appears to reduce ovarian response to stimulation
- No difference in pregnancy rate and miscarriage rate

POSSIBLE ADVANTAGES OF PROXIMAL TUBAL OCCLUSION

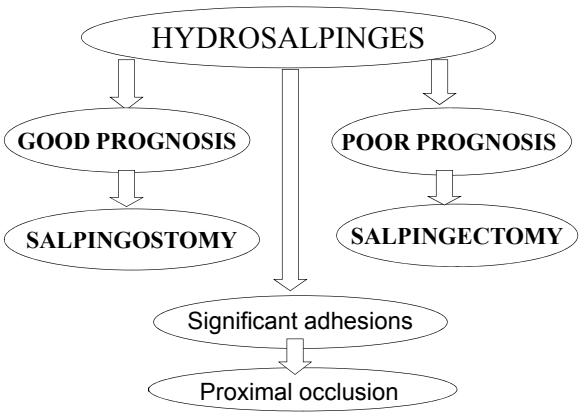
- Simpler operation than salpingectomy
- ? Less likely to affect blood supply to ovary and therefore ovarian response in IVF treatment cycles

Disadvantages of proximal tubal occlusion

- Pain may get worse
- Risk of recurrent infection and pyosalpinx
- May require further surgery to remove the diseased tube at a later date
- The data on possible benefit is not as robust as that of salpingectomy

RCT : proximal tubal occlusion Vs salpingectomy
Kontoravdis et al, Fertil Steril 2006

	Ongoing pregnancy rate per transfer
Tubal occlusion (n=45)	37.8%
Salpingectomy (n=47)	48.9%
No treatment (n=14)	7.1%



How can Surgery improve the results of ART

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ENDOMETRIAL SCRATCH -1

- RCT of repeated endometrial biopsies in the cycle immediately preceding IVF treatment significantly increased (~doubled) the implantation, pregnancy and live birth (28%, 67% & 49%) rates in women who had one or more IVF failure compared with control subjects (14%, 30% and 23%) (Barash et al 2003)

ENDOMETRIAL SCRATCH - 2

- Cohort study of repeated endometrial biopsies in the cycle immediately preceding IVF treatment significantly increased the implantation & pregnancy (11% & 30%) rates in 60 women who had more than 4 fresh embro transfer compared with 57 control subjects (4% & 12%) (Raziel et al 2007)

Endometrial Scratch -3

- RCT
- 115 women with at least two implantation failures
- Endometrial biopsy in the luteal phase of cycle preceding IVF/ICSI

Karimzadeh et al, 2009
Aust NZJ Obstet Gynaecol 49: 677-80

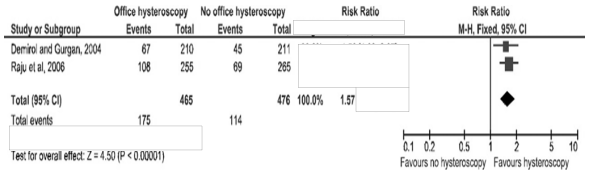
Endometrial scratch

	Biopsy Gp	Control Gp	p
Implantation rate	10.9%	3.4%	<0.05
Pregnancy rate	27.1%	8.9%	<0.05

Karimzadeh et al, 2009
Aust NZJ Obstet Gynaecol 49: 677-80

Office Hysteroscopy versus No Hysteroscopy in Patients with Two or More Failed IVFs

Outcome: Clinical pregnancy



RR = 1.7 (95% CI: 1.5-2.0)

Bosteels, J. et al. Hum Reprod Update 2010 16:1-11

Human Reproduction Update

Summary

Office hysteroscopy performed in the preceding menstrual cycle improves CPR after recurrent implantation failure

WHAT IS RECURRENT IVF FAILURE?

What is Recurrent Implantation Failure?

RECURRENT IMPLANTATION FAILURE

- About 2/3 of centres in UK defined recurrent IVF failure as a failure to achieve a pregnancy after 3 completed fresh IVF-ET cycles (often excluding FER) (Tan et al 2005)
- Failure to achieve a pregnancy after 3 IVF cycles, in which reasonably good embryos were transferred (Margalioth et al 2006)
- Failure to achieve a pregnancy after a total of 10 or more embryos had been transferred to the uterus (Stern et al 2003)

Recurrent IVF Failure
Recurrent Implantation Failure

- How many cycles? How many embryos?
- Should it refer only to those with good quality embryo replaced?
- Age limit?
- Have standard investigations been performed to establish the underlying causes?

RECURRENT IMPLANTATION FAILURE

- Failure to achieve a clinical pregnancy
- following the transfer of at least four embryos
- in at least 3 fresh or frozen cycles
- in which good quality embryos were transferred
- in women aged less than 40 years

THANKYOU