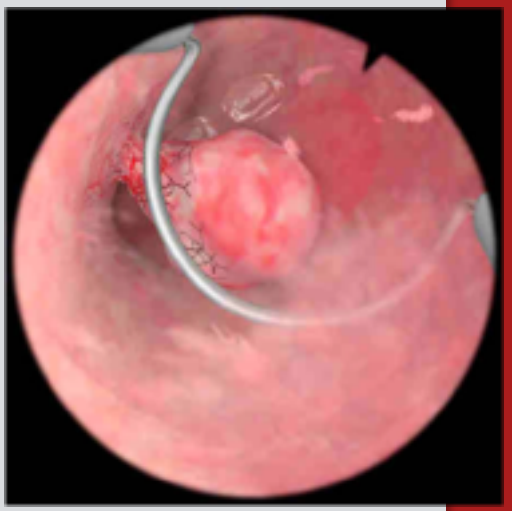
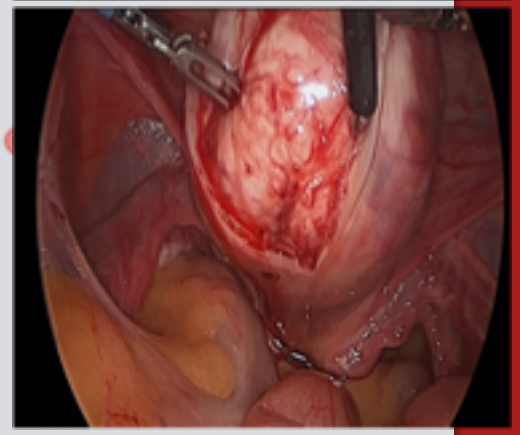
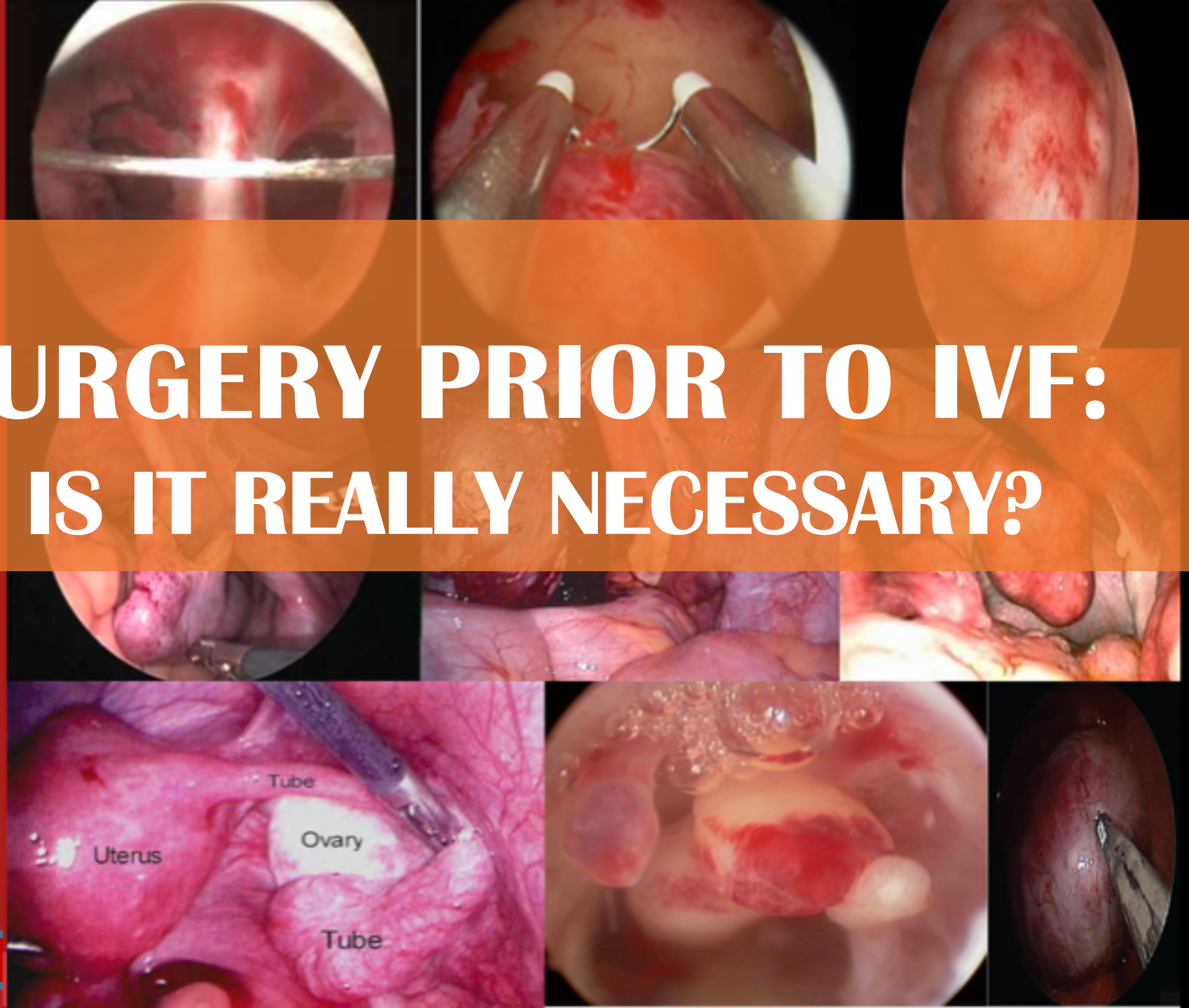
SURGERY PRIOR TO IVF:
IS IT REALLY NECESSARY?

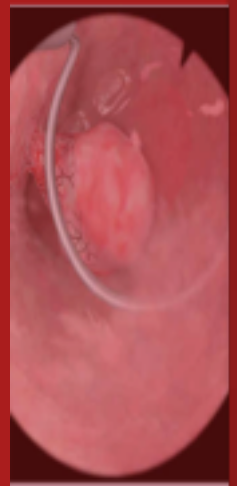
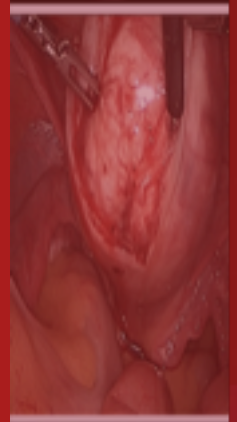
Ina S. Irabon, MD, FPOGS, FPSRM, FPSGE
Obstetrics and Gynecology
Reproductive Endocrinology and Infertility





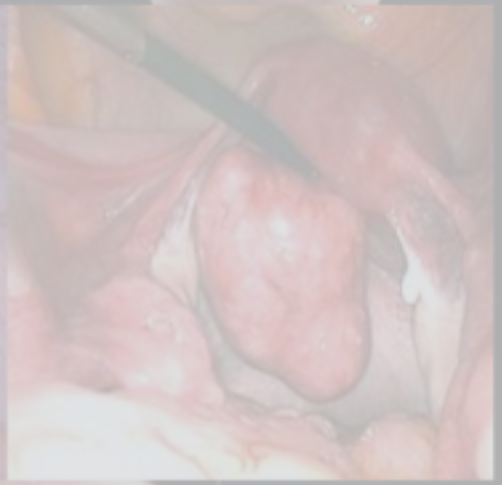
SURGERY PRIOR TO IVF:
IS IT REALLY NECESSARY?



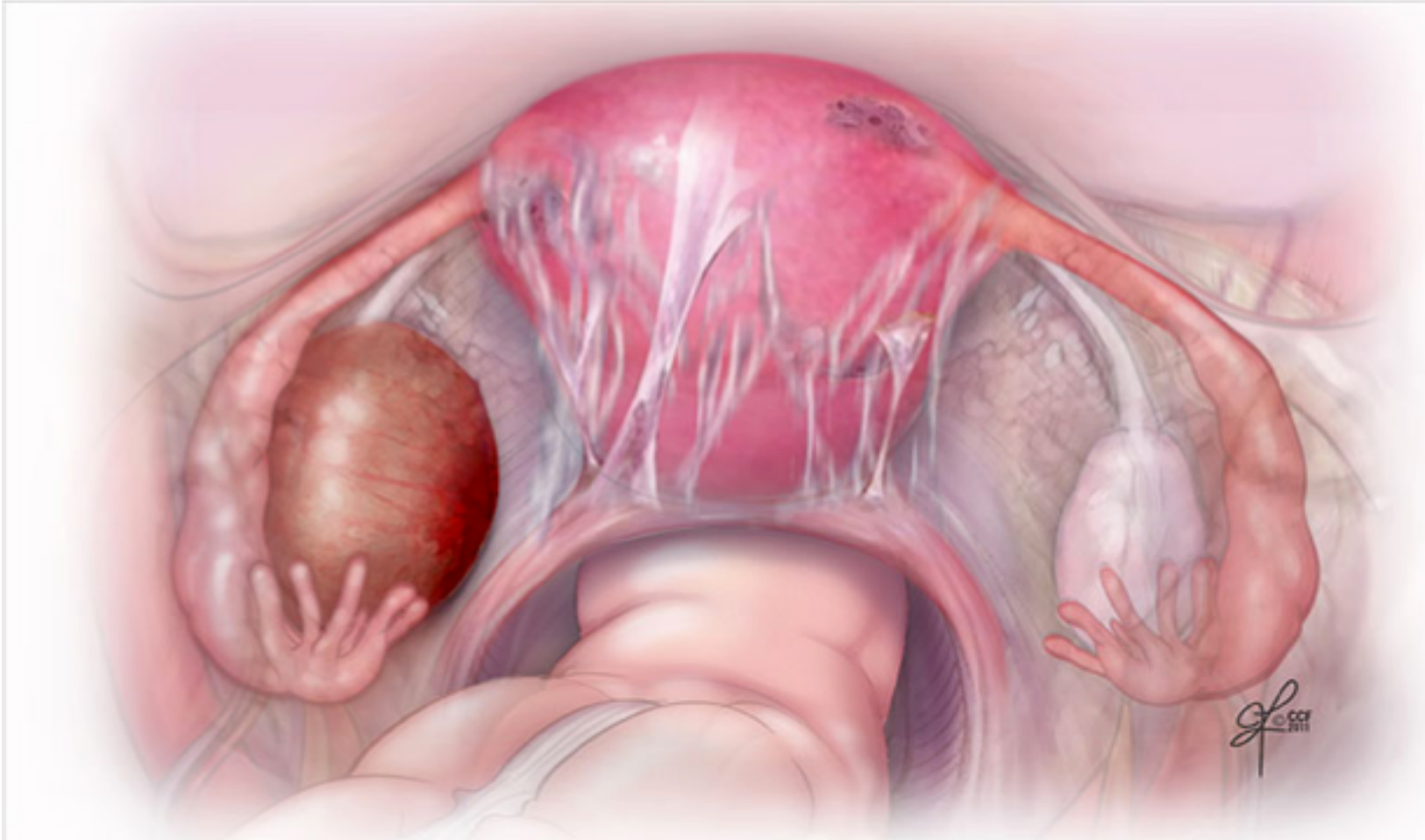




Outline

- Surgery for :
  - Endometriotic cysts
  - Hydrosalpinx
  - Myoma uteri
  - Endometrial polyps
  - Uterine septum
  - Endometrial injury/scratching

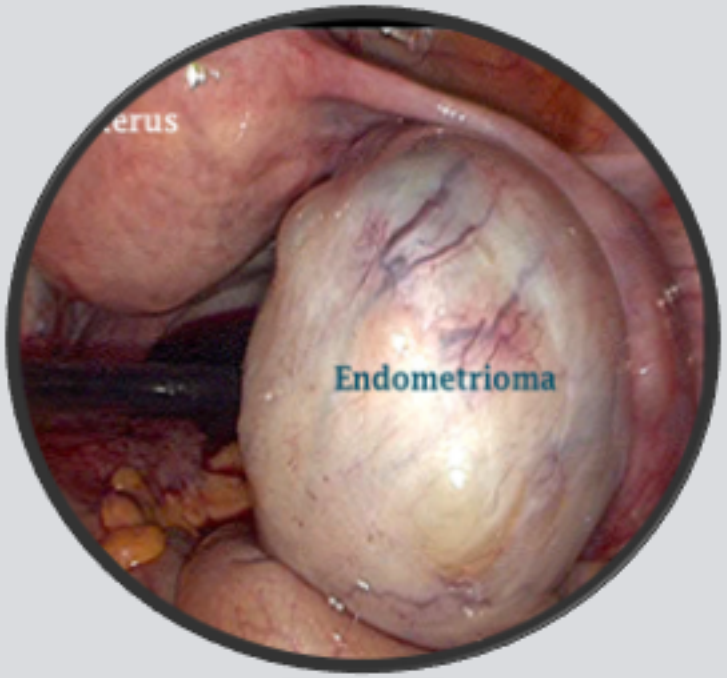


1. Endometriotic cyst



Pelvic Endometriosis

- Affects 6–10% of reproductive-aged women, with a reported higher prevalence among women affected by infertility.
- Ovarian endometrioma(s) can be found in up to 17–44% of women with endometriosis and are often associated with the severe form of the disease.

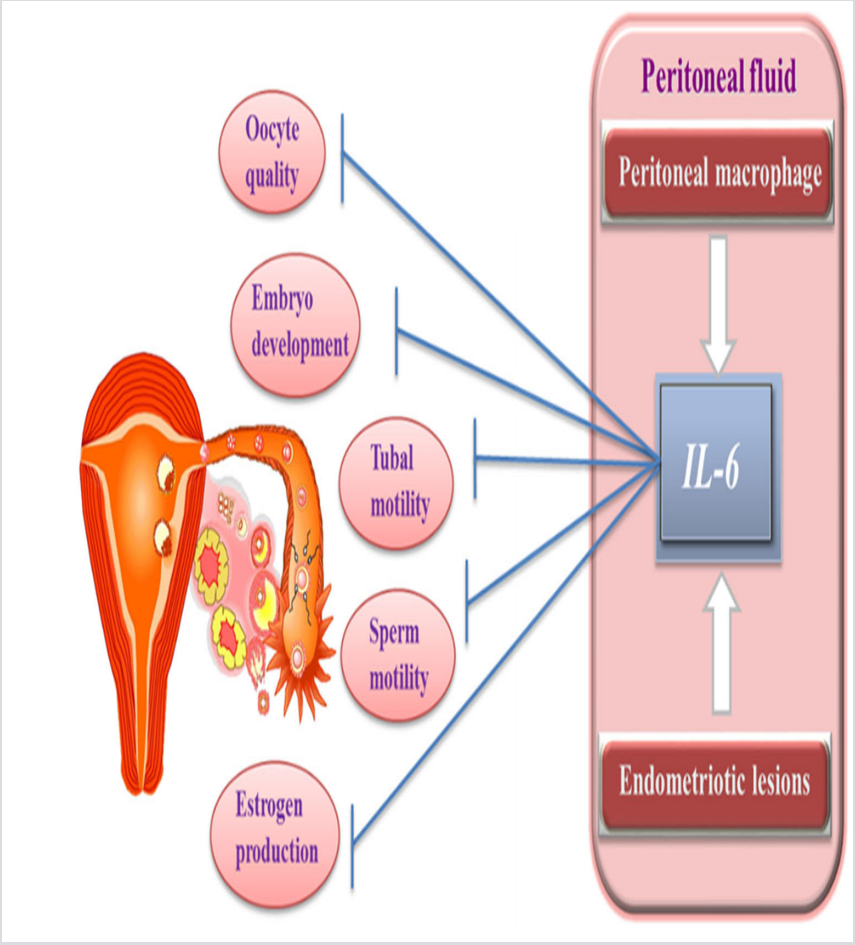


- The presence of an endometrioma can often present a clinical dilemma during the course of fertility treatment.

Jayaprakasan K, Becker C, Mittal M on behalf of the Royal College of Obstetricians and Gynaecologists. The Effect of Surgery for Endometriomas on Fertility. Scientific Impact Paper No. 55. BJOG 2017; 125:e19–e28.

