<table>
<thead>
<tr>
<th>sFGR - MCDA</th>
<th>sFGR - DCDA</th>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
</tr>
</thead>
</table>

Asma Khalil
St George’s Hospital, University of London, UK
Predictive accuracy of embryonic discordance for fetal loss

CRL discordance at 7+0 to 9+6 weeks is a predictor of the risk of single fetal demise in the first trimester (DR of 74% for an FPR of 5%)

AUC 0.93
Embryonic growth discordance and Early fetal loss

CRL discordance at 7-10 weeks is predictive of subsequent single fetal demise in 1st trimester

Optimal cut-off at 19% of CRL discordance

D’Antonio 2013: n=1,356 twin pregnancies (288 MC and 1068 DC)

AUC 0.93 (95% CI = 0.91–0.94)
What are the implications of discordance in NT or CRL?

- The management of twin pregnancies with CRL discordance $\geq 10\%$ or of NT discordance $\geq 20\%$ should be discussed with a fetal medicine expert.
How should twin pregnancies discordant for fetal anomaly be managed?

- Twin pregnancies discordant for fetal anomaly should be referred to a regional fetal medicine center.

- Lethal abnormality with a high risk of intrauterine demise:
  - DC twins: conservative management
  - MC twin: selective termination to protect the healthy cotwin against the adverse effects of spontaneous demise.
### Indications

- Discordant anomaly/aneuploidy
- Advanced TTTS stage
- Severe early-onset sFGR
- TRAP
- TAPS
- Uncomplicated higher order multiples
In DC/TC pregnancies: TA ultrasound-guided 20-22 gauge needle, intracardiac or intrafunicular injection of KCl or lignocaine, preferably in the first trimester.

When the diagnosis is made in the second trimester, women might opt for late selective termination in the third trimester, if the law permits.

MC pregnancies: cord occlusion, intrafetal coagulation (Laser or radiofrequency ablation)
- Survival >80%
- Premature rupture of the membranes and PTB <32 weeks 20%
- Adverse neurological sequelae
Reduction in Triplets – Systematic Review

In trichorionic triplets, embryo reduction to twins:
• does not improve the chance of survival
• significantly increases the gestation at delivery
• reduction in preterm birth may have an impact on disability

• Continue whole pregnancy
• Terminate whole pregnancy
• Embryo reduction

Papageorghiou 2006, Wimalasundera 2010
Timing of selective termination

Evans et al. 1994

<table>
<thead>
<tr>
<th>Gestation at delivery (wks)</th>
<th>≤16 wks</th>
<th>&gt;16 wks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss</td>
<td>5%</td>
<td>14%</td>
</tr>
<tr>
<td>25 - 28</td>
<td>0%</td>
<td>6%</td>
</tr>
<tr>
<td>29 - 32</td>
<td>6%</td>
<td>14%</td>
</tr>
<tr>
<td>33 - 36</td>
<td>31%</td>
<td>24%</td>
</tr>
<tr>
<td>37 - 42</td>
<td>63%</td>
<td>57%</td>
</tr>
</tbody>
</table>

12 wks
- Miscarriage: 5%
- Delivery <33w: 6%

20 wks
- Miscarriage: 14%
- Delivery <33w: 20%
<table>
<thead>
<tr>
<th></th>
<th>Miscarriage (%)</th>
<th>PTB &lt;34 weeks (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCTA expectant</td>
<td>3</td>
<td>52</td>
</tr>
<tr>
<td>TCTA ER to 2</td>
<td>7</td>
<td>21</td>
</tr>
<tr>
<td>TCTA ER to 1</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>DCTA expectant</td>
<td>9</td>
<td>67</td>
</tr>
<tr>
<td>DCTA ER to 2</td>
<td>13</td>
<td>31</td>
</tr>
<tr>
<td>DCTA ER to 1</td>
<td>17</td>
<td>9</td>
</tr>
</tbody>
</table>

Chaveeva et al *Fetal Diagn Ther* 2013
Timing of selective termination

**Triplet pregnancy**

**Which fetus to reduce?**

- All three normal
- 1 and 2 monochorionic
- 1 anencephalic
- 2 and 3 increased NT
Cord Occlusion

