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Is measurement of nuchal translucency thickness a useful screening tool for heart malformations? A study in 16 383 fetuses.

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Key words: Nuchal translucency measurement, Congenital cardiac defect, Ultrasonography, Screening, Prenatal diagnosis

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Abstract

Objective: The aim of this study was to estimate the sensitivity and false positive rate of increased nuchal translucency (NT) as a marker of congenital heart malformation.

Study Design: Our population consists of 16 383 consecutive euploid fetuses in whom an NT measurement was obtained. They are derived from an unselected pregnant population. The following cut-offs for increased risk of heart malformation were chosen à priori and tested prospectively: $NT \geq 95^{\text{th}}$ percentile for crown rump length, $NT \geq 3\text{mm}$, and $NT \geq 3.5\text{ mm}$. The sensitivity and false positive rate (1 minus specificity) of the risk cut-offs and their positive and negative likelihood ratios (+LR, -LR) with regard to congenital heart malformation were calculated.

Result: Among the 16 383 fetuses with an NT measurement there were 127 cases with a diagnosis of heart malformation confirmed by cardiac investigations after birth or at autopsy; 55 malformations were defined as major, of these 52 were isolated (no other malformations, no chromosomal aberrations) corresponding to a prevalence of major heart malformation in chromosomally normal fetuses/ newborns of 3.3/1000. The sensitivity, false positive rate, +LR and -LR of $NT \geq 95^{\text{th}}$ percentile with regard to isolated major heart malformation were: 13.5%, 2.6%, 5.2 and 0.9; of $NT \geq 3.0\text{ mm}$: 9.6%, 0.8%, 12.0 and 0.9; and of $NT \geq 3.5\text{ mm}$: 7.7%, 0.3%, 25.6 and 0.9.

Conclusion: NT measurement is a poor screening method for isolated major congenital heart malformation. A method with a much higher detection rate and with a reasonably low false-positive rate is needed. **However, as increased NT indicates increased risk of fetal heart malformation, women carrying fetuses with increased NT should be offered fetal echocardiography in the second trimester.**

Introduction

Cardiac malformations are among the most common congenital abnormalities. They account for most deaths from congenital defects in childhood.¹ The prevalence is 4 – 8 per 1000 live births^{1, 2, 3, 4}. Lethal cardiac defects and those requiring intervention within the first year of life are usually classified as major^{1, 5}. The estimated prevalence of major congenital heart malformations is 4 per 1000 live births¹⁻⁵. Prenatal detection of congenital heart malformations is currently based on examination of the four-chamber view of the heart at a second trimester routine ultrasound examination. Measurement of fetal nuchal translucency thickness (NT) in the late first trimester has become an established method of identifying fetuses at risk of aneuploidy^{6, 7}. Increased NT may also be associated with structural fetal malformations, among them congenital cardiac malformations^{8, 9}. It has even been suggested that NT measurement can be used as a screening tool for fetal cardiac defects⁹. NT increases with increasing fetal crown rump length, and the use of different cutoffs for NT to identify a risk group of adverse outcome will yield different detection rates and false positive rates.

The aim of this study was **to determine the performance of NT measurement as a method to screen for congenital heart malformations among fetuses with normal karyotype, i.e., to estimate the area under its receiver operating characteristic (ROC) curve and the sensitivity, specificity, positive and negative likelihood ratios of increased NT using different cut offs.**

Subjects and methods

Study design

Our population is a subgroup of the Swedish NUPP-trial (NUPP is an abbreviation for NackUPPklarning which is Swedish for nuchal translucency). This national multicenter trial involved eight Swedish hospitals and included almost 40 000 unselected pregnancies¹⁰. It was approved by the Ethics Committees at the Karolinska Institute in Stockholm, and those of the

