Università degli Studi di Padova
Dipartimento di Scienze Ginecologiche e della Riproduzione Umana
Scuola di Specializzazione in Ginecologia e Ostetricia
Direttore Prof. Giovanni Battista Nardelli

Embryo-transfer

- ***Dott.ssa Denise Capuzzo***

Casi clinici

36 aa, sterilità primaria idiopatica

In anamnesi 3 IUI facili

- Primo ET: difficile, attesa e buscopan 1 fl IM-> facile

  No gravidanza

- Secondo ET (no buscopan per reazione allergica): difficile (pinza e dilatazione): gravidanza singola

40 aa, sterilità secondaria tubarica.

- ET a fresco: difficile, pinza dilatazione-> non gravidanza

HSC diagnostica: sinechie a livello cervicale.

- ET successivo: più di un tentativo, non dilatazione, non pinza, non sangue-> no gravidanza

39 aa, sterilità secondaria maschile

- ET a fresco non riuscito: embrioni congelati
- ET di prova (ecoguidato): non si passa OUI

HSC diagnostica: piccola lesione a livello della cervice, procedura mal tollerata dalla paziente.

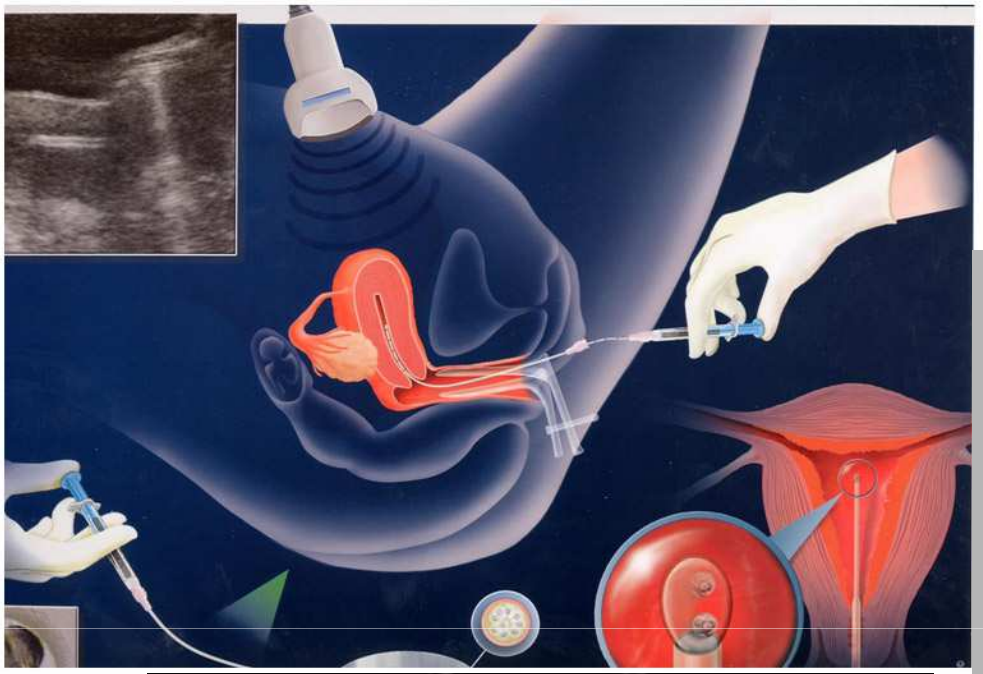
- ET il mese successivo: facile-> no gravidanza

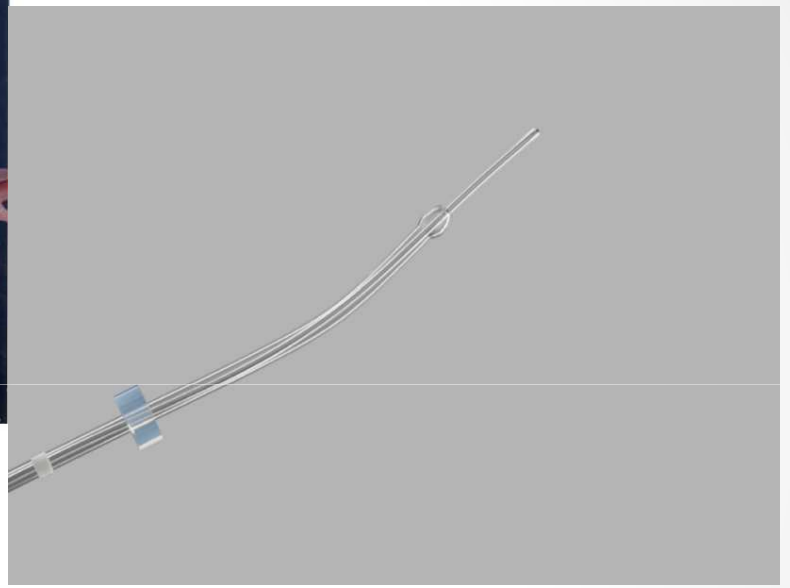
- E’ uno degli step fondamentali della fecondazione in vitro

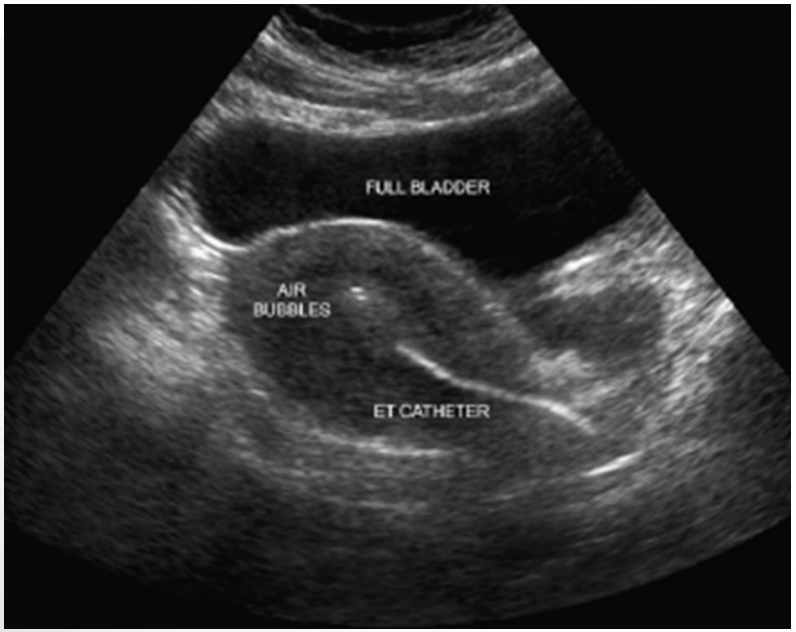
- Sembra essere lo step più «inefficiente»

la maggior parte delle pazienti che si sottopone ad ART raggiunge lo stadio di ET, solo 1/3 di queste arrivano ad una gravidanza clinica

