Should all women have third trimester ultrasound screening? What the data show

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Learning Objectives

- Identify common indications for third-trimester ultrasound
- Role of late ultrasound in detection of fetal abnormalities.
- Compare the evidence for and against routine third-trimester ultrasound screening.

Questions

- True or False: The evidence supporting obtaining universal third-trimester ultrasound can categorized as Level A.
- True or false: There is evidence that universal third-trimester ultrasound can prevent stillbirth.
- True or False: Universal third-trimester ultrasound detect a significant number of fetal anomalies

Common indications for third-trimester Ultrasound

- Current clinical practice are examples of selective screening:
  - Pre-pregnancy risk factors e.g. hypertension, diabetes, renal disease
  - Current pregnancy complications e.g. preeclampsia or GDM
  - Uterine size / symphyseal fundal height discrepancy
  - Anatomy survey for late prenatal care

Goals of Ultrasound Examinations

- Detect fetal abnormalities
- Diagnose growth disorders
- Adjunctive management of complex pregnancies

Is a routine ultrasound in the third trimester justified?

Manegold G et al Ultraschall Med 2011

- Aim: To evaluate the additional benefit of routine USS at 28-32 weeks if prior anatomy US were normal.
- Methods: Prospective study of 5044 pregnancies.
- Results: Overall incidence of anomalies – 289 (3.6%), 40% detected between 11-13 weeks, 35% at 18-24 weeks and additional 15% in 3rd trimester.
Value of routine ultrasound examination at 35-37 weeks’ gestation in diagnosis of fetal abnormalities. Ficara et al UOG 2019

- **Aim:** To investigate the value of routine USS for fetal abnormalities at 35-37 weeks
- **Method:** Prospective study of 52,400 pregnancies that had routine anatomy USS at 18-24 weeks
- **Routine screening performed at 35-37 weeks**

Examples of common anomalies detected in the 3rd trimester: Ficara et al UOG 2019

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>1st or 2nd Trim</th>
<th>2nd Trim</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS anomalies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild VM</td>
<td>68</td>
<td>22</td>
<td>6</td>
</tr>
<tr>
<td>Mild VM</td>
<td>8</td>
<td>3</td>
<td>5</td>
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<tr>
<td>Severe VM</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Arachnoid cyst</td>
<td>12</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Microcephaly</td>
<td>5</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Heart</td>
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<td></td>
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</tr>
<tr>
<td>VSD</td>
<td>120</td>
<td>93</td>
<td>22</td>
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<tr>
<td>CoA</td>
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<td>6</td>
<td>4</td>
</tr>
<tr>
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<td>10</td>
<td>9</td>
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<tr>
<td>GU Tract</td>
<td></td>
<td></td>
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<tr>
<td>Hydronephrosis</td>
<td>118</td>
<td>48</td>
<td>70</td>
</tr>
<tr>
<td>Duplex Kidneys</td>
<td>60</td>
<td>42</td>
<td>18</td>
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Cochrane SR 2015: Bricker et al

- **Aim:** To assess the effects on pregnancy outcome of routine late pregnancy ultrasound (>24 weeks) in low-risk pregnancies
- **Selection criteria:** All RCTs of routine ultrasound in late pregnancy
- **Results:**
  - 13 trials recruiting 34,980 women
  - Low risk of bias

Cochrane SR 2015: Bricker et al; Risk of bias scale

Note: This summary reflects authors' judgment about each risk of bias item for each included study.

Cochrane SR 2015: Bricker et al; Birth weight <10th percentile
Cochrane SR 2015: Bricker et al; Post-term delivery > 42 weeks

- Routine late pregnancy ultrasound was not associated with improvements in overall perinatal mortality.
- No difference in preterm birth < 37 weeks, cesarean delivery and induction of labor rates.
- Decreased post-term deliveries.
- Data lacking for psychological effects, and neurodevelopment at age two.

Don't throw the baby out with the bath water......