Medical Faculties of Lund University and Uppsala University. Women were recruited to the trial between March 1999 and December 2002 from maternity care units affiliated to the hospitals involved. Those who consented to take part were randomized to a routine ultrasound examination either at 12–14 gestational weeks (gws) or at 18 gws. The 12-week scan included NT screening for Down's syndrome. The present study includes only those pregnancies that were randomized to a routine ultrasound examination at 12–14 gws. Of 19 796 women randomised to a 12–14 week scan 17 973 were found to have at least one living fetus at the routine scan. Of these, 16 567 had an NT measurement. Absent information on NT in 1699 fetuses is explained by the woman being too advanced in her pregnancy for NT measurement to be possible (crown rump length > 84 mm), difficulties with obtaining an accurate measurement, administrative mistakes and, in a few cases, obvious lethal fetal malformations, e.g., anencephaly. After exclusion of 80 fetuses with any chromosomal anomaly and 104 fetuses lost to follow up our study population comprised 16 383 fetuses.

The scans were performed by 46 specially trained midwives. In addition, 26 obstetricians with special interest in fetal medicine were involved. Their role was to confirm abnormal findings and to provide counselling. All midwives and obstetricians were certified by the Fetal Medicine Foundation as being competent to perform NT screening for chromosomal anomalies. The quality of our NT measurements was regularly checked by the Fetal Medicine Foundation. The ultrasound examinations included pregnancy dating, measurement of NT in accordance with the technical guidelines published by the Fetal Medicine Foundation¹¹ and screening for fetal malformations. They were performed transabdominally. Only on rare occasions was a transvaginal examination by an obstetrician added. If the NT thickness was ≥ 3.5 mm – or if a cardiac malformation was suspected – the woman was referred for fetal echocardiography by a pediatric cardiologist or an obstetrician with special training in fetal echocardiography.

Information on pregnancy outcome was retrieved from delivery records, from departments of neonatology, pediatric cardiology, pediatric surgery, neurosurgery, plastic surgery, clinical genetics and pathology providing services to the hospitals involved, and from the National Registry of Congenital Anomalies. To facilitate follow-up all women were given a questionnaire at their routine scan where they were asked to report pregnancy outcome. Newborns were followed up with regard to heart malformation until 12 months of age. The cardiac defects were subdivided into major and minor malformations by the pediatric cardiologist of our team (GB). A major heart malformation was defined as one requiring surgery or catheter intervention – except intervention for persisting arterial duct or atrial septal defect (ASD) secundum – within the first 12 months of life. In addition, a ventricular septal defect (VSD) was regarded as a major cardiac malformation if the child was symptomatic despite pharmacological treatment. The major heart defects were divided into two groups 1) isolated major congenital heart malformation, and 2) major congenital heart malformation with associated extracardiac malformations. For consistency and to facilitate comparison of our results with those of others, cardiac defects were grouped into eight categories modified after Makrydimas *et al.*¹²

1) Left heart lesions (including hypoplastic left heart syndrome, aortic atresia with or without mitral atresia, aortic valve stenosis, and coarctation of the aorta with or without VSD).

2) Right heart lesions (including tricuspid atresia, tricuspid valve dysplasia, Ebstein's anomaly, pulmonary atresia with or without VSD, and pulmonary stenosis)

3) Septal defects (including ASD and VSD, and atrio-ventricular septal defects with normal situs)

4) Outflow tract anomalies (including transposition of the great arteries with or without VSD, common arterial trunk, tetralogy of Fallot with or without atresia of the pulmonary valve, and absent pulmonary valve syndrome).

- 5) Laterality anomalies (including left and right atrial isomerism)
- 6) Complex abnormalities (including atrio-ventricular to ventriculo-atrial discordance, double outlet right ventricle, and double inlet ventricle).
- 7) Other lesions (e.g., cardiomyopathy, abnormal pulmonary venous drainage)
- 8) Non-classifiable cases