- Fattori implicati: recettività endometriale,
  competenza embrione,
  EMBRYO TRANSFER






FULL BLADDER
AIR
BUBBLES
ET CATHETER

In general the procedure starts by placing a speculum in the vagina to visualize the cervix, which is cleansed with saline solution or culture media. Additional mucus in the cervical canal can be aspirated using a sterile syringe. After confirmation of the patient's identity, a transfer catheter is loaded with the embryos and handed to the clinician. The catheter is inserted through the cervical canal and advanced into the uterine cavity where the embryos are deposited. The catheter is then withdrawn and handed to the embryologist, who inspects it for retained embryos.

The goal of a successful ET is to deliver the embryos atraumatically to a location in the uterus where implantation is maximized.

Potential reasons for a failed transfer include disruption of the endometrium by the catheter, induction of uterine contractions, deposition of the embryos in a suboptimal location, or damage to the embryos during the process. Numerous technical aspects of this procedure have been studied to minimize these complications and determine their effect on pregnancy outcome. Although much of

Optimizing the technique of embryo transfer

Lindsay Mains, M.D., and Bradley J. Van Voorhis, M.D.

Fertility and Sterility® Vol. 94, No. 3, August 2010

- Preparazione della paziente
- Evitare contaminazione
- Practicing
- Ecoguida
- Difficoltà ET
- Sangue
- Tipo catetere
- Standardizzazione esecuzione
- Bed rest

Preparazione

- Conoscere le caratteristiche anatomiche della paziente

Anamnesi

Visita

Screening ecografico pre stimolazione ed eventuale isteroscopia con bonifica della cavità uterina prima della stimolazione (polipi, miomi, malforamzioni uterine)

RICONOSCERE fattori di rischio per stenosi del canale cervicale-> embrio transfer di prova

- Valutazione ecografica pre/durante la stimolazione
- Eventuale correzione condizioni che aumentano la probabilità di ET difficile (polipi endometriali, del canale cervicale,miomi, stenosi del canale cervicale)

Embryo transfer di prova

- Timing:
  - prima della stimolazione
  - durante la stimolazione
  - al pick up
  - prima del ET

Alcuni studi riportano una minore PR se ET di prova eseguito nell'ultima fase del trattamento (induzione contrazioni uterine, danneggiamento dell'endometrio,...)

Does the timing of mock embryo transfer affect in vitro fertilization implantation and pregnancy rates?

Comparison of patients who underwent early mock embryo transfer (MET) and patients who had MET during oocyte retrieval, 3 to 5 days before embryo transfer.

Parameter	Early MET (n = 103)	Oocyte retrieval MET (n = 186)	*P* value or OR (95% CI)
Age (years)	33.2	33.2	.936
Body mass index	25.8	25.4	.670
ICSI	46 (44.6%)	72 (38.7%)	.324
Peak estradiol	1844	2435	.006
No. of oocytes	12.0	11.0	.441
No. of mature oocytes	11.5	11.6	.917
No. of embryos	8.1	8.0	.822
No. of embryos transferred	2.2	2.4	.005
Difficult transfer	9.7%	15.1%	.270
Mean length of cavity at MET	7.6 ± 0.85 cm	7.9 ± 0.94 cm	.003
Mean depth of cavity at actual ET	6.7 ± 0.91 cm	6.9 ± 0.85 cm	.080
Positive hCG (per ET)	59.2%	60.8%	0.94 (0.56, 1.58)
Clinical pregnancy (per ET)	55.3%	53.2%	1.09 (0.65, 1.82)
Implantation rate (gestational sacs/ET)	40.1% (75/187)	33.2% (126/339)	1.34 (0.95, 1.90)
Ongoing pregnancy (per ET)	47.6%	48.4%	0.97 (0.58, 1.61)

Katariya. Mock embryo transfer. Fertil Steril 2007.

In summary, our study demonstrated that the timing of MET does not affect IVF implantation or pregnancy rates. Performing a MET at the time of oocyte retrieval, 3 to 5 days before ET, does not have a deleterious effect on the endometrium. In addition, there was a statistically significant difference in the uterine cavity length at the time of early MET when compared with MET performed at oocyte retrieval. This suggests that the uterus is dynamic; measurement of the uterine cavity length may be longer when measured closer to the time of actual ET. It is possible that assessment of the uterine cavity length closer to the time of the actual ET may be more accurate and identify yet another potential variable associated with ET success.

Katariya et al.

Vol. 88, No. 5, November 2007

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Katariya et al.

Vol. 88, No. 5, November 2007

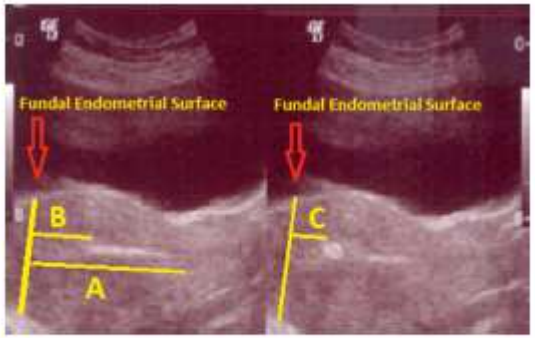


Fig. 1. (A) The length of uterine cavity, (B) the distance between the end of the fundal endometrial surface and the tip of inner catheter, and (C) the distance between fundal endometrial surface and air bubbles.

