NUCHAL TRANSLUCENCY AND CARDIAC DEFECTS

Julene S Carvalho MD, PhD, FRCPH
Consultant Fetal Cardiologist Bromtpon Fetal Cardiology, Royal Brompton Hospital
Fetal Medicine Unit, St. George's Hospital, London, UK
j.carvalho@rbh.nthames.nhs.uk

Introduction

Nuchal translucency (NT) - a well described sonographic sign at 11-14 weeks of gestation is imaged as a sonotranslucent area behind the fetal neck. Normal NT thickness (measured in mm) is dependent on fetal size i.e. crown-rump length. Increased NT thickness - initially recognised as a sonographic marker for chromosomal defects[1] has subsequently been shown also to be associated with major congenital heart disease (CHD). Whilst the initial reports pointed towards such an association in fetuses with aneuploidy,[2-4] this has also been demonstrated in chromosomally normal fetuses.[5] Data from nearly 1,500 fetuses with increased NT strongly suggested this to be a potentially useful marker for major cardiac defects and also suggested that the incidence of CHD increased with increasing NT measurements.[5] Over the last decade there has been growing evidence to support increased NT at 11-14 weeks of gestation as a new marker for major CHD.[6-13]

Increased NT – an indication for fetal echocardiography

The higher the NT measurement in a chromosomally normal fetus, the higher the risk of encountering a major heart abnormality. Much of the published data still refer to NT thickness of 2.5 mm as a cut-off point for the 95th centile as these studies reflect early information in this field even though it is now clear that reference ranges for the 95th centile depend on fetal size. For the 99th centile however, a value of 3.5 mm can be taken as this centile limit for different fetal sizes.

The risk of a major cardiac abnormality in fetuses with NT ≥99th centile (i.e., NT ≥3.5 mm) appears to be around 5-10% (7;8;12;14). Thus, this is a clear indication for specialised fetal echocardiography. On the other hand, for NT measurements ≥2.5mm but <3.5 mm, the incidence seems to be marginally higher (17/1000)[14] than that of the general population. This NT related risk (1.7%) is similar to other risk factors generally accepted as indications for detailed assessment of the fetal heart such as a previous child with CHD.[15] Based on this, NT ≥2.5 mm also constitutes an indication for referral. However, if this cut-off point is to be used, approximately 5% of the population would have to be referred for fetal echocardiography. Available human and financial resources will limit the utility of using this cut-off point when the risk of major CHD is still very close to that of the general population.

Knowing the absolute value of NT provides further stratification of risks.[8] For example, if NT lies between 3.5-4.4 mm the risk is around 3%, but increases further to ~ 10% and ~ 20% if NT ranges are 4.5-6.5 mm and 6.5-8.5 mm respectively.[16] As most fetuses with CHD will still have normal NT measurements,[7;17] this marker ought to be seen as an additional tool to help detecting CHD prenatally. It is still very important that at the time of the routine 'anomaly scan', all fetuses have a good obstetric screening using the the four-chamber view and possibly great vessel assessment as this remains the most important means of effectively diagnosing CHD before birth.[18]

Following detection of an increased NT and exclusion of any associated chromosomal defect it is not possible to predict the type of structural cardiac abnormality to be found if there is one. Many different forms of CHD have been reported in association with previously increased NT with many reports showing there to be a wide spectrum of abnormalities.[7;8;17;19-21] Knowing that NT was increased allows referral for specialist fetal echocardiography to be made earlier[17] particularly if NT >4 mm.

Increased NT and early fetal echocardiography

One of the reported advantages of knowing the increased risk of having a child with major CHD following NT assessment at the time of the '11-14 week scan' is the awareness that such risk exists early in the pregnancy. The feasibility of performing transabdominal[22] as well as transvaginal echocardiography from the late first trimester together with realisation of NT-related risks have contributed enormously to the growing interest in performing fetal echocardiography at less than 16 weeks of gestation[6;21;23-29] Referral for early cardiac assessment (from around 12-13 weeks), however, is not widely available. If performing an early fetal echo, it is important to realise that an important proportion of euploid fetuses with increased NT will have a normal heart and that a proportion of these will have significant extracardiac abnormalities. This stresses the importance also to consider early obstetric assessment if patients are referred for early fetal echocardiography.[29]