**Counselling and techniques**

- **Survival (80%)**
- **Techniques:**
  - Bipolar cord coagulation
  - Laser cord coagulation
  - Cord ligation
- 3.8mm operative sleeve
- MCMA twin: BCC + cord transection

**Complications**

- **Co-twin IUD (15-20%)**
- **Bleeding:**
  - Introduction site
  - Placental surface
- **PPROM (10-15%)**
- **Chorioamnionitis**
- **Neurological damage (15%)**
Limitations: anhydramnios, short umbilical cord, small target mass

Loss rate 21%
Birth < 32w 28%

3 mm port
Local anaesthesia

Courtesy to Professor Lewi

RFA: 17-gauge (1.4 mm) diameter probe, US guided

Loss rate 23%
Birth < 32w 24%

- 16-18 g needle
- Local anaesthesia

Courtesy to Professor Lewi

Intrafetal coagulation

**Interstitial Laser**

- 400–600 micron Laser fibre passed down a 17- or 18-gauge needle
- US guided
- NdYag and diode
- Difficulty in maintaining correct positioning of the Laser fibre during repeated Laser applications

Choice of the technique depends on the expertise and available equipment

**Risks**

- Larger diameter device
- Risk of PPROM/PTL

**Benefits**

- Complete mechanical cord occlusion
- MCMA

**Cord occlusion**

**RFA/Interstitial Laser**

- Slower occlusion: risk of co-twin IUD

**Benefits**

- Smaller diameter device
- Oligohydramnios and anhydramnios
Predictive accuracy of discordance for perinatal loss

D’Antonio 2013: n=2,161 twin pregnancies

Discordance in Twins

- EFW discordance: 61%
- 2nd trimester AC discordance: 32%
- CRL discordance: 23%
Discordance and Perinatal Loss

<table>
<thead>
<tr>
<th></th>
<th>DR</th>
<th>FPR</th>
<th>+ LR</th>
<th>- LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>EFW Discordance</td>
<td>75%</td>
<td>9%</td>
<td>9.3</td>
<td>0.27</td>
</tr>
<tr>
<td>CPR Discordance</td>
<td>44%</td>
<td>4%</td>
<td>10.6</td>
<td>0.59</td>
</tr>
<tr>
<td>Combination</td>
<td>88%</td>
<td>7%</td>
<td>13.1</td>
<td>0.13</td>
</tr>
</tbody>
</table>

n= 620 twin pregnancies (n=1240 fetuses)

Khalil A et al., AJOG 2015
Growth Discordance in MC twins and neonatal morbidity

<table>
<thead>
<tr>
<th>Discordance in twins</th>
<th>Smaller vs larger twin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BWD ≥25% (n=47 twin pairs)</strong></td>
<td></td>
</tr>
<tr>
<td>Larger twin</td>
<td>Smaller twin</td>
</tr>
<tr>
<td>Severe neonatal morbidity</td>
<td>38%</td>
</tr>
<tr>
<td>RDS</td>
<td>32%</td>
</tr>
</tbody>
</table>

Lopriore E et al. Twin Res Hum Genet 2012
Severe cerebral injury: twice in the larger compared to the smaller twin

Etiology:

- **ANTENATAL:** intermittent AREDF → feto-fetal shifts of blood → temporary hypovolemia → hypoxic injury
- **Periods of bradycardia and low BP** more often in the smaller twin → volume shift and hypoxic damage in the larger twin *(Gratacos 2004)*
- **POSTNATAL:** iatrogenic premature delivery
The degree of EFW discordance associated with fetal loss during 3rd trimester. EFW discordance threshold for intervention should vary according to GA.

One size does not fit all

D'Antonio et al., FDT 2015
• Respiratory morbidity
• Infectious morbidity
• Neurological morbidity
• Hypoglycemia
• Hypothermia
• Jaundice and need for phototherapy
• Necrotizing enterocolitis
• Retinopathy of prematurity

SGA of one or both twins
Monochorinicity
GA at delivery
BW decile
BW Discordance

D’Antonio, UOG 2017
### How best to screen for FGR in twin pregnancy?

- **A combination of head, abdomen and femur measurements performs best in calculating the EFW.**  
  - B

- **If inter-twin discordance is ≥25%, a referral should be made to a tertiary fetal medicine centre.**  
  - ✔️

---

NICE 2011; Khalil et al UOG 2016
Multiple pregnancy

The management of twin and triplet pregnancies in the antenatal period

- Estimate fetal weight discordance at each scan from 20 wk.
- Do not scan more than 28 days apart.
- Consider a ≥ 25% difference in size as clinically important and refer woman to a 3ry level fetal medicine centre.

