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First-trimester detection of structural abnormalities and the role of aneuploidy markers

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KEYWORDS: aneuploidy markers; congenital defects; first-trimester ultrasound; structural anomalies

ABSTRACT

Objectives *To determine the sensitivity of first-trimester ultrasound for diagnosing different structural anomalies in chromosomally normal pregnancies, and to establish the role of aneuploidy markers in the detection of abnormalities.*

Methods *This was a retrospective study of chromosomally normal singleton pregnancies with an 11–14-week scan performed in our center during 2002–2009. The ultrasound examination included an early fetal anatomy survey and assessment of nuchal translucency, ductus venosus blood flow and nasal bone.*

Results *Among 13 723 scanned first-trimester pregnancies with no genetic anomalies and complete follow-up, 439 fetuses (3.2%) were found to present with structural anomalies (194 with major anomalies and 245 with only minor anomalies). Forty-nine per cent of major structural anomalies were detected during the first-trimester scan, the highest rates corresponding to acrania (17/17), holoprosencephaly (three of three), hypoplastic left heart syndrome (10/10), omphalocele (six of six), megacystis (seven of eight) and hydrops (eight of nine). Higher than expected detection rates were obtained for skeletal (69%) and cardiac (57%) defects, coincidentally showing the highest presence of an increased nuchal translucency or abnormal ductus venosus blood flow (38% and 52%, respectively). The finding of an absent nasal bone did not appear to be associated with structural defects.*

Conclusion *About half of major structural abnormalities can be diagnosed in the first trimester. Increased nuchal translucency or abnormal ductus venosus blood flow appear to be associated with cardiac and skeletal defects and may facilitate early detection. Copyright © 2012 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Routine prenatal ultrasound during the first trimester of pregnancy (11–13 weeks) is increasingly being offered to pregnant women in many developed countries in addition to the second-trimester scan (at 16–22 weeks)[1–4], which is considered the standard of care in the prenatal detection of fetal structural anomalies[5]. First-trimester ultrasound was introduced in order to more accurately estimate gestational age[1,6], identify multiple pregnancies and diagnose non-viable pregnancies[7], and, more recently, to measure nuchal translucency (NT) as part of aneuploidy screening schemes[8]. Ductus venosus (DV) blood flow used in aneuploidy screening has also been suggested to have a role as a marker for cardiac defects, similarly to NT[9–11].

During the past decade, tertiary centers have reported their experience using first-trimester ultrasound to detect structural abnormalities, including defects of the central nervous system (CNS) and abdominal wall[12], and, more recently, cardiac and facial defects. A screening program for structural anomalies based on two ultrasound examinations, at 11–13 and 18–22 weeks, is gaining acceptance owing to the detection of an increasing number of anomalies in the first trimester[13]. Current clinical effectiveness of the 11–13-week sonogram in the diagnosis of birth defects is controversial, given the wide differences between reported studies. A range of 18–71% has been recently quoted in a systematic review, with a 29% overall pooled detection rate[2].

We present our experience of first-trimester scans of 13 723 pregnancies at a single center between 2002 and 2009. An early anatomical survey was carried out of all the fetuses, together with an assessment of sonographic markers of aneuploidy. This is one of the largest studies from a single center to assess the capacity of the first-trimester scan to detect fetal structural anomalies in chromosomally normal singleton pregnancies. We sought

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to determine the detection rate for common anomalies and to evaluate a potential association between an increase in early detection with the finding of abnormal aneuploidy markers, increased NT, abnormal DV blood flow or an absent nasal bone (NB).

METHODS

Population

During an 8-year period (January 2002 to December 2009) a total of 16 301 pregnant women with singleton pregnancies were scanned between 11 and 14 weeks in our center and were included in the study. Chromosomally abnormal fetuses and multiple pregnancies were excluded from the analysis. Continuing pregnancies were followed up until neonatal discharge, and structural anomalies detected either prenatally during one of the three routine scans typically scheduled in each trimester at 11–14, 20–22 and 32–35 weeks, or postnatally at either neonatal examination or postmortem examination, were noted. Women with a first-trimester scan were enrolled in the study after giving informed consent for Doppler studies, including women who received their prenatal care at our facility and those who were referred for ultrasound only. The study was approved by the Hospital Institutional Review Board.

