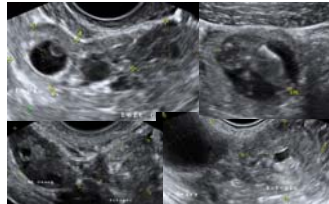


ART and Ectopic Pregnancy: Risk and Diagnosis



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Conflict of Interest

- None

Ectopic Pregnancy After IVF

- Reported rates of 1.4-5.4%
- Rates higher than after natural conception
- Why?
 1. Risk factors in infertile women
 2. Other predisposing risks
 3. The ART method itself

1. Risk Factors for Ectopic Pregnancy in Infertile Women

- Tubal pathology
- Pelvic inflammatory disease
- Previous pelvic surgery
- Uterine cavity abnormalities

2. Other predisposing risk factors for ectopic pregnancy

- Smoking
- Advanced maternal age
- Uterine fibroids
- Endometriosis
- Obesity
- Previous history of ectopic pregnancy

3. ART method as a risk factor for ectopic pregnancy

- Number of embryos transferred
- Transfer techniques
- Day of transfer
- Fresh or frozen cycle
- Ovarian hyperstimulation

The number of embryos transferred

- Higher rate of EP, the more embryos that are transferred.
- Chance of a heterotopic pregnancy ~ 1/100
 - ~1/45 if > 4 embryos transferred.
- Increased risk if history of tubal factor infertility.

Day of transfer

- Blastocyst transfer (day 5) has been shown previously to reduce the risk of EP.
- In a spontaneous cycle, the embryo enters the uterine cavity at the blastocyst stage.
- When transferred in IVF at this stage, it has a larger diameter, shorter time before implantation and a lower likelihood of migration to the tube.
- Lower uterine contractility (cervix to fundus) due to progesterone influence (day 6-7 after oocyte pick up) could minimize retrograde travel of the embryo.

Day of transfer

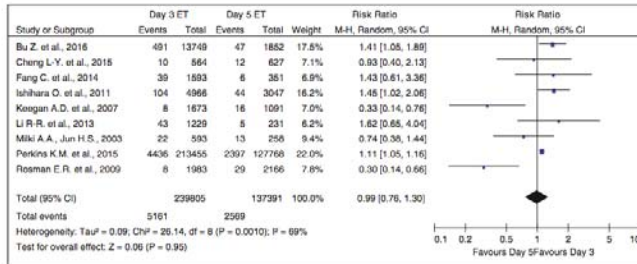


Figure 1. Forest plot of the comparison of ectopic pregnancy rates following day 3 versus day 5 embryo transfer (random effect model).

Muller et al., 2016

- Meta-analysis suggests that the embryo stage does not affect incidence of EP

Fresh or frozen cycle

- Higher risk of EP in fresh non-donor IVF cycles.

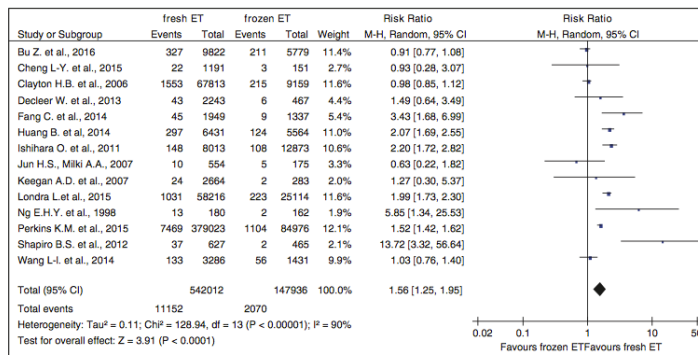


Figure 2. Forest plot of the comparison of ectopic pregnancy rates following fresh versus frozen/thawed embryo transfer (random effect model).

