The ultrasound diagnosis of ectopic pregnancy

Emma Kirk

Transvaginal sonography (TVS) is an accurate diagnostic test for ectopic pregnancy with a high sensitivity (87.0-99.0%) and specificity (94.0-99.9%)

Braffman et al., 1994, Shalev et al., 1998, Atri et al., 2003, Condous et al., 2005

Diagnosis based on positive visualisation of an extra-uterine pregnancy, rather than the inability to visualise an intra-uterine pregnancy

Appearance of an Ectopic Pregnancy on TVS

Tubal
Gestational sac and CRL
Visible cardiac activity
**Appearance of an Ectopic Pregnancy on TVS**

### Tubal

- ‘Bagel Sign’
- Inhomogeneous Mass

<table>
<thead>
<tr>
<th>Image 1</th>
<th>Image 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.jpg" alt="Bagel Sign" /></td>
<td><img src="image2.jpg" alt="Inhomogeneous Mass" /></td>
</tr>
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</table>

### Cervical

- An empty endometrial cavity, with a gestational sac present below the level of the uterine arteries.
- An absent “sliding sign”.
- Visible blood flow around the gestation sac using colour Doppler.

### Interstitial

- An empty endometrial cavity with products of conception located outside of the endometrial echo, surrounded by a continuous rim of myometrium, within the interstitial area.
Appearance of an Ectopic Pregnancy on TVS

Non - Tubal Caesarean Section Scar

- An empty endometrial cavity and cervical canal with a gestational sac implanted within the lower anterior segment of uterine wall
- Evidence of myometrial dehiscence

Diagnosis on the initial TVS examination?

- Studies reporting high sensitivities examined women using TVS immediately prior to laparoscopy, and correlated sonographic features to surgical findings
- Results are therefore possibly misleading as not all ectopic pregnancies would have been visualised on the initial TVS examination

Positive Pregnancy Test

- TVS
  - 90% Intra-Uterine Pregnancy (IUP)
  - 10% Ectopic Pregnancy (EP)
  - 10% Pregnancy of unknown location
    - IUP Failing EP PUL
Pregnancy of Unknown Location (PUL)
- Positive pregnancy test
- No pregnancy visualised on scan
- Not interchangeable with 'ectopic pregnancy'

X Pregnancy of Unknown Location (PUL)

Early Intra-uterine Gestational Sac

Fluid in the endometrial cavity
Diagnostic effectiveness of the initial TVS to diagnose ectopic pregnancy

- A prospective observational study including all women attending the Early Pregnancy Unit with a positive pregnancy test over a one-year period
- Outcome measure = ectopic pregnancy
- The sensitivity, specificity, PPV, NPV and likelihood ratio with 95% confidence intervals (CI) for the initial USS to diagnose ectopic pregnancy were calculated

Kirk et al, Hum Reprod 2007
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%)

Why are some ectopic pregnancies missed on the initial scan?

<table>
<thead>
<tr>
<th>Initial TVS result</th>
<th>Ectopic Pregnancy</th>
<th>PUL</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>363</td>
<td>58</td>
<td>-</td>
</tr>
<tr>
<td>Maternal age (years) Mean (SD)</td>
<td>30.4 (5.9)</td>
<td>32.0 (6.3)</td>
<td>0.0551</td>
</tr>
<tr>
<td>Bleeding n (%)</td>
<td>216 (61.2)</td>
<td>39  (67.2)</td>
<td>0.4657</td>
</tr>
<tr>
<td>Pain n (%)</td>
<td>233 (66.0)</td>
<td>34 (58.6)</td>
<td>0.2997</td>
</tr>
<tr>
<td>ET mm Mean (SD)</td>
<td>10.1 (5.7)</td>
<td>11.1 (5.3)</td>
<td>0.098</td>
</tr>
</tbody>
</table>

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<th>PUL</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (days) Mean (SD)</td>
<td>45.6 (14.5)</td>
<td>41.4 (13.5)</td>
<td>0.0317</td>
</tr>
<tr>
<td>hCG IU/L Median (IQR)</td>
<td>1286 (3394, 478-3826)</td>
<td>635 (1796, 234-2039)</td>
<td>0.0010</td>
</tr>
<tr>
<td>Prog nmol/L Median (IQR)</td>
<td>19 (27, 9-36)</td>
<td>30 (26, 19-45)</td>
<td>0.0095</td>
</tr>
</tbody>
</table>
Why are some ectopic pregnancies missed on the initial scan?