Endometriosis-related infertility

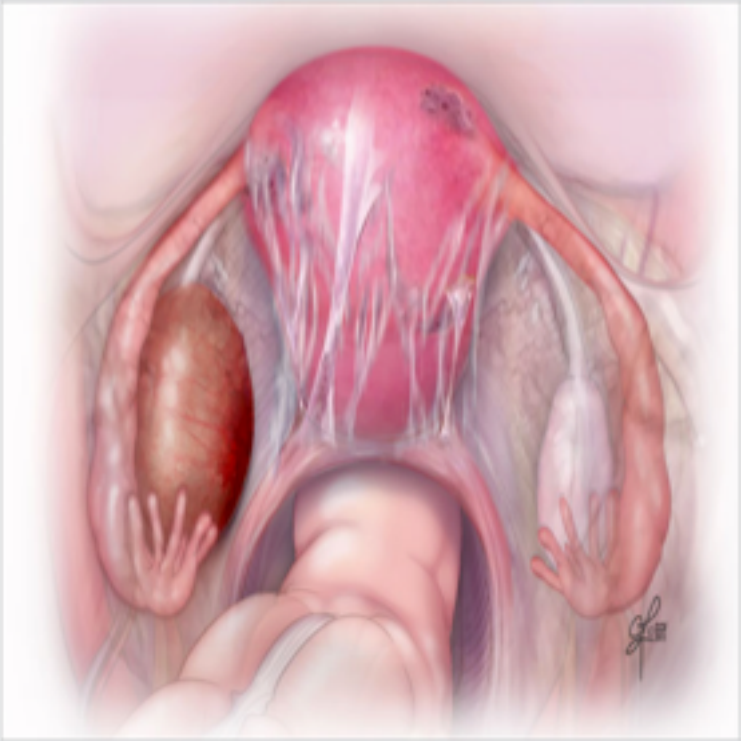
- **Theories:**
  1. Tubo-ovarian anatomic distortion
  2. Chronic inflammation
  3. Reduced endometrial receptivity
  4. Decreased ovarian reserve
  5. Altered oocyte and embryo quality



Jayaprakasan K, Becker C, Mittal M on behalf of the Royal College of Obstetricians and Gynaecologists. The Effect of Surgery for Endometriomas on Fertility. Scientific Impact Paper No. 55. BJOG 2017; 125:e19–e28.

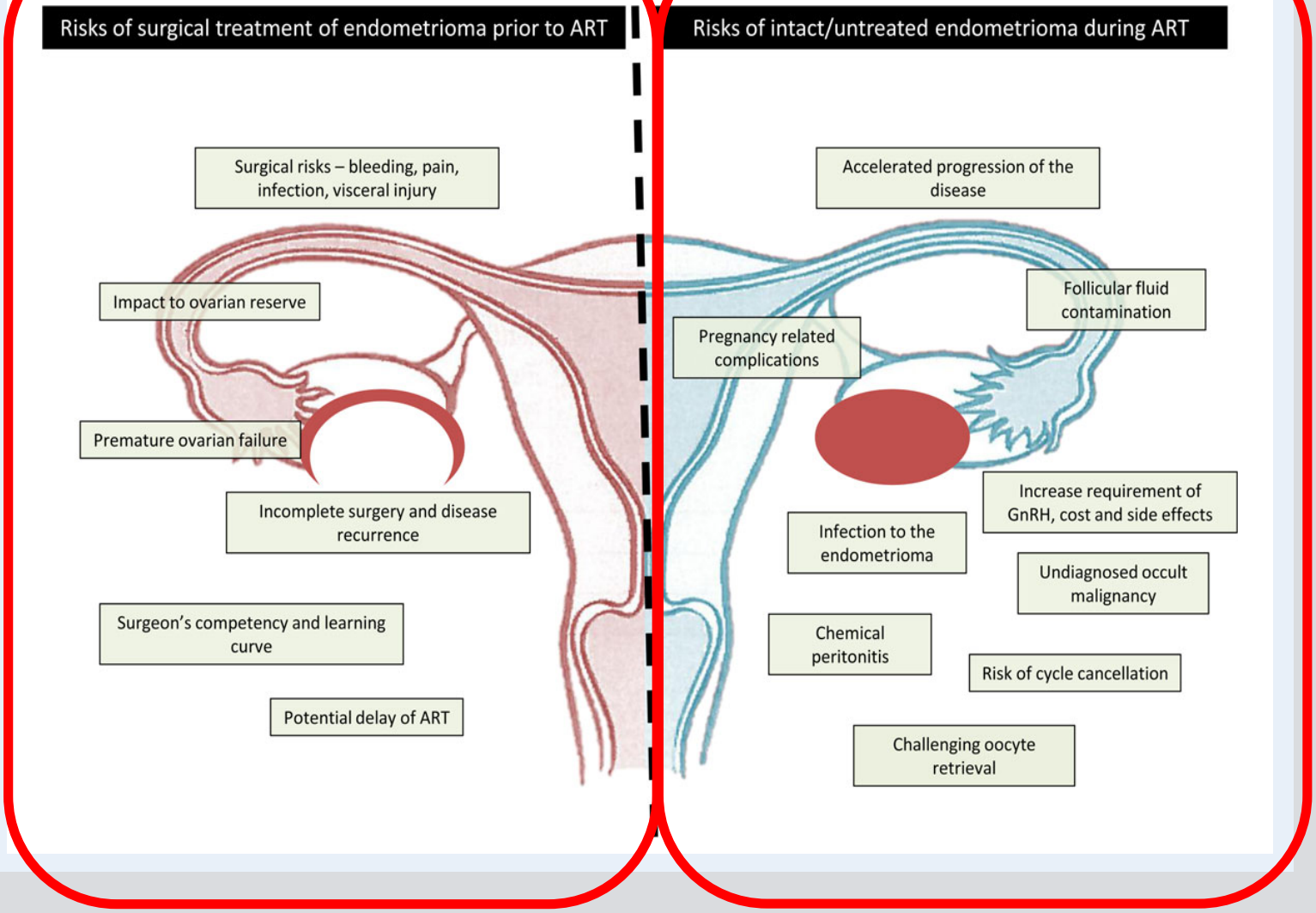
Endometriosis-related infertility

- Surgical treatment of endometriosis and endometrioma prior to IVF/ICSI is widely practiced
- Surgical treatment on endometrioma could be detrimental to ovarian reserve and adversely affect IVF/ICSI reproductive outcomes

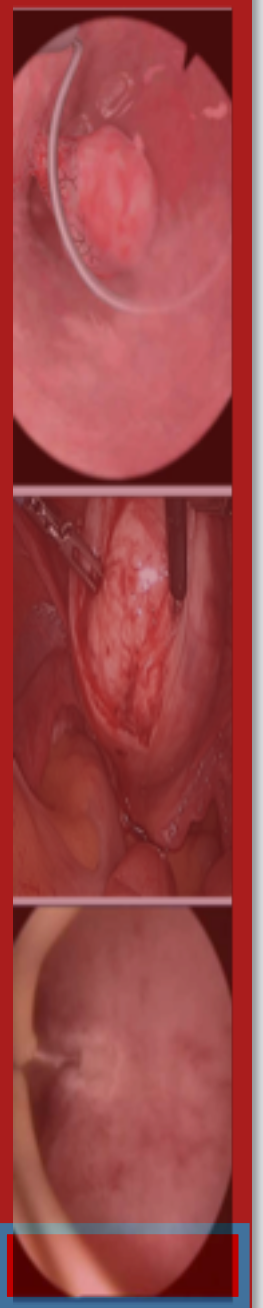


Jayaprakasan K, Becker C, Mittal M on behalf of the Royal College of Obstetricians and Gynaecologists. The Effect of Surgery for Endometriomas on Fertility. Scientific Impact Paper No. 55. BJOG 2017; 125:e19–e28.

Risks of surgical treatment of endometrioma before ART and risks of intact endometrioma during ART.



Hamdan M, Dunselman G, Li TC, Cheong Y. The impact of endometrioma on IVF/ICSI outcomes: a systematic review and metaanalysis. Hum Reprod Update. 2015 Nov-Dec;21(6):809-25. doi: 10.1093/humupd/dmv035. Epub 2015 Jul 12. **Review**.



Endometriosis-related infertility

- Expectant vs surgical management?
- The recommended treatment should be guided by:
  - the woman's symptoms
  - fertility prognostic factors, including age and ovarian reserve
  - previous treatment history
  - nature of the cyst
  - wishes of the woman

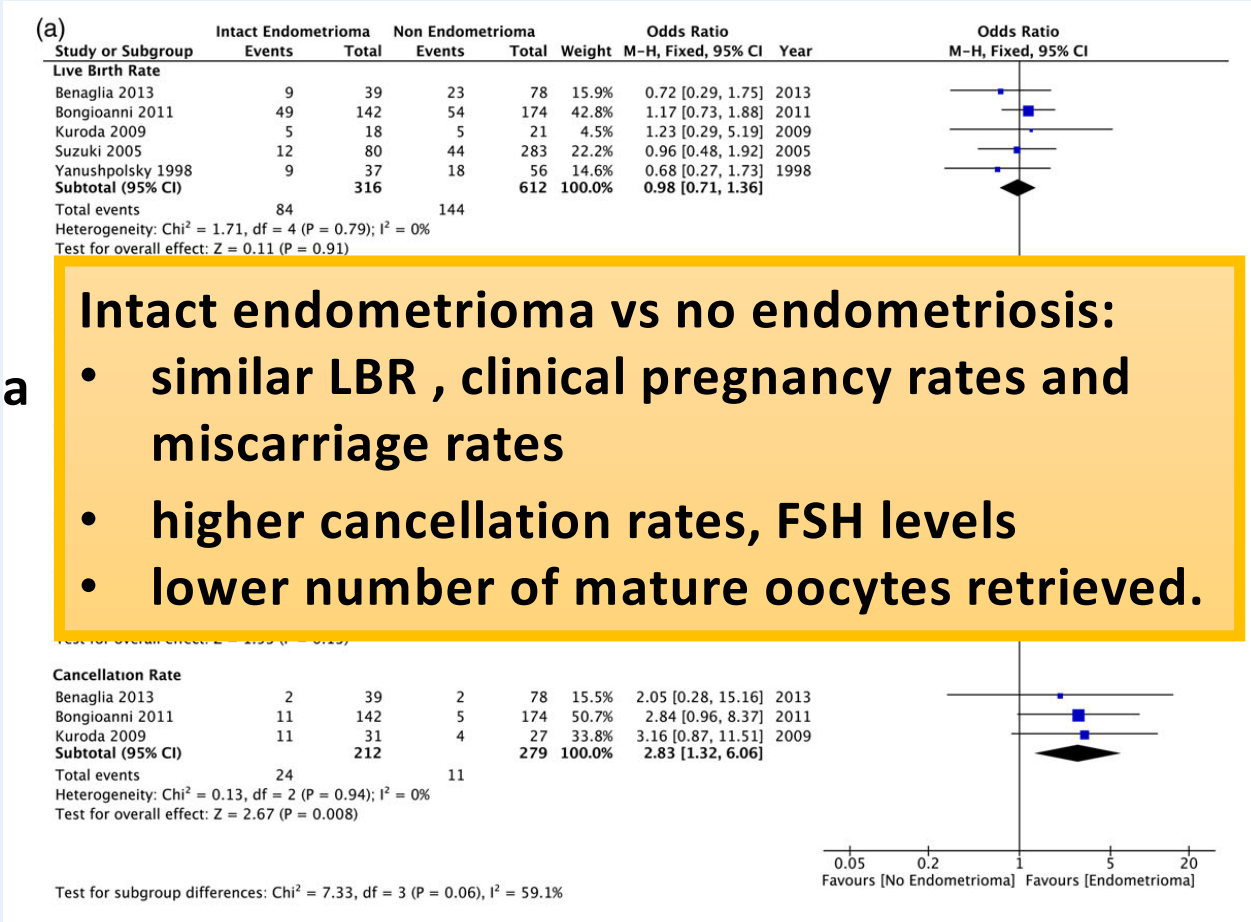
Human Reproduction Update, Vol.21, No.6 pp. 809–825, 2015
Advanced Access publication on July 12, 2015 doi:10.1093/humupd/dmv035

human reproduction update

The impact of endometrioma on IVF/ICSI outcomes: a systematic review and meta-analysis

M. Hamdan[1,2,3], G. Dunselman[4], T.C. Li[5], and Y. Cheong[1,3,*]

Effect of intact endometrioma on IVF/ICSI outcomes

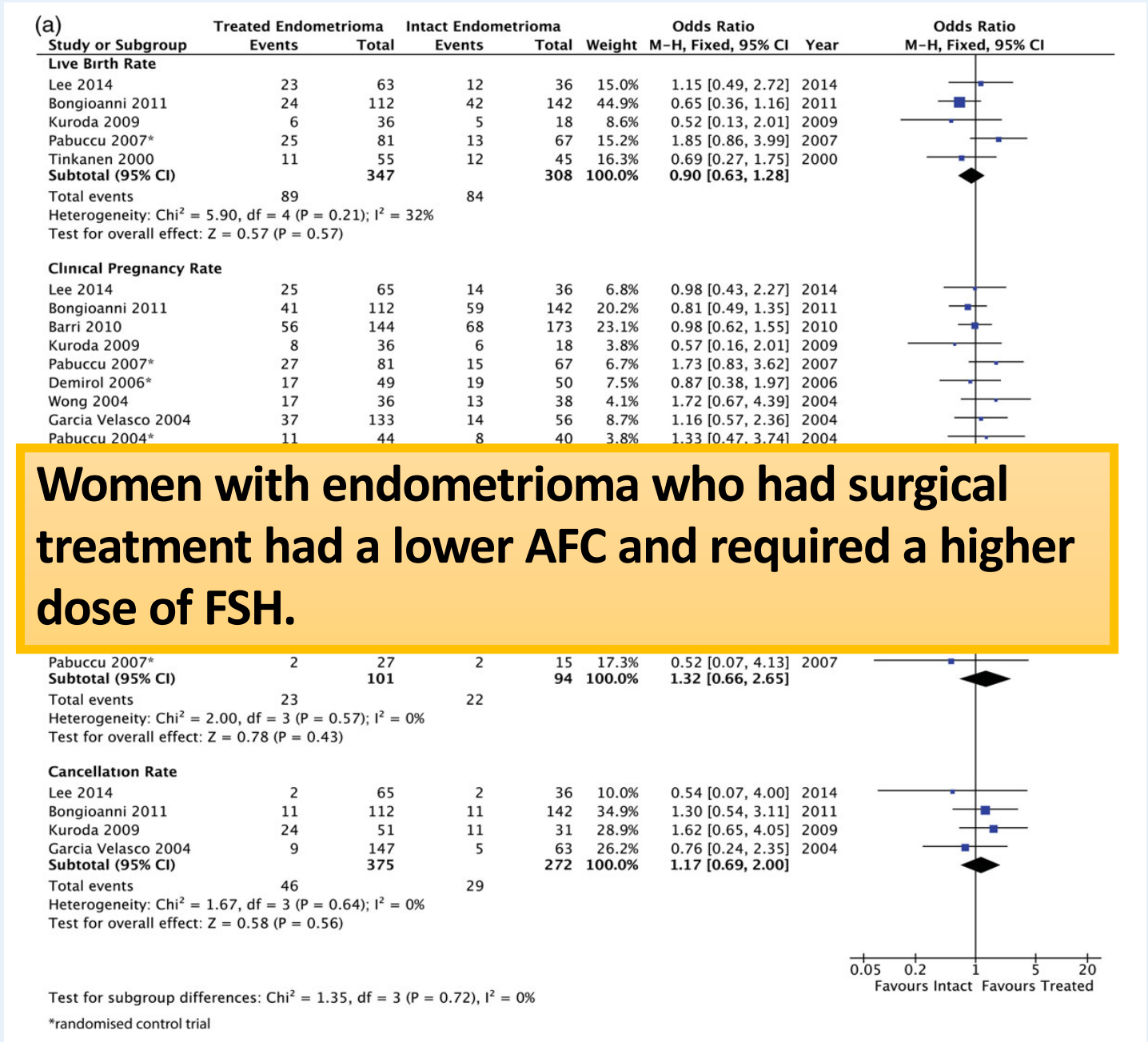


Intact endometrioma vs no endometriosis:

- **similar LBR , clinical pregnancy rates and miscarriage rates**
- **higher cancellation rates, FSH levels**
- **lower number of mature oocytes retrieved.**

Impact of surgical intervention of endometrioma on IVF/ICSI outcomes:

Endometrioma (surgically treated) versus intact endometrioma



Women with endometrioma who had surgical treatment had a lower AFC and required a higher dose of FSH.