First-trimester scan

First-trimester scans were performed by 19 obstetricians using primarily three ultrasound machines: Power Vision 6000 SSA-370 (Toshiba Medical Systems, Tokyo, Japan); Acuson Antares (Siemens Medical Solutions, Malvern, PA, USA); and Voluson 730 Pro (GE Healthcare, Milwaukee, WI, USA). Doppler examinations were performed with safety indices minimized according to the ALARA (as low as reasonably achievable) principle. The time slot assigned to perform a routine first-trimester scan was 25 min. The vast majority of examinations included both transvaginal and transabdominal imaging (3.5–7 MHz). In all cases, we attempted to evaluate the fetal head (cranium, falx and choroid plexus), chest (lungs, four-chamber view and diaphragm), abdomen (stomach, cord insertion and kidneys) and the four limbs (long bones, hands and feet). Cystic hygroma was only considered to be a fetal defect distinct from an increased NT[14], when in a cross-sectional view of the fetal neck free-fluid-filled cavities were clearly depicted. Data on gestational age, NT measurement, DV blood flow and presence of NB were also noted. In pregnancies in which an increased risk for fetal trisomies by means of the Combined Test[15] or a fetal structural defect were found, women were offered chorionic villus sampling for fetal karyotyping. Early fetal echocardiograms were performed at 14–16 weeks when a cardiac defect was suspected or when an increased fetal NT ($> 97.5^{th}$ percentile from 2002 to 2005; and $> 99^{th}$ percentile from 2006 to 2009)[16], and/or an abnormal DV blood flow (absent or reversed flow) were observed[9]. Cardiac anomalies diagnosed before 17 weeks because of an abnormal ultrasound marker observed at 11–14 weeks were considered to be detected in the first trimester. The algorithm for increased NT also included a repeat anatomical survey at 14 weeks and re-evaluation at 20 weeks with an anatomical survey, echocardiogram and nuchal fold measurement.

Pregnancy follow-up

In pregnancies monitored at our hospital (unselected pregnancies and referred pregnancies that were monitored and delivered in our hospital), data on second- and third-trimester scans, pregnancy outcome and neonatal follow-up or postmortem examinations were obtained from hospital records. Postmortem examination was systematically performed at fetal demise after 10 weeks' gestation. In some pregnancies delivered in other centers, questionnaires were given to women and returned to us by mail. Otherwise, private obstetricians or the women were contacted by telephone to collect these data. Pregnancies with unknown pregnancy outcome were excluded from the study.

Classification of fetal structural anomalies

Fetal anomalies were divided into two categories according to severity, following EUROCAT (European Surveillance of Congenital Anomalies) guidelines: major malformations (those considered lethal, severe or moderate) and minor malformations (those excluded from the EUROCAT Registry)[17]. Minor anomalies were grouped into seven system/organs: CNS, facial, cardiac, gastrointestinal, nephrourinary, genital, skeletal, and other. Fetuses with a single major anomaly were included in the corresponding EUROCAT group for this major anomaly, irrespective of whether associated minor anomalies were present. Fetuses with two or more major malformations were classified as a polymalformed fetus. Fetuses with more than one minor anomaly were classified according to the most relevant anomaly. Anomalies were also classified according to the time of the diagnosis: first, second or third trimester, or postnatally.

Data entry

Maternal and clinical data, data obtained from the first-trimester ultrasound examination and pregnancy outcome were registered in a Statistical Package for the Social Sciences (SPSS) database. The detection rate for each anomaly was calculated as the number of affected fetuses with a first-trimester diagnosis divided by the total number of affected fetuses. Each fetus represented a single entry in the analysis.

RESULTS

Among 16 301 scanned first-trimester pregnancies, complete perinatal follow up was achieved in 14 368 (88%).

Table 1 Detection of major structural defects prenatally (first, second and third trimesters) and postnatally, and pregnancy outcome