Why Screening tests can yield negative results

- Test is poorly performed e.g. poor diagnostic effectiveness of US for FGR
  - Perhaps due to poor QA.
  - Definition of FGR - charts, customization etc.
  - Potential role for Delphi consensus definition of FGR (Gordijn S et al UOG 2016)

- Lack of an effective intervention
- How FGR cases are managed
- No effective therapeutic or monitoring strategies

Studies analyzing them are flawed e.g. underpowered
- Cochrane review include 34,980 women from 13 trials
- Definition of screen positive differed among 13 trials
- Was underpowered to address stillbirth and did not provide any data on NNT
  - Flenady V et al; Lancet 2016 (need 130,000 women)
  - Smith GCS; BJOG 2017
National Institute for Health and Care Excellence (NICE) recommendation

- NICE systematic review on universal screening for SGA in 2008:
  "the methods by which [SGA] can be identified antenatally are poorly developed or not tested by rigorous methodology"
- NICE: London 2008
- Recommendation – against universal 3rd trimester USS
- Mostly based on the negative Cochrane SR.

The Pregnancy Outcome Prediction (POP) study – Sovio et al Lancet: 2015

- Prospective cohort study of nulliparous women recruited at time of dating US
- Participants had clinically indicated ultrasonography in the third trimester as per routine clinical care (selective ultrasound)
  - All participants also had research ultrasonography, including fetal biometry at 28 and 36 weeks' gestational age.
  - Results not available to participants or clinicians (Universal ultrasound)
- Outcomes:
  - Screen positive for SGA = EFW <10th percentile for GA
  - Composite neonatal morbidity / severe adverse outcome e.g. stillbirth and neonatal death
  - Data available for 3977 women recruited over a 4-year period

The Pregnancy Outcome Prediction (POP) study – Sovio et al Lancet: 2015

<table>
<thead>
<tr>
<th>SGA (&lt;10th Centile)</th>
<th>Severe SGA (&lt;3rd Centile)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Selective</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>20% (15–24)</td>
</tr>
<tr>
<td>Specificity</td>
<td>98% (98–99)</td>
</tr>
<tr>
<td>PPV</td>
<td>50% (42–58)</td>
</tr>
<tr>
<td>NPV</td>
<td>93% (92–93)</td>
</tr>
<tr>
<td>Positive LR</td>
<td>10.3 (7.5–14.1)</td>
</tr>
<tr>
<td>Negative LR</td>
<td>0.8 (0.8–0.9)</td>
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- Screening of nulliparous women with universal third-trimester ultrasound almost tripled detection of SGA
- Combination of fetal biometry + fetal growth velocity identified FGR fetuses at highest risk for neonatal morbidity
Universal vs Selective USS for LGA – Sovio et al UOG 2018

- Secondary analysis of data from the Pregnancy Outcome Prediction study
- Outcomes LGA (BW > 90th percentile) and predefined neonatal morbidity

Results
- Universal USS detected more LGA infants – sensitivity 38% vs 27% for selective
- LGA fetuses with increased ACGV had a relative risk of any neonatal morbidity of 2.0 (95% CI, 1.1-3.6)

Strengths and Limitations of Pregnancy Outcome Prediction study

- Large prospective study
- “Blinding” of clinicians to research ultrasound is the closest surrogate to a RCT available
- Cost of improved sensitivity of universal screening – For every additional SGA newborn detected, about two false positive diagnoses were made
  - Romero R and Deter R; Lancet 2015
- Only UA Doppler evaluated.

Cost-effectiveness of Universal 3rd trimester screening for LGA (Wastlund et al; BJOG 2019)

- Simulation model used to compare long-term maternal-fetal health and cost outcomes for two detection strategies
- Universal ultrasound at approx. 36 weeks versus selective ultrasound,
  - Combined with three management strategies (planned cesarean section versus induction of labor versus expectant management) of suspected fetal macrosomia.
  - Expected costs to the NHS and quality-adjusted life-years (QALYs) gained from each strategy
- Results: Universal ultrasound increased QALYs by 0.0038 (95% CI 0.0012-0.0076), but also costs by £123.50 (95% CI 99.6-149.9).
- Conclusion: Universal ultrasound scanning for macrosomia in late-stage pregnancy is not cost-effective.

Ongoing RCT

- IRIS Trial in Netherlands (Henrichs et al; BMC Pregnancy Childbirth. 2016)
  - This nationwide stepped wedge cluster-randomized trial
  - Plan to recruit 15000 women – 7500 in intervention and 7500 to routine group
  - Primary composite outcome is ‘severe adverse perinatal outcome’ up to 7 days after birth
- Cost-effectiveness and cost utility

Conclusion

- Detects additional significant fetal abnormalities
- Improve the detection of SGA neonates
- More screening / diagnostic studies are needed
- RCT versus high quality observational studies
- Interventional studies focused on additional fetal surveillance or timing of delivery are also needed

Questions

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