Figure 5 (**a**) Forest plot of LBR, CPR, MR and CR for women with treated endometrioma versus intact endometrioma. (**b**) Forest plot of MNOR, Baseline FSH, Total FSH and AFC for women with treated endometrioma versus intact endometrioma.

Human Reproduction, Vol.29, No.3 pp. 400–412, 2014
Advanced Access publication on January 15, 2014 doi:10.1093/humrep/det457

human reproduction

ORIGINAL ARTICLE *ESHRE pages*

ESHRE guideline: management of women with endometriosis†

G.A.J. Dunselman[1,*], N. Vermeulen[2], C. Becker[3], C. Calhaz-Jorge[4], T. D'Hooghe[5], B. De Bie[6], O. Heikinheimo[7], A.W. Horne[8], L. Kiesel[9], A. Nap[10], A. Prentice[11], E. Saridogan[12], D. Soriano[13], and W. Nelen[14]

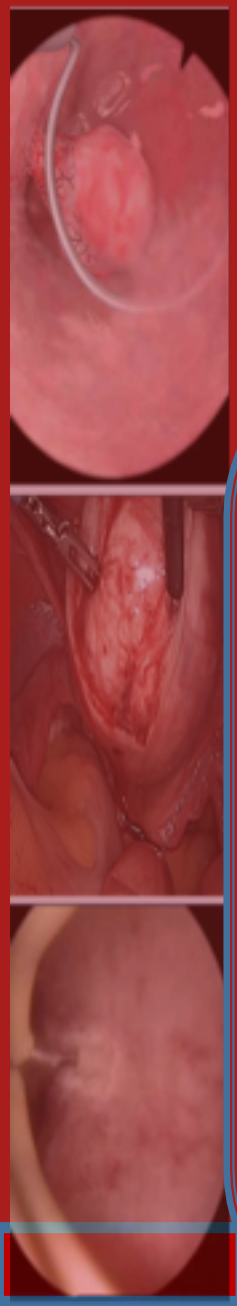
Recommendations:

1. Cystectomy for an endometrioma, prior to undergoing IVF treatment, does not improve pregnancy rates.
2. Surgery prior to ART can be considered for:
    1. management of endometriosis-associated pain
    2. increasing the accessibility of the follicles during oocyte retrieval procedures, or
    3. to ameliorate any concern for malignancy.

Human Reproduction, Vol.29, No.3 pp. 400–412, 2014
Advanced Access publication on January 15, 2014 doi:10.1093/humrep/det457

human reproduction

ORIGINAL ARTICLE *ESHRE pages*



ESHRE guideline: management of women with endometriosis†

Recommendations:

3. Counsel women about the risk of reduced ovarian function following surgical intervention and even the possible risk of an oophorectomy.

4. The decision to proceed with surgery for an endometrioma should be carefully considered:

    1. Age of the woman
    2. ovarian reserve status
    3. unilaterality /bilaterality of the disease
    4. number and size of the cysts
    5. symptoms
    6. presence or absence of suspicious radiological features
    7. extent of extraovarian disease
    8. history of previous ovarian surgery.

Interventions for women with endometrioma prior to assisted reproductive technology (Review)

Benschop L, Farquhar C, van der Poel N, Heineman MJ

Cochrane Database of Systematic Reviews 2010, Issue 11. Art. No.: CD008571.

Results:

- Aspiration was associated with greater number of mature oocytes retrieved (MD 0.50, 95% CI 0.02 to 0.98) and increased ovarian response (E2 levels on day of hCG injection) (MD 685.3, 95% CI 464.50 to 906.10) compared to expectant management.
- Aspiration versus cystectomy showed no evidence of a difference in CPR or the NMOR.

Human Reproduction, Vol.24, No.3 pp. 496–501, 2009
Advanced Access publication on December 4, 2008 doi:10.1093/humrep/den398

human reproduction OPINION

Management of endometriomas in women requiring IVF: to touch or not to touch

Juan A. Garcia-Velasco[1,*] and Edgardo Somigliana[2]

Recommendations:

1. Laparoscopic surgical removal of ovarian endometriotic cysts prior to IVF does not offer any additional benefit in terms of fertility outcomes.

2. We recommend proceeding directly to IVF to reduce time to pregnancy, to avoid potential surgical complications and to limit patient costs.

3. Surgery should be reserved for specific cases such as: treat concomitant **pain symptoms** or **when malignancy cannot be reliably ruled out**, or in the **presence of large cysts**.

Human Reproduction, Vol.24, No.3 pp. 496–501, 2009
Advanced Access publication on December 4, 2008 doi:10.1093/humrep/den398

human reproduction OPINION

Management of endometriomas in women requiring IVF: to touch or not to touch

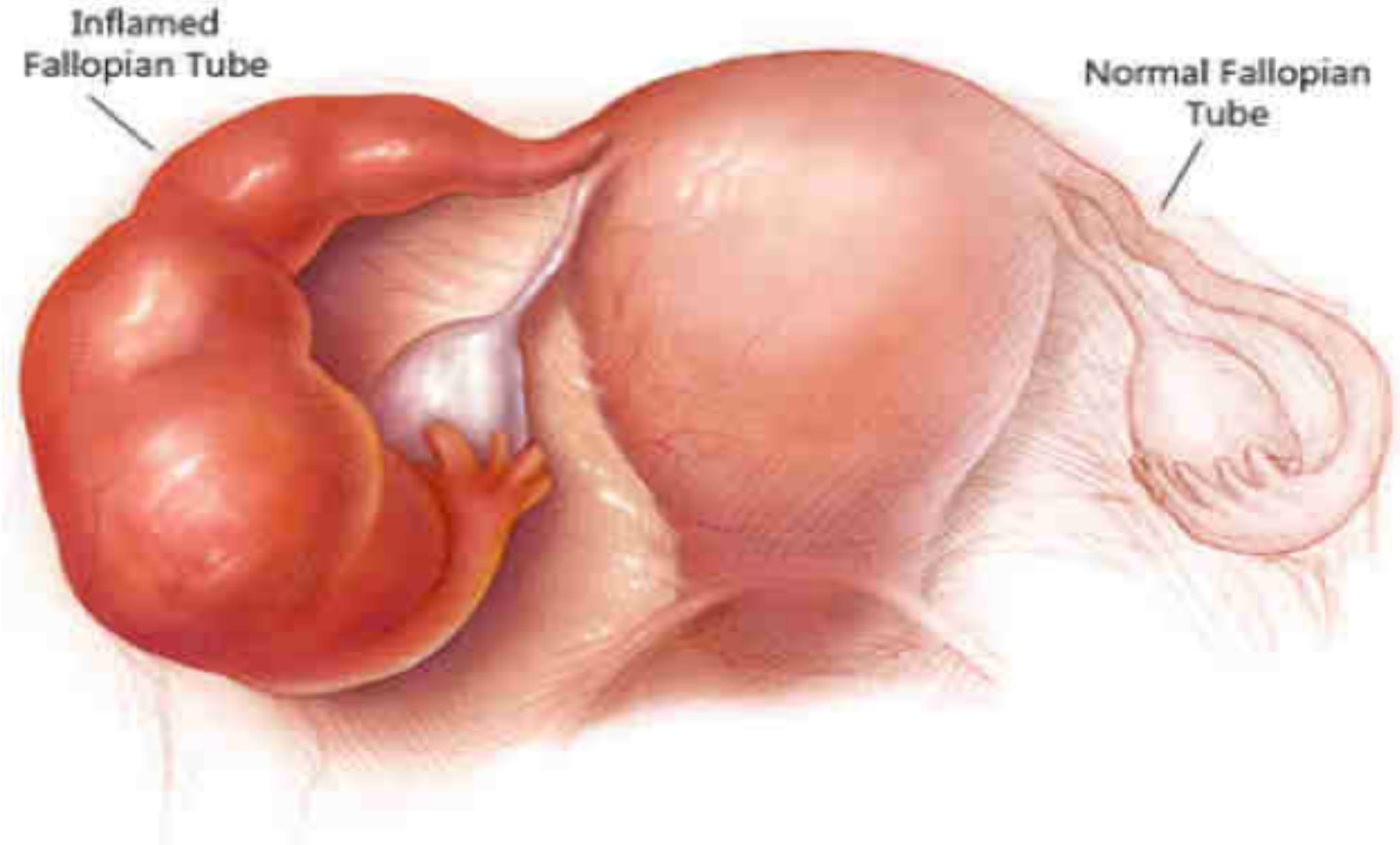
Juan A. Garcia-Velasco[1,*] and Edgardo Somigliana[2]

Table I Clinical variables to be considered when deciding whether to perform surgery or not in women with endometriomas selected for IVF

Characteristics	Favours surgery	Favours expectant management
Previous interventions for endometriosis	None	≥ I
Ovarian reserve[a]	Intact	Damaged
Pain symptoms	Present	Absent
Bilaterality	Monolateral disease	Bilateral disease
Sonographic feature of malignancy[b]	Present	Absent
Growth	Rapid growth	Stable

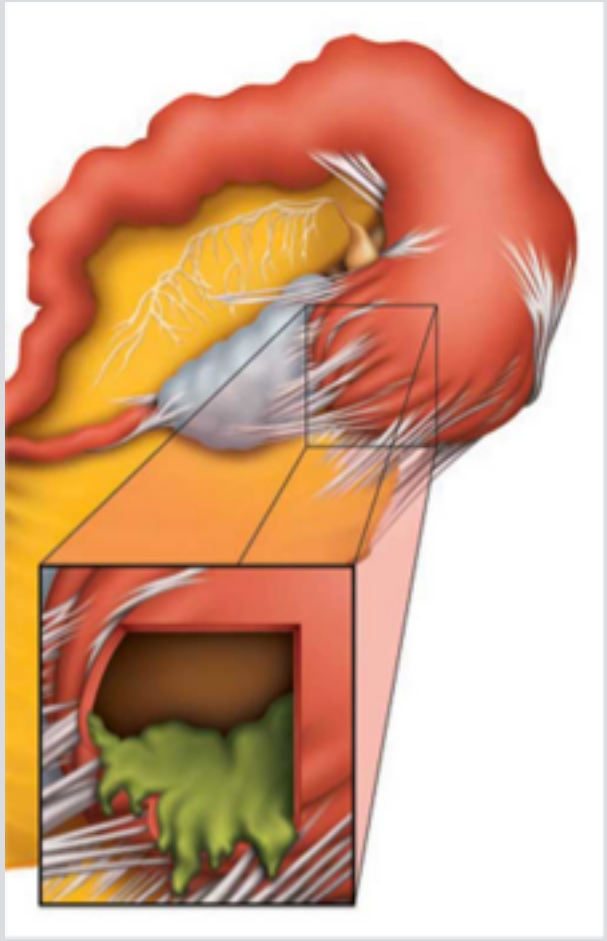
[a]Ovarian reserve is estimated based on serum markers or previous hyperstimulation cycles; [b]sonographic feature of malignancy refers to solid components, locularity, echogeniety, regularity of shape, wall, septa, location and presence of peritonal fluid.

2. Hydrosalpinx



Hydrosalpinx AND IVF

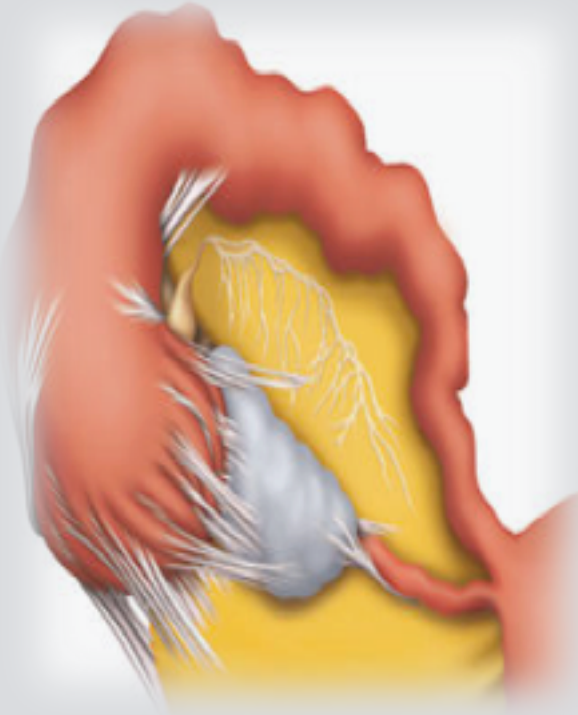
- Lower live birth rate of patients with hydrosalpinges undergoing IVF
- The adverse impact of hydrosalpinges on implantation may be attributed to:
    1. direct embryotoxic effect
    2. mechanical effect (accumulated fluid may flush the embryo out of the uterus)
    3. negative effect on endometrial receptivity.
    4. Low leukaemia inhibitory factor (cytokine essential for successful implantation)



Coughlan C, Ledger W, Wang Q, Liu F, Demirol A, Gurgan T, Cutting R, Ong K, Sallam H, Li TC. Recurrent implantation faiklure: definition and management. Reprod Biomed Online. 2014 Jan;28(1):14-38. doi: 10.1016/j.rbmo.2013.08.011. Epub 2013 Sep 14. Review.

Hydrosalpinx AND IVF

- Salpingectomy before embryo transfer has been shown to improve endometrial receptivity.
- A prophylactic salpingectomy prior to IVF is done to eliminate possible tubal inflammation and toxins that might damage the embryo.
- Studies have reported enhanced ovarian response and increased pregnancy rates following salpingectomy.



Zhang Y, Sun Y, Guo Y, Li, Tin C, Duan H.Salpingectomy and Proximal Tubal Occlusion for Hydrosalpinx Prior to In Vitro Fertilization : A Meta-analysis of Randomized Controlled Trials. Obstetrical & Gynecological Survey. January 2015, Volume 70 (1), p 33–38

Volume 70, Number 1
OBSTETRICAL AND GYNECOLOGICAL SURVEY

Salpingectomy and Proximal Tubal Occlusion for Hydrosalpinx Prior to In Vitro Fertilization: A Meta-analysis of Randomized Controlled Trials

Ying Zhang, MD,* Yurong Sun, MD,† Yinshu Guo, MD,‡ Tin Chiu Li, PhD,§ and Hua Duan, MD¶

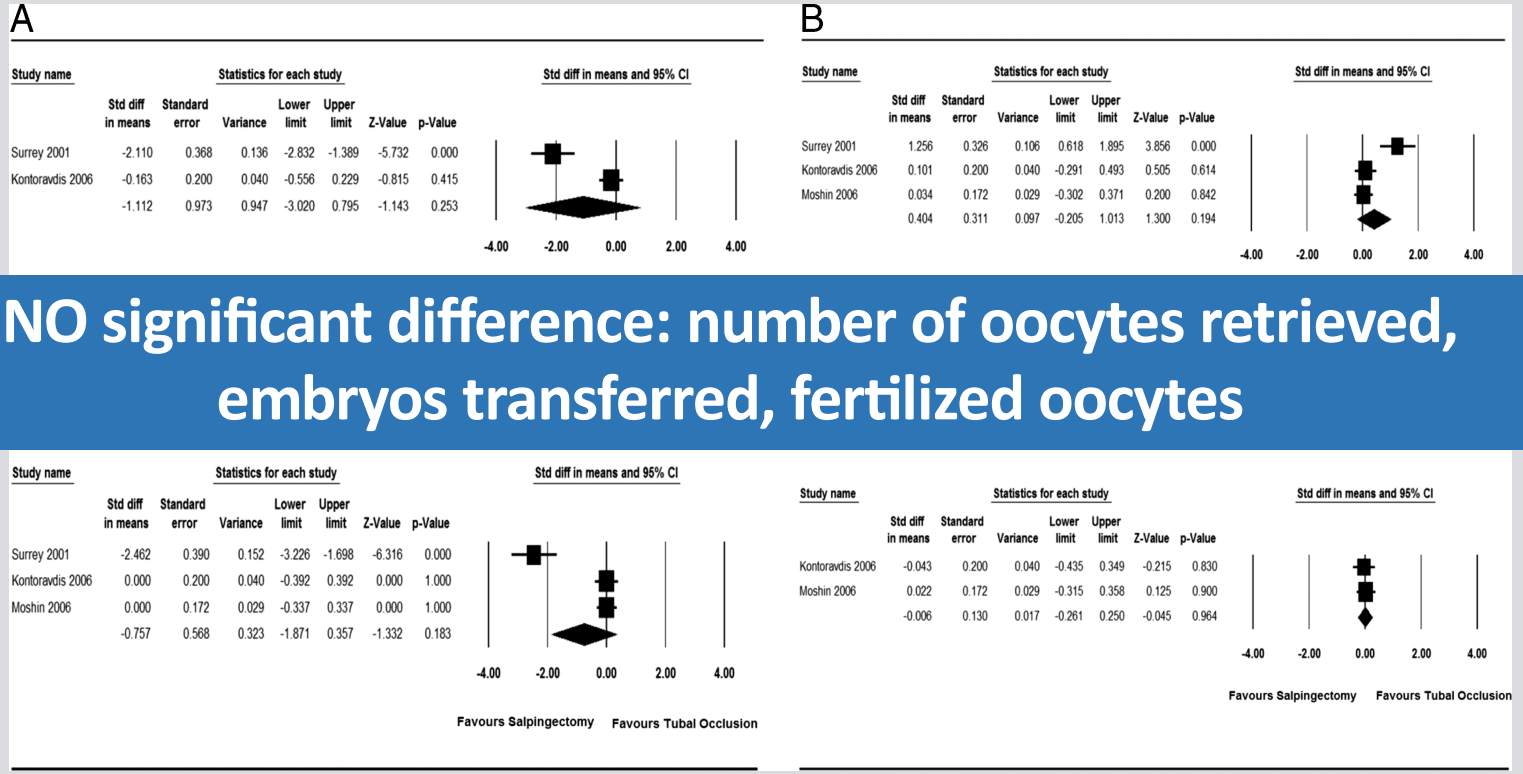


FIG. 2. Forest plot for the aggregate ovarian response in hydrosalpinx patients treated with salpingectomy or proximal tubal occlusion prior to IVF. A, The response days to controlled ovarian hyperstimulation. B, The number of oocytes retrieved. C, The embryos transferred per cycle. D, Fertilized oocytes.

