Ultrasound in Multiple Pregnancy
Joshua F. Nitsche, MD, PhD

Disclosures
• None

Learning Objectives
After completion of this lecture attendees should understand:
• The proper use of ultrasound in first trimester of multiple gestations to establish chorionicity
• How ultrasound should be used to screen for aneuploidy and congenital anomalies in multiple gestations
• The role of ultrasound in the management of multiple gestations in the second and third trimester

Birth Rate of Multiples
From 1980 – 2002
• 65% increase in twin births
• 404% increase in triplet and higher order multiples
• 3.1% of all pregnancies in the US contained multiples in 2002

In ART pregnancies
• Twins – 22 times the general population
• Triplets and higher order – 50 times the general population

Diagnosis of Multiple Gestation
• As many as 50% diagnosed at delivery if ultrasound is not performed.
• Diagnosis in the first trimester is theoretically error-free.
• Vanishing embryos can occur in up to 21% of twin pregnancies imaged in the 1st trimester
• Important to determine chorionicity at time of diagnosis

Zygosity and Chorionicity
• Zygosity
  • Refers to the genetic makeup of the pregnancy
  • Is determined by type of fertilization, i.e. monozygotic or dizygotic

  • Chorionicity
  • Refers to the membrane complement of the pregnancy
  • Is determined by the occurrence, and timing of embryo splitting
Zygosity and Chorionicity

- **Zygosity** can only be determined by genetic analysis of both fetuses.
- **Chorionicity**, determined non-invasively by ultrasound, can be used to determine the likelihood of zygosity.

Zygosity

- Twins resulting from 2 ova fertilized by 2 sperm.
- These are ALWAYS dichorionic.

Monozygotic Pregnancy

One ovum fertilized by one sperm that subsequently splits

<table>
<thead>
<tr>
<th>Days</th>
<th>DC/DA</th>
<th>MC/DA</th>
<th>MC/MA</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3</td>
<td>20-30%</td>
<td>70%</td>
<td>2-4%</td>
</tr>
<tr>
<td>3-8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-13</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Separate Gestation Sacs and Chorionicity

- Scan performed in the first trimester before multiple sacs have had time to grow and coalesce.
- Should be almost 100% accurate.
- Sacs that are clearly separate should be observed.
- Each sac is surrounded by an echogenic ring.
- A thin dividing membrane, or no apparent dividing membrane, suggests a monochorionic diamniotic gestation.

Conjoined twins

Scan performed in the first trimester before multiple sacs have had time to grow and coalesce.

- Should be almost 100% accurate.
- Sacs that are clearly separate should be observed.
- Each sac is surrounded by an echogenic ring.
- A thin dividing membrane, or no apparent dividing membrane, suggests a monochorionic diamniotic gestation.

Number of Yolk Sacs and Amnionicity

- At less than 8 weeks the amnionicity of a monochorionic pregnancy may be difficult to identify.
- Retrospective study of 20 MC/DA and 2 MC/MA pregnancies.
  - In all DA pregnancies scanned <8 weeks no dividing membranes were seen – 2 yolk sacs seen in all but 1 case.
  - In each of the MA pregnancies only 1 yolk sac was seen.

Number of Yolk Sacs and Amnionicity

- The number of yolk sacs in early monochorionic pregnancies provides an indirect method of determining amnionicity.
- The finding of 2 fetal poles and 1 yolk sac is consistent with a monoamniotic twin gestation.
- When this diagnostic tool is used, additional scans later in the pregnancy are recommended for verification.
Diagnosis of Chorionicity
“Twin Peak” or “Lambda” Sign

Initially described by Bessis and Papiernik in 1981.

This sign is created by the projection of placental tissue into the inter-twin membrane.

Evaluation of the Twin Peak/Lambda Sign in DC Gestation

<table>
<thead>
<tr>
<th>Frequency of Twin Peak Sign in DC Gestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fused Placentas</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>N 7</td>
</tr>
<tr>
<td>10-14 weeks</td>
</tr>
<tr>
<td>16 weeks</td>
</tr>
<tr>
<td>20 weeks</td>
</tr>
</tbody>
</table>

0% False Positive Rate at 10-weeks

Zygosity Based on Conception

<table>
<thead>
<tr>
<th>Conception</th>
<th>Dizygotic</th>
<th>Monozygotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural</td>
<td>67%</td>
<td>33%</td>
</tr>
<tr>
<td>ART</td>
<td>93%</td>
<td>7%</td>
</tr>
</tbody>
</table>

The percentage of naturally conceived dizygotic twins varies with maternal age and ethnicity (1 in 4 to 1 in 1000).

