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Screening for trisomy 21 in monochorionic twins by measurement of fetal nuchal translucency thickness

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KEYWORDS: monochorionic twins; nuchal translucency; screening; trisomy 21; ultrasound

ABSTRACT

Objective *To determine whether in screening for trisomy 21 by measurement of fetal nuchal translucency (NT) thickness in monochorionic twin pregnancies it is preferable to use the higher, smaller or average NT.*

Methods *We retrospectively examined 769 monochorionic twin pregnancies that had undergone NT screening. The selection criteria were that first, in each pregnancy both fetuses were alive at the 11 to 13 + 6-week scan and second, the fetal karyotype had been determined by prenatal invasive testing or the pregnancy outcome was known. In each pregnancy the risk for trisomy 21 was calculated by a combination of maternal age and fetal NT for crown–rump length (CRL). Three estimates of risk for each pregnancy were made using the higher, smaller and average NT and these were compared for detection and false positive rates.*

Results *The median maternal age was 33 (range, 16–45) years, the CRL was 62 (range, 45–84) mm and gestational age was 12 (range, 11 to 13 + 6) weeks. Either the fetal karyotype was normal, or phenotypically normal babies were born, in 761 cases. The karyotype was abnormal in eight cases, including six with trisomy 21. The estimated risk using the higher, smaller and average NT was 1 in 300 or more in 6 (100%), 4 (66.7%) and 6 (100%) of the trisomy 21 pregnancies and in 148 (19.4%), 57 (7.5%) and 106 (13.9%) of the normal pregnancies. For a detection rate of 100%, the false positive rates using the higher, smaller and average NT would be 5.1%, 45.9% and 4.2%, respectively.*

Conclusion *In monochorionic twins, effective screening for trisomy 21 is best provided by using the average NT measured in the two fetuses. Copyright © 2005 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

In twin pregnancies effective screening for chromosomal abnormalities is provided by a combination of maternal age and fetal nuchal translucency (NT) thickness[1–4]. In dichorionic twins, patient-specific risks for trisomy 21 are calculated for each fetus based on maternal age and fetal NT, and the detection rate (75–80%) and false positive rate (5% per fetus or 10% per pregnancy) are similar to those in singleton pregnancies[2]. Therefore effective screening and diagnosis of major chromosomal abnormalities can be achieved in the first trimester, allowing the possibility of earlier and hence safer selective fetocide for those parents that choose this option[3].

In monochorionic twins, which are always monozygotic, the maternal age-related risk for chromosomal abnormalities is the same as in singleton pregnancies, and in the vast majority of cases both fetuses are affected. The false-positive rate of NT screening (13% per pregnancy) is higher than in dichorionic twins, because increased NT in at least one of the fetuses is an early manifestation of twin-to-twin transfusion syndrome[5,6].

The aim of this study was to determine whether in screening for trisomy 21 by measurement of fetal NT in monochorionic twins it is preferable to use the higher, smaller or average NT in estimating the risk for the pregnancy as a whole.

METHODS

In the Harris Birthright Research Centre for Fetal Medicine and the Fetal Medicine Centre, London, UK, screening for trisomy 21 is based on maternal age and the measurement of fetal NT and crown–rump length (CRL) at 11 to 13 + 6 weeks of gestation[7]. Essentially, the maternal age and gestational age-related risk is multiplied by a likelihood ratio corresponding to the deviation in fetal NT thickness from the appropriate normal median

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for CRL. In twin pregnancies fetal NT and CRL are measured in each fetus and chorionicity is determined by examining the intertwin membrane at its junction with the placenta[8].

Demographic characteristics and ultrasound findings are recorded in a fetal database at the time of the examination. In those cases undergoing chorionic villus sampling or amniocentesis both fetuses are sampled and the results of fetal karyotype are also entered in the database when they are made available. Data on pregnancy outcome are obtained from the patients themselves, their general practitioners or the maternity units in which they deliver.

A computer search was made to identify all monochorionic–diamniotic twin pregnancies that had NT screening between January 1993 and May 2004. The selection criteria were that first, in each pregnancy both fetuses were alive at the 11 to 13 + 6 weeks scan and second, the fetal karyotype had been determined by prenatal invasive testing or the pregnancy outcome was known. In each pregnancy the risk for trisomy 21 was calculated by a combination of maternal age and fetal NT for CRL. Three estimates of risk for trisomy 21 in each pregnancy were made using the higher, smaller and average NT, and these were compared for detection and false positive rates. For a detection rate of 100%, the false positive rates using the higher, smaller and average NT were calculated and the significance of the observed differences was determined using the Comparison of Proportions test (StatsDirect, Version 2.2.4, 2003, Oxford, UK).

RESULTS

The computer search identified 769 monochorionic twin pregnancies. The median maternal age was 33 (range, 16–45) years, the median fetal CRL was 62 (range, 45–84) mm and the median gestational age was 12 (range, 11 to 13 + 6) weeks. Either the fetal karyotype was normal, or phenotypically normal babies were born, in 761 cases. The karyotype was abnormal in eight cases, including six with trisomy 21, one with trisomy 18 and one with triple X.

The NT thickness was successfully measured in all fetuses. In the chromosomally normal pregnancies the NT thickness was equal to or above the 95th centile of the normal range in 10.5% of the fetuses, and there were 4.2% pregnancies with increased NT in both fetuses and 12.6% with increased NT in only one of the fetuses. In each pregnancy the average NT for CRL between the two fetuses was above the 95th centile of the normal range in 10.8% of the cases (Table 1). In the trisomy 21 pregnancies the NT thickness was equal to or above the 95th centile of the normal range in 83.3% of the fetuses and there were 66.7% pregnancies with increased NT in both fetuses and 33.3% with increased NT in only one of the fetuses (Table 1 and Figure 1). The average NT for CRL between the two fetuses in each pregnancy was equal to or above the 95th centile of the normal range in all six cases. In the trisomy 18 pregnancy both fetuses had increased NT, and in the triple X pregnancy neither fetus had increased NT.