Importanza della valutazione delle dimensioni uterine:

- lunghezza della cervice uterina (OUE-OUI)
- Importanza del posizionamento della punta del catetere esterno appena all'interno dell'OUI
- lunghezza della cavità uterina
- Distanza catetere morbido-fondo uterino ->

Miglior posizione per ET

(Frankfurter al. 2003, Cenksoy 2013)

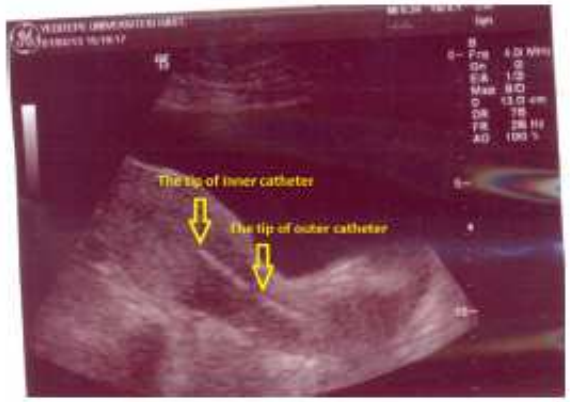


Fig. 2. The location of the tip of inner and outer catheter.

P.O. Cenksoy et al./ European Journal of Obstetrics & Gynecology and Reproductive Biology 172 (2014) 46–50

Studio del 2011

- 150 pazienti randomizzate per eseguire ET di prova al 21 giorno del ciclo precedente o in sesta giornata di stimolazione.

NON differenze di pregnancy rate o implantation rate

Yoldemir T et al. 2011

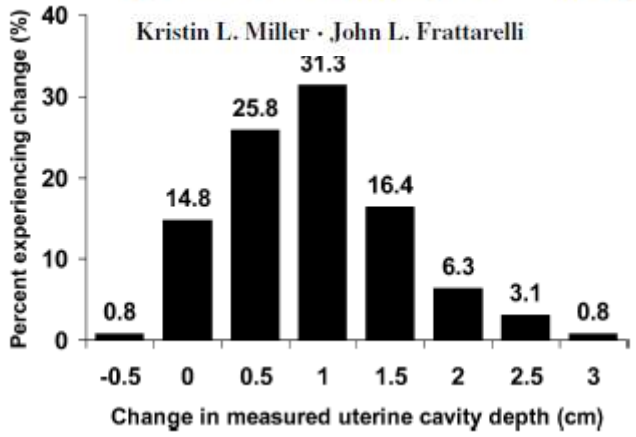
ET di prova prima della stimolazione:

- Predittivo per difficoltà ET
- Non predittivo per posizione ideale degli embrioni all'ET

modificazioni uterine legate alla stimolazione

The pre-cycle blind mock embryo transfer is an inaccurate predictor of anticipated embryo transfer depth

Kristin L. Miller · John L. Frattarelli



J Assist Reprod Genet (2007) 24:77–82

Sia modificazioni legate alla lunghezza della cavità uterina che alla flessione uterina

Contaminazione

BATTERICA

- Non eseguibile disinfezione con antisettici normalmente utilizzati in ginecologia.

Da circa vent'anni evidenze su impatto negativo su ovociti ed embrioni (anche nella fase del pick up) riduzione del pregnancy rate aumento del tasso di gravidanze biochimiche.

Hannoun A et al. 2008; van Os et al 1992

- Solitamente la detersione aviene con soluzione fisiologica o terreno di coltura.

Human Reproduction Vol.21, No.11 pp. 2911–2915, 2006

A randomized controlled trial of prophylactic antibiotics (co-amoxiclav) prior to embryo transfer

N.Brook[1], Y.Khalaf[1,3], A.Coomarasamy[1], J.Edgeworth[2] and P.Braude[1]

Table II. The effect of antibiotics on assisted reproduction technique outcome

	Co-amoxiclav group (%)	Control group (%)	Relative risk (95% CI)	*P*-value
Contamination of catheter tips	76/154 (49.4)	81/130 (62.3)	0.79 (0.64 – 0.97)	<0.03
Clinical pregnancy	64/178 (36.0)	61/172 (35.5)	1.01 (0.81 – 1.24)	0.83

Table IV. Effect of grade of bacterial contamination of the embryo transfer catheter on clinical pregnancy and implantation rates

Level of contamination	Clinical pregnancy rate (%)	Crude (Unadjusted OR)	Adjusted[a] OR
No growth	60/126 (47.2)	1[b]	1[b]
GP+	36/90 (40.0)	0.73	0.61
GP++	12/37 (32.4)	0.53	0.41
GP+++	3/19 (15.8)	0.21	0.18
GN	2/11 (18.2)	0.22	0.16

GP, gram positive; GN, gram negative.
The overall unadjusted *P*-value for the association of the level of bacterial contamination and clinical pregnancy rates was 0.03. Following adjustment for the above factors, the *P*-value was found to be 0.01, showing an even stronger association between the level of contamination and clinical pregnancy rates.
[a]Adjusted for female age, cause of infertility, duration of infertility, cycle number, basal FSH level, embryo transfer operator and type of assisted reproduction technique (IVF, ICSI or PGD).
[b]Reference group for the comparisons.

- PR non correlato all'antibioticoprofilassi ma al livello di contaminazione batterica.
  Importanza dello screening ed eventuale terapia prima del trattamento di IVF.

Examination of bacterial contamination at the time of embryo transfer, and its impact on the IVF/ pregnancy outcome

Helmy Selman · Monica Mariani · Nicoletta Barnocchi · Antonella Mencacci · Francesco Bistoni · Saverio Arena · Silvana Pizzasegale · Gian Francesco Brusco · Antonio Angelini

Table 2 Distribution of patients based on each isolated bacterium and its correlation with pregnancy outcome

Isolated microbial organisms	Number of positive patients		Number of negative patients		*P*
	Pregnant (%)	Not pregnant (%)	Pregnant (%)	Not pregnant (%)	
Lactobacillus	3 (15.8)	16 (84.2)	46 (34.6)	87 (65.4)	ns
Entrobacteriaceae	22 (22.2)	77 (77.8)	27 (51)	26 (49)	≤0.001
Staphylococcus spp.	12 (17.6)	56 (82.4)	37 (44)	47 (56)	≤0.001
Streptococcus spp.	18 (41.8)	25 (58.1)	31 (28.4)	78 (71.6)	ns
Others[a]	12 (42.8)	16 (57.2)	37 (29.8)	87 (70.2)	ns

ns Not significant

[a]Other microorganisms include: *S agalactiae*, *G. vaginalis*, Mycoplasma and yeast

