Early Pregnancy Cerclage – vaginal or abdominal?

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Setting the scene

- Early pregnancy figures in UK
- Trends and shifts
- Care provision
- New horizons
UK Figures (2008)

- 700,000 births per annum in UK
- 200,000 terminations
- >250,000 miscarriages
- 15,000 ectopic pregnancies

Trends and Shifts

• Increasing average maternal age
• Increasing demand for all EP events
• Increasing knowledge about early pregnancy events (17,500,000 entries on Google)
• Patient Choice an important driver for management and shared decision making based on evidence based practice
Standards in Early Pregnancy + Ectopic Pregnancy + Recurring Miscarriage

RCOG Standards in Gynaecology (2008)

AEPU   Roy Farquharson, Chair, Association of Early Pregnancy Units
       Lesley Regan, Hon President, AEPU

Website: earlypregnancy.org.uk        rcog.org.uk/standards
June 2008

2. EARLY PREGNANCY LOSS
3. ECTOPIC PREGNANCY
4. RECURRING MISCARRIAGE
<table>
<thead>
<tr>
<th>Standard</th>
<th>CORE</th>
<th>Aspirational</th>
</tr>
</thead>
</table>
| Patient Information   | Designated Reception Area  
Universal use of clear, understandable terminology by all staff | Dedicated staff constantly at reception desk to provide greeting, obtain patient details and explain structure and triage function of EPU |
| Patient Choice In Management | Education of patient relevant to diagnosis and management  
Open explanation of expectant, medical and surgical options | Dedicated phone line for patient queries and electronic access to protocols from outside unit |
| Dedicated Quiet Room  | Room for breaking bad news away from work area                       | Single-use room only with soft furnishing and absence of medical equipment |
| Availability of Service | 5 day opening during office hours                                      | 7/24 opening and service provision with full staffing and daily scan support |
| Competence of Scanning | Recognised ultrasound training and preceptor assessment and validation (RCOG/BMUS)  
Register of staff competent at scanning | Lead Clinician Presence of RCOG/BMUS trainer in EPU  
Annual assessment of audited activity |
| Blood HCG level measurement | Laboratory access to blood HCG measurement and result within 48 hours of sampling | Same day sampling and result with electronic result link to laboratory |
| Written Information Leaflets | Visible open access to written information leaflets in EPU | Online external access to PIL |
| Acknowledgment of Privacy and Dignity | To provide individualised patient support and acknowledge confidentiality | Place one to one care as best practice at all times |
| Bereavement Counselling | All staff trained in emotional aspects of early pregnancy loss  
To enable access to counselling and provide immediate support | To provide all emotional and psychological counselling requirements within EPU and supported by dedicated staff and related agencies |
| Site of EPU           | Geographically separate from all maternity areas                      | Own EPU entrance/exit                                                      |
What does an Early Pregnancy Clinic/Unit do?

- All early pregnancy problems are seen by a multidisciplinary team in a dedicated area with easy patient access and privacy (for breaking bad news) plus good quality scan service and laboratory backup (HCG result computer link)
- Adapted (MEWS-based) Triage Assessment on presentation (~ 1-2% score>4)
- Diagnosis & surveillance of PUL/PUV/ectopic
- Treatment & Surveillance of EP loss, ectopic failed PUL/molar pregnancy/hyperemesis
- Initiation of Management Plan for Medical/Surgical/Expectant protocols & options
Inherited Thrombophilia Tests
UK National EPU Survey 2008
(Norrie et al, Brit J Haem, 2009, 144, 241-4)

• 70% response rate (115/164 EPU’s) in UK
• Heritable Thrombophilias (eg FVL, Prot C, S) tested for late miscarriage (80%), recurrent miscarriage (76%) and placental abruption (88%)
• Highly variable range of tests between EPU’s which frequently led to heparin/aspirin administration in next pregnancy
• Evidence based practice for testing and intervention inconsistent across UK
Opportunityisnowhere
Historical Perspective
(Cervical Weakness)

• Described in 1658 by Grant:

“the orifice of the womb is so slack that it cannot rightly contract itself to keep in the seed; which is chiefly caused by abortion or hard labour and childbirth, whereby the fibres of the womb are broken in pieces from one another and they, and the inner orifice of the womb overmuch slackened.”
First Presentation with Midtrimester Loss (MTL)  
~2% risk between 12 to 24 weeks gestation
<table>
<thead>
<tr>
<th>EVENT versus CAUSE</th>
<th>CERVIX</th>
<th>LIQUOR PV</th>
<th>FETAL HEART ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical Weakness</td>
<td>OPEN</td>
<td>Absent until expulsion of sac</td>
<td>Present</td>
</tr>
<tr>
<td>Maternal Thrombophilia Eg APS</td>
<td>Closed</td>
<td>Absent</td>
<td>ABSENT (Intrauterine death)</td>
</tr>
<tr>
<td>Bacterial Vaginosis</td>
<td>Closed</td>
<td>PRESENT</td>
<td>Present ? until sac expulsion</td>
</tr>
</tbody>
</table>
Investigation Protocols for MTL