Issue date: September 2011
Heterogeneous definitions of sFGR in the existing literature

- EFW <10th centile
- EFW <5th centile
- AC centile <10th centile
- EFW <10th centile + EFW discordance ≥25%
- EFW <10th centile + EFW discordance ≥20%
- AC (<22wk) or EFW (≥22wk) <5th centile + discordance ≥25%

<table>
<thead>
<tr>
<th>Condition</th>
<th>Incidence (%)</th>
<th>Poon</th>
<th>Stirrup</th>
</tr>
</thead>
<tbody>
<tr>
<td>EFW &lt;3rd centile</td>
<td>13</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>EFW &lt;10th centile</td>
<td>21</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>EFW &lt;10th centile + EFW discordance ≥25%</td>
<td>8</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>
What are the diagnostic criteria for selective FGR?

- **DC twin**: one fetus with EFW < 10th centile
- **MC twin**: one fetus with EFW < 10th centile + inter-twin EFW discordance ≥ 25%

☑️

☑️
Diagnostic features

**DC twins**

- **Solitary:** EFW <3<sup>rd</sup> centile
- **Contributory:** at least 2/3
  - EFW <10<sup>th</sup> centile
  - EFW discordance ≥25%
  - Umbilical PI >95<sup>th</sup> centile

**MC twins**

- **Solitary:** EFW <3<sup>rd</sup> centile
- **Contributory:** at least 2/4
  - EFW <10<sup>th</sup> centile
  - EFW discordance ≥25%
  - Umbilical PI >95<sup>th</sup> centile
  - AC <10<sup>th</sup> centile
Singleton (n=4280)

- Predictions within ±10%: 62.2%
- Predictions within ±15%: 81.5%

Twins (n=586)

- Predictions within ±10%: 49.7%
- Predictions within ±15%: 68.5%

Khalil A et al., UOG 2013
<table>
<thead>
<tr>
<th>First Author</th>
<th>Correctly identified</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>LR+</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combs</td>
<td>0.86</td>
<td>0.44</td>
<td>0.96</td>
<td>0.74</td>
<td>11.56</td>
<td>0.90</td>
</tr>
<tr>
<td>Hadlock 2</td>
<td>0.85</td>
<td>0.53</td>
<td>0.93</td>
<td>0.65</td>
<td>7.47</td>
<td>0.89</td>
</tr>
<tr>
<td>Hadlock 3</td>
<td>0.85</td>
<td>0.53</td>
<td>0.93</td>
<td>0.65</td>
<td>7.47</td>
<td>0.89</td>
</tr>
<tr>
<td>Hadlock 5</td>
<td>0.84</td>
<td>0.60</td>
<td>0.90</td>
<td>0.62</td>
<td>6.28</td>
<td>0.90</td>
</tr>
<tr>
<td>Hadlock 6</td>
<td>0.85</td>
<td>0.59</td>
<td>0.91</td>
<td>0.64</td>
<td>6.85</td>
<td>0.90</td>
</tr>
<tr>
<td>Ott</td>
<td>0.85</td>
<td>0.47</td>
<td>0.95</td>
<td>0.68</td>
<td>8.49</td>
<td>0.89</td>
</tr>
<tr>
<td>Shinozuka</td>
<td>0.86</td>
<td>0.58</td>
<td>0.94</td>
<td>0.70</td>
<td>9.03</td>
<td>0.89</td>
</tr>
<tr>
<td>Jordaan 2</td>
<td>0.87</td>
<td>0.58</td>
<td>0.94</td>
<td>0.72</td>
<td>10.16</td>
<td>0.90</td>
</tr>
</tbody>
</table>

Khalil A et al., UOG 2013
• 9866 ultrasound examinations
  • 1802 DCDA
  • 323 MCDA
• Biometry in twins:
  • 40th centile in singletons at 18 weeks
  • 35th centile at 25 weeks
  • 30th centile at 35 weeks
• MCDA smaller than DCDA twin pregnancies

ONS 2013: n=641,861 singletons, n=20,448 twins
Twin Growth Reference Charts

**Dichorionic/Monochorionic**

(a) AC (mm) vs. Gestational age (weeks)

(b) FL (mm) vs. Gestational age (weeks)

(c) BPD (mm) vs. Gestational age (weeks)

(d) HC (mm) vs. Gestational age (weeks)

**EFW (DCDA/MCDA)**

- EFW (g) vs. Gestational age (weeks)
- EFW (g) vs. Gestational age (weeks)

Stirrup O, et al UOG 2014
How should monochorionic twin pregnancies complicated by sFGR be classified?