Volume 70, Number 1
OBSTETRICAL AND GYNECOLOGICAL SURVEY

Salpingectomy and Proximal Tubal Occlusion for Hydrosalpinx Prior to In Vitro Fertilization: A Meta-analysis of Randomized Controlled Trials

Ying Zhang, MD,* Yurong Sun, MD,† Yinshu Guo, MD,‡ Tin Chiu Li, PhD,§ and Hua Duan, MD¶

NO significant difference: clinical pregnancy rate and implantation rate

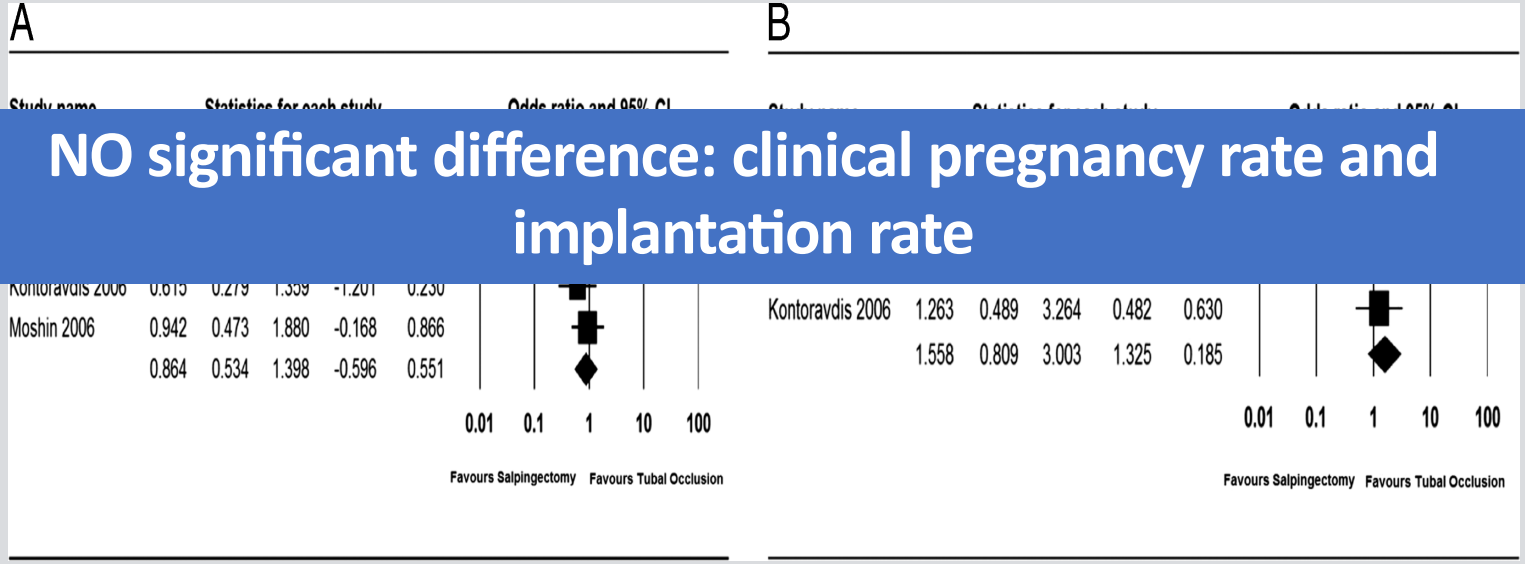


FIG. 3. Forest plot for the aggregate pregnancy outcomes in hydrosalpinx patients treated with salpingectomy or proximal tubal occlusion prior to IVF. A, The clinical pregnancy rate. B, The implantation rate.

BMC Women's Health

Ultrasound guided aspiration of hydrosalpinx fluid versus salpingectomy in the management of patients with ultrasound visible hydrosalpinx undergoing IVF-ET: a randomized controlled trial

Usama M Fouda*, Ahmed M Sayed, Hatem I Abdelmoty and Khaled A Elsetohy *BMC Women's Health* (2015) 15:21

Table 2 IVF cycle characteristics

	Salpingectomy group (n = 80)	Aspiration group (n = 80)	*P* value
Stimulation period (days)	11.4 ± 1.13	11.68 ± 1.52	0.197
Consumed HP-uFSH units	2752.5 ± 664.5	2869.5 ± 681.75	0.272
Follicles > 18 mm on the day of HCG administration	10.93 ± 4.35	11.33 ± 4.76	0.580
Fertilization rate	551/688 (80.09%)	585/737 (79.38%)	0.742
No. of embryos transferred	2.53 ± 0.5	2.57 ± 0.49	0.691
Grade I & II embryos /transferred embryos	146/190 (76.84%)	153/195 (78.46%)	0.715

Values are expressed as mean ± SD or n/n (%).

NO significant difference: FSH dose, # of follicles, retrieved oocytes, metaphase oocytes, fertilization rate, # of embryos transferred

BMC Women's Health

Ultrasound guided aspiration of hydrosalpinx fluid versus salpingectomy in the management of patients with ultrasound visible hydrosalpinx undergoing IVF-ET: a randomized controlled trial

Usama M Fouda*, Ahmed M Sayed, Hatem I Abdelmoty and Khaled A Elsetohy *BMC Women's Health* (2015) 15:21

Table 3 Reproductive outcomes

	Salpingectomy group (n = 80)	Aspiration group (n = 80)	Odd ratio (95% CI)	P value
No. of transfer cycles	75	76		
Clinical pregnancy/started cycle	32/80 (40%)	22/80 (27.5%)	1.76 (0.9,3.41)	0.132
Implantation rate	36/190 (18.95%)	25/195 (12.82%)	1.59 (0.91,2.77)	0.124
Spontaneous abortion rate n/IUP	3/32 (9.38%)	3/22 (13.64%)	0.66 (0.12, 3.59)	0.678

Values are expressed as n/n (%) unless otherwise indicated. IUP = intrauterine pregnancy.

NO significant difference: clinical pregnancy rate, ongoing pregnancy rate, implantation rate

BMC Women's Health

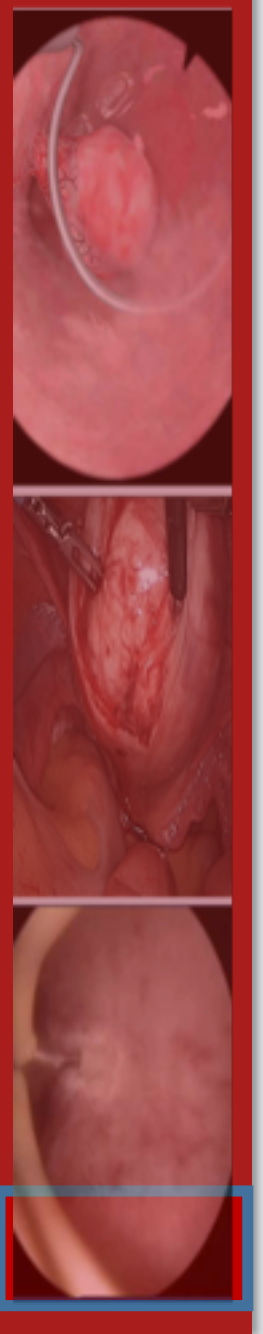
Ultrasound guided aspiration of hydrosalpinx fluid versus salpingectomy in the management of patients with ultrasound visible hydrosalpinx undergoing IVF-ET: a randomized controlled trial

Usama M Fouda*, Ahmed M Sayed, Hatem I Abdelmoty and Khaled A Elsetohy *BMC Women's Health* (2015) 15:21

Table 4 Patients' characteristics and reproductive outcomes per transfer cycle in the salpingectomy group and the subgroups of the aspiration group

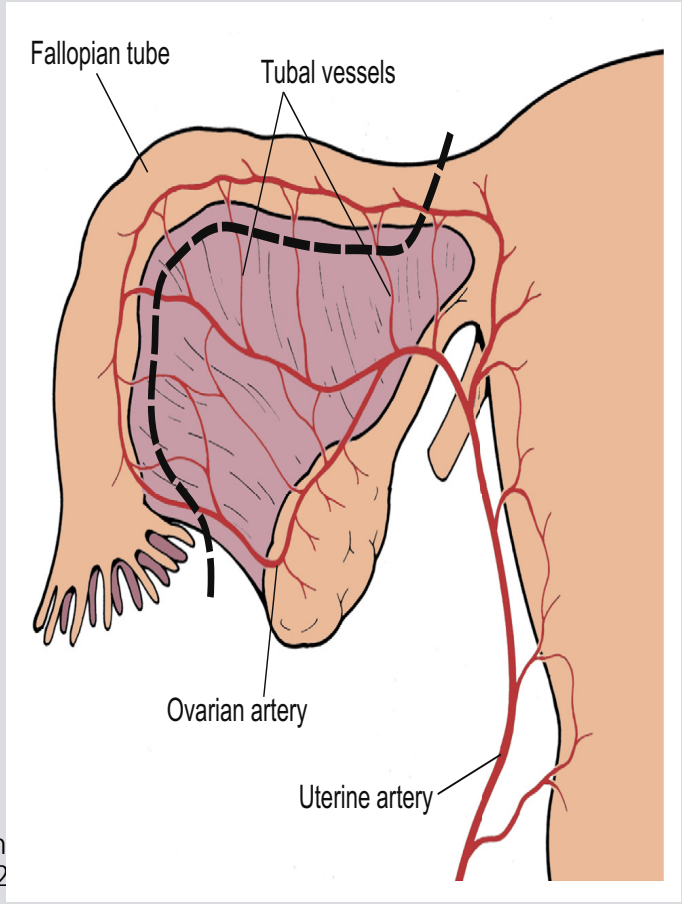
	Salpingectomy (Group 1)	No re-accumulation of hydrosalpinx fluid (Group 2)	Re-accumulation of hydrosalpinx fluid (Group 3)	G1 Vs G2	G1 Vs G3	G2 Vs G3
No. of transfer cycles	75	50	26			
Age	27.92 ± 3.59	28.2 ± 3.63	27.04 ± 3.01	0.672	0.228	0.143
Body mass index (Kg/m^2)	25.68 ± 2.03	25.36 ± 1.96	25.19 ± 1.81	0.379	0.257	0.711
Bilateral hydrosalpinx	15/75 (20%)	12/50 (24%)	7/26 (26.92%)	0.660	0.582	0.786
Duration of infertility	3.56 ± 1.8	3.26 ± 1.69	3.54 ± 2	0.346	0.962	0.548
Basal FSH (IU/L)	6.35 ± 2.09	6.29 ± 2.17	5.81 ± 1.68	0.872	0.188	0.288
No. of embryos transferred	2.53 ± 0.5	2.58 ± 0.49	2.54 ± 0.51	0.61	0.965	0.735
Grade I & II embryos/ transferred embryos	146/190 (76.84%)	103/129 (79.84%)	50/66 (75.76%)	0.582	0.867	0.582
Implantation rate	36/190 (18.95%)	20/129 (15.5%)	5/66 (7.58%)	0.457	0.032	0.173
Clinical pregnancy	32/75 (42.67%)	17/50 (34%)	5/26 (19.23%)	0.356	0.036	0.286
Ongoing pregnancy	29/75 (38.67%)	15/50 (30%)	4/26 (15.38%)	0.346	0.031	0.264

Values are expressed as n/n (%) unless otherwise indicated, G = group.



SALPINGECTOMY PRIOR TO IVF

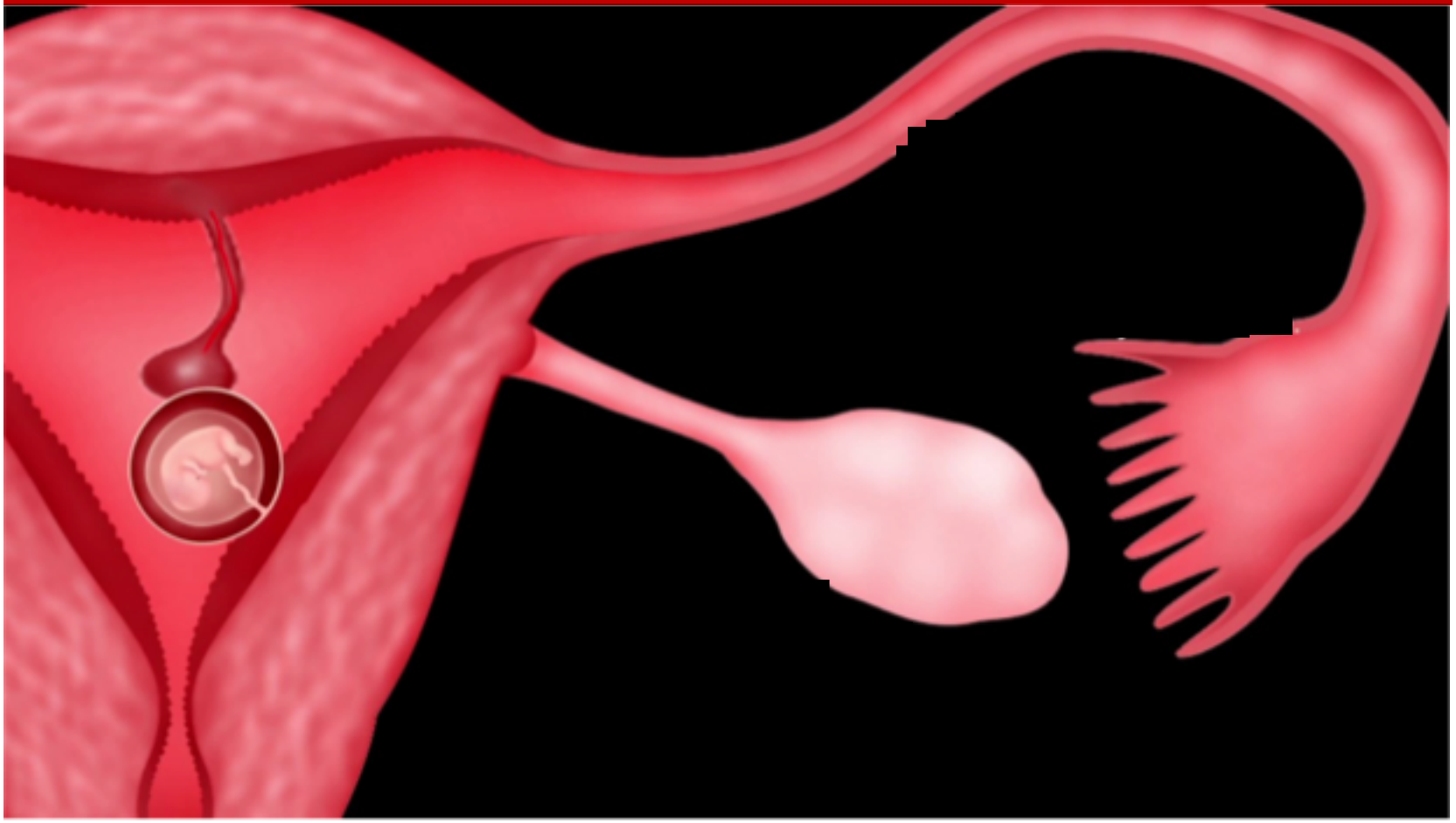
- Diathermize and incise as close to the fallopian tube as possible and as far away from the ovary as possible to avoid disruption to the ovarian blood supply
- Salpingectomy had no short-term effect on serum AMH levels



Coughlan C, Ledger W, Wang Q, Liu F, Demirol A, Gurgan T, Cutting R, On faiklure: definition and management. Reprod Biomed Online. 2014 Jan;2 10.1016/j.rbmo.2013.08.011. Epub 2013 Sep 14. Review.