Statistical analysis

Fetuses were grouped as being or not being at increased risk of congenital heart malformation using the following cut-offs chosen *à priori*: $NT \geq 3.0$ mm, $NT \geq 3.5$ mm, and $NT \geq 95^{\text{th}}$ percentile for crown-rump length, the definition of the 95^{th} percentile being that used by the Fetal Medicine Foundation at the time of the trial ⁷. The sensitivity and false-positive rate (1 minus specificity) of these risk cut-offs **chosen *à priori*** and their positive and negative likelihood ratios with regard to congenital heart malformations were calculated. In addition, ROC¹³ curves were drawn to determine the **overall** diagnostic performance of NT and NT percentiles with regard to identifying congenital heart malformations. **The NT percentiles used when drawing the ROC curves were those derived from our own study population (15 866 fetuses without chromosomal aberrations and structural congenital malformations and with crown rump length 47 – 84 mm).** The area under the ROC curve and the 95% confidence interval (CI) of this area were calculated. If the lower limit of the CI for the area under the ROC curve was ≥ 0.5 , the test was considered to have discriminatory potential. ROC curves were also used to determine the best cut-off value **from a strictly mathematical point of view**, the **mathematically** best cut-off value being defined as the one corresponding to the point on the ROC curve situated most far away from the reference line¹³.

Our outcome variables were 1) all congenital heart malformations 2) major congenital heart malformations 3) major isolated congenital heart malformations.

Statistical analyses were carried out using the Statistical package for the Social Sciences (SPSS Inc, Chicago, IL, USA, 2003, version 12.0.1). The 95% confidence intervals of likelihood ratios were calculated using StatXact, version 4 (Cytel Software Corporation, Cambridge, MA, USA, 1999). The ROC curve for NT percentiles was drawn manually using the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles **calculated from our own study population** as cut-offs, and the area under this ROC curve was calculated using MATLAB (6.5.0.180913A). **The other ROC curves were drawn and their area calculated using the SPSS software.**

Results

None of the 104 fetuses lost to follow-up had NT ≥ 3 mm but two fetuses had NT $\geq 95^{\text{th}}$ percentile. There were 127 fetuses/babies with a diagnosis of a congenital heart malformation either confirmed by postnatal cardiac investigation or at autopsy, 55 of them having a major heart malformation and 52 having an isolated major heart malformation. Seventy-two fetuses/babies had a minor heart malformation, 66 of these being isolated. This corresponds to a prevalence of congenital heart malformation of 7.8/1000 and a prevalence of major congenital heart malformations of 3.3/1000 in euploid fetuses/newborns. In Table 1 the heart defects are described according to the classification modified after Makrydimas *et al*¹¹. The sensitivity, specificity, false positive rate, positive and negative likelihood ratios of the cutoffs defined à priori (NT ≥ 3 mm, NT ≥ 3.5 mm, NT $\geq 95^{\text{th}}$ percentile for crown rump length) are shown in Table 2. The sensitivity was generally low. The positive likelihood ratios for NT ≥ 3.0 mm and ≥ 3.5 mm with regard to major (isolated) heart malformations were high, the negative likelihood ratios were close to 1.0. Areas under ROC curves with sensitivity, false-positive rate, positive and negative likelihood ratios of the **mathematically best** cutoff selected on the basis of the ROC curves are shown in Table 3. **ROC-curves for absolute nuchal translucency measurements are shown in Figures 1.** According to the ROC curves NT could not reliably discriminate between fetuses with and without congenital heart malformation, **irrespective of which NT cutoff was chosen.** Table 4 shows detection rates for different types of major heart malformation. Cases identified by increased NT had either left heart lesions, septal defects or outflow tract anomalies. Right heart lesions and complex anomalies were not identified by increased NT.

