Nuchal Translucency in First-Trimester Ultrasound Screening for Trisomy 21

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“Nuchal translucency-based screening for fetal abnormalities has truly become an indispensable aspect of contemporary obstetric practice.”

(Soha Said, Clinical Obstetrics and Gynecology, March 2008)
Agenda

- Introduction to Our Patients
- Definition of Nuchal Translucency and Measurement Criteria
- NT in Trisomy 21 Screening
- Advantages/Limitations of NT Screening
- Differential Diagnosis of Increased NT
- Mechanisms of Increased NT
- Fetal Anomalies associated with Increased NT
- Follow-up on Our Patients
Two Patients With Increased Fetal Risk for Trisomy 21

**Our First Patient**
- 41 year-old, G5P2, with singleton pregnancy
- Presents for early OB ultrasound (<14 weeks)
- Nuchal translucency = 4mm

**Our Second Patient**
- 40 year-old, G3P1, with singleton pregnancy
- Presents for early OB ultrasound
- Nuchal translucency = 2.7mm
Defining Nuchal Translucency

- Fluid between skin and soft tissue at back of fetal neck

- Can be seen sonographically in all first trimester fetuses

- Criteria for Increased NT:
  - NT > 3mm
  - Depends on gestational age (Most accurately expressed as multiple of the median) [3]
Criteria for NT Measurement (1)

1. Crown-Rump Length = 45-84mm (approximately 11-14wks).
2. Mid-sagittal plane with fetus in neutral position: Neck flexion decreases NT; Neck extension increases NT.
3. Enlarge image: upper 2/3 of fetus.
4. Identify potential false positives: non-fused amnion, nuchal cord, neck extension.
5. Measure maximal translucency in greatest dimension: from outer soft tissue edge to inner nuchal membrane edge.
Inaccurate NT Measurement

1. Not midline view: Nasal bone and chin not visible.
2. Difficult to separate fetal skin from amnion.
How does Nuchal Translucency fit into screening for Trisomy 21?
The Combined Test

- Nuchal Translucency measurement between 11-14 weeks

- Maternal Serum Markers
  1. Free beta-hCG: Elevated in T21
ACOG 2007: All women should be offered aneuploidy screening before 20wks gestation.
- using maternal age alone to triage patients into diagnostic testing misses 50% of T21 pregnancies that occur in women <35 y/o.
- noninvasive screening tests enable women to be more certain of their actual risk for T21, which they can then weigh against the risk of invasive diagnostic testing.

Ideal Screening: “Combined Test” in First Trimester with follow-up depending on results.
Choose type of screening based on tests available in your area, patient’s wishes, and patient’s risk factors.

Comparing Screening Methods for T21

<table>
<thead>
<tr>
<th>Method</th>
<th>Gestational Age</th>
<th>Detection Rate/Sensitivity</th>
<th>False Positive Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nuchal Translucency + Maternal Age</td>
<td>11-14 weeks</td>
<td>72-77%</td>
<td>4.2-5%</td>
</tr>
<tr>
<td>Combined Test: Age + NT + PAPP-A + Beta-hCG</td>
<td>11-14 weeks</td>
<td>85%</td>
<td>4.8</td>
</tr>
<tr>
<td>Full Integrated Test: Combined Test + Quad Screen</td>
<td>11-14 weeks + 15-18 weeks</td>
<td>85% 90-95%</td>
<td>1% 2.6-5%</td>
</tr>
<tr>
<td>Serum Integrated Test: PAPP-A + Quad Screen (No U/S)</td>
<td>11-14 weeks + 15-18 weeks</td>
<td>85%</td>
<td>3.5%</td>
</tr>
<tr>
<td>Quad Screen: serum AFP, uE3, hCG, inhibin A</td>
<td>15-18 weeks</td>
<td>85%</td>
<td>6.8%</td>
</tr>
</tbody>
</table>

*All data from FASTER (First and Second Trimester Evaluation of Risk) and SURUSS (Serum, Urine and Ultrasound Screening Study) Trials.
# Advantages of Screening with The Combined Test

**Abnormal Test**
- First-trimester identification of patients at high-risk for fetal anomalies.
- Allows for early therapeutic abortion.
- Enables pre-natal planning for care of affected child.
- Triage patients for further testing, which improves cost-effective use of resources.