Fetal abnormality	n	*Detection rate* (n *(%))*				*Detection (%): first-trimester review**	*Outcome†*	
		First trimester	*Second trimester*	*Third trimester*	*Postnatally*		*Liveborn* (n *(%))*	*TOP* (n *(%))*
Central nervous system	43	23 (53)	9 (21)	9 (21)	2 (5)	40	13 (30)	30 (70)
Acrania-exencephaly	17	17 (100)	0 (0)	0 (0)	0 (0)	88	0 (0)	17 (100)
Holoprosencephaly (alobar)	3	3 (100)	0 (0)	0 (0)	0 (0)	92	0 (0)	3 (100)
Hydrocephaly	14	1 (7)	6 (43)	7 (50)	0 (0)	16	10 (71)	4 (29)
Encephalocele	1	1 (100)	0 (0)	0 (0)	0 (0)	—	0 (0)	1 (100)
Agenesis of corpus callosum	3	0 (0)	1 (33)	2 (67)	0 (0)	—	1 (33)	2 (67)
Microcephaly	1	0 (0)	0 (0)	0 (0)	1 (100)	—	1 (100)	0 (0)
Spina bifida	4	1 (25)	2 (50)	0 (0)	1 (25)	18	1 (40)	3 (60)
Face and neck	13	4 (31)	5 (38)	0 (0)	4 (31)	—	9 (69)	4 (31)
Cystic hygroma	3	3 (100)	0 (0)	0 (0)	0 (0)	—	0 (0)	3 (100)
Facial clefting	7	0 (0)	4 (57)	0 (0)	3 (43)	43	7 (100)	0 (0)
Other	3	1 (33)	1 (33)	0 (0)	1 (33)	—	2 (67)	1 (33)
Thoracic	45	25 (56)	16 (36)	2 (4)	2 (4)	17	10 (22)	32 (71)
HLHS and left heart defects	10	10 (100)	0 (0)	0 (0)	0 (0)	—	0 (0)	10 (100)
Right heart defects	7	5 (71)	2 (29)	0 (0)	0 (0)	—	0 (0)	7 (100)
Atrioventricular canal	5	4 (80)	0 (0)	0 (0)	1 (20)	—	1 (20)	4 (80)
Tetralogy of Fallot	7	3 (43)	3 (43)	1 (14)	0	—	3 (43)	3 (43)
Great arteries defects	8	2 (25)	5 (63)	0 (0)	1 (13)	—	4 (50)	2 (25)
Other cardiac	7	1 (14)	5 (71)	1 (14)	0 (0)	—	2 (29)	5 (71)
Lung	1	0 (0)	1 (100)	0 (0)	0 (0)	—	0 (0)	1 (100)
Digestive	12	9 (75)	0 (0)	2 (17)	1 (8)	29	9 (75)	2 (17)
Omphalocele	6	6 (100)	0 (0)	0 (0)	0 (0)	75	4 (67)	1 (17)
Diaphragmatic hernia	3	1 (33)	0 (0)	1 (33)	1 (33)	20	3 (100)	0 (0)
Gastroschisis	1	1 (100)	0 (0)	0 (0)	0 (0)	67	1 (100)	0 (0)
Large wall defects	1	1 (100)	0 (0)	0 (0)	0 (0)	—	0 (0)	1 (100)
Other	1	0 (0)	0 (0)	1 (100)	0 (0)	0	1 (100)	0 (0)
Nephrourinary	40	10 (25)	16 (40)	14 (35)	0 (0)	25	28 (70)	9 (23)
Megacystis	8	7 (88)	1 (13)	0 (0)	0 (0)	67	1 (13)	5 (63)
Hydronephrosis	17	1 (6)	8 (47)	8 (47)	0 (0)	6	17 (100)	0 (0)
Cystic kidney	4	1 (25)	2 (50)	1 (25)	0 (0)	11	3 (75)	1 (25)
Persistent cloaca	1	1 (100)	0 (0)	0 (0)	0 (0)	—	0 (0)	0 (0)
Renal agenesis	8	0 (0)	5 (63)	3 (38)	0 (0)	22	5 (63)	3 (38)
Other	2	0 (0)	0 (0)	2 (100)	0 (0)	—	2 (100)	0 (0)
Skeletal	16	11 (69)	5 (31)	0 (0)	0 (0)	16	1 (6)	13 (81)
Osteochondrodysplasias	7	6 (86)	1 (14)	0 (0)	0 (0)	33	0 (0)	5 (71)
Limb reduction defects	7	4 (57)	3 (43)	0 (0)	0 (0)	20	1 (14)	6 (86)
Arthrogryposis	2	1 (50)	1 (50)	0 (0)	0 (0)	—	0 (0)	2 (100)
Other	25	13 (52)	8 (32)	2 (8)	2 (8)	—	4 (16)	15 (60)
Hydrops	9	8 (89)	1 (11)	0 (0)	0 (0)	82	0 (0)	7 (78)
Polymalformation	12	4 (33)	6 (50)	0 (0)	2 (17)	—	1 (8)	7 (58)
Tumors	4	1 (25)	1 (25)	2 (50)	0 (0)	—	3 (75)	1 (25)
Total	194	95 (49)	59 (30)	29 (15)	11 (6)	29	74 (38)	105 (54)

*First-trimester detection rates in a recent systematic review are also shown for comparison (Borrell *et al.*[2], 2011). †Cases of fetal or neonatal demise are not included. HLHS, hypoplastic left heart syndrome; TOP, termination of pregnancy.