Discussion

NT measurement cannot reliably discriminate between fetuses with and without congenital heart malformation irrespective of which cut-off of NT thickness is used (lower 95% confidence limit of area under ROC curves <0.5). In a screening situation, i.e., when examining an unselected asymptomatic population for a condition of low prevalence, it is desirable to keep the risk group reasonably restricted for both economical and ethical reasons. According to our ROC curve, the **mathematically best** cut-off of NT with regard to major congenital heart malformation was 2.1 mm. The use of this cut-off would yield a risk group of 19% of all pregnancies for a theoretical detection rate of 36%, i.e., substantial health care resources would be needed to potentially detect only one third of fetuses with a major congenital heart defect. Nor did any of the NT cut-offs chosen **à priori** perform well enough to defend NT measurement as a screening tool for either major congenital heart malformations, major isolated heart malformations, or any type of heart malformations. **For instance, the 3.5 mm cutoff yielded a detection rate of major isolated heart malformations of only 5.8% albeit for a very low false-positive rate of 0.3%.**

Our results suggest that increased NT thickness may be associated mainly with left heart lesions and septal defects, an observation made also by others^{9,14,15}. However, both our study and the studies cited included few cases and the observation that increased NT seems to be selectively associated with specific types of heart malformations may be explained by chance (wide confidence intervals of detection rates). The results of a study by Makrydimas *et al.*¹² including 399 major congenital heart malformations did not support the hypothesis that increased NT is selectively associated with specific types of cardiac anomalies.

A literature search for original articles assessing the diagnostic performance of NT screening for congenital heart malformations yielded nine studies^{9,14-21}. The design and results of these studies are summarized in Table 5. All studies were performed in unselected populations and included only chromosomally normal fetuses. Two studies included all congenital heart malformations^{14,18}, while

the others included only major heart malformations^{9,15,16,17,19,20,21}. In all but one¹⁵ of the studies cited it is unclear, if the cases included had isolated cardiac malformations, or if cases with extra-cardiac malformations were included as well. Five studies were prospective and four retrospective. The detection rate of cardiac malformations varied between 11% and 56%. The highest detection rate (56%) was reported by Hyett *et al.*⁹ Their study was retrospective, and the prevalence of major cardiac malformations was low (1.7/1000), indicating that their follow-up may have been incomplete. Incomplete follow-up results in falsely high detection rates. In a prospective study, Bilardo *et al.*¹⁶ reported NT screening to be associated with a 50% detection rate of congenital heart malformations. However, their study included only four cases of major heart malformations, which means that the 95% confidence interval of their reported detection rate was extremely large (7 – 93%). Michailidis *et al.*¹² reported a detection rate of 36%, but their study, too, was retrospective and follow-up may have been incomplete, because the prevalence of major congenital heart malformations in their study was only 1.7/1000. Two prospective studies^{19, 21} reported a prevalence of major congenital malformations in accordance with epidemiological data, 3.3/1000. In these two studies, the sensitivity of increased NT with regard to congenital heart malformations was lower (28% and 15%) than that in most of the other studies^{9,14, 16,17,18}.

The positive likelihood ratios varied between the studies, but it was usually high. The negative likelihood ratios were high in all studies (close to 1.0), indicating that a normal result of an NT measurement does not substantially decrease the odds of a fetus having a major cardiac malformation. Quite clearly, there is an association between enlarged NT and major congenital heart malformation, and increased NT – e.g. $NT \geq 3.5\text{mm}$ – is an indication to perform fetal echocardiography. However, because only a small proportion of fetuses with a cardiac malformation manifest increased NT, NT measurement is not a suitable screening test for congenital cardiac malformation. A method with much higher detection rate and with a reasonably low false-positive rate is needed.

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Legends

Figure 1. Receiver operating characteristics curve describing the diagnostic performance of nuchal translucency measurements (absolute values) with regard to detecting any heart malformation, major heart malformation, and isolated major heart malformation.