The frequency of MZ twinning is essentially constant at 4 per 1000 births.
The Risk of Aneuploidy in Twin Gestations

- The risk of aneuploidy is related to zygosity
- Dizygotic twins have independent risks for aneuploidy, and this, like singletons, is related to maternal age.
- Monozygotic twins usually have the same karyotype, and their risk for aneuploidy is also related to maternal age.
- Monozygotic twins are at increased risk of congenital anomalies, which can be discordant between twins.

Risk of at least One Affected Twin

<table>
<thead>
<tr>
<th>Maternal Age</th>
<th>Singleton</th>
<th>Dizygotic (2x age risk)</th>
<th>Monozygotic (age risk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>641</td>
<td>320</td>
<td>641</td>
</tr>
<tr>
<td>31</td>
<td>610</td>
<td>305</td>
<td>610</td>
</tr>
<tr>
<td>32</td>
<td>481</td>
<td>240</td>
<td>481</td>
</tr>
<tr>
<td>33</td>
<td>384</td>
<td>192</td>
<td>384</td>
</tr>
<tr>
<td>34</td>
<td>303</td>
<td>151</td>
<td>303</td>
</tr>
<tr>
<td>35</td>
<td>237</td>
<td>118</td>
<td>237</td>
</tr>
<tr>
<td>40</td>
<td>69</td>
<td>34</td>
<td>69</td>
</tr>
</tbody>
</table>

NT Screening in Twins

Feasibility of Measuring NT in Twins

- 120 fetuses in 60 twin pregnancies were compared with 120 singletons matched for CRL and maternal age.
- All were scanned at 10-14 weeks.
- NTs were obtained in all cases and the mean measurements (MoM) and median measurements (mm), as well as values at 5%, 50%, and 95% were almost identical in the twins and controls.

Sebire et al. BJOG;1996:103,999

NT Screening in Twins

- 16 pregnancies developed severe TTS at 15-22 wks.
- The remaining 116 pregnancies – no TTS.
- Results: NT>95% PPV - 38% NPV – 91%
  LR – 4.4 (1.6 - 9.7)
  NT<95% LR – 0.7 (0.4 - 0.9)

Conclusion: The underlying hemodynamic changes associated with TTS may manifest as increased fetal NT thickness at 10-14 weeks of gestation.
Combined First Trimester Screening

Detection rate with a 5% FPR

<table>
<thead>
<tr>
<th>Pregnancy</th>
<th>Combined Test (%)</th>
<th>Integrated Test (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monochorionic</td>
<td>84</td>
<td>93</td>
</tr>
<tr>
<td>Dichorionic</td>
<td>70</td>
<td>78</td>
</tr>
<tr>
<td>All Twins</td>
<td>72</td>
<td>80</td>
</tr>
<tr>
<td>Singleton</td>
<td>85</td>
<td>95</td>
</tr>
</tbody>
</table>

Wald and Ruh, Prenat Diagn, 2003; 25: 740-745

Detection of Fetal Morphologic Anomalies

- Increased incidence of major congenital anomalies in twins
  - 0.6% in singletons
  - 1.0% in DZ twins
  - 2.7% in MZ twins


- 88% anomaly detection rate with routine ultrasound
  - VACTERL systems are particularly affected:
  - Recommend a very detailed scan or even 2 anatomy scans especially if sub-optimal visualization of any structures

Evaluation of Fetal Growth in Twins

- As twins are excluded from standard growth curves, it is often presumed that these curves cannot be used accurately for twins
- There is no significant difference between singleton and twin growth curves


- Singleton growth curves are appropriate for use in twins
- BPD measurements can be different in multiple pregnancies due to dolichocephalic fetuses in noncephalic presentations

Evaluation of Fetal Growth

- Studies on 103 sets of twins at 4-6 week intervals revealed BPD and AC measurements fell away from singleton norms after 31 and 32 weeks respectively, while FL remained similar to singleton norms throughout gestation.


Evaluation of Fetal Growth

<table>
<thead>
<tr>
<th>GA</th>
<th>TWINS</th>
</tr>
</thead>
<tbody>
<tr>
<td>35-36 wks</td>
<td>13%</td>
</tr>
<tr>
<td>37-38 wks</td>
<td>23%</td>
</tr>
<tr>
<td>39+41 wks</td>
<td>58%</td>
</tr>
</tbody>
</table>

Risk of low birthweight increases dramatically in the late 3rd trimester


Common errors

- Assuming that it is normal for twins to have less than normal measurements (twins are particularly susceptible to IUGR).
- Using one fetus as the yardstick for the other.
- One fetus may develop differently, but normally, from the other because of genetic predestination– either smaller or larger.
- Both may be macrosomic, or have IUGR.
- Assuming that marked disparity in biometric measurements is a sign of TTTS in MC pregnancies.
Growth Discordance/IUGR