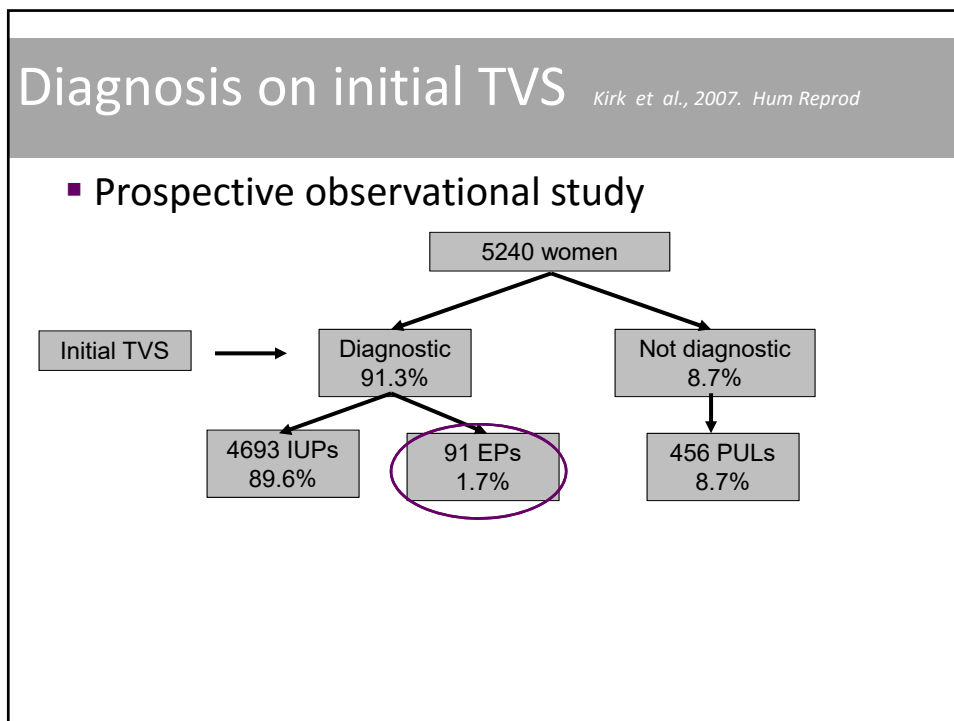
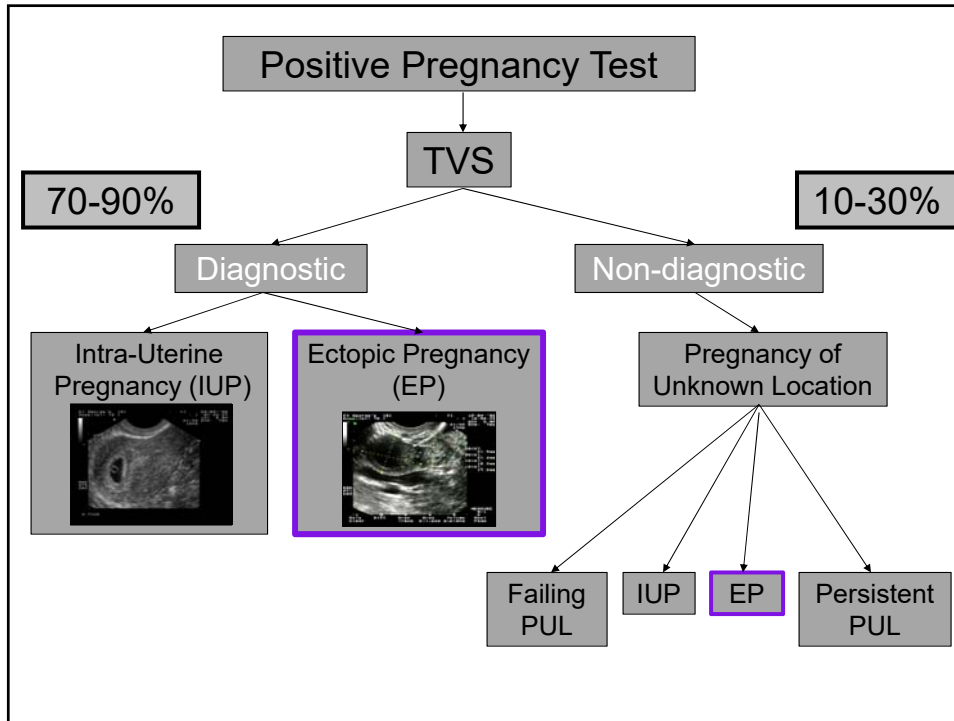
Fresh or frozen cycle