- Non-uniform
- Inconsistent
- Restricted testing of important variables and causative factors
- Small cohort analysis & description
- Randomised trials - rare
# Investigation Protocols for Published Vaginal or Abdominal Cerclage Studies

<table>
<thead>
<tr>
<th>First Author &amp; Year of Publication</th>
<th>Number of Patients Vaginal (TVS) or Abdominal (TAC)</th>
<th>Hysteroscopy before pregnancy</th>
<th>Antiphospholipid Syndrome (APS) Testing</th>
<th>Bacterial Vaginosis (BV) or Infection Screening</th>
<th>TVU of CLM +/- Funnelling surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Davis et al (2000)</td>
<td>40 TAC</td>
<td>4 Mullerian Anomalies</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Rust et al (2000)</td>
<td>61 RCT of TVS v. TLC</td>
<td>NO</td>
<td>YES</td>
<td>BV &amp; AF Sample</td>
<td>Inclusion Criteria at 16-24/40</td>
</tr>
<tr>
<td>Althuisius et al (2000)</td>
<td>67 RCT of TVS v. TLC</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Inclusion criteria</td>
</tr>
<tr>
<td>Gibb et al, (1998)</td>
<td>50 TAC</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Occlusion 2005</td>
<td>TVS +/- occlusion</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Farquharson et al (2005)</td>
<td>40 TAC</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Standardised Investigation Protocol

- Consecutive cases of second trimester loss
- Continuous Care provision by same team at one hospital (Liverpool Women’s Hospital)
- Uniform application of standardised investigation pathway
- Management plan constructed after full investigation prepregnancy

References:
- Farquharson et al, Transabdominal cerclage: the significance of dual pathology and increased preterm delivery, BJOG, 2005, 112, 1424-26
Midtrimester Loss Investigations

- Antiphospholipid Syndrome
  (APS testing & Bone mineral density prepregnancy)
- Significant Thrombophilia
  (inherited or acquired APCR, Protein C/S deficiency)
- Bacterial Vaginosis
- Thyroid Function
- Cervical assessment and Hysteroscopy
- Dual Pathology found in 10% of ALL MTL cases
What’s Missing?

• Reproducible and accurate assessment of internal os integrity
• Preconceptual and T1 testing for APS & BV
• Accurate prediction of efficacy for vaginal suture insertion and next treatment intervention if vaginal cerclage fails
• Considered, informed prepregnancy counselling before Transabdominal Cerclage insertion following appropriate investigation and full risk disclosure
Bacterial Vaginosis

- Imbalance in type and number of vaginal bacterial population eg. anaerobes, clue cells with a 14% prevalence in antenatal group (Oakeshott, 2002, BMJ)
- Effective eradication/suppression proven by RCT’s in pregnancy (Okun et al., O&G, 2005, 105, 857-68 Systematic Review)
- Clindamycin RCT given for 5 days at 12-16 weeks reduces MTL (RR 0.20, 95% CI 0.04-0.89) (Ugwumadu et al, Lancet, 2003)

Liverpool Women's Hospital
Thrombophilia Screen: Antiphospholipid Syndrome (DRVVT, ACA IgG/IgM); Activated Protein C resistance (APCR/ACPRV (acquired), Factor V Leiden (inherited); Protein C/S level

Autoimmune screen (ANA/dsDNA/ENA:RO, La/SMA)

ABO grouping: RH grouping/ Antibody

Hb: WCC & platelets

FSH/LH/E2/Test/Prog/PRL/Thyroid Function tests+/−Thyroid Peroxidase

Viral screen CMV/Rubella/TXP/Parvo

Random blood sugar

BONE MINERAL DENSITY preconceptual and/or ULTRASOUND

DAY CASE HYSTEROSCOPY

SWABS X2 preconceptual and T1

BACTERIAL VAGINOSIS

PREGNANCY LOSS CHROMOSOMES KARYOTYPED (by CGH)
MidTrimester Loss (1995-2005)
(n=451 consecutive cases at Liverpool Women’s)

- Idiopathic (46%)
- Thrombophilia (18%)
- Cervical Weakness (21%)
- Anatomical (3%)
- BV (11%)
- Hypothyroid (1%)
Next Pregnancy Outcome LWH (n=351, 1995-2003)