152 pazienti, tampone vaginale, catetere, colture media

J Assist Reprod Genet (2007) 24:395–399

- Valutazione batteriuria: origine urinaria della contaminazione
- Prevalenza batteriuria asintomatica nelle donne in età riproduttiva: circa 5% (Hooton TM et al, 2000)
- Fattore prognostico per sviluppo di infezioni sintomatiche nella seconda fase del trattamento di PMA/in gravidanza

Prevenzione complicanze urinary tract related in gravidanza

PROGESTERONE

Recente studio su modello murino in vitro. Coltura di embrioni con concentrazioni variabili di progesterone (crinone gel, progesterone micronizzato): aumento del apoaptosi, riduzione cellulare e riduzione della formazione della blastocisti (Ying LY et al. 2014)

MUCO
Contaminazione da muco, se in minima quantità non sembra interferire con l'impianto.

- Screening ed eventuale terapia di coppia prima del trattamento per la riduzione della contaminazione batterica
- Accurata pulizia prima dell'embryo transfer, minimizzare la contaminazione esterna.

Practicing

Almeno 50 embryo transfer

(Papageorgiu 2001)

11-99 ET per raggiungere gli standard di un ginecologo esperto

(Dessolle 2010)

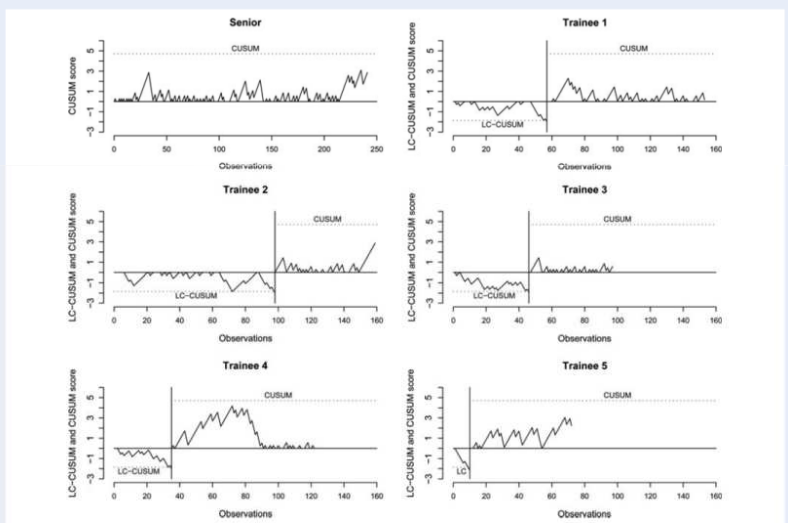


Figure 1 LC-CUSUM and CUSUM curves for embryo transfer (positive hCG) in five trainees and a senior gynaecologist. The first embryo transfers performed by five trainees were monitored. LC-CUSUM and CUSUM scores are plotted in terms of the successive procedures, evaluating performance by the results of hCG tests. CUSUM was also used to monitor 241 consecutive transfers performed by a senior gynaecologist. LC-CUSUM is applied until acceptable performance has been reached and CUSUM is used thereafter to ensure that adequate level is maintained. For the LC-CUSUM, as long as the score remains over the limit *h* (dotted line), the trainee is not considered as proficient; when the LC-CUSUM score crosses this limit, the trainee is considered to have learned the procedure. For the CUSUM, as long as the score remains under the limit, the operator is considered to maintain an acceptable performance.

Human Reproduction, Vol.25, No.2 pp. 380–386, 2010

Alcuni studi riportano un'alta variabilità interoperatore (Hearn Stokes et. Al 2000), così forte da poter essere un grosso bias nello studio nell'efficacia dell'utilizzo di diversi tipi di cateteri (casistica di 1400 casi da tre operatori diversi)(Yao 2009).

US guide/vs clinical touch

- Standard nella maggior parte dei centri: US guide
- Standardizzazione della procedura, minimizzazione del fattore operatore dipendente

Ultrasound versus 'clinical touch' for catheter guidance during embryo transfer in women (Review)

Brown J, Buckingham K, Abou-Setta AM, Buckett W

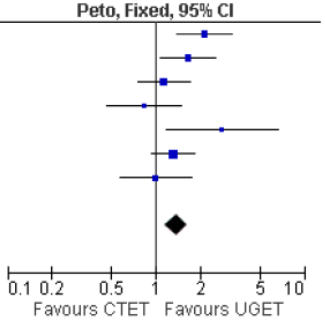
For a population of women with a 25% chance of pregnancy using clinical touch this would be increased to 32% (28% to 46%) by using UGET

THE COCHRANE COLLABORATION®

Figure 4. Forest plot of comparison: 1 Pregnancy, outcome: 1.2 Ongoing pregnancies (per woman randomised).

Study or Subgroup	UGET Events	UGET Total	Clinical touch Events	Clinical touch Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Coroleu 2000	85	182	52	180	16.8%	2.13 [1.39, 3.25]
Eskander 2008	68	183	50	190	15.9%	1.65 [1.07, 2.55]
Garcia-Velasco 2002	100	187	94	187	18.4%	1.14 [0.76, 1.70]
Kosmas 2007	36	101	38	95	9.1%	0.83 [0.47, 1.48]
Marconi 2003	22	41	12	42	4.0%	2.79 [1.17, 6.65]
Tang 2001	94	400	76	400	26.3%	1.31 [0.93, 1.84]
Weissman 2003	36	160	28	124	9.6%	1.00 [0.57, 1.74]
Total (95% CI)		**1254**		**1218**	**100.0%**	**1.38 [1.16, 1.64]**
Total events	441		350			

Heterogeneity: Chi² = 12.40, df = 6 (P = 0.05); I² = 52%
Test for overall effect: Z = 3.65 (P = 0.0003)

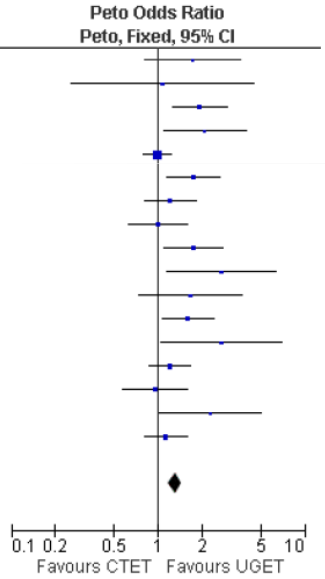


Non differenze statisticamente significative per quanto riguarda il live birth rate (solo 4 studi); non differenze statisticamente significative per eventi avversi (gravidanze gemellari, aborti, GEU)

Figure 5. Forest plot of comparison: 1 Pregnancy, outcome: 1.3 Clinical pregnancies (per woman randomised).