- Higher risk in fresh cycles may be due to adverse effect of ovarian hyperstimulation:
 - Elevated hormonal levels alter uterine environment affecting implantation
 - Supra-physiological levels of oestrogen and progesterone lead to enhanced uterine contractility, affect tubal peristalsis and ciliary beat possibly contributing to retrograde embryo movement

Diagnosis of ectopic pregnancy

- Specific ultrasound criteria for most types of ectopic pregnancy

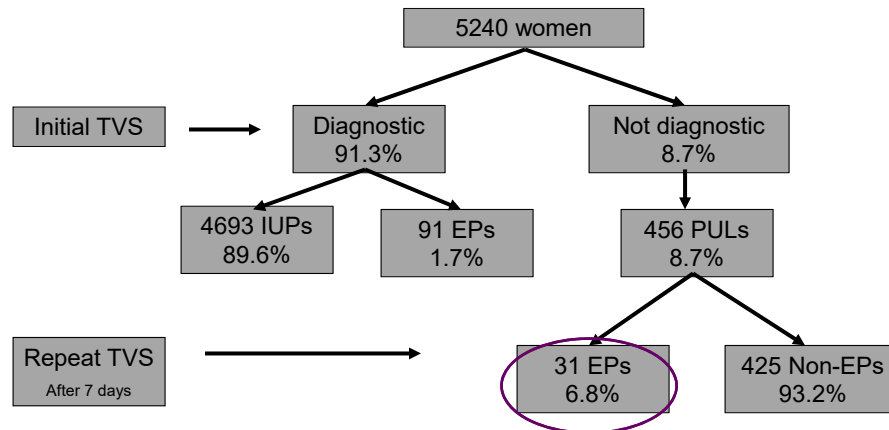




Diagnosis on initial TVS

Kirk et al., 2007. Hum Reprod

■ Prospective observational study



Sensitivity of TVS to detect ectopic pregnancy

■ Initial TVS:

- Sensitivity 73.9% (95% CI: 55.7 – 81.2%)
- Specificity 99.9% (99.8-100.0%)
- PPV 96.7% (91.6 – 99.2%)
- NPV 99.4% (99.1 – 99.6%)

■ Overall (including follow-up scans):

- Sensitivity 98.3% (95% CI: 94.1 - 99.8%)
- Specificity 99.9% (99.8 - 100.0%)
- PPV 97.5% (92.9 - 99.5%)
- NPV 100% (99.9 - 100.0%)

Scanning Ectopic Pregnancies

1. Demographics
2. Presenting complaints
3. Serum Biochemistry
4. USS findings
 1. Endometrium
 2. Free Pelvic Fluid
 3. Visualization of an ectopic mass

Scanning Ectopic Pregnancies

- ~~1. Demographics~~
- ~~2. Presenting complaints~~
3. Serum Biochemistry
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Serum Biochemistry

- * Initial serum hCG level 1299 IU/L (6-129,956 IU/L)
- * Initial serum hCG level < 500 IU/L 24.9%
- * Initial serum hCG level < 1000 IU/L 41.7% **45%
- * Initial serum hCG level < 1500 IU/L 51.4%

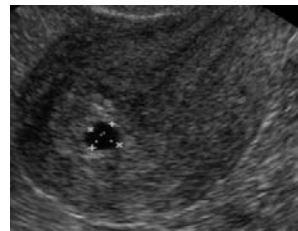
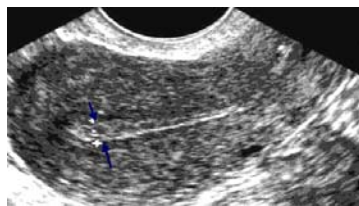
- * Initial progesterone level 19 nmol/L (1-178 nmol/L)

- *hCG < 1000 IU/L – 72% visualised on the initial TVS
- *hCG > 1000 IU/L – 83% visualised on the initial TVS

*** Data from 697 consecutive tubal ectopic pregnancies - unpublished*

** Data from 422 consecutive tubal ectopic pregnancies Kirk et al., 2008*

Empty uterus....