----- Any heart malformation
..... Major heart malformation
..... Isolated major heart malformation

ROC Curve

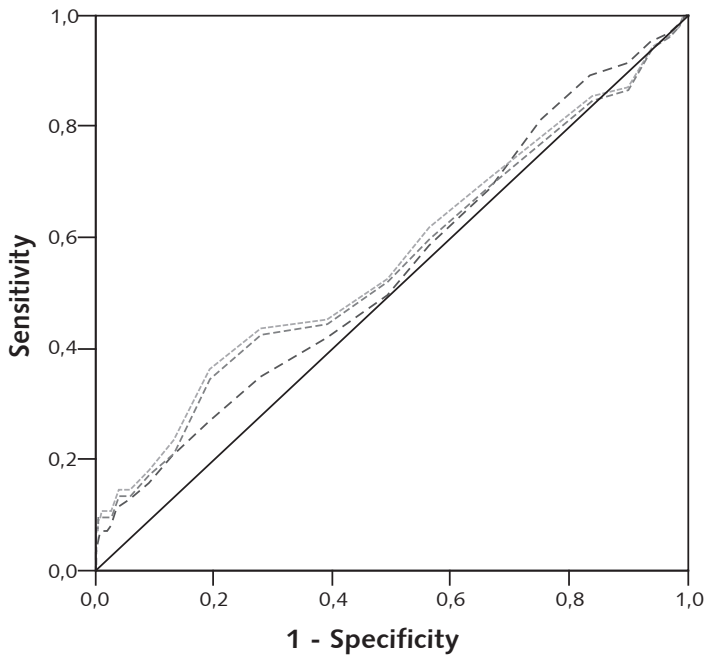


Table1. Congenital heart defects

	Number
Major malformations (n=55)	
Left heart lesion	12
Right heart lesion	10
Septal defect	18 (one with associated malformations)
Outflow tract anomaly	10
Laterality anomaly	2 (one with associated malformations)
Complex abnormality	2 (one with associated malformations)
Other lesion	1
Minor malformations (n=72)	
ASD	8 (two with associated malformations)
VSD	59 (four with associated malformations)
Unclassifiable cases	5

Table 2. Sensitivity, false positive rate, positive and negative likelihood ratio of increased nuchal translucency with regard to congenital heart malformation using nuchal translucency cutoffs defined à priori.

	Sensitivity, % (95% CI)	False positive rate, % (95% CI)	Positive likelihood ratio, (95% CI)	Negative likelihood ratio, (95% CI)
<i>Any heart malformation</i>				
<i>(n=127)</i>				
NT≥95th percentile*		2.6 (2.4–2.9)	3.9 (2.1-7.0)	0.9 (0.85-0.97)
	10.2 (4.9–15.6) (13/127)	(424/16_256)		
NT≥3.0 mm		0.8 (0.7–0.9)	7.9 (3.0-17.8)	0.9 (0.88-0.98)
	6.3 (2.0–10.6) (8/127)	(130/16_256)		
NT≥3.5 mm		0.3 (0.2–0.4)	10.5 (1.6-36.5)	1.0 (0.91-0.99)
	3.1 (0.1–6.2) (4/127)	(49/16_256)		
<i>Major heart malformation</i>				
<i>(n=55)</i>				
NT≥95th percentile*		2.6 (2.4–2.9)	5.6 (2.4-11.4)	0.9 (0.73-0.96)
	14.5 (4.9–24.2) (8/55)	(426/16_328)		
NT≥3.0 mm		0.8 (0.7–0.9)	11.3 (3.2-30.4)	0.9 (0.78-0.98)
	9.0 (1.3– 16.9)	(131/16_328)		

(5/55)

NT≥3.5 mm 5.4 (**0.7–** 0.3 (**0.2–0.4**) 18.0 (**2.1-73.7**) 0.9 (**0.83-0.99**)

11.7

(49/16_328)

(3/55)

Major isolated congenital heart malformation (n=52)

NT≥95th percentile* 13.5 2.6 (**2.4–2.9**) 5.2 (**2.1-11.0**) 0.9 (**0.74-0.97**)

(**3.4–23.1**) (7/52) (427/16_331)

NT≥3.0 mm 9.6 (**1.3–17.9**) 0.8 (**0.7–0.9**) 12.0 (**3.4-32.1**) 0.9 (**0.77-0.97**)

(5/52) (131/16_331)

NT≥3.5 mm 5.8 (**0.8–12.3**) 0.3 (**0.2–0.4**) 19.3 (**2.2-77.7**) 0.9 (**0.82-0.99**)

(3/52) (49/16_331)

NT, nuchal translucency; CI, confidence interval
* The definition of the 95th percentile is that used by the Fetal Medicine Foundation at the time of the trial ⁷

Table 3 Area under the receiver operating characteristic (ROC) curve for nuchal translucency thickness with regard to predicting congenital heart malformation, and the sensitivity, specificity, and positive and negative likelihood ratio associated with the **mathematically best** cut-off chosen on the basis of the ROC curve.