- 90 (25%) women did not become pregnant again (Brigham et al, 1999, Hum Rep, 14, 2868-71)
- of 261 MTL cases, 58 cases miscarried (30 in T1=12%) and 28 in T2 =11%).
- of 203 deliveries, 41 (20%) delivered before 34 weeks and 56 (28%) before 37 weeks
- rate of PET (3%), IUGR (3%), Abruption (2.5%) and SB (1 case)
Cervical Assessment Process

- Clinical History and **Time Order of Events** vital in assessment eg. silent dilatation of Cx first or primary SROM (+/- evidence of infection).
- Preconceptual Hysteroscopy to exclude anomaly (CUA), synechiae or denuded endometrium, integrity of internal cervical os and length
- Swab for BV and repeat in T1
- Ultrasound measurement of cervical length (TVU of CLM) at 16, 20 and 24 weeks (T2)
Cervical Length Measurement (CLM) and Funnelling

- Normal CLM circa 50mm

- Funnelling often appears after 16 weeks
TVU of Open Cervix at 16 weeks
Vaginal Cerclage

- CIPRACT RCT: cerclage v. bed rest (Althuisius, AmJOg, 2001)
- Prophylactic cerclage or Serial TVU of CLM (Berghella et al, AmJOg, 2002)
- Cochrane (Issue 1) review (Drakeley et al, O&G, 2003)
- Abdominal versus vaginal cerclage: systematic review (Zaveri, AmJOg, 2002)
- Cerclage and cervical insufficiency: an evidence based analysis (Harger, O&G, 2002)
- Occlusion RCT (2005)
Occlusion Trial

- Retaining the mucus plug by second suture
- Primary McDonald suture higher around ectocervix
- RCT of primary +/- second suture
- Multicentre international trial
Elective Vaginal Suture (LWH 2001-08)

OUTCOME

Miscarriages n=12/46 25% Failure Rate

<table>
<thead>
<tr>
<th>Gestation</th>
<th>Aetiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>BV+TCW</td>
</tr>
<tr>
<td>25</td>
<td>APS+TCW+BV</td>
</tr>
<tr>
<td>14</td>
<td>TCW</td>
</tr>
<tr>
<td>17</td>
<td>TCW+Thrombophilia</td>
</tr>
<tr>
<td>14,17(twins)</td>
<td>TCW+Thrombophilia+BV</td>
</tr>
<tr>
<td>13</td>
<td>TCW+APS+BV</td>
</tr>
<tr>
<td>22</td>
<td>BV</td>
</tr>
<tr>
<td>16</td>
<td>TCW+BV+overactive thyroid</td>
</tr>
<tr>
<td>18</td>
<td>BV+overactive thyroid</td>
</tr>
<tr>
<td>22</td>
<td>TCW+APS+BV</td>
</tr>
<tr>
<td>23</td>
<td>TCW+BV</td>
</tr>
<tr>
<td>18</td>
<td>BV+Thrombophilia</td>
</tr>
</tbody>
</table>
Transabdominal Cerclage Technique

- Uterine vessels
- Knot
- Double-stranded nylon suture
- Uterosacral ligaments
Trans Abdominal Cerclage - pre-conceptual suture insertion
Transabdominal Cerclage -- tying the knot anterior.
TA Cerclage: Indications

- History of Mid-trimester losses (12 weeks to 24 weeks)
- Cervical weakness
- Failed elective transvaginal cerclage (TVC)
  - Study exclusions: Preterm deliveries <34/40
  - Extensive cervical surgery and absent cervix (following repeated cone biopsy; radical trachellectomy)
Standardised Investigation Protocol

- Consecutive referred cases of second trimester loss
- Continuous Care provision by same team at one centre (Liverpool Women’s) before and during pregnancy
- Universal application of standardised investigation pathway
- Management plan constructed after full investigation prepregnancy
Pregnancy after TAC

- Subsequent delivery → mandatory C/S
- Suture permanent
- Can be utilised for > 1 pregnancy
- 3 patients → 2 successful pregnancies with 1 TAC in situ and single case of twins
Reported operative complications

- Injury to bladder
- Small bowel injury \(\text{(Mingione et al, 2003)}\)
- Large bowel fistula \(\text{(Debbs et al, 2007)}\)
- Rupture of membranes, pregnancy loss

→ Preconceptual (PC TAC) after 2005
TAC procedures

- All procedures performed at the Recurrent miscarriage (RM) unit - tertiary centre
- Referrals from 15 UK locations
- RM history
- $\geq 1$ previous MTL & cervical weakness
- 1 failed elective vaginal suture (TVC)
Patient demographics and summary of pre-pregnancy investigation