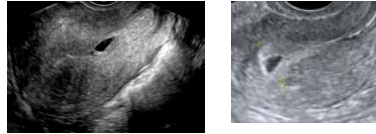
Endometrium

- No specific endometrial appearance that can be used to diagnose an ectopic pregnancy

*ET 9.3mm (1.7 – 36.0 mm)

*24.1% Disrupted 75.8% Intact

- 'Pseudosac' reported in up to 20% of cases
 - May occasionally contain internal debris - ? embryonic structures

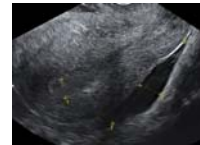
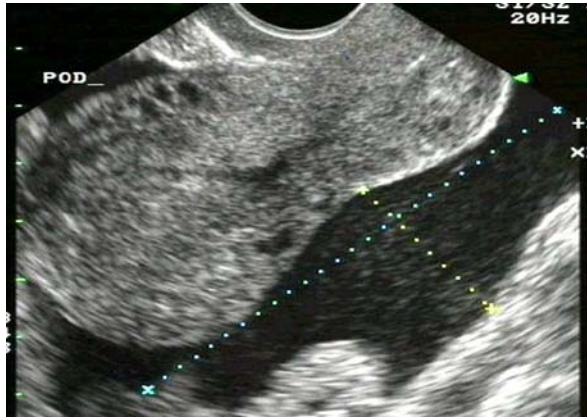


* Data from 422 consecutive tubal ectopic pregnancies Kirk et al., 2008

Endometrium



Free Fluid.....



Free Fluid

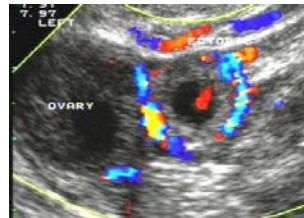
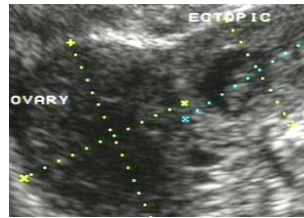
- Small amount of anechoic fluid common in intra- and extra-uterine pregnancies
- Echogenic fluid present in 28-56% (Nyberg et al., 1991, Fleischer et al., 1990)
 - *Anechoic free fluid in 19.5%
 - *Echogenic fluid in 35.8%
- Amount of fluid found on TVS correlates well with operative findings
- Significant if reaches fundus of uterus, is in utero-vesical pouch or Morrison's pouch



* Data from 422 consecutive tubal ectopic pregnancies Kirk et al., 2008

Tubal Ectopic Pregnancy

Gestational sac and CRL or yolk sac



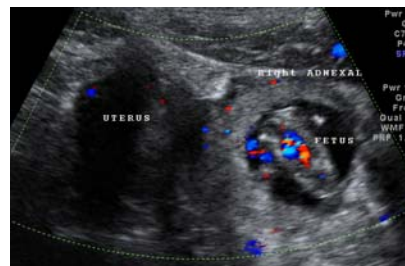
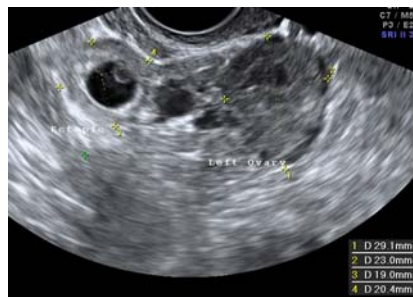
*19%