- depends on the pattern of the end-diastolic velocity in the umbilical artery Doppler.

<table>
<thead>
<tr>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>![Type 1 Image]</td>
<td>![Type 2 Image]</td>
<td>![Type 3 Image]</td>
</tr>
</tbody>
</table>
What is the optimal GA for delivery in sFGR?

- If there is a substantial risk of fetal demise of the smaller twin (e.g. reversed a-wave in DV)
  - >26 weeks: consider delivery
  - <26 weeks: consider selective termination

Delivery
- sFGR type 1: 34-36 weeks
- sFGR type 2 and 3: 32 weeks or earlier if deterioration
**What is the protocol for screening for TTTS?**

- **Start at 16 weeks and repeat every 2 weeks thereafter**

**What is the prognosis for MC twin pregnancies with amniotic fluid discordance?**

- **Follow up on a weekly basis for progression to TTTS**

**• Good outcome (93% overall survival)**

**• Low risk of progression to severe TTTS (14%)**
Dichorionic Twin Pregnancy

11-14 week
- Dating, labelling
- Chorionicity
- Screening for trisomy 21

20-22 week
- Detailed anatomy
- Biometry
- Amniotic fluid volume
- Cervical length

24-26 week
- Assessment of fetal growth
- Amniotic fluid volume
- Fetal Doppler

28-30 week
- Assessment of fetal growth
- Amniotic fluid volume
- Fetal Doppler

32-34 week
- Assessment of fetal growth
- Amniotic fluid volume
- Fetal Doppler

36-37 week
- Assessment of fetal growth
- Amniotic fluid volume
- Fetal Doppler

Delivery

Monochorionic Twin Pregnancy

11-14 week
- Dating, labelling
- Chorionicity
- Screening for trisomy 21

16 week
- Fetal growth, DVP
- UA PI

18 week
- Fetal growth, DVP
- UA PI

20 week
- Detailed anatomy
- Biometry, DVP
- UA PI, MCA PSV
- Cervical length

22 week
- Fetal growth, DVP
- UA PI, MCA PSV

24 week
- Fetal growth, DVP
- UA PI, MCA PSV

26 week
- Fetal growth, DVP
- UA PI, MCA PSV

28 week
- Fetal growth, DVP
- UA PI, MCA PSV

30 week
- Fetal growth, DVP
- UA PI, MCA PSV

32 week
- Fetal growth, DVP
- UA PI, MCA PSV

34 week
- Fetal growth, DVP
- UA PI, MCA PSV

36 week
- Fetal growth, DVP
- UA PI, MCA PSV
**Deepest vertical point:**
- **16-20 weeks:** >8cm AND <2cm
- **>20 weeks:** >10cm AND <2cm

**Modified Diagnostic Criteria of TTTS**

- **>18 weeks**
  - Oligohydramnios (DVP ≤ 2cm)
  - Polyhydramnios (DVP ≥ 6cm)
- **18-20 weeks**
  - Oligohydramnios (DVP ≤ 2cm)
  - Polyhydramnios (DVP ≥ 8cm)
- **>20 weeks**
  - Oligohydramnios (DVP ≤ 2cm)
  - Polyhydramnios (DVP ≥ 10cm)
• Chronic feto-fetal transfusion
• Large inter-twin Hb differences, without signs of TOPS
• Few minuscule anastomoses at the placental surface (<1mm) allowing a slow transfusion of blood

Slaghekke et al, Fetal Diagn Therap 2010
Lopriore et al, Placenta 2007
# Diagnostic Criteria

## ANTENATAL
- MCA-PSV $>1.5$ MoM in the donor
- MCA-PSV $<1.0$ MoM in the recipient

## POSTNATAL
- Intertwin Hb difference $>8.0$ g/dl
- at least one of the following:
  - Reticulocyte count ratio $>1.7$
  - Placenta with only small ($<1$mm) vascular anastomoses