Study or Subgroup	UGET Events	UGET Total	Clinical touch Events	Clinical touch Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Bar Harva 2003	22	65	15	66	2.0%	1.72 [0.81, 3.68]
Chen 2007	5	27	4	23	0.6%	1.08 [0.26, 4.52]
Coroleu 2000	91	182	61	180	6.8%	1.93 [1.27, 2.93]
Coroleu 2002	32	93	18	91	2.8%	2.09 [1.09, 3.99]
Drakeley 2008	207	834	204	815	23.6%	0.99 [0.79, 1.24]
Eskander 2008	75	183	54	190	6.5%	1.74 [1.14, 2.66]
Garcia-Velasco 2002	112	187	103	187	7.0%	1.22 [0.81, 1.83]
Kosmas 2007	63	150	63	150	5.6%	1.00 [0.63, 1.58]
Li 2005	66	178	38	152	5.4%	1.75 [1.10, 2.78]
Marconi 2003	25	41	15	42	1.6%	2.72 [1.15, 6.40]
Martins 2004	21	50	15	50	1.8%	1.67 [0.74, 3.77]
Matorras 2002	67	255	47	260	6.8%	1.61 [1.06, 2.44]
Moraga-Sanchez 2004	21	33	13	34	1.3%	2.72 [1.05, 7.04]
Tang 2001	104	400	90	400	11.3%	1.21 [0.88, 1.67]
Weissman 2003	49	160	39	124	4.6%	0.96 [0.58, 1.60]
Wisanto 1989	19	98	9	98	1.8%	2.29 [1.03, 5.09]
Zakova 2008	105	308	97	309	10.4%	1.13 [0.81, 1.58]
Total (95% CI)		**3244**		**3171**	**100.0%**	**1.31 [1.18, 1.46]**
Total events	1084		885			

Heterogeneity: Chi² = 27.28, df = 16 (P = 0.04); I² = 41%
Test for overall effect: Z = 4.92 (P < 0.00001)



The exact mechanism by which UGET increases pregnancy rates remains unclear. The main suggestions remain the confirmation of the catheter in the uterine cavity , "ease of transfer" positioning of the catheter and avoiding touching the fundus or indenting the endometrium.

Transvaginal versus transabdominal ultrasound guidance for embryo transfer in donor oocyte recipients: a randomized clinical trial

Daniel Bodri, M.D., M.Sc., Ph.D.,[a] *Marta Colodrón, M.D.,*[a] *Désirée García, Pharm.D.,*[b] *Albert Obradors, M.Sc., Ph.D.,*[a] *Valérie Vernaeve, M.D., Ph.D.,*[a] *and Oriol Coll, M.D., Ph.D.*[a]

[a] Clínica EUGIN; and [b] Fundació privada Eugin, Barcelona, Spain

Objective: To compare pregnancy and implantation rates with transvaginal (TV) versus transabdominal (TA) ultrasound-guided embryo transfer (ET).
Design: Randomized, clinical trial registered at clinicaltrials.gov (NCT 01137461).
Setting: Private, infertility clinic.
Patient(s): Three-hundred thirty randomized recipients of donor oocytes.
Intervention(s): Embryo transfer using TV (with empty bladder, using the Kitazato ET Long catheter) versus TA ultrasound guidance (with full bladder, using the echogenic Sure View Wallace catheter).
Main Outcome Measure(s): Overall pregnancy, clinical pregnancy, implantation, and ongoing pregnancy rates. Duration and difficulty of ET. Patient-reported uterine cramping and discomfort, as evaluated by questionnaire.
Result(s): No statistically significant differences were observed in clinical pregnancy 50.9% versus 49.4% (95% confidence interval of the difference: −9.2 to +12.2%), implantation 34.5% versus 31.4% (95% CI of the difference: −4 to +10.3%) between the TV and TA ultrasound-guided groups. Transfer difficulty (6% versus 4.2%) and uterine cramping (27.2% versus 18.3%) were not statistically significantly different between treatment groups. Total duration (154 ± 119 versus 85 ± 76 seconds) was statistically significantly higher in the TV ultrasound group. Light to moderate-severe discomfort related to bladder distension was reported by 63% of the patients in the TA ultrasound group.
Conclusion(s): Transvaginal ultrasound-guided ET yielded similar success rates compared with the TA ultrasound-guided procedure without requiring the assistance of a sonographer. It was associated with increased patient comfort due to the absence of bladder distension. (Fertil Steril® 2011;95:2263–8. ©2011 by American Society for Reproductive Medicine.)

Fertility and Sterility® Vol. 95, No. 7, June 2011

Transvaginal ultrasound image of the uterus after injecting the embryos with the Kitazato ET Long catheter.

Bodri. Transvaginal ultrasound-guided ET. Fertil Steril 2011.

Ultrasound-guided embryo transfer does not offer any benefit in clinical outcome: a randomized controlled trial

Human Reproduction Vol.22, No.5 pp. 1327–1334, 2007

BACKGROUND: Ultrasound-guided embryo transfer (ET) is widely suggested as a standard clinical practice that improves overall embryo implantation and pregnancy rates. Various studies of this issue suffer from methodological pitfalls, so that a randomized controlled trial, which overcomes these problems, might be valuable. **METHODS:** Three hundred women aged <40, who underwent fresh ET, were included in this randomized, double-blind controlled trial. The K-J-SPPE echo tip soft catheter was used for the ultrasound-guided ET and the traditional K-Soft catheter for ETs not using ultrasound. One experienced operator performed all ETs. The primary study outcome was overall pregnancy rate (defined as the number of positive hCG results per transfer). **RESULTS:** No significant differences between groups were found regarding baseline patient and embryological characteristics, except for male factor and unexplained infertility (higher in the blind and ultrasound-guided ET group, repectively, $P < 0.05$). Overall pregnancy rates were 53.3 and 51.3% in the ultrasound-guided and blind ET group, respectively. Two ectopic pregnancies were reported in each group. Difficulty in cervical negotiation did not differ between the two groups. **CONCLUSIONS:** In patients undergoing ET by an experienced operator, ultrasound guidance did not provide any benefit in terms of overall clinical pregnancy and embryo implantation rates.