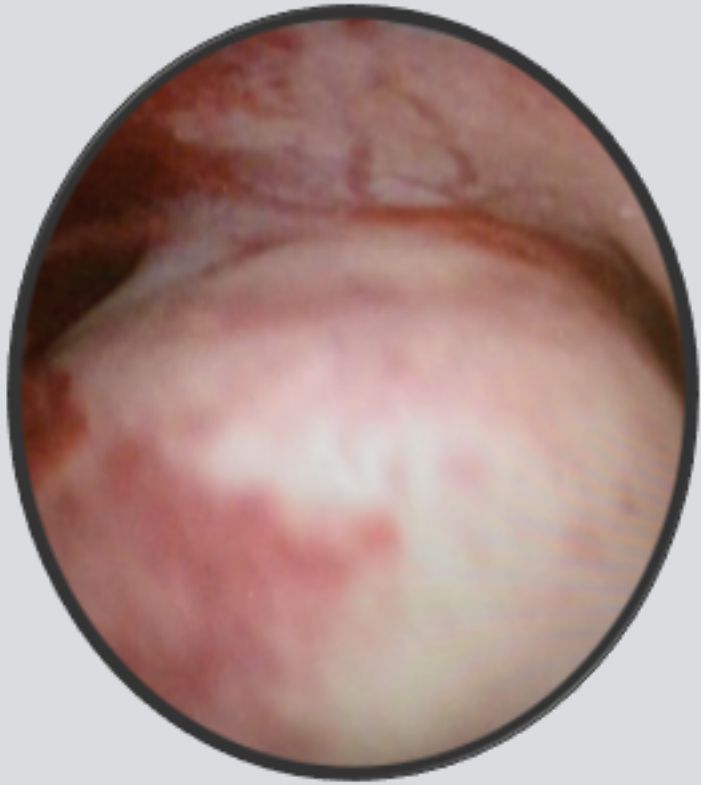
Grynnerup AG, Lindhard A, Sorensen S, Orskov M, Petersen K, Madsen L, Pilsgaard F, Lossi K, Pinborg A. Serum AMH concventration before and after salpingectomy for ectopic pregnancy. Reproductive Biomedicine Online 2018 August. 37:2; pp145-152.

3. Endometrial polyps



ENDOMETRIAL POLYPS AND INFERTILITY

- Polyps are common among women with unexplained infertility and repeated implantation failure following IVF
- For asymptomatic women undergoing IVF, prevalence of endometrial polyps (as determined by hysteroscopy): 6-8%

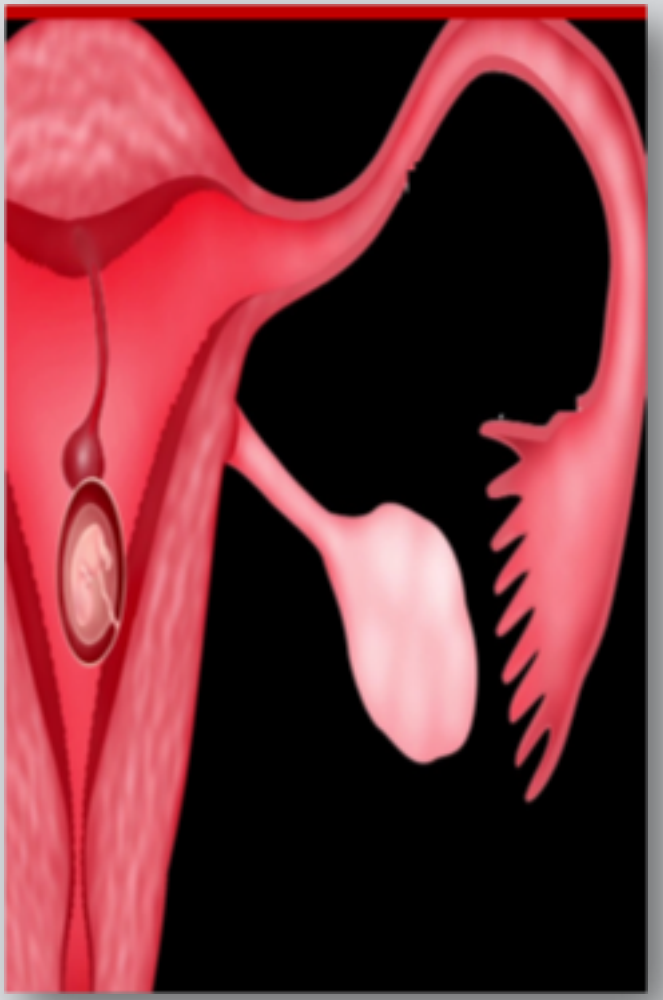


Kodaman PH. Hysteroscopic polypectomy for women undergoing IVF treatment: when is it necessary? Curr Opin Obstet Gynecol 2016, 28::184-90

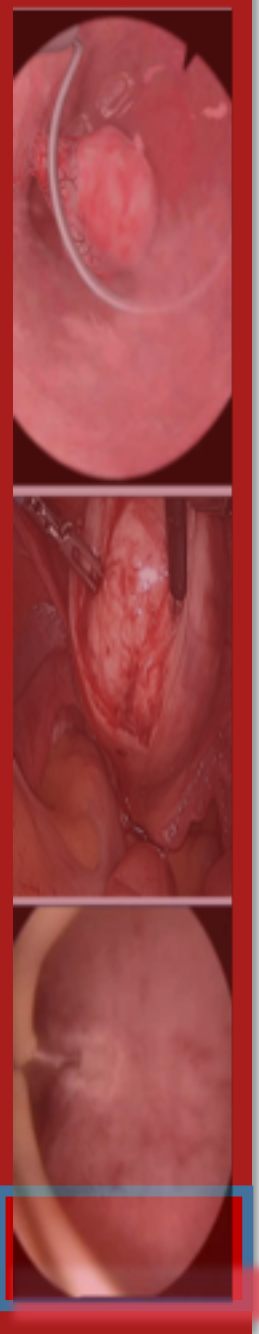
ENDOMETRIAL POLYPS AND INFERTILITY

Detrimental effects of polyp on fertility:

- Remains incompletely understood
- May be an underlying cause of unexplained infertility
- Several potential mechanisms:
  - Mechanical obstruction of the ostium such that sperm and/or embryo transport is hindered
  - Inflammatory changes
  - Altered endometrial receptivity
  - Elevated glycodelin levels may impair sperm binding to the zona pelucida

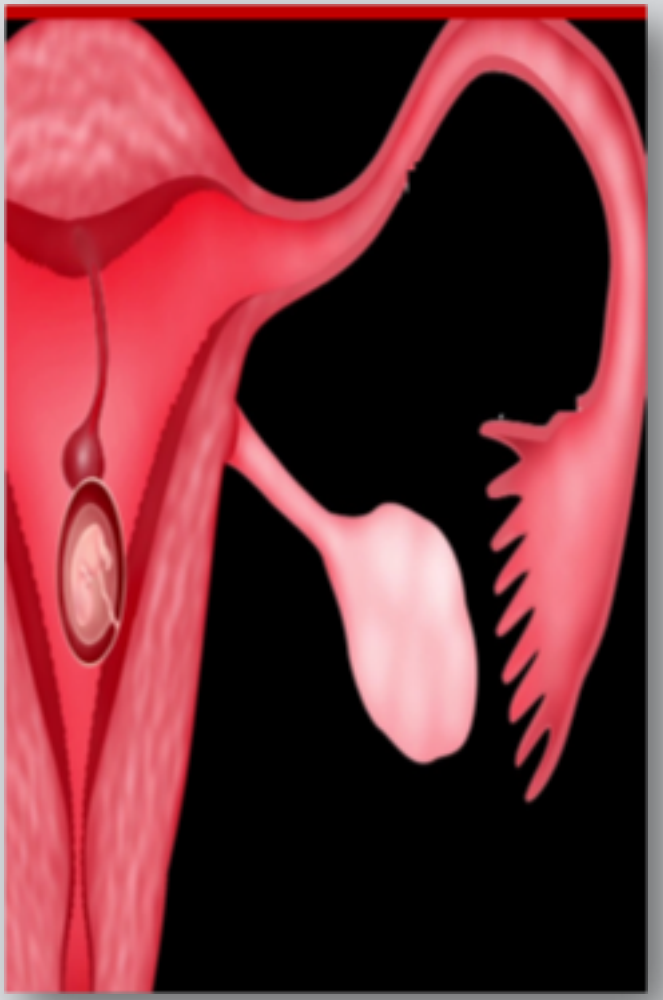


Kodaman PH. Hysteroscopic polypectomy for women undergoing IVF treatment: when is it necessary? Curr Opin Obstet Gynecol 2016, 28::184-90



HYSTEROSCOPIC POLYPECTOMY AND FERTILITY

- hysteroscopic polypectomy is generally recommended to restore normal anatomy prior to fertility treatments.
- There is sufficient data to support hysteroscopy if a polyp is discovered incidentally or otherwise.
- Hysteroscopy should be strongly considered *after a failed IVF cycle and in the setting of recurrent implantation failure.*



Kodaman PH. Hysteroscopic polypectomy for women undergoing IVF treatment: when is it necessary? Curr Opin Obstet Gynecol 2016, 28::184-90

HYSTEROSCOPIC POLYPECTOMY AND FERTILITY

Human Reproduction Vol.20, No.6 pp. 1632–1635, 2005
Advance Access publication March 10, 2005
doi:10.1093/humrep/deh822

Endometrial polyps and their implication in the pregnancy rates of patients undergoing intrauterine insemination: a prospective, randomized study

Tirso Pérez-Medina[1], José Bajo-Arenas, Francisco Salazar, Teresa Redondo, Luis Sanfrutos, Pilar Alvarez and Virginia Engels

Table II. Number and percentage of pregnancies after hysteroscopic polypectomy ($n = 204$)

	Polypectomy		*P*-value
	Study ($n = 101$)	Control ($n = 103$)	
Pregnancy (%)			<0.001
Yes	64 (63.4)	29 (28.2)	
No	37 (36.6)	74 (71.8)	

RR 2.1 (95% CI 1.5–2.9).

HYSTEROSCOPY after failed IVF

RBM Online - Vol 16. No 5. 2008 712-719 Reproductive BioMedicine Online; www.rbmonline.com/Article/3207 on web 11 March 2008

Article

Outpatient hysteroscopy and subsequent IVF cycle outcome: a systematic review and meta-analysis

Tarek El-Toukhy[1], Sesh Kamal Sunkara, Arri Coomarasamy, Jan Grace, Yakoub Khalaf
Assisted Conception Unit, Guy's and St. Thomas' Hospital NHS Foundation Trust, London SE1 9RT, UK
[1]Correspondence: Tel: +44 207 188 0496; Fax: +44 207 188 0490; e-mail: tarekeltoukhy@hotmail.com

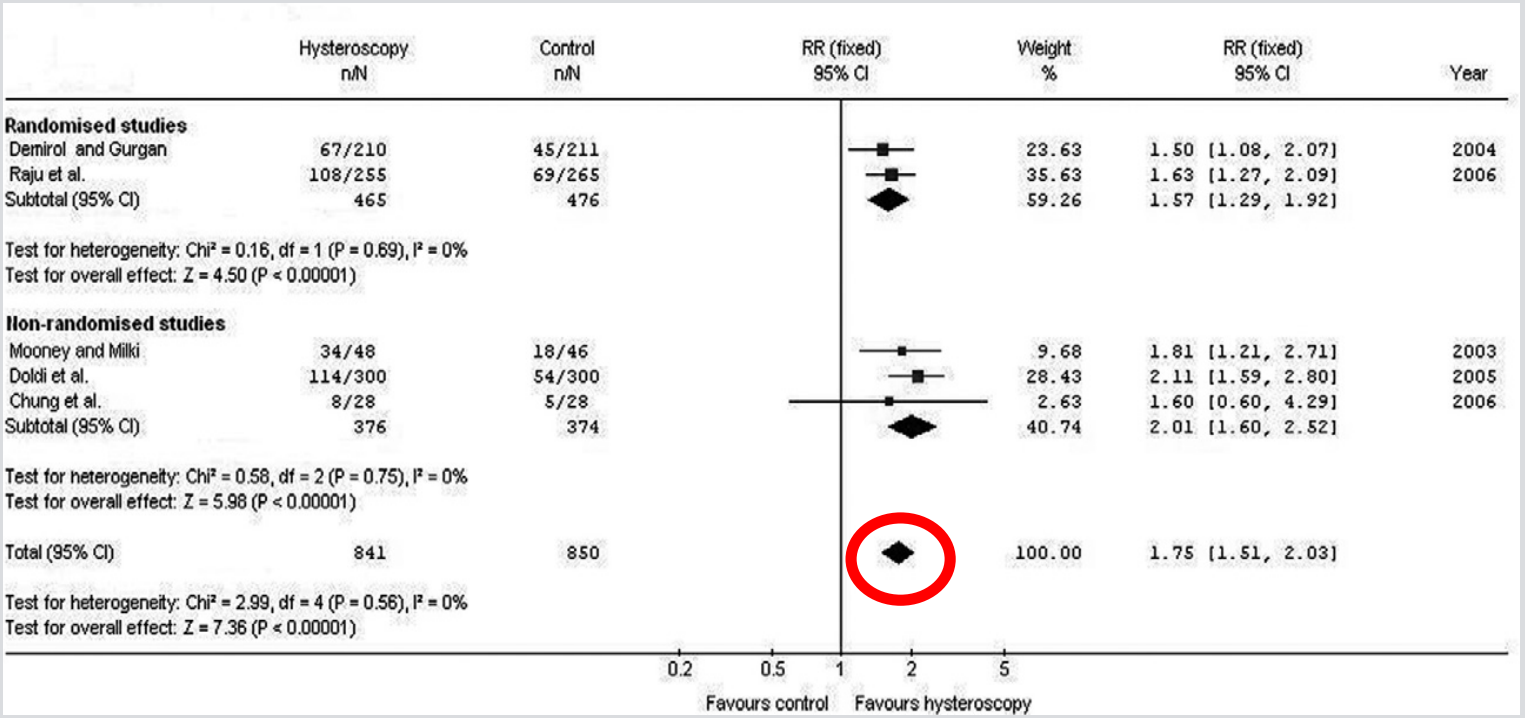


Figure 2. Summary of the outcome for the five studies included in the systematic review. CI = confidence interval, df = degrees of freedom, RR = relative risk.