*Cardiac activity in 29%
*5.5% of all visualised EPs

Median hCG 9072 IU/L
Range 378 – 129,956 IU/L

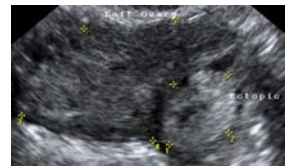
Tubal Ectopic Pregnancy

Gestational sac and CRL or yolk sac



Tubal Ectopic Pregnancy

Empty Gestational Sac

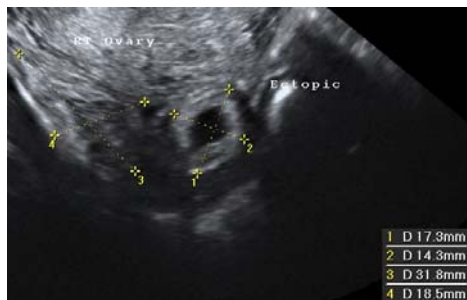


*20%

Median hCG 1576 IU/L
Range 63 – 47,302 IU/L

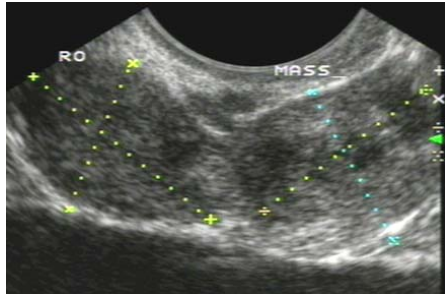
Tubal Ectopic Pregnancy

Empty Gestational Sac



Tubal Ectopic Pregnancy

Inhomogeneous Mass



*62%

Median hCG 667 IU/L
Range 10 – 31,169 IU/L


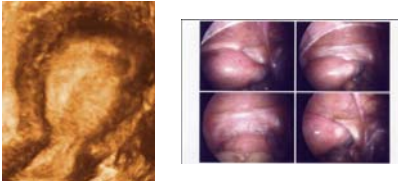


Tubal Ectopic Pregnancy

Inhomogeneous Mass



Interstitial Ectopic Pregnancy

- Empty uterine cavity
 - Gestational sac or trophoblastic mass located in the interstitial area surrounded by a continuous rim of myometrium
 - Interstitial line sign (thin echogenic line extending from central uterine cavity echo to periphery of interstitial sac)
- 2-4% of all ectopic pregnancies
- 
- 

Cornual Ectopic Pregnancy

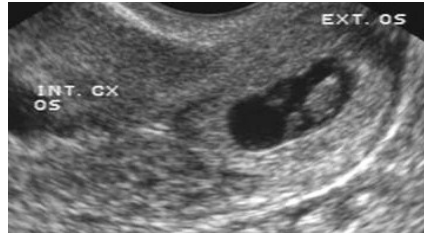
- A single interstitial portion of Fallopian tube in the main uterine body
 - A gestational sac or trophoblastic mass mobile and separate from the main uterine body but surrounded by myometrium
 - A vascular pedicle joining the gestational sac to the unicornuate uterus
- Implantation in the non-communicating horn of a unicornuate uterus.
 - 1 in 76,000 pregnancies
 - 0.27% of all ectopics

Cervical Ectopic Pregnancy

- Empty uterine cavity
- Barrel shaped cervix
- Gestational sac or trophoblastic mass below level of the internal os
- Absence of 'sliding sign'

(when pressure is applied to cervix using the probe in a miscarriage, the gestational sac slides against the endocervical canal, but does not in an implanted cervical pregnancy)

- Evidence of peritrophoblastic flow on Color Doppler examination



- <1% of all ectopic pregnancies

Caesarean Section Scar Pregnancy

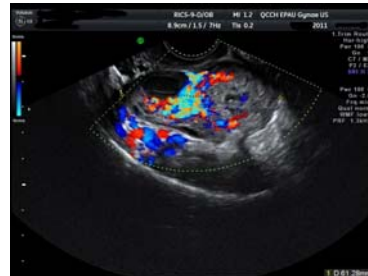
- Empty uterine cavity
- Gestational sac or trophoblastic mass located anteriorly at the level of the internal os covering the visible or presumed site of the previous lower uterine segment caesarean section scar
- Absent 'sliding sign'
- Evidence of peritrophoblastic flow on color Doppler examination



- 1 in 1800 pregnancies
- 6% of ectopics in women with a previous LSCS

Ovarian Ectopic Pregnancy

- Empty uterine cavity
- Gestational sac or trophoblastic mass with a wide echogenic ring on or within the ovary, generally seen separately from the corpus luteum



- Up to 3% of all ectopic pregnancies

Intra-mural Ectopic Pregnancy

- Empty uterine cavity
- Gestational sac or trophoblastic mass completely surrounded by myometrium and separate to the endometrial cavity



- Rare
- Risk factors: IVF, adenomyosis, uterine trauma from instrumentation

Heterotopic Pregnancy

- An ectopic pregnancy with an intra-uterine pregnancy
- 1 in 30,000 spontaneous conceptions
- 1-3 in 100 pregnancies conceived via ART



Abdominal Pregnancy

- Empty uterine cavity
 - No evidence of a dilated Fallopian tube or complex adnexal mass
 - Gestational sac or trophoblastic mass surrounded by loops of bowel and separated by peritoneum
- 1° – original implantation site is within the peritoneal cavity
 - 2° – result of tubal abortion and re-implantation into the abdominal cavity