	Area under ROC curve		Optimal	Sensitivity,	False-	+LR	-LR
			cutoff	%	positive rate,		
	Estimate	95% CI			%		
All heart malformations							
NT, absolute value	0.539	(0.487–0.592)	2.1	27	19	1.4	0.9
NT, percentile*	0.534		90th	20	12	1.7	0.9
Major heart malformation							
NT, absolute value	0.565	(0.479–0.650)	2.1	36	19	1.9	0.8
NT, percentile*	0.550		75th	45	29	1.6	0.8
Major isolated heart malformation							
NT, absolute value	0.552	(0.464–0.640)	2.1	34	19	1.8	0.8
NT, percentile*	0.540		75th	44	29	1.5	0.8

NT, nuchal translucency; + LR, positive likelihood ratio; - LR, negative likelihood ratio

* The definition of the 95th percentile is that derived from our own study population

Table 4 Detection rates of increased nuchal translucency with regard to different types of major isolated heart malformations.

	NT \geq 95 th percentile* Estimate 95% CI	NT \geq 3.0 mm Estimate 95% CI	NT \geq 3.5 mm Estimate 95% CI
Left heart lesions	25% (3/12) (5–57)	17 % (2/12) (2–48)	8 % (1/12) (0.2–38)
Right heart lesions	0% (0/10) (0–31)	0% (0/10) (0–30)	0% (0/10) (0–30)
Septal defects	11% (2/17) (1–36)	11% (2/17) (1–36)	11% (1/17) (1–36)
Outflow tract defect	20% (2/10) (3–56)	10% (1/10) (0.3–44)	10% (1/10) (0.3–44)
Laterality defects	0/1	0/1	0/1
Complex defects	0/1	0/1	0/1
Other lesions	0/1	0/1	0/1
NT, nuchal translucency			

* The definition of the 95th percentile is that used by the Fetal Medicine Foundation at the time of the trial ⁷

Table 5.
Studies investigating nuchal translucency as a marker of congenital heart defect

	<i>Orvos et al. 2002</i> ¹⁴	<i>Michailidis et al. 2001</i> ¹⁷	<i>Hafner et al. 2003</i> ¹⁵	<i>Hyett et al. 1999</i> ⁹	<i>Josefsson et al. 1999</i> ¹⁸
<i>Study design</i>	Retrospective	Retrospective	Retrospective	Retrospective	Prospective
<i>No. included</i>	3655	6606	12978	29154	1460
<i>No. CHD</i>	35	11	27	50	13
<i>Type of CHD</i>	All	Major	Major Major isolated	Major	All
<i>Prevalence</i>	9.6/1000	1.7/1000	2.1/1000	1.7/1000	8.9/1000
<i>Definition of major CHD</i>	Not defined	Not defined	All but ASD secundum, VSD, and PDA	Not defined	Not defined
<i>NT cut-off</i>	≥ 3.0 mm	I) ≥ 95 th percentile II) ≥ 99 th percentile	≥ 95 th percentile	≥ 95 th percentile	I) ≥ 2.5 mm, II) ≥ 3.5 mm
<i>Follow-up time</i>	4 days	Not defined	Not defined	2 months	Not defined
<i>Follow-up mode</i>	Medical record (examined by neonatologist)	Questionnaire	Routine feed back from pediatric department.	Medical record, feed-back from GP and maternal care units, questionnaire	National Registry of malformations, medical records
<i>Sensitivity (95%)</i>	51% (34 – 69)	I) 36% (11 – 69)	Major 26% (11	56% (41 – 70)	I) 38% (14 – 68), II) 0%