Posizionamento degli embrioni

Letteratura contrastante, negli ultimi anni

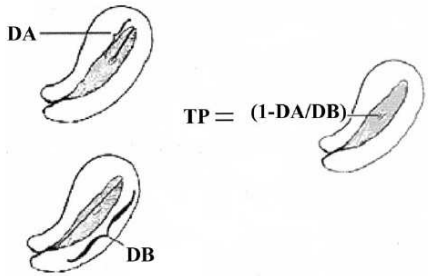
Fundal ET

Middle to lower uterine segment embryo transfer improves implantation and pregnancy rates compared with fundal embryo transfer

David Frankfurter, M.D., James B. Trimarchi, Ph.D., Celso P. Silva, M.D., and David L. Keefe, M.D.

FERTILITY AND STERILITY®
VOL. 81, NO. 5, MAY 2004

Representation of transfer point (TP) equation. DA represents the distance from the middle of the transfer flash to the fundal extent of the endometrium. DB represents the endometrial length from the internal os to the fundus. TP represents the relative depth of transfer normalized for the length of the endometrial cavity and is calculated based on the following formula: 1 − DA/DB. Based on this formula, the greater the value of TP, the closer to the fundus was the transfer.



Frankfurter. Middle to lower uterine embryo transfer and IVF success. Fertil Steril 2004.

Patient and cycle-specific parameters in fundal and lower to middle groups.

Characteristic	Fundal (n = 393)	Lower–mid (n = 273)	*P* value
Live births (% of ET)[a]	103 (26.2)	93 (34.1)	.03
Clinical pregnancies (% of ET)[a]	123 (31.2)	115 (39.6)	.005
Implantations (sacs/embryos trans)[a]	192 (0.141)	174 (0.206)	.001
Age[b,c]	34 (32–38)	35 (31–38)	.19
Basal FSH (mIU/mL)[b,c]	6.2 (5.1–7.5)	5.8 (4.7–7.4)	.19
Peak 17 E_2 (pg/mL)[b,c]	1,712 (1,160–2,617)	2,010 (1,088–2,448)	.20
No. oocytes fertilized (%)[b,c]	3,085 (64.3)	1,858 (62.4)	.09
No. of ICSI cycles[a]	181 (46.1)	105 (38.5)	.06
No. of 6-cell embryos[b,c]	3 (1–4)	2 (1–4)	.74
No. of embryos transferred[b,c]	3 (2–4)	3 (2–4)	.51
No. of traumatic ETs (%)	70 (17.8)	61 (22.3)	.18
No. blastocyst transfers (%)[a]	22 (5.6)	8 (2.8)	.18

[a] χ^2.
[b] Values are medians with inner quartile ranges.
[c] Binary logistic regression. Significance set at $P<.05$.

Frankfurter. Middle to lower uterine embryo transfer and IVF success. Fertil Steril 2004.

The importance of the length of uterine cavity, the position of the tip of the inner catheter and the distance between the fundal endometrial surface and the air bubbles as determinants of the pregnancy rate in IVF cycles

Pınar Ozcan Cenksoy[a,*], Cem Fıcıcıoglu[a,1], Mert Yesiladali[a,2], Oya Alagoz Akcin[a,3], Cigdem Kaspar[b,4]

European Journal of Obstetrics & Gynecology and Reproductive Biology 172 (2014) 46–50

The optimal distance between the fundal endometrial surface and the tip of inner catheter is 1.5–2 cm.

Tiras 2011: studio su 5055 ET

PR aumentata se bolle a distanza dal fondo <10 mm.

Gold standard: punta del catetere a 10-20 mm

Easy vs difficult

- Difficult ET= lower pregnancy rate
  - Time consuming
  - Require of firmer catheter
  - Cause discomfort
  - Additional instrumentation

- Meccanismo diminuzione PR
  - Modificazione dell'attività contrattile uterina (insulto meccanico, Rilascio Pg e ossitocina,...?)
  - Insulto diretto endometriale (sangue sulla punta del catetere)