<table>
<thead>
<tr>
<th>Mean (range)</th>
<th>T1 TAC (n= 40)</th>
<th>PC TAC (n= 38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (21-41 years)</td>
<td>30 (21-41 years)</td>
<td>27 (22-40 years)</td>
</tr>
<tr>
<td>Parity (3-13)</td>
<td>5 (3-13)</td>
<td>4 (3-12)</td>
</tr>
<tr>
<td>Previous MTL (2-10)</td>
<td>3 (2-10)</td>
<td>3 (2-9)</td>
</tr>
<tr>
<td>Previous vaginal suture (1-4)</td>
<td>1 (1-4)</td>
<td>1 (1-4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dual Pathology</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APS (27%)</td>
<td>11 (27%)</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Bacterial Vaginosis (17%)</td>
<td>7 (17%)</td>
<td>11 (29%)</td>
</tr>
</tbody>
</table>
Preconception TAC

TAC procedures
n=38

Conceived
n=31
(PC to LMP: 25 wks; 2-64)

empty sac pregnancy loss in T1
n=2

currently pregnant n=4:
13/40
17/40
22/40
30/40

30-34 weeks
n=3

34 – 38 weeks
n=15

>38 weeks
n=6
Index Pregnancy losses between 12 to 24 weeks (n=5)

- T1TAC n= 4 (14/40;19/40;23/40;24/40)
- PC TAC n=1 (19/40)
- No correlation between success and number of previous losses &/or number of previous vaginal sutures

- All 5 failures associated with co-morbidity APS (n=3) or BV (n=2)
## Gestation at Delivery
*(after 24 weeks)*

<table>
<thead>
<tr>
<th>Gestation (weeks) at delivery</th>
<th>First trimester TAC (n=40) % (n= )</th>
<th>PreConc’al TAC (n=25) % (n= )</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;38/40</td>
<td>7% (3)</td>
<td>24% (6)</td>
</tr>
<tr>
<td>34-38/40</td>
<td>55% (22)</td>
<td>60% (15)</td>
</tr>
<tr>
<td>30-34/40</td>
<td>20% (8)</td>
<td>12% (3)</td>
</tr>
<tr>
<td>24-30/40</td>
<td>7% (3)</td>
<td>0% (0)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>90 % (36)</td>
<td>96 % (24)</td>
</tr>
</tbody>
</table>
Comparison of vaginal (TVS) and abdominal (TAC) cerclage for treatment of cervical weakness for Midtrimester Loss based on consecutive cohort data from Liverpool Women’s Hospital (2001-2008)

<table>
<thead>
<tr>
<th></th>
<th>Vaginal (n=58)</th>
<th>Abdominal (n=78)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Success Rate</strong></td>
<td>75%</td>
<td>93%</td>
</tr>
<tr>
<td><strong>Preterm Delivery rate</strong></td>
<td>25%</td>
<td>30% (60% if dual pathology)</td>
</tr>
<tr>
<td><strong>Insertion</strong></td>
<td>12 weeks gestation</td>
<td>10 weeks gestation or Preconceptual with less morbidity</td>
</tr>
<tr>
<td><strong>Morbidity</strong></td>
<td>Minimal</td>
<td>Haemorrhage Trauma to bladder/bowel</td>
</tr>
<tr>
<td><strong>Long Term Delivery</strong></td>
<td>Removal at 36 weeks</td>
<td>Permanent</td>
</tr>
<tr>
<td><strong>Delivery</strong></td>
<td>Option of vaginal</td>
<td>Mandatory Caesarean Section</td>
</tr>
</tbody>
</table>
Summary & Overview

- Midtrimester Loss between 12 to 24 weeks occurs in approx 2% of all pregnancies
- Causal factors are known in 50% of cases
- Patient friendly approach involves a specialised team with standardised investigation protocol and agreed management plan
- IVF or spontaneous pregnancies share a uniform approach
Conclusion

• TAC associated with high (90% or >) successful pregnancy outcome of >24/40
• Preconceptual TAC insertion is equally efficacious compared to T1 TAC
• PC TAC is technically easier to insert and greater precision of suture placement
• Avoids significant surgical morbidity of hemorrhage, bowel and bladder damage
Acknowledgements

LWH: AnneMaria Ellard, Kelly Macnamee, Jo Topping

Thanks to all colleagues and referring hospitals from across the UK

Thank you for your attention
Standards for Management

- Investigation of Causal Factors
- Surveillance in T1 & T2
- Treatment Interventions during pregnancy