<i>confidence interval)</i>	II) 27% (6 – 61) – 46)			
	Major isolated 14% (3 –35)			
<i>False positive rate</i>	2.3%	I) 3.5%, II) 1%	Not given	6.1%
				I) 8.9%, II) 0.4%
<i>Positive likelihood ratio</i>	22.3	I) 10.3 II) 24.5	-	9.2
				I)4.3, II) 0
<i>Negative likelihood ratio</i>	0.5	I) 0.7 II) 0.7	-	0.5
				I) 0.7 , II) 1.0
<i>Conclusion</i>	Increased NT is highly associated with CHD	Increased NT is a marker of high-risk pregnancy in euploid fetuses. Follow-up should include fetal echocardiography	Increased NT can be used as an indication for fetal echocardiography	Measurement of NT is a more sensitive method than the midtrimester 4-chamber view for screening of major heart defects.

	<i>Bilardo et al. 1998¹⁶</i>	<i>Hafner et al. 1998¹⁹</i>	<i>Schwärzler et al. 1999²⁰</i>	<i>Mavridis et al. 2001²¹</i>	<i>Westin et al. 2005</i>
<i>Study design</i>	Prospective	Prospective	Prospective	Prospective	Prospective
<i>No. included</i>	1590	4214	4474	7339	16383
<i>No. CHD</i>	4	14	9	26	52

<i>Type of CHD</i>	Major	Major	Major	Major	Major isolated
<i>Prevalence</i>	2.5/1000	3.3/1000	2.0/1000	3.5/1000	3.3/1000
<i>Definition of major CHD</i>	Not defined	All but ASD secundum, VSD, and PDA	Complex	Lethal; termination or post natal longterm follow-up	Intervention \leq 12 months of age
<i>NT cut-off</i>	≥ 3.0 mm	≥ 2.5 mm	≥ 2.5 mm	I) ≥ 2.5 mm, II) ≥ 3.5 mm	I) ≥ 95 percentile, II) ≥ 3.0 mm, III) ≥ 3.5 mm
<i>Follow-up time</i>	Until dismissed from postnatal care	Not defined	Until dismissed from postnatal care	3 months	12 months
<i>Follow-up mode</i>	Questionnaire	Routine feed-back from department of pediatrics.	Postnatal examination	Cardiology database	Feed back from departments of pediatrics, pathology, pediatric cardiology; questionnaire, National Registry of malformations
<i>Sensitivity (95% confidence interval)</i>	50% (7 – 93)	28% (8 – 58)	11% (0.3 – 48)	I) 15% (4 – 35), II) 11% (2 – 30)	I) 13.5% (6 – 26), II) 9.6% (3 – 21) III) 7.7% (2 – 19)
<i>False positive rate</i>	2.8%	1.4%	2.4%	I) 3.4%, II) 0.8%	I) 2.6%, II) 0.8%, III) 0.3%
<i>Positive likelihood ratio</i>	17.8	20	4.6	I) 4.4, II) 13.8	I) 5.2, II) 12.0, III) 25.6
<i>Negative likelihood ratio</i>	0.5	0.7	0.9	I) 0.9, II) 0.9	I) 0.9, II) 0.9, III) 0.9
<i>Conclusion</i>	There is a strong association between enlarged NT and NT measurement is a valuable marker of CHD				
	NT is not an effective screening tool for major	Fetuses with NT ≥ 3.5 mm have a high risk of CHD, but the	NT measurement is a poor screening method for isolated major CHD		

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congenital structural
abnormalities

CHD

low sensitivity of NT
for CHD makes it
unreliable as a major
screening tool for
CHD

No, number; CHD, congenital heart defect; NT, nuchal translucency; ASD, atrial septal defect; VSD, ventricular septal defect; PDA,
persistent arterial duct; GP, general practitioner