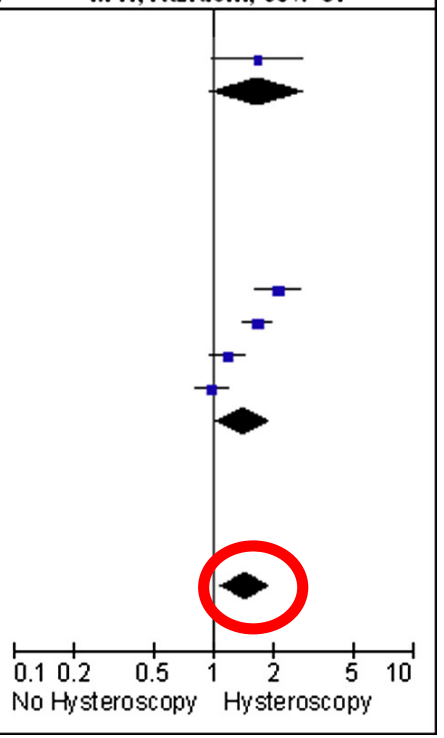
ROUTINE HYSTEROSCOPY PRIOR TO IVF ???

REVIEW Reproductive BioMedicine Online (2014) 28, 151–161

Hysteroscopy prior to the first IVF cycle: A systematic review and meta-analysis

Jyotsna Pundir [a,*], Vishal Pundir [b], Kireki Omanwa [c], Yacoub Khalaf [a], Tarek El-Toukhy [a]

Study or Subgroup	Hysteroscopy Events	Total	No Hysteroscopy Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 RCTs						
El-Nashar et al., 2011	25	62	15	62	13.3%	1.67 [0.98, 2.84]
Subtotal (95% CI)		**62**		**62**	**13.3%**	**1.67 [0.98, 2.84]**
Total events	25		15			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.87 (P = 0.06)						
1.1.2 Non - RCTs						
Doldi et al., 2005	114	300	54	300	20.1%	2.11 [1.59, 2.80]
Karayalcin et al., 2012	184	407	155	571	22.9%	1.67 [1.40, 1.98]
Trninic et al., 2011	84	193	106	287	21.7%	1.18 [0.95, 1.47]
Yu et al., 2012	92	215	124	284	22.1%	0.98 [0.80, 1.20]
Subtotal (95% CI)		**1115**		**1442**	**86.7%**	**1.41 [1.03, 1.94]**
Total events	474		439			
Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 26.51$, df = 3 (P < 0.00001); $I^2 = 89\%$						
Test for overall effect: Z = 2.11 (P = 0.03)						
Total (95% CI)		**1177**		**1504**	**100.0%**	**1.44 [1.08, 1.92]**
Total events	499		454			
Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 26.96$, df = 4 (P < 0.0001); $I^2 = 85\%$						
Test for overall effect: Z = 2.51 (P = 0.01)						
Test for subgroup differences: $Chi^2 = 0.28$, df = 1 (P = 0.60), $I^2 = 0\%$						



Clinical pregnancy rate per cycle for routine hysteroscopy versus no hysteroscopy prior to IVF/ICSI.

ROUTINE HYSTEROSCOPY PRIOR TO IVF???

Archives of Gynecology and Obstetrics
January 2015, Volume 291, Issue 1, pp 193–199 | Cite as

Routine office hysteroscopy prior to ICSI vs. ICSI alone in patients with normal transvaginal ultrasound: a randomized controlled trial

Authors Authors and affiliations

Khaled Ahmed Abdel Aziz Elsetohy, Ahmed H. Askalany, Mohamed Hassan, Zamam Dawood

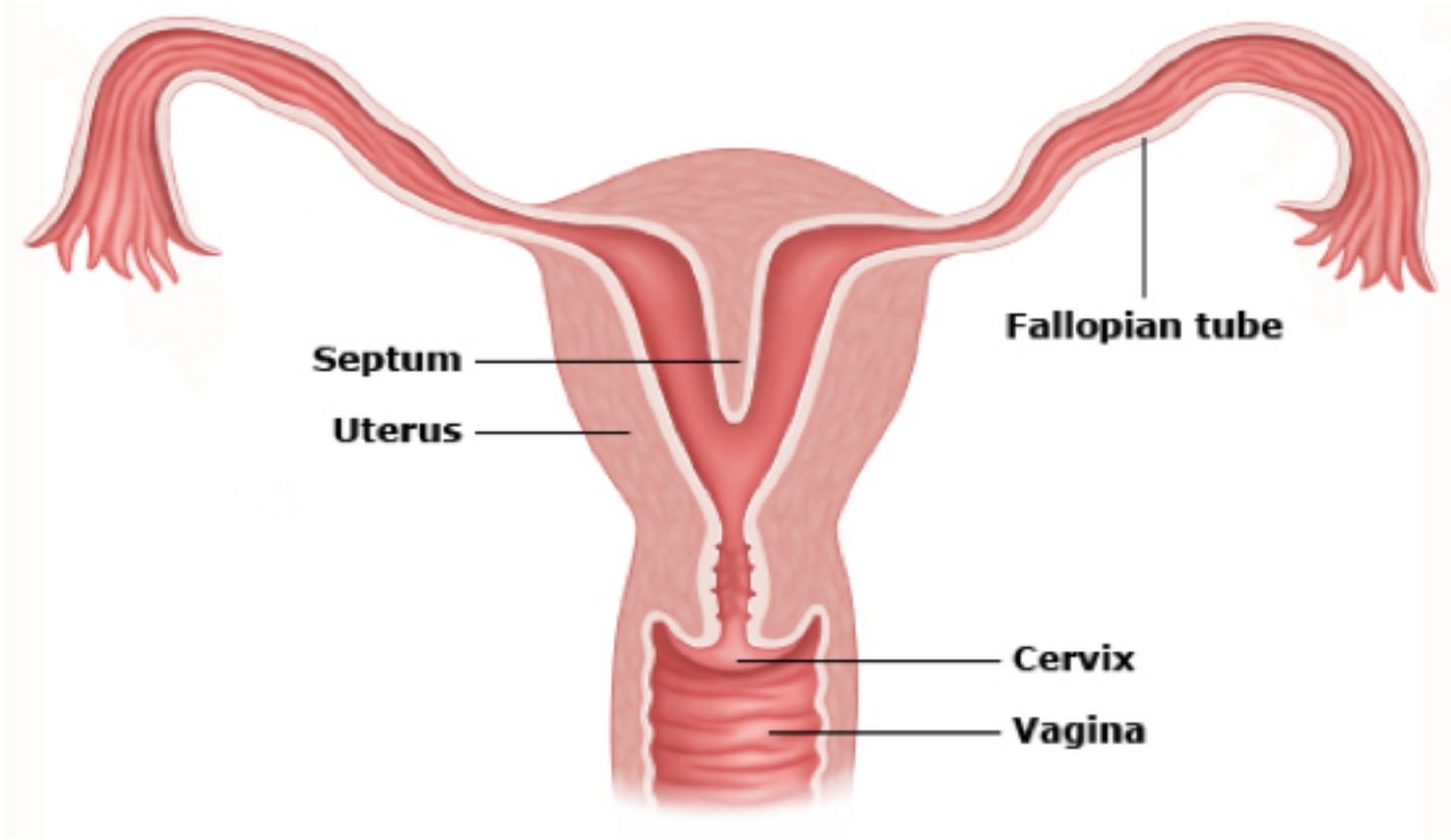
Results:

- There is statistically significant association between the use of hysteroscopy prior to ICSI and the rate of pregnancy (OR 2.77, 95 % CI [1.53–5.00]).
- In addition, hysteroscopy had detected abnormalities in near half of cases (43%) whose ultrasound was normal.

Conclusion:

- Routine office hysteroscopy is an essential step for infertility workup before ICSI even in patients with normal TV/US.

4. Uterine septum



Uterine septum/Septate uterus

- one of the most common forms of congenital uterine malformations
- The incidence has been reported to be as high as 3-4% in the general female population → significantly higher in patients with infertility and recurrent pregnancy loss
- may affect female reproductive health in three ways:
  - (i) obstetric complications
  - (ii) recurrent miscarriages
  - (iii) infertility
-

Nouri K, Ott J, Huber JC, Fischer EM, Stögbauer L, Tempfer CB. Reproductive outcome after hysteroscopic septoplasty in patients with septate uterus- a retrospective cohort study and systematic review of the literature . Reproductive Biology and Endocrinology 2010, **8**:52

Septate, subseptate and arcuate uterus decrease pregnancy and live birth rates in IVF/ICSI

T Tomaževič *, H Ban-Frangež, I Virant-Klun, I Verdenik, B Požlep, E Vrtačnik-Bokal

Reproductive BioMedicine Online (2010) 21, 700–705

Table 4 Analysis of all embryo transfers in the study and in the control groups regardless of the number and quality of embryos transferred (1993–2005).

Variable	*Study*	*Control*	*OR (95% CI)*	*P-value*
Live birth	49 (18.6)	115 (21.9)	1.222 (0.843–1.772)	NS

Values are *n* (%) unless otherwise indicated.
NS = not statistically significant.

Results:

Pregnancy rates before hysteroscopic metroplasty were significantly lower, both in women with subseptate and septate uterus.

After surgery, the pregnancy rate was comparable to the pregnancy rate in women with a normal uterus

Clinical implications of congenital uterine anomalies: a meta-analysis of comparative studies

Christos A Venetis [a,b,*], Stamatis P Papadopoulos [a], Rudi Campo [c], Stephan Gordts [d], Basil C Tarlatzis [a], Grigoris F Grimbizis [a,c]

Reproductive BioMedicine Online (2014) **29**, 665–683

b) Spontaneous abortion rate

Study or subgroup	Treatment Events	Total	No treatment Events	Total	Weight (%)	Risk ratio M-H, random, 95% CI
Heinonen *et al.*, 1997	4	28	11	42	14.7	0.55 [0.19, 1.54]
Total (95% CI)		**167**		**124**	**100.0**	**0.37 [0.25, 0.55]**
Total events	28		55			

Heterogeneity: Tau² = 0.00; Chi-squared = 4.69, df = 5 (P = 0.45); I² = 0%

Test for overall effect: Z = 4.91 (P < 0.00001)

Risk ratio M-H, random, 95% CI

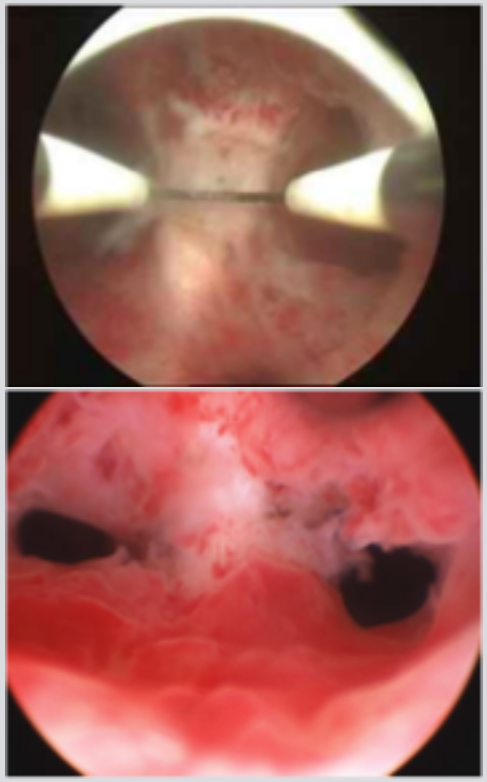
0.01 0.1 1 10 100

Favours treatment Favours no treatment

The spontaneous abortion rate was increased in women with uterine septum.

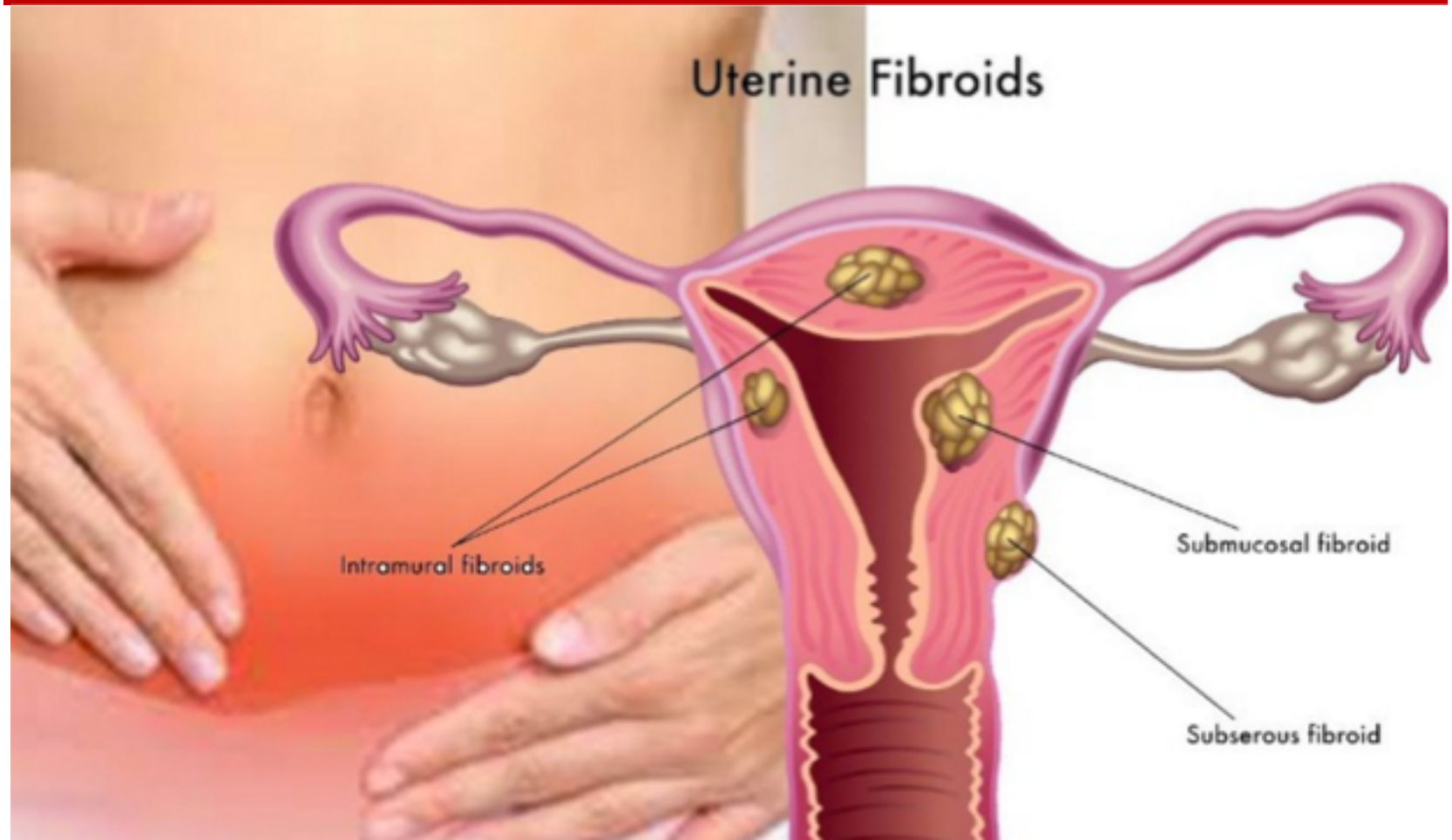
Uterine septum/Septate uterus

- In a patient with infertility, prior pregnancy loss, or poor obstetrical outcome it is reasonable to consider septum incision. (Grade C)
- In a patient without infertility or prior pregnancy loss, it may be reasonable to consider septum incision following counseling regarding potential risks and benefits of the procedure. (Grade C)



Practice Committee of the American Society for Reproductive Medicine. Uterine Septum: a guideline. Fertil Steril. 2016 Sep 1;106(3):530-40. doi: 10.1016/j.fertnstert.2016.05.014. Epub 2016 May 25. Review.

