Nuchal Translucency Thresholds for Predicting Fetal Anomalies in Low-Risk cfDNA

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Background

Nuchal translucency (NT) is a well-established first-trimester ultrasound marker for aneuploidy and structural anomalies. Frequency and perceived clinical utility of NT assessment have declined since cell-free DNA (cfDNA).

Objective

Evaluate the predictive role of NT in pregnancies with low-risk cfDNA results and identify optimal thresholds for detection of fetal anomalies

Study Design

- Retrospective cohort study of pregnancies with NT ≥ 3 mm between 11 to 14 weeks and a low risk cfDNA from 2012 to 2024
- Primary outcome: composite major abnormal ultrasound (US)
- Secondary outcomes: abnormal diagnostic testing and composite abnormal soft US marker
- Statistical analysis: Chi-square or Fisher-exact to assess outcomes by NT measurement, multivariate logistic regression to calculate adjusted odds ratio (aOR), area under curve (AUC) from receiver operating characteristic (ROC) curves to assess optimal NT cutoff to predict major anomalies

Results

- 211 pregnancies had low risk cfDNA and NT ≥ 3 mm
  - 30 (14.2%) had composite major abnormal US (Table 1)
  - 11 (5.2%) had composite abnormal soft US marker (Table 1)
- Diagnostic testing performed in 82 (40%) of patients (Table 1)
- Abnormal diagnostic testing in 12 (14.8%), Figure 2
- Median NT was higher for abnormal US (3.9 mm, IQR 3.5-6.4) than normal US (3.3 mm, IQR 3.1-3.6), p<0.01
- Increased NT associated with higher rates of composite abnormal US (p<0.01), Figure 1
- NT of > 4.5 mm compared to 3.0-3.4 mm had a significantly increased risk of fetal anomalies (aOR 32.5, 95% CI 8.7-121.4)
- NT threshold of 3.3-3.8 mm and 4.5 mm had significantly higher AUC than 3.1 mm on ROC curves, Figure 3

Conclusion

- Rate of abnormal US in low-risk cfDNA pregnancies was only 14% but higher NT measurement is associated with significantly increased risk of abnormal US
- 1st trimester US and NT remain valuable tools in prenatal screening, but higher threshold for increased NT measurement may be considered when evaluating risk of fetal anomalies

A higher **NT threshold** should be considered when evaluating risk of fetal **anomalies** in **low-risk cfDNA** population.

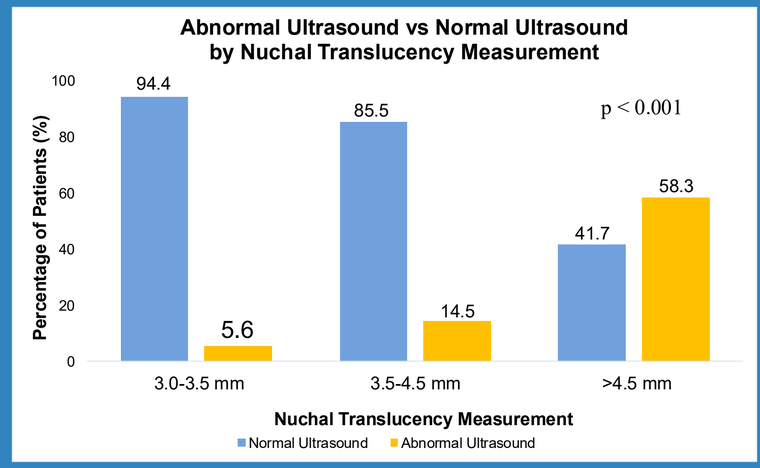

Figure 1: Rate of composite abnormal ultrasound versus normal ultrasound by nuchal translucency measurement

Questions?
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Table 1: Fetal and obstetric outcomes by nuchal translucency measurement among low risk cell-free DNA