**Normal Test**
- Lowers overall risk of advanced maternal age patients.
- Decreases use of invasive diagnostic procedures (CVS, amniocentesis)
- Decreases procedure-associated fetal loss.
- Reduces anxiety.
Limitations of The Combined Test

- NT measurement is operator dependent and requires special training.
- A significant number of patients do not get prenatal care until the 2\textsuperscript{nd} trimester.
- 20\% of obstetric patients are not being offered this test in spite of research demonstrating its efficacy.
- Anxiety-provoking when positive. If patients do not want CVS, they must wait 4 weeks for amniocentesis.
You identify a neck mass during first trimester ultrasound screening. What do you need to rule out before diagnosing increased nuchal translucency?
Differential Diagnosis: 1st Trimester Neck Mass

- Hydrops fetalis
- Cystic Hygroma
- Nonfused amnion
- Nuchal cord

Less Common: Branchial cleft cyst, hemangioma, neuroblastoma.

Trans-abdominal OB U/S, axial view of fetal head

Potential Mechanisms for Increased Nuchal Translucency

1. Heart strain/failure
2. Abnormal lymphatic drainage – increased # or size of lymphatics, irregular connection between lymphatics and veins, impaired fetal movement.
3. Abnormal extracellular matrix
## Fetal Abnormalities Associated with Increased NT

<table>
<thead>
<tr>
<th>Chromosomally Abnormal</th>
<th>Chromosomally Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trisomy 13</td>
<td>CNS defects</td>
</tr>
<tr>
<td>Trisomy 18</td>
<td>Diaphragmatic hernia</td>
</tr>
<tr>
<td>Trisomy 21</td>
<td>Omphalocele</td>
</tr>
<tr>
<td>Turner’s Syndrome</td>
<td>Myotonic Dystrophy</td>
</tr>
<tr>
<td>Triploidy</td>
<td>Esophageal Atresia</td>
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<tr>
<td>Unbalanced translocations</td>
<td>Infantile PCKD</td>
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<td></td>
<td>Achondroplasia</td>
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<tr>
<td></td>
<td>Fetal Anemia</td>
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<tr>
<td></td>
<td>Metabolic defects</td>
</tr>
<tr>
<td></td>
<td>(and others)</td>
</tr>
</tbody>
</table>

(and others)
Increased NT and Fetal Abnormalities: An Important Caveat

Increased NT is NOT a fetal anomaly in and of itself.

- 90% of chromosomally normal fetuses with NT<4.5mm go on to be healthy, live-born infants.

- If there are no abnormalities on targeted ultrasound at 20-22 weeks, there is no increased risk of poor outcome.

- There is no increased prevalence of developmental delay associated with increased NT.
Back to Our First Patient
Patient 1: Fetal Ultrasound

- 41 y/o G5P2
- Sent for early OB ultrasound to evaluate NT secondary to Advanced Maternal Age
- PAPP-A and beta-hCG levels unknown
- CRL = 55.2mm
Patient 1: NT Measurement on Fetal US

Trans-abdominal OB U/S, midline sagittal view

NT = 4.1mm
Outcome for Our First Patient: Trisomy 21

Final NT Measurement = 4.0mm

Follow-up:
1. Amniocentesis at 16 weeks: 47, XX, +21
2. Full Fetal Survey at 21w6d: common AV canal.
3. Ultrasound at 33w2d: size<dates, oligohydramnios, no duodenal atresia.
4. Uncomplicated delivery at 38w6d.
Patient 2: Fetal Ultrasound

- 40 y/o G3P1
- Combined Test Results:
  1. Decreased PAPP-A
  2. Increased hCG
  3. Ultrasound - CRL = 63.6mm
Patient 2: NT Measurement on Fetal US

Trans-abdominal OB U/S, midline sagittal view

NT = 2.7mm
Outcome for Our Second Patient: Normal Fetus

- Final NT Measurement = 2.6mm

Follow-up:
1. Full Fetal Survey at 16w0d: No abnormalities.
2. Patient declined amniocentesis.
3. Quad Screen at 19w1d: Lowered T21 risk
4. Delivered healthy baby girl at 40w5d.
**Summary**

- Nuchal Translucency, as part of the Combined Test, is an effective and accurate method of screening for fetal anomalies, especially Trisomy 21.
- Sensitive, non-invasive screening tests ensure that only those pregnancies at high-risk for abnormalities undergo invasive diagnostic procedures.
- Ultrasonographers must be carefully trained in NT measurement.
- All women who receive aneuploidy screening should be appropriately counseled and provided with thorough follow-up.
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Resources

- Benacerraf, BR. “The sonographic diagnosis of fetal aneuploidy.” UpToDate 16.1. (5/16/08)