5. Leiomyoma uteri



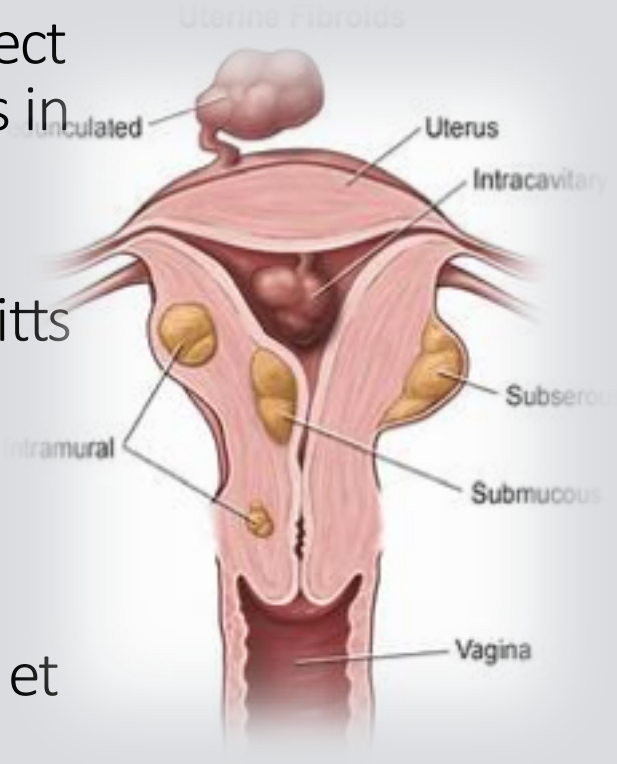
WHAT IS THE IMPACT OF LEIOMYOMAS ON REPRODUCTIVE OUTCOME?

- Uterine leiomyomas can cause anatomical disruption of the uterine architecture.
- submucosal leiomyomas may impact the endometrial cavity, thereby plausibly impacting embryo implantation and development.
- Intramural or subserosal leiomyomas may grow to large sizes prior to inducing symptoms of pelvic pressure or pain, but could potentially disrupt fertility and maintenance of pregnancy.

Practice Committee of the American Society for Reproductive Medicine. Removal of myomas in asymptomatic patients to improve fertility and/or reduce miscarriage rate: a guideline. Fertil Steril! 2017;108:416–25. !2017 by American Society for Reproductive Medicine

IMPACT OF NON-CAVITY-DISTORTING LEIOMYOMAS

- Remains controversial
- Some studies suggest an adverse effect on implantation and pregnancy rates in women undergoing IVF, particularly with large fibroids >4 cm
- 3 meta-analyses (Metwally 2011; Pritts 2009; Sunkara 2010): **reduced implantation rates**
- Myomectomy did not appear to significantly increase the clinical pregnancy and live birth rates (Pritts et al., 2009)



Coughlan C, Ledger W, Wang Q, Liu F, Demirol A, Gurgan T, Cutting R, Ong K, Sallam H, Li TC. Recurrent implantation faiklure: definition and management. Reprod Biomed Online. 2014 Jan;28(1):14-38. doi: 10.1016/j.rbmo.2013.08.011. Epub 2013 Sep 14. Review.

Human Reproduction, Vol.25, No.2 pp. 418–429, 2010
Advanced Access publication on November 12, 2009 doi:10.1093/humrep/dep396

human reproduction

META-ANALYSIS *Infertility*

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

Sesh Kamal Sunkara[1], Mohammed Khairy, Tarek El-Toukhy, Yacoub Khalaf, and Arri Coomarasamy

Assisted Conception Unit, Guy's and St Thomas' Hospitals NHS Foundation Trust, 11th Floor, Tower Wing Guy's Hospital Great Maze Pond, London SE1 9RT, UK

[1]Correspondence address. E-mail: sksunkara@hotmail.com

CONCLUSION: The presence of non-cavity-distorting intramural fibroids is associated with adverse pregnancy outcomes in women undergoing IVF treatment.

RESULTS: We identified 19 observational studies comprising 6087 IVF cycles. Meta-analysis of these studies showed a significant decrease in the live birth (RR = 0.79, 95% CI: 0.70–0.88, $P < 0.0001$) and clinical PRs (RR = 0.85, 95% CI: 0.77–0.94, $P = 0.002$) in women with non-cavity-distorting intramural fibroids compared with those without fibroids, following IVF treatment.

CONCLUSION: The presence of non-cavity-distorting intramural fibroids is associated with adverse pregnancy outcomes in women undergoing IVF treatment.

Key words: intramural fibroids / IVF / pregnancy / observational studies

Human Reproduction, Vol.25, No.2 pp. 418–429, 2010
Advanced Access publication on November 12, 2009 doi:10.1093/humrep/dep396

human reproduction

META-ANALYSIS *Infertility*

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

Sesh Kamal Sunkara[1], Mohammed Khairy, Tarek El-Toukhy, Yacoub Khalaf, and Arri Coomarasamy

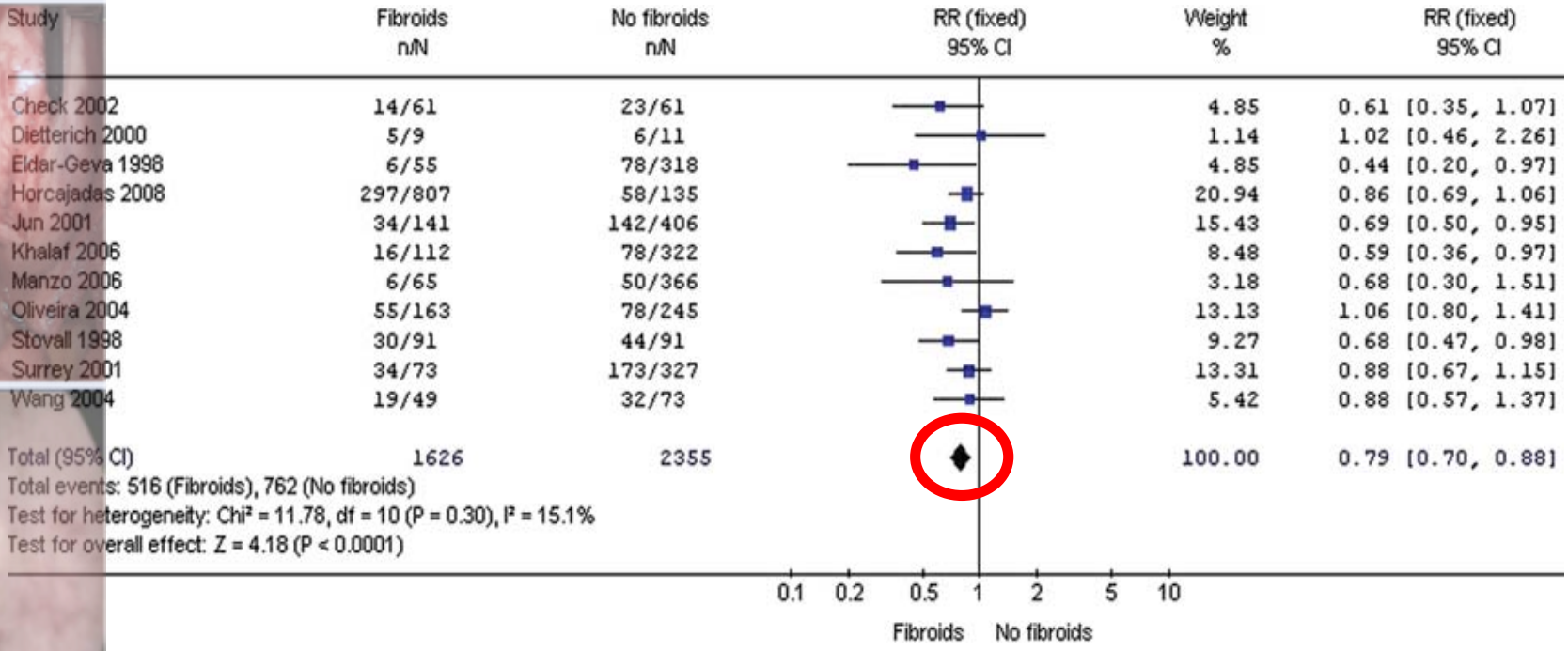


Figure 3 Forest plot of studies of non-cavity-distorting intramural fibroids versus no fibroids in women undergoing IVF treatment for outcome of live birth rates.

Human Reproduction, Vol.25, No.2 pp. 418–429, 2010
Advanced Access publication on November 12, 2009 doi:10.1093/humrep/dep396

human reproduction

META-ANALYSIS *Infertility*

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

Sesh Kamal Sunkara[1], Mohammed Khairy, Tarek El-Toukhy, Yacoub Khalaf, and Arri Coomarasamy

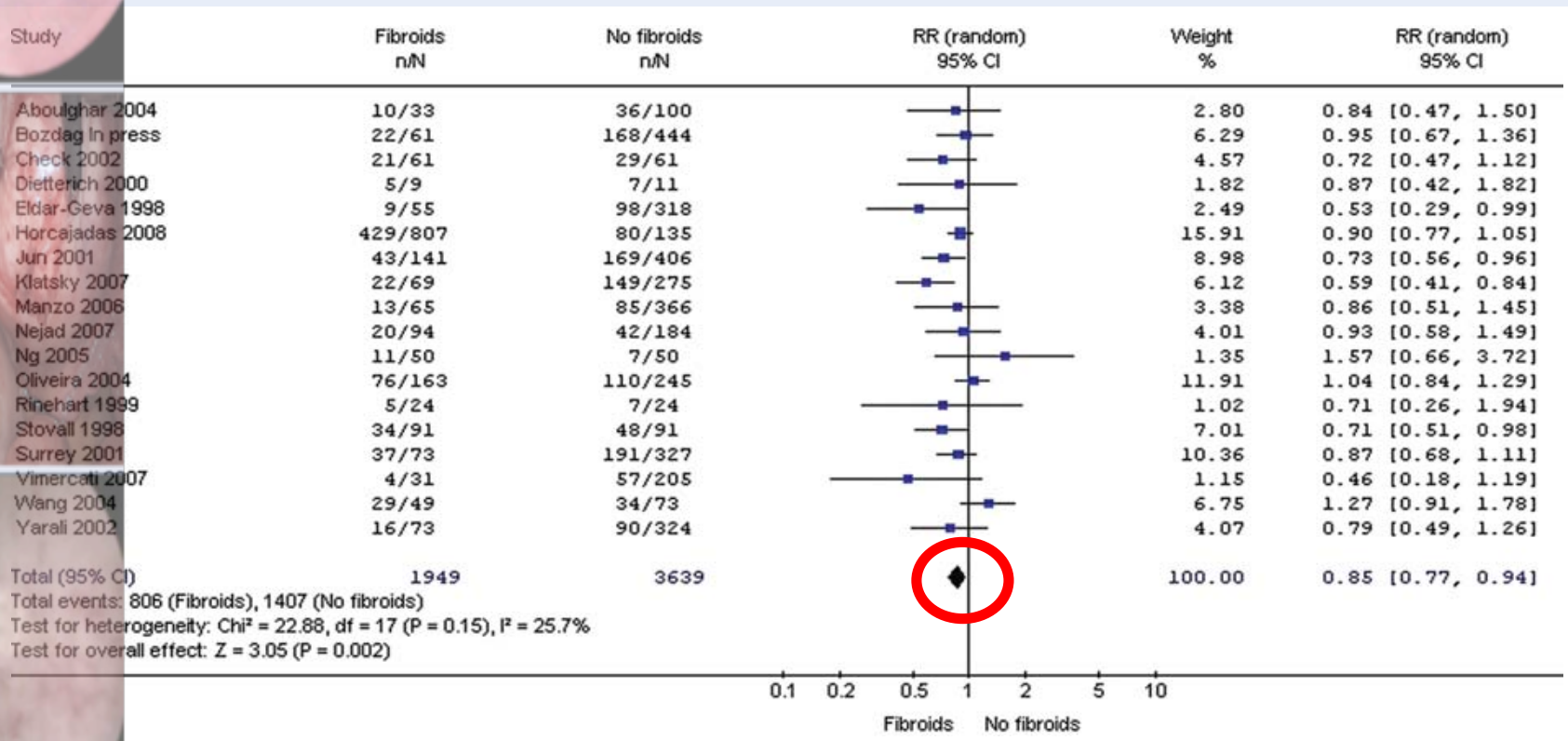
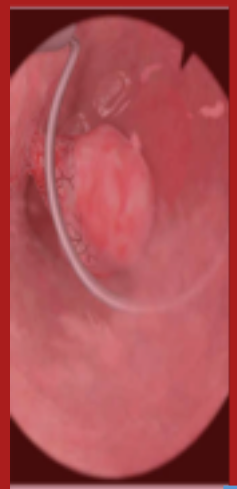
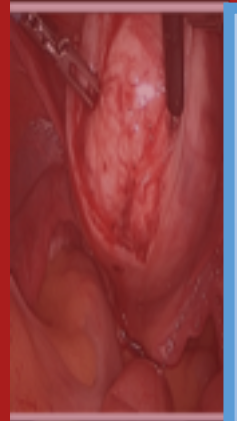


Figure 7 Forest plot of studies of non-cavity-distorting intramural fibroids versus no fibroids in women undergoing IVF treatment for outcome of clinical PRs.





BJOG An International Journal of Obstetrics and Gynaecology

DOI: 10.1111/1471-0528.14362
www.bjog.org

General gynaecology

Fibroids that do not distort the uterine cavity and IVF success rates: an observational study using extensive matching criteria

G Christopoulos,[a] A Vlismas,[a] R Salim,[a,b] R Islam,[a] G Trew,[a] S Lavery[a]

RESULTS:

The presence of non-cavity-distorting fibroids negatively affect clinical pregnancy rates and live birth rates in patients undergoing IVF/ICSI.

The deleterious effects on LBR was significant in women with ≥ 2 fibroids and fibroids ≥ 3cm

stimulating hormone (FSH), number of embryos transferred (one or two), day of transfer (day 3 or day 5), and no uterine fibroids identified by transvaginal ultrasound.

Main outcome measures Clinical pregnancy and live birth rates.

Results Our study demonstrates that the presence of non-cavity-distorting fibroids appears to negatively affect clinical pregnancy (odds ratio, OR 0.62; 95% confidence interval, 95% CI 0.41–0.94) and live birth rates (OR 0.58; 95% CI 0.48–0.78) in patients

surgical interventions in patients with intramural and subserosal fibroids before undergoing fertility treatment.

Keywords Infertility, IVF, leiomyoma, uterine fibroid.

Tweetable abstract Non-cavity-distorting fibroids negatively affect pregnancy rates after IVF.

Linked article This article is commented on by F van der Veen, p. 622 in this issue. To view this mini commentary visit http://dx.doi.org/10.1111/1471-0528.14461.

- Of the systematic reviews published, most concluded that there is insufficient evidence regarding the effect of removal of intramural myomas (laparoscopic or open) on reproductive outcomes in infertile women

WHAT IS THE IMPACT OF LEIOMYOMAS ON REPRODUCTIVE OUTCOME?

- There is **no consensus on whether or not intramural fibroids** in women undergoing IVF should be removed.
- Many clinicians would recommend removal of intramural fibroids if they are more than 4 cm in diameter.
- There is a lower threshold to removing an intramural fibroid if it is situated in the anterior lower uterine segment as it may pose problems in delivery of the fetus, especially if Caesarean section is required.
- The pros and cons of myomectomy should be carefully explained in each case.

Coughlan C, Ledger W, Wang Q, Liu F, Demirol A, Gurgan T, Cutting R, Ong K, Sallam H, Li TC. Recurrent implantation faiklure: definition and management. Reprod Biomed Online. 2014 Jan;28(1):14-38. doi: 10.1016/j.rbmo.2013.08.011. Epub 2013 Sep 14. Review.

6. Endometrial injury

Endometrial injury

- intentional damage to the endometrium performed with the objective of improving the reproductive outcomes of women or couples desiring pregnancy.
- The most common intervention is endometrial scratching performed using a pipelle.
- The movements made during endometrial sampling are believed to result in some disturbance or “injury” to the endometrium.

Nastri CO, Lensen SF, Gibreel A, Raine-Fenning N, Ferriani RA, Bhattacharya S, Martins WP. Endometrial injury in women undergoing assisted reproductive techniques. *Cochrane Database of Systematic Reviews* 2015, Issue 3. Art. No.: CD009517.