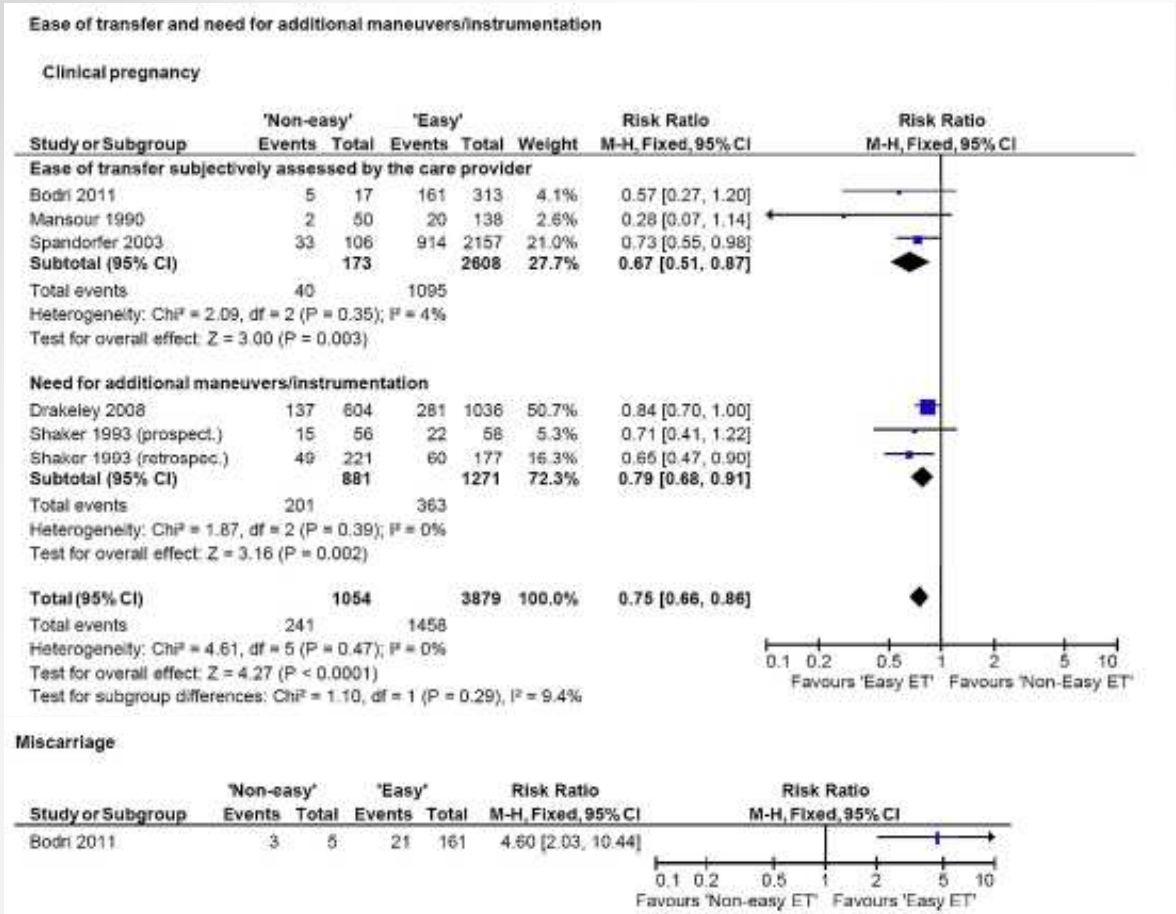


Fig. 2. Forest plots for clinical pregnancy and miscarriage: comparison between 'Non easy' versus 'Easy' embryo transfers.

Difficult embryo transfers or blood on catheter and assisted reproductive outcomes: a systematic review and meta-analysis

James A.S. Phillips [a], Wellington P. Martins [b,c,d,*], Carolina O. Nastri [b,c], Nicholas J. Raine-Fenning [a]

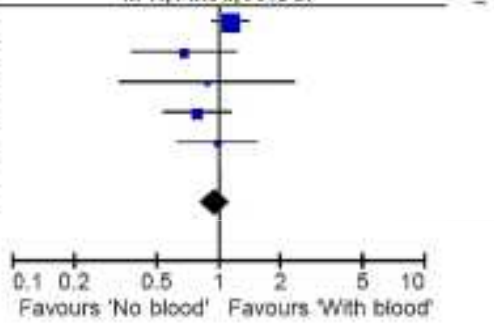
J.A.S. Phillips et al. / European Journal of Obstetrics & Gynecology and Reproductive Biology 168 (2013) 121–128

Presence of blood on the transfer catheter

Clinical pregnancy

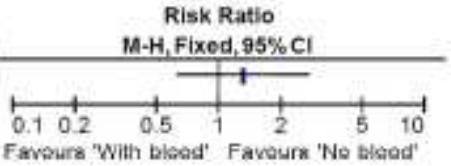
Study or Subgroup	With blood Events	Total	No blood Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bodri 2011	65	119	101	211	48.0%	1.14 [0.92, 1.42]
Eskandar 2008	9	37	120	336	15.7%	0.68 [0.38, 1.22]
Karande 2002	2	4	140	247	2.9%	0.88 [0.33, 2.36]
Rhodes 2005	17	38	95	167	23.2%	0.79 [0.54, 1.15]
Rhodes 2007	9	15	51	84	10.2%	0.99 [0.63, 1.55]
Total (95% CI)		**213**		**1045**	**100.0%**	**0.96 [0.82, 1.14]**
Total events	102		507			

Heterogeneity: Chi² = 4.86, df = 4 (P = 0.30); I² = 18%
Test for overall effect: Z = 0.44 (P = 0.66)



Miscarriage

Study or Subgroup	With blood Events	Total	No blood Events	Total	Risk Ratio M-H, Fixed, 95% CI
Bodri 2011	11	65	13	101	1.31 [0.63, 2.76]



Localizzazione sangue su catetere

Correlation of technical difficulty during embryo transfer with rate of clinical pregnancy

Neeta Singh, Prerna Gupta, Suneeta Mittal, and Neena Malhotra

J Hum Reprod Sci. 2012 Sep-Dec; 5(3): 258–261.

Characteristics of cycle between bloodless transfers and transfers with blood at outer catheter or catheter tip

	Bloodless transfer ($n = 241$)	Blood on outer catheter ($n = 71$)	Blood on catheter tip ($n = 30$)	P value
Age	31.29 ± 3.9	31.6 ± 4.12	31.8 ± 4.3	NS
No. of oocytes retrieved	11.6 ± 6.8	10.5 ± 6.9	11.9 ± 5.8	NS
No. of grade I embryos	5.4 ± 3.6	6.2 ± 3.4	5.8 ± 2.9	NS
No. of embryos transferred	2.7 ± 0.5	2.7 ± 0.5	2.7 ± 0.5	NS
Clinical pregnancy rate	24.1	21.2	13.3	0.032

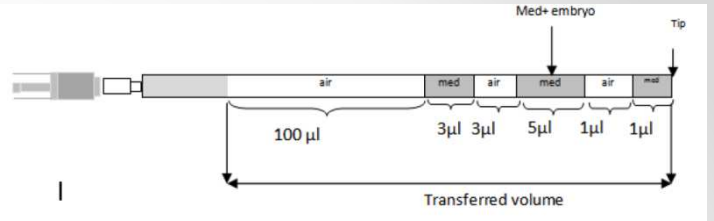
Tipo di catetere

Catetere morbido e flessibile per indurre minor traumatismo possibile a livello della cavità uterina.

Numerosi trial randomizzati, metanalisi.

(Abou Setta 2005; Buckett 2006)

L'uso di mandrino rigido, altra strumentazione (es. Pinza da collo) sono da utilizzare solo in caso di ET difficile.