References

1. Nicolaides KH, Azar G, Byrne D, Mansur C, Marks K. Fetal nuchal translucency: ultrasound screening for chromosomal defects in first trimester of pregnancy. BMJ 1992; 304(6831):867-869.
2. Hyett JA, Moscoso G, Nicolaides KH. Cardiac defects in 1st-trimester fetuses with trisomy 18. Fetal Diagn Ther 1995; 10(6):381-386.
3. Hyett JA, Moscoso G, Nicolaides KH. First-trimester nuchal translucency and cardiac septal defects in fetuses with trisomy 21. Am J Obstet Gynecol 1995; 172(5):1411-1413.
4. Hyett J, Moscoso G, Nicolaides K. Abnormalities of the heart and great arteries in first trimester chromosomally abnormal fetuses. Am J Med Genet 1997; 69(2):207-216.
5. Hyett JA, Perdu M, Sharland GK, Snijders RS, Nicolaides KH. Increased nuchal translucency at 10-14 weeks of gestation as a marker for major cardiac defects. Ultrasound Obstet Gynecol 1997; 10(4):242-246.
6. Haak MC, Bartelings MM, Gittenberger-De Groot AC, Van Vugt JM. Cardiac malformations in first-trimester fetuses with increased nuchal translucency: ultrasound diagnosis and postmortem morphology. Ultrasound Obstet Gynecol 2002; 20(1):14-21.
7. Mavrides E, Cobian-Sanchez F, Tekay A, Moscoso G, Campbell S, Thilaganathan B et al. Limitations of using first-trimester nuchal translucency measurement in routine screening for major congenital heart defects. Ultrasound Obstet Gynecol 2001; 17(2):106-110.
8. Ghi T, Huggon IC, Zosmer N, Nicolaides KH. Incidence of major structural cardiac defects associated with increased nuchal translucency but normal karyotype. Ultrasound Obstet Gynecol 2001; 18(6):610-614.
9. Michailidis GD, Economides DL. Nuchal translucency measurement and pregnancy outcome in karyotypically normal fetuses. Ultrasound Obstet Gynecol 2001; 17(2):102-105.
10. McAuliffe FM, Hornberger LK, Winsor S, Chitayat D, Chong K, Johnson JA. Fetal cardiac defects and increased nuchal translucency thickness: a prospective study. Am J Obstet Gynecol 2004; 191(4):1486-1490.
11. Hafner E, Schuller T, Metzenbauer M, Schuchter K, Philipp K. Increased nuchal translucency and congenital heart defects in a low-risk population. Prenat Diagn 2003; 23(12):985-989.
12. Galindo A, Comas C, Martinez JM, Gutierrez-Larraya F, Carrera JM, Puerto B et al. Cardiac defects in chromosomally normal fetuses with increased nuchal translucency at 10-14 weeks of gestation. J Matern Fetal Neonatal Med 2003; 13(3):163-170.
13. Orvos H, Wayda K, Kozinszky Z, Katona M, Pal A, Szabo J. Increased nuchal translucency and congenital heart defects in euploid fetuses. The Szeged experience. Eur J Obstet Gynecol Reprod Biol 2002; 101(2):124-128.
14. Hyett J. Does nuchal translucency have a role in fetal cardiac screening? Prenat Diagn 2004; 24(13):1130-1135.
15. Allan LD, Crawford DC, Chita SK, Anderson RH, Tynan MJ. Familial recurrence of congenital heart disease in a prospective series of mothers referred for fetal echocardiography. Am J Cardiol 1986; 58(3):334-337.
16. Carvalho JS. The fetal heart or the lymphatic system or ...? The quest for the etiology of increased nuchal translucency. Ultrasound Obstet Gynecol 2005; 25(3):215-220.
17. Makrydimas G, Sotiriadis A, Huggon IC, Simpson J, Sharland G, Carvalho JS et al. Nuchal translucency and fetal cardiac defects: A pooled analysis of major fetal echocardiography centers. Am J Obstet Gynecol 2005; 192(1):89-95.
18. Carvalho JS, Mavrides E, Shinebourne EA, Campbell S, Thilaganathan B. Improving the effectiveness of routine prenatal screening for major congenital heart defects. Heart 2002; 88(4):387-391.
19. Simpson JM, Sharland GK. Nuchal translucency and congenital heart defects: heart failure or not? Ultrasound Obstet Gynecol 2000; 16(1):30-36.
20. Makrydimas G, Sotiriadis A, Ioannidis JP. Screening performance of first-trimester nuchal translucency for major cardiac defects: a meta-analysis. Am J Obstet Gynecol 2003; 189(5):1330-1335.

21. Huggon IC, Ghi T, Cook AC, Zosmer N, Allan LD, Nicolaides KH. Fetal cardiac abnormalities identified prior to 14 weeks' gestation. Ultrasound Obstet Gynecol 2002; 20(1):22-29.
22. Carvalho JS, Moscoso G, Ville Y. First-trimester transabdominal fetal echocardiography. Lancet 1998; 351(9108):1023-1027.
23. Areias JC, Matias A, Montenegro N, Brandao O. Early antenatal diagnosis of cardiac defects using transvaginal Doppler ultrasound: new perspectives? Fetal Diagn Ther 1998; 13(2):111-114.
24. Zosmer N, Souter VL, Chan CS, Huggon IC, Nicolaides KH. Early diagnosis of major cardiac defects in chromosomally normal fetuses with increased nuchal translucency. Br J Obstet Gynaecol 1999; 106(8):829-833.
25. Carvalho MH, Brizot ML, Lopes LM, Chiba CH, Miyadahira S, Zugaib M. Detection of fetal structural abnormalities at the 11-14 week ultrasound scan. Prenat Diagn 2002; 22(1):1-4.
26. Comas GC, Galindo A, Martinez JM, Carrera JM, Gutierrez-Larraya F, de la FP et al. Early prenatal diagnosis of major cardiac anomalies in a high-risk population. Prenat Diagn 2002; 22(7):586-593.
27. Haak MC, Twisk JW, Van Vugt JM. How successful is fetal echocardiographic examination in the first trimester of pregnancy? Ultrasound Obstet Gynecol 2002; 20(1):9-13.
28. Favre R, Cherif Y, Kohler M, Kohler A, Hunsinger MC, Bouffet N et al. The role of fetal nuchal translucency and ductus venosus Doppler at 11-14 weeks of gestation in the detection of major congenital heart defects. Ultrasound Obstet Gynecol 2003; 21(3): 239-243.
29. Carvalho JS, Moscoso G, Tekay A, Campbell S, Thilaganathan B, Shinebourne EA. Clinical impact of first and early second trimester fetal echocardiography on high risk pregnancies. Heart 2004; 90(8):921-926.