Endometrial injury

- The underlying mechanism of how endometrial injury may improve endometrial receptivity remains unclear
- Hypotheses:
  - mechanical effect of local injury to the proliferative endometrium induces endometrial decidualisation, a process that naturally occurs in preparation for pregnancy and therefore favours implantation
  - the injury induces a wound healing response, which involves recruitment of immune system cells to the site of healing
  - endometrial injury retards endometrial maturation, leading to better synchronicity between the endometrium and the transferred embryo

Endometrial injury in women undergoing assisted reproductive techniques

Carolina O Nastri[1], Sarah F Lensen[2], Ahmed Gibreel[3], Nick Raine-Fenning[4], Rui A Ferriani[1], Siladitya Bhattacharya[5], Wellington P Martins[1]

Cochrane Database of Systematic Reviews 2015, Issue 3. Art. No.: CD009517. DOI: 10.1002/14651858.CD009517.pub3.

Summary of findings for the main comparison. Effect of endometrial injury performed between day 7 of the previous cycle and day 7 of the ET cycle vs no injury

Patient or population: subfertile women undergoing IVF/ICSI

Settings: private and academic clinics

Intervention: endometrial injury performed between day 7 of the previous cycle and day 7 of the ET cycle vs no control

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	NNTB (95% CI)	Quality of the evidence (GRADE)	Comments (study authors' interpretation)
	Control	Endometrial injury					
Live birth/Ongoing pregnancy per randomly assigned woman	**26.0 per 100**	**34.2 per 100** (28.1-48.1)	**RR 1.42** (1.08-1.85)	1496 (9 studies)	12 (5-48)	⊕⊕⊕⊖ **Moderate**[a]	Benefit
Clinical pregnancy per randomly assigned woman	**29.8 per 100**	**38.6 per 100** (33.4-48.0)	**RR 1.34** (1.12-1.61)	1972 (13 studies)	11 (5-28)	⊕⊕⊕⊖ **Moderate**[b]	Benefit
Miscarriage per clinical pregnancy	**15.8 per 100**	14.7 per 100 (10.0-24.2)	**RR 0.99** (0.63-1.53)	500 (8 studies)	-	⊕⊕⊖⊖ **Low**[c,d]	-

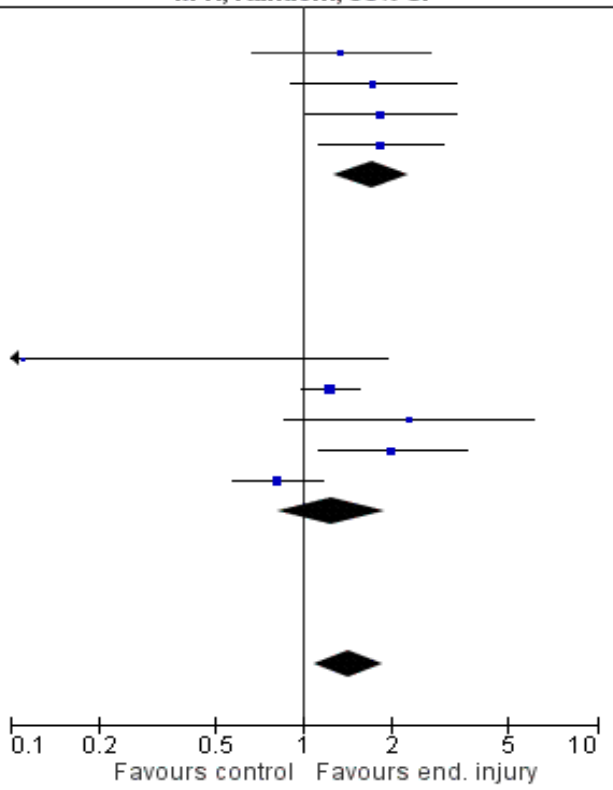
Endometrial injury in women undergoing assisted reproductive techniques

Carolina O Nastri[1], Sarah F Lensen[2], Ahmed Gibreel[3], Nick Raine-Fenning[4], Rui A Ferriani[1], Siladitya Bhattacharya[5], Wellington P Martins[1]

Cochrane Database of Systematic Reviews 2015, Issue 3. Art. No.: CD009517. DOI: 10.1002/14651858.CD009517.pub3.

1. Endometrial injury between day 7 of the previous cycle and day 7 of the ET cycle versus control: live birth/ongoing pregnancy

Study or Subgroup	End. Injury Events	End. Injury Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 No intrauterine manipulation in control group						
Aleyamma 2013	13	40	10	41	9.2%	1.33 [0.66, 2.68]
Guven 2014	19	62	11	62	10.0%	1.73 [0.90, 3.32]
Inal 2012	22	50	12	50	11.3%	1.83 [1.02, 3.29]
Nastri 2013	33	79	18	79	13.7%	1.83 [1.13, 2.97]
Subtotal (95% CI)		**231**		**232**	**44.2%**	**1.71 [1.28, 2.30]**
Total events	87		51			
Heterogeneity: Tau² = 0.00; Chi² = 0.62, df = 3 (P = 0.89); I² = 0%						
Test for overall effect: Z = 3.59 (P = 0.0003)						
1.1.2 Intrauterine manipulation in control group						
Baum 2012	0	18	4	18	0.9%	0.11 [0.01, 1.92]
Gibreel 2015	91	193	74	194	20.8%	1.24 [0.98, 1.56]
Narvekar 2010	11	49	5	51	5.7%	2.29 [0.86, 6.11]
Shohayeb 2012	28	105	14	105	11.4%	2.00 [1.12, 3.58]
Yeung 2014	39	150	48	150	17.1%	0.81 [0.57, 1.16]
Subtotal (95% CI)		**515**		**518**	**55.8%**	**1.25 [0.82, 1.90]**
Total events	169		145			
Heterogeneity: Tau² = 0.12; Chi² = 11.90, df = 4 (P = 0.02); I² = 66%						
Test for overall effect: Z = 1.02 (P = 0.31)						
Total (95% CI)		**746**		**750**	**100.0%**	**1.42 [1.08, 1.85]**
Total events	256		196			
Heterogeneity: Tau² = 0.08; Chi² = 17.10, df = 8 (P = 0.03); I² = 53%						
Test for overall effect: Z = 2.55 (P = 0.01)						
Test for subgroup differences: Chi² = 1.48, df = 1 (P = 0.22), I² = 32.5%						



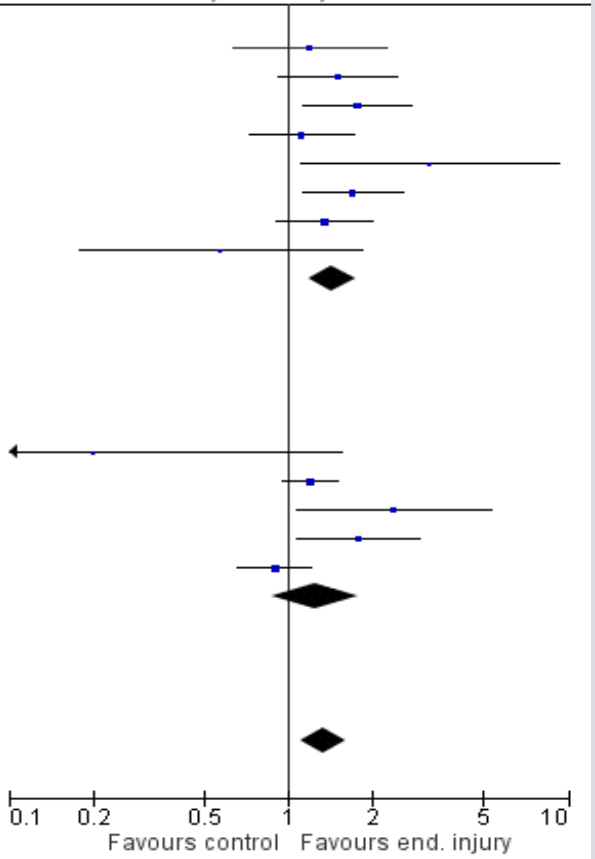
Endometrial injury in women undergoing assisted reproductive techniques

Carolina O Nastri[1], Sarah F Lensen[2], Ahmed Gibreel[3], Nick Raine-Fenning[4], Rui A Ferriani[1], Siladitya Bhattacharya[5], Wellington P Martins[1]

Cochrane Database of Systematic Reviews 2015, Issue 3. Art. No.: CD009517. DOI: 10.1002/14651858.CD009517.pub3.

1. Endometrial injury between day 7 of the previous cycle and day 7 of the ET cycle versus control: clinical pregnancy rate

Study or Subgroup	End. Injury Events	End. Injury Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.4.1 No intrauterine manipulation in control group						
Aleyamma 2013	14	40	12	41	6.0%	1.20 [0.63, 2.26]
Guven 2014	27	62	18	62	8.5%	1.50 [0.93, 2.43]
Inal 2012	30	50	17	50	9.2%	1.76 [1.13, 2.76]
Karim Zadeh 2008	29	80	26	80	9.6%	1.12 [0.73, 1.71]
Karimzadeh 2009	13	58	4	57	2.7%	3.19 [1.11, 9.21]
Nastri 2013	39	79	23	79	10.1%	1.70 [1.13, 2.56]
Polanski 2014	30	52	21	49	10.3%	1.35 [0.90, 2.00]
Safdarian 2011	4	50	7	50	2.3%	0.57 [0.18, 1.83]
Subtotal (95% CI)		**471**		**468**	**58.7%**	**1.44 [1.18, 1.74]**
Total events	186		128			
Heterogeneity: Tau² = 0.01; Chi² = 7.82, df = 7 (P = 0.35); I² = 11%						
Test for overall effect: Z = 3.67 (P = 0.0002)						
1.4.2 Intrauterine manipulation in control group						
Baum 2012	1	18	5	18	0.8%	0.20 [0.03, 1.55]
Gibreel 2015	95	193	80	194	15.4%	1.19 [0.96, 1.49]
Narvekar 2010	16	49	7	51	4.3%	2.38 [1.07, 5.28]
Shohayeb 2012	32	105	18	105	7.9%	1.78 [1.07, 2.96]
Yeung 2014	51	150	57	150	12.9%	0.89 [0.66, 1.21]
Subtotal (95% CI)		**515**		**518**	**41.3%**	**1.24 [0.87, 1.78]**
Total events	195		167			
Heterogeneity: Tau² = 0.09; Chi² = 11.55, df = 4 (P = 0.02); I² = 65%						
Test for overall effect: Z = 1.18 (P = 0.24)						
Total (95% CI)		**986**		**986**	**100.0%**	**1.34 [1.11, 1.62]**
Total events	381		295			
Heterogeneity: Tau² = 0.05; Chi² = 22.27, df = 12 (P = 0.03); I² = 46%						
Test for overall effect: Z = 3.08 (P = 0.002)						
Test for subgroup differences: Chi² = 0.48, df = 1 (P = 0.49), I² = 0%						



Endometrial injury in women undergoing assisted reproductive techniques

Carolina O Nastri[1], Sarah F Lensen[2], Ahmed Gibreel[3], Nick Raine-Fenning[4], Rui A Ferriani[1], Siladitya Bhattacharya[5], Wellington P Martins[1]

Cochrane Database of Systematic Reviews 2015, Issue 3. Art. No.: CD009517. DOI: 10.1002/14651858.CD009517.pub3.

2. Endometrial injury on the day of oocyte retrieval versus control: live birth/clinical pregnancy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	NNTH (95% CI)	Quality of the evidence (GRADE)	Comments (study authors' interpretation)
	Control	Endometrial injury on the day of oocyte retrieval					
Live birth per randomly assigned woman	**29 per 100**	**9 per 100** (4-20)	**RR 0.31** (0.14-0.69)	156 (1 study)	5.0 (4.0-11.1)	⊕⊕⊖⊖ **Low**[3]	Harm
Clinical pregnancy per randomly assigned woman	**33 per 100**	**12 per 100** (6-23)	**RR 0.36** (0.18-0.71)	156 (1 study)	4.8 (3.7-10.0)	⊕⊕⊖⊖ **Low**[3]	Harm

*The assumed risk in the control group was determined as the median value across studies. The assumed risk in the endometrial injury group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** oocyte retrieval; **RR:** Risk ratio; **NNTH:** number needed to treat for an additional harmful outcome.

Endometrial injury in women undergoing assisted reproductive techniques

Carolina O Nastri[1], Sarah F Lensen[2], Ahmed Gibreel[3], Nick Raine-Fenning[4], Rui A Ferriani[1], Siladitya Bhattacharya[5], Wellington P Martins[1]

Cochrane Database of Systematic Reviews 2015, Issue 3. Art. No.: CD009517. DOI: 10.1002/14651858.CD009517.pub3.

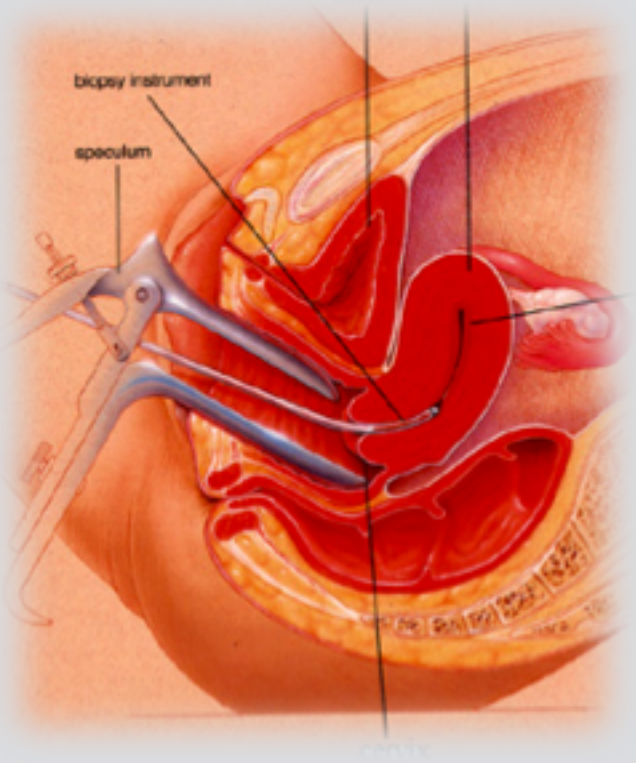
Authors' conclusions

1. Endometrial injury performed between day 7 of the previous cycle and day 7 of the embryo transfer (ET) cycle is associated with an improvement in live birth and clinical pregnancy rates in women with more than two previous embryo transfers.

2. Endometrial injury on the day of oocyte retrieval is associated with a reduction of clinical and ongoing pregnancy rates.

Endometrial injury

- studies suggests that endometrial scratch should be carried out **approximately 7 days prior to the onset of menstruation**, immediately before the start of ovarian stimulation for IVF treatment.
- Couples should be advised regarding the importance of protected intercourse in the month of the endometrial scratch



Coughlan C, Ledger W, Wang Q, Liu F, Demirol A, Gurgan T, Cutting R, Ong K, Sallam H, Li TC. Recurrent Implantation failure: definition and management.Reprod Biomed Online. 2014 Jan;28(1):14-38. doi: 10.1016/j.rbmo.2013.08.011. Epub 2013 Sep 14.

Summary of Recommendations:

1. ENDOMETRIOMA
   - Laparoscopic surgical removal of ovarian endometriotic cysts prior to IVF does not offer any additional benefit in terms of fertility outcomes.
   - Surgery prior to ART can be considered for:
     1. management of endometriosis-associated pain
     2. increasing the accessibility of the follicles during oocyte retrieval procedures, or
     3. to ameliorate any concern for malignancy.
   - It is recommend to proceed directly to IVF to reduce time to pregnancy, to avoid potential surgical complications and to limit patient costs.

2. Hydrosalpinx
   - Salpingectomy before embryo transfer has been shown to improve endometrial receptivity.

3. Endometrial Polyps
   - hysteroscopy should be considered before IVF and is highly recommended after one, otherwise unexplained, failed IVF cycle and in the setting of recurrent implantation failure

Summary of Recommendations

4. Septum
   - Hysteroscopic septum incision is associated with a reduction in subsequent miscarriage rates and improvement in live-birth rates in patients with a history of recurrent pregnancy loss.

5. Intramural Myoma uteri (non-cavity-distorting)
   - While most studies suggest an adverse effect on implantation and pregnancy rates in women with intramural fibroids, there is insufficient evidence to conclude that myomectomy improves IVF outcomes.

6. Endometrial scratching
   - Endometrial injury performed between day 7 of the previous cycle and day 7 of the embryo transfer (ET) cycle is associated with an improvement in live birth and clinical pregnancy rates in women

Thank you for you kind attention

Wordpress: Doc Ina Ob Gyne