	Total (N=211)	NT 3.0-3.5 mm (n=125)	NT 3.5-4.5 mm (n=62)	NT > 4.5 mm (n=24)	P-value
Composite Abnormal Ultrasound*					**<0.001**[1]
Normal	181 (85.8%)	118 (94.4%)	53 (85.5%)	10 (41.7%)	
Abnormal	30 (14.2%)	7 (5.6%)	9 (14.5%)	14 (58.3%)	
Composite Abnormal Soft Ultrasound Marker†					0.30[2]
Normal	200 (94.8%)	116 (92.8%)	61 (98.4%)	23 (95.8%)	
Abnormal	11 (5.2%)	9 (7.2%)	1 (1.6%)	1 (4.2%)	
Diagnostic Testing Performed					**0.002**[2]
No	123 (60.0%)	86 (69.4%)	29 (50.0%)	8 (34.8%)	
Yes	82 (40.0%)	38 (30.6%)	29 (50.0%)	15 (65.2%)	
Diagnostic Testing Result					**<0.001**[2]
Normal	69 (85.2%)	36 (97.3%)	26 (89.7%)	7 (46.7%)	
Abnormal	12 (4.8%)	1 (2.7%)	3 (10.3%)	8 (53.3%)	
Major Abnormal Ultrasound Finding					
Cystic Hygroma					**<0.001**[1]
No	191 (91.0%)	122 (98.4%)	57 (91.9%)	12 (50.0%)	
Yes	19 (9.0%)	2 (1.6%)	5 (8.1%)	12 (50.0%)	
Body Wall Edema					**<0.001**[2]
No	201 (95.7%)	124 (100.0%)	59 (95.2%)	18 (75.0%)	
Yes	9 (4.3%)	0 (0.0%)	3 (4.8%)	6 (25.0%)	
Cardiac Anomaly					0.14[2]
No	206 (98.1%)	123 (99.2%)	59 (95.2%)	24 (100.0%)	
Yes	4 (1.9%)	1 (0.8%)	3 (4.8%)	0 (0.0%)	
Central Nervous System Anomaly					0.33[2]
No	182 (97.8%)	115 (98.3%)	55 (98.2%)	12 (92.3%)	
Yes	4 (2.2%)	2 (1.7%)	1 (1.8%)	1 (7.7%)	
Gastrointestinal Anomaly					1.00[2]
No	185 (99.5%)	116 (99.1%)	56 (100.0%)	13 (100.0%)	
Yes	1 (0.5%)	1 (0.9%)	1 (1.8%)	0 (0.0%)	
Skeletal Anomaly					0.61[2]
No	184 (98.9%)	116 (99.1%)	55 (98.2%)	13 (100.0%)	
Yes	2 (1.1%)	1 (0.9%)	1 (1.8%)	0 (0.0%)	
Renal Anomaly					--
No	185 (100.0%)	117 (100.0%)	55 (100.0%)	13 (100.0%)	
Yes	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	

All data presented as n (%) unless otherwise indicated
* Composite abnormal ultrasound was defined as one or more of the following: cystic hygroma, body wall edema, major structural anomaly (cardiac, central nervous system, gastrointestinal, skeletal, renal)
† Composite abnormal soft ultrasound marker was defined as one or more of the following: echogenic intracardiac focus, echogenic bowel, pyelectasis, short long bones, single umbilical artery
[1]Chi-Square, [2]Fisher Exact, [3]Kruskal-Wallis

Figure 2. Abnormal Diagnostic Testing Flowsheet

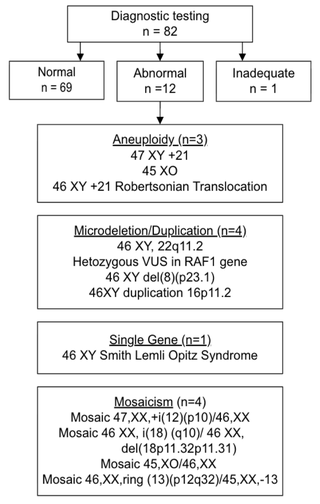

Figure 3: Receiver operating characteristic curve for prediction of major abnormal ultrasound by increasing nuchal translucency thresholds in low risk cell-free DNA