The estimated risk for trisomy 21 in each pregnancy using the higher, smaller and average NT was 1 in 300 or more in 6 (100%), 4 (66.7%) and 6 (100%) of the trisomy 21 pregnancies and in 148 (19.4%), 57 (7.5%) and 106 (13.9%) of the normal pregnancies (Table 2). For any given estimated risk cut-off the false positive rate was highest using the higher NT and lowest using the smaller NT. For a detection rate of 100%, the false positive rates using the higher, smaller and average NT would be 5.1% (39 of 761), 45.9% (349 of 761), and 4.2% (32 of 761), respectively (comparison of proportions: higher vs. smaller NT, $Z = -18.2$, $P < 0.001$; smaller vs. average NT, $Z = 18.6$, $P < 0.0001$; average vs. higher NT, $Z = -0.85$, $P = 0.40$). In order to demonstrate that the observed difference in false positive rates of 0.9% between the use of the average and higher NT is significant (alpha = 0.05, power = 80%) we would need to investigate 8813 monochorionic twins.

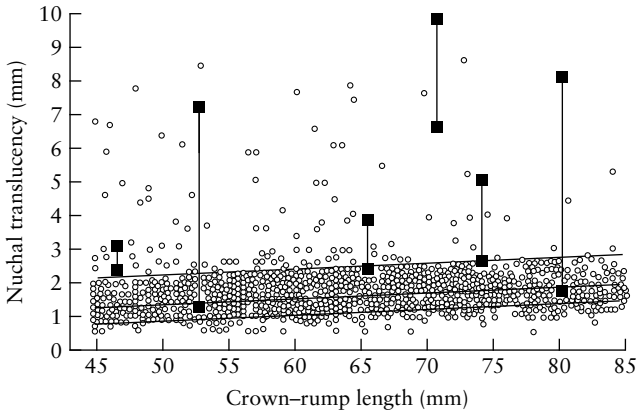

Figure 1 Fetal nuchal translucency thickness in chromosomally normal (○) and trisomy 21 (■) fetuses in monochorionic twin pregnancies plotted on the normal range for crown–rump length in singletons (median, 5th and 95th centiles)[7].

Table 1 Prevalence of nuchal translucency (NT) thickness equal to or above the 95th centile of the normal range in the chromosomally normal and the trisomy 21 monochorionic twin pregnancies

NT ≥ 95th centile	*Normal*	*Trisomy 21*
Total fetuses with increased NT	160/1522 (10.5%)	10/12 (83.3%)
Pregnancies with increased NT in both fetuses	32/761 (4.2%)	4/6 (66.7%)
Pregnancies with increased NT in only one fetus	96/761 (12.6%)	2/6 (33.3%)
Pregnancies with increased average NT between the two fetuses	82/761 (10.8%)	6/6 (100%)

Table 2 Prevalence of estimated risk for trisomy 21 of 1 in 300 or more in each pregnancy in the chromosomally normal and the trisomy 21 pregnancies, using the higher, smaller and average nuchal translucency (NT) thickness

Estimated risk ≥ 1 in 300	*Normal*	*Trisomy 21*
Fetus with higher NT	148/761 (19.4%)	6/6 (100%)
Fetus with smaller NT	57/761 (7.5%)	4/6 (66.7%)
Average NT between the fetuses	106/761 (13.9%)	6/6 (100%)

DISCUSSION

The findings of this study suggest that in monochorionic twins, effective screening for trisomy 21 is best provided by using the average of NT measured in the two fetuses. If the fetus with the smaller NT is considered the detection rate of trisomy 21, for a given false positive rate or risk cut-off, is substantially lower than using the average NT measured in the two fetuses. For a given detection rate, the false positive rate of screening using the average NT was lower than with the higher NT, but the number of cases examined was not sufficiently high to demonstrate that this difference was significant.

In dichorionic twin pregnancies the detection and false positive rates of screening for trisomy 21 by fetal NT thickness are similar to those in singleton pregnancies[2]. In monochorionic twin pregnancies the prevalence of increased NT in at least one of the fetuses is higher than in singletons and in dichorionic twins[5,6]. All monochorionic twins are monozygotic and they are invariably concordant for fetal karyotype. Discordancy for chromosomal abnormalities is very rare, with only a handful of reported cases[9–11]. In our cases there was no such discordancy. Consequently, in monochorionic twins the finding of increased NT in one of the fetuses should not lead to the erroneous conclusion of discordant risk for a chromosomal abnormality but rather should stimulate the search for alternative causes.

In general, the suggested mechanisms for increased NT are cardiac dysfunction in association with abnormalities of the heart and great arteries, venous congestion in the head and neck in association with the constriction of the fetal body in amnion rupture sequence or superior mediastinal compression found in diaphragmatic hernia or the narrow chest in skeletal dysplasia, failure of lymphatic drainage due to abnormal or delayed development of the lymphatic system or impaired fetal movements in various neuromuscular disorders, altered composition of the subcutaneous connective tissue and fetal anemia or hypoproteinemia[12,13]. In our cases there were no obvious malformations in any of the fetuses, and a possible explanation for the discordancy in NT, in at least some of the pregnancies, is twin-to-twin transfusion syndrome with the recipient twin presenting with increased NT and the donor with decreased NT[5,6].

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