- Significant growth discordance:
  - 20-25% difference in EFW between the twins, expressed as percentage of larger fetal weight
  - Investigate the cause
  - Consider fetal surveillance

Surveillance of Fetal Growth and Management of Growth Disorders

- Serial growth scans for ALL twin gestations
- If growth discordance is evident:
  - Investigate etiology
  - Antenatal testing if IUGR suspected
  - Steroids and delivery for non-reassuring testing

Wake Forest School of Medicine

Confirmation of Fetal Well-Being

- Most techniques testing fetal well-being have simply been extrapolated from experience with singletons.
- An NST may be technically difficult in higher order gestations. BPP is better.
- BPP is advantageous because it gives incidental data about the amniotic fluid volume.

Risk of Stillbirth in Multiple Gestation Pregnancies

- Risk of SB increased from 1:3333 at 28 weeks to 1:69 at 39 weeks or more
- Risk of SB in multiples at 37-38 weeks is equal to that of postterm singletons
- Risk of SB in multiples at 39 weeks surpassed that of postterm singletons.

Sairam et al. ObstetGynecol 2002;100:638-41

Management of Dichorionic Twins

- Perform ultrasounds:
  - At 11 to 14 weeks establish chorionicity and evaluate nuchal translucency
  - At 18 weeks perform fetal anatomic survey and document cord insertions (velementous insertion is very common in multiple gestations)
  - Every 4-6 weeks to assess growth
  - Twice weekly for BPPs if FGR develops

Management of Monochorionic Twins

- Perform ultrasounds:
  - At 11 to 14 weeks establish chorionicity and evaluate nuchal translucency
  - At 18 weeks perform fetal anatomic survey and document cord insertions (velementous insertion is very common in multiple gestations)
  - Every 2 weeks until approximately 28-30 weeks gestation for evidence of twin-twin transfusion syndrome (if all is well, frequency could decrease after this point in time until delivery)
  - Every 4 weeks to assess growth
  - Twice weekly for BPPs
  - In all monochorionic twins???
  - Only if FGR or TTTS develops???
When should twins be delivered?

- A rational practice would be to offer elective delivery at or during the 38th week in well-dated, uncomplicated twin pregnancies.
- Prolonging a twin pregnancy beyond 38 weeks requires convincing evidence of appropriate fetal growth, normal AF, normal UA Doppler studies, and unequivocally reassuring fetal testing.
- Prolonging a twin pregnancy beyond 39 weeks is NOT recommended.


Twin-Twin Transfusion Syndrome

- Incidence: 15 – 20% of MC twins
- Untreated: 60% to 100% mortality
- Treatment options:
  - Pregnancy termination
  - Selective termination
  - Serial amnio-reduction
  - Septosotomy
  - Laser ablation

Twin-Twin Transfusion Syndrome

- Sonographic criteria to diagnose TTTS:
  - Gender concordance and MC placentation
  - AFI discrepancy ("oligo/poly")
  - Significant growth discordance (usually > 20%)
  - Hydrops may be evident in the recipient twin
- Differential diagnosis includes:
  - Differential uteroplacental insufficiency
  - Velamentous cord insertion of 1 fetus
  - Fetal anomaly (aneuploidy, urinary tract anomaly)

Twin-Twin Transfusion Syndrome

<table>
<thead>
<tr>
<th>Stage</th>
<th>Poly/Oligo</th>
<th>Absent Bladder</th>
<th>Abnormal Doppler</th>
<th>Hydrops</th>
<th>Demise</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>


TTTS Treatment

- Early determination of chorionicity
- Serial U/S beginning at 14-16 weeks of gestation
- Severe TTTS < 26 weeks
  - Refer for laser ablation
- TTTS > 26 weeks:
  - Stage 1: Weekly sonographic evaluation
  - Stage 2-4: twice weekly sonographic evaluation
  - Amnioreduction as needed
  - Planned delivery of all MC twins by ~34-36 weeks

Single Intrauterine Fetal Demise

- Vanishing twin is common in first trimester – no significance for the remaining fetus.
- Single fetal loss seen after first trimester in 5% of twins and 15% of triplets.
- Prognosis good if dichorionic.
- Increased risk if monochorionic:
  - Death of remaining fetus is possible.
  - 12-17% incidence of multi-cystic encephalomalacia.
  - Morbidity due to hypotension at time of IUFD.
Single Intrauterine Fetal Demise

- Fetal surveillance after a single IUFD in an MC pregnancy cannot predict neurologic injury in the surviving fetus.

- Immediate delivery after a single IUFD in an MC pregnancy may not prevent neurologic injury in the surviving twin.

Questions???

Contact Info
jnitsche@wakehealth.edu