## Incidence
- Spontaneous: 3-5% MC twin pregnancies
- Post-laser: 2-13% TTTS cases

**Placenta:** minute ($<1$mm) AV anastomoses

Slaghekke et al, Fetal Diagn Therap 2010
Lopriore et al, Prenat Diagn 2010
**AN staging**

Stage 1: MCA-PSV donor >1.5 MoM and MCA-PSV recipient <1.0 MoM, without other signs of fetal compromise

Stage 2: MCA-PSV donor >1.7 MoM and MCA-PSV recipient <0.8 MoM, without other signs of fetal compromise

Stage 3: stage 1 or 2, with cardiac compromise of donor (AREDF in UA, pulsatile flow in UV, increased PI or reversed flow in DV)

Stage 4: Hydrops of donor

Stage 5: IUD of one or both fetuses preceded by TAPS

**PN staging**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Intertwin Hb difference, g/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt;8.0</td>
</tr>
<tr>
<td>2</td>
<td>&gt;11.0</td>
</tr>
<tr>
<td>3</td>
<td>&gt;14.0</td>
</tr>
<tr>
<td>4</td>
<td>&gt;17.0</td>
</tr>
<tr>
<td>5</td>
<td>&gt;20.0</td>
</tr>
</tbody>
</table>

Slaghekke et al, Fetal Diagn Therap 2010  
Lopriore et al, Prenat Diagn 2010
Management options

- Expectant
- IOL
- IUT
- Selective feticide
- Fetoscopic laser

Lopriore et al, AJOG 2008
Herway et al, UOG 2009
Slaghekke et al, Fetal Diagn Ther 2010
Lopriore et al, Placenta 2007
Genova et al, Fetal Diagn Ther 2013
Slaghekke et al, UOG 2014
Lopriore et al, Prenat Diagn 2010
Intrauterine transfusion combined with partial exchange transfusion for twin anemia polycythemia sequence: Modeling a novel technique

F. Slaghekke a,*, J.P.H.M. van den Wijngaard b, c, J. Akkermans a, M.J.C. van Gemert b, J.M. Middeldorp d, F.J. Klumper a, D. Oepkes a, E. Lopriore d
### TAPS: Outcome

#### DONOR
- Healthy (Hb discordance)
- Neonatal morbidity
  - Severe anemia
  - Cerebral injury
- NND

#### RECIPIENT
- Healthy (Hb discordance)
- Neonatal morbidity
  - Severe polycythemia
  - Thrombocytopenia
  - Ischemic limb necrosis
  - Cerebral injury
- NND

Slaghekke et al, Fetal Diagn Therap 2010
Lopriore et al, Prenat Diagn 2010
• The prenatal diagnosis of TAPS is based on the finding of discordant MCA Doppler abnormalities.

• Little evidence about the outcome and optimal management of TAPS; therefore treatment options should be individualized and discussed with parents.
• Screening: MCA PSV should be measured in all MC twins and during the follow-up of treated TTTS cases
• Prevention: Solomon fetoscopic laser ablation technique
• Spontaneous MCDA twin pregnancy
• 18 wk: TTTS treated with Laser
• 20 wk: Post-Laser TAPS
• 20+4 wk: Repeat Laser + IUT
• 22 wk: Unilateral VM + Intraventricular hemorrhage
• 22+4 weeks: selective cord occlusion

Ventriculomegaly
Intraventricular hemorrhage
Periventricular white matter abnormality

Acquired brain injury

- Spontaneous MCDA twin pregnancy
- 22+6 wk: sFGR + TAPS
- Smaller twin: MCA PSV <1MoM
- Larger twin: MCA PSV >1.5MoM

Brain abnormality

- 24 weeks: selective cord occlusion
Take Home Messages

- Discordance <10 weeks: high risk of early fetal loss
- Discordance in CRL or NT: aneuploidy/anomalies
- Size + Doppler Discordance: risk of perinatal mortality
- TTTS: Discordance in fluid (polyhydramnios)
- TAPS: MCA PSV discordance
- sFGR: Discordance in size
- Anomalies: Discordant anomaly/aneuploidy
- Consider early referral to 3ry fetal medicine centre