Tecnica ET

- Velocità di iniezione

Pressure changes during embryo transfer

Cezary Grygoruk, M.D., Ph.D.,[a] Piotr Sieczynski, M.Sc., Ph.D.,[b] Piotr Pietrewicz, M.Sc.,[a] Malgorzata Mrugacz, M.D., Ph.D.,[c] Jerzy Gagan, M.Sc., Ph.D.,[d] and Grzegorz Mrugacz, M.D., Ph.D.[a]

Pressure changes, time and speed of injection of transferred volume recorded during 30 mock embryo transfers.

	Mean	SD	Minimum	Maximum
Peak pressure during transfer (mm Hg)	76	37	14	155
Pressure increase slope (mm Hg/s)	26,682	16,595	2,656	72,437
Pressure decrease slope (mm Hg/s)	61,742	34,209	8,375	144,250
Time of injection of transferred volume (s)	0.021	0.006	0.011	0.032
Speed of injection of transferred volume (m/s)	12.1	3.5	7.5	21.8

Grygoruk. Embryo transfer: part I. Fertil Steril 2011.

minor traumatismo
possibile per gli embrioni

Pressure changes (in mm Hg) recorded during ejection of transferred volume for doctor A (10 transfers), doctor B (10 transfers), and doctor C (10 transfers).

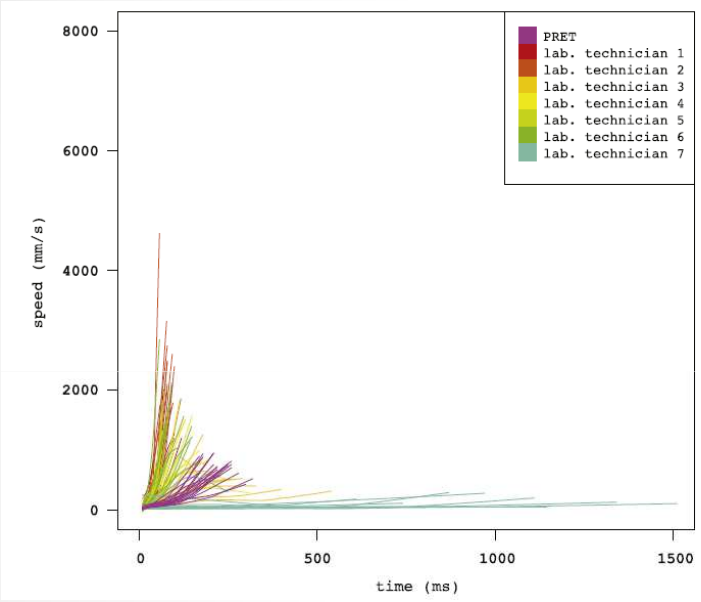
	Doctor A	Doctor B	Doctor C	Together
Mean peak pressure (SD)	116 (25)[a]	66 (25)	47 (20)	76 (37)
Minimum	76	31	14	14
Maximum	155	95	73	155

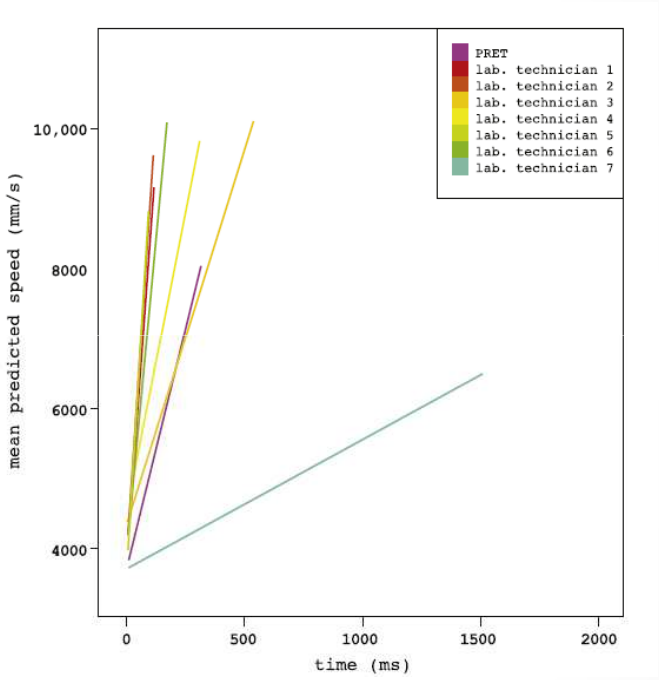
[a] $P < 0.05$.

Grygoruk. Embryo transfer: part I. Fertil Steril 2011.

Standardization of catheter load speed during embryo transfer: comparison of manual and pump-regulated embryo transfer

E Groeneveld [a,*], B de Leeuw [b], CG Vergouw [a], OW Visser [c], MJ Lambers [a], MW Heymans [d], LH Langeveld [b], R Schats [a], PGA Hompes [a]





technique. Their injection speeds were compared with that of a PRET device. The results indicate that in manually performed transfers, even after standardization of the protocol, there is still a large variation in injection speed, while a PRET device generates a reliable and reproducible injection speed and therefore brings new possibilities for further standardization of the embryo-transfer procedure. Future research should reveal whether these experiments mimic real clinical circumstances and if a standardized injection speed results in more exact positioning of the transferred embryos and therefore higher pregnancy rates.

Evitare la fuoriuscita degli embrioni

- Terreno ricco di acido ialuronico (es. Embryo glue)
- Togliere il caterere dopo 30-60 secondi dalla fine della procedura.

Quando togliere il catetere: immediate vs delayed removal

Sroga et al.2010: non differenze statisticamente significative tra le due tecniche.

Importante non creare pressione negativa che possa dislocare gli embrioni appena trasferiti

- Mantenimento dello speculum per qualche minuto con lo scopo di mantenere disteso il collo uterino

Controllo catetere post ET

- Controllare che non ci siano embrioni ritenuti all'interno del catetere.
- Se si ripetere la procedura.
- Non sembra interferire sul PR.

Bed rest

- In passato consigliato per 24 ore post ET
- Attualmente 10-15 minuti bed rest (Abou-Setta et al., 2009)
- the bed rest period did not affect clinical pregnancy rate (Purcell et al.,2007)