<table>
<thead>
<tr>
<th>TVS to visualise ectopic pregnancy</th>
<th>Initial TVS</th>
<th>Subsequent TVS</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>hCG IU/L Median (IQR)</td>
<td>1256 (5344, 472-4820)</td>
<td>1258 (2657, 946-2997)</td>
<td>0.2431</td>
</tr>
<tr>
<td>Prog nmol/L Median (IQR)</td>
<td>19 (7, 9-36)</td>
<td>20 (17, 11-28)</td>
<td>0.7334</td>
</tr>
<tr>
<td>Appearance on TVS:</td>
<td></td>
<td></td>
<td>0.1029</td>
</tr>
<tr>
<td>Inhomogeneous mass n (%)</td>
<td>222 (62.8)</td>
<td>25 (71.4)</td>
<td></td>
</tr>
<tr>
<td>Empty gestational sac n (%)</td>
<td>77 (21.8)</td>
<td>9 (25.7)</td>
<td></td>
</tr>
<tr>
<td>Gestational sac with yolk sac/fetal pole n (%)</td>
<td>54 (15.3)</td>
<td>1 (2.8)</td>
<td></td>
</tr>
<tr>
<td>Mean size of ectopic mass mm (SD)</td>
<td>22.2 (9.3)</td>
<td>19.4 (5.3)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Why are some ectopic pregnancies missed on the initial scan?

- Compared to ectopic pregnancies visualised on the initial TVS, ectopic pregnancies initially classified as PULs had:
  - Lower mean gestational age
  - Lower mean initial hCG,
  - Higher mean progesterone level at presentation

- However, at the time of visualization: serum hCG, serum progesterone levels and the appearance were not significantly different between the two groups

Why are some ectopic pregnancies missed on the initial scan?

- Failure of visualization of the ectopic pregnancy on the initial TVS may be due to the fact that they are too small and probably too early in the disease process
Diagnosis of ectopic pregnancies in PUL population

1. Hormones
2. Surgical intervention
3. Mathematical models

PUL Management

- Serum hCG and progesterone
- ± TVS ± Curettage ± Laparoscopy
- Intrauterine Pregnancy (IUP)
- Failing PUL
- Ectopic Pregnancy (EP)

CURRENT CRITERIA

- IUP - hCG rise > 66% in 48 hrs
- Failing PUL - Serum progesterone < 20 nmol/L
- Ectopic Pregnancy - hCG rise < 66% in 48 hours

PUL Management

1. Hormones
   - Human chorionic gonadotrophin (hCG)
   - Progesterone
   - Other:
     - CA 125
     - Creatine kinase
     - Activin A
     - Inhibin A
2. Surgical Intervention

- Laparoscopy
  - The combination of a positive pregnancy test and the absence of an IUP on TVS is an accepted indication for laparoscopy

- Curettage
  - Serial measurements of hCG and progesterone, TVS and uterine curettage have been combined into various diagnostic algorithms when a pregnancy cannot be seen on TVS

3. Use of mathematical models

- Mathematical models have been developed to predict the outcome of PULs

- They do not require any understanding of the behaviour of serum biochemistry in early pregnancy and could possibly lead to more standardised management protocols

Summary

- TVS has a high sensitivity for the detection of ectopic pregnancy:

  - Diagnosis is based on positive visualisation of an ectopic mass
  - ~75% of ectopic pregnancies can be visualised on the initial TVS examination
  - Those missed on the initial TVS should be classified as pregnancies of unknown location
  - Overall >90% can be visualised on TVS prior to treatment
Summary

Detecting ectopic pregnancy in the PUL population:

- The majority of PULs are not ectopic pregnancies
- Expectant management is safe
- There is no role for the routine use of uterine curettage or laparoscopy in the management of PULs

Summary

Detecting ectopic pregnancy in the PUL population:

- A discriminatory zone level of serum hCG is not helpful in a PUL population where ectopic pregnancy diagnosis is TVS based
- Mathematical models do allow prediction of PUL outcome
- There is the possibility to rationalise the follow-up of PULs