After the exclusion of 312 (2.2%) cases with chromosomal anomalies, 103 (0.7%) single-gene disorders and 230 (1.6%) spontaneous losses, the study group included 13 723 pregnancies. The mean gestational age at scanning was 12 + 2 weeks, being distributed as follows: 17% at 11 weeks, 48% at 12 weeks, 31% at 13 weeks and 4% at 14 weeks. Of these, 439 (3.2%) fetuses were found to carry at least one anomaly, 194 (1.4%) had one or more major structural anomalies and 245 (1.8%) carried one or more minor structural anomalies. The proportion of referrals was 13% among the whole study population and 23% among fetuses with anomalies. The detection rates achieved for major anomalies were 49% (95/194) in the first trimester, 30% in the second trimester, 15% in the third trimester and 6% postnatally (Table 1). Abnormal aneuploidy marker rates in structurally abnormal fetuses were 23% for NT (> 99th percentile), 17% for DV blood flow (absent or reversed flow) and 5% for NB (absence) (Table S1), while in non-abnormal fetuses the corresponding rates were 1.3%, 1.8% and 0.8%.

CNS anomalies

The first-trimester detection rate for major CNS anomalies was 53% (23/43) (Table 1). All fetuses presenting with acrania/exencephaly (17/17), alobar holoprosencephaly (three of three) and encephalocele (one of one) were

Table 2 Detection of minor structural defects prenatally (first, second and third trimesters) and postnatally, and pregnancy outcome

Type of fetal abnormality	*Total* n	*Detection rate* (n *(%))*				*Outcome**	
		First trimester	*Second trimester*	*Third trimester*	*Postnatally*	*Liveborn* (n *(%))*	*TOP* (n *(%))*
Central nervous system	6	0 (0)	2 (33)	3 (50)	1 (17)	5 (83)	1 (17)
Facial	15	0 (0)	0 (0)	1 (7)	14 (93)	15 (100)	0 (0)
Cardiac	80	3 (4)	23 (29)	28 (35)	26 (32)	80 (100)	0 (0)
Nephrourinary	77	1 (1)	28 (36)	41 (53)	7 (9)	76 (99)	0 (0)
Genital	39	0 (0)	0 (0)	1 (3)	38 (97)	39 (100)	0 (0)
Skeletal	23	2 (9)	6 (26)	0 (0)	15 (65)	21 (91)	2 (9)
Other	5	0 (0)	0 (0)	0 (0)	5 (100)	5 (100)	0 (0)
Total	245	6 (2)	59 (24)	74 (30)	106 (43)	241 (98)	3 (1)

*One case with nephrourinary anomaly died *in utero*. TOP, termination of pregnancy.

diagnosed during the first trimester (Table 1). On the contrary, the detection rates for hydrocephaly (7%; one of 14) and spina bifida (25%; one of four) were poor, and typically were diagnosed in the second (50% of spina bifida cases) or third (50% of hydrocephalus cases) trimesters. Agenesis of corpus callosum and microcephaly cannot be detected in the first trimester, and were usually observed during the third trimester. Nine per cent of fetuses with a CNS abnormality presented with an abnormal NT or DV blood flow but none presented with an absent NB (Table S1). The few minor CNS anomalies of this series (cerebral cysts) went undetected during the first-trimester sonogram (Table 2).

Facial and neck anomalies

Major facial anomalies, such as facial clefting (cleft lip and/or palate), were overlooked in the first trimester, with the exception of one congenital malformation of eye orbits (one of seven cases) (Table 1). Although several cases were referred to our center with a 'cystic hygroma', only three fetuses (three of three cases) near 14 weeks were considered to have that diagnosis using strict criteria. Among these fetuses, 23% presented with an increased NT or abnormal DV blood flow and 15% with an absent NB (Table S1). None of the minor facial anomalies, such as facial asymmetry, preauricular appendage, Pierre–Robin malformation and congenital cataracts, was detected in the first trimester (Table 2).

Thoracic anomalies

A 57% (25/44) detection rate for major cardiac defects was achieved during the first trimester (Table 1). High detection rates were achieved for hypoplastic left heart syndrome (HLHS) (100%; 10/10 cases), and for atrioventricular (AV) canal (80%; four of five cases) and right heart (71%; five of seven cases) defects. In contrast, detection rates were low for transposition of the great arteries (25%; two of eight cases) and for AV block (14%; one of seven cases). Among 44 fetuses carrying a major cardiac defect, 16 had an abnormal NT, 16 an abnormal DV blood flow and four an absent NB, leading to a 52% rate of abnormal NT or DV blood flow (three of five had AV canal, three of seven had tetralogy of Fallot, five of seven had right heart defects, seven of 10 had HLHS left heart defects and three of eight had great arteries defects) (Table S1). Minor cardiovascular defects, such as ventricular septal defect (VSD), atrioventricular septal defect (AVSD), persistent foramen ovale and aberrant right subclavian artery (ARSA) were detected in the first trimester in only 4% of the cases (Table 2). The single lung anomaly in our series, congenital cystic adenomatoid malformation of the lung, went undetected in the first trimester.

Digestive and abdominal wall anomalies

Seventy-five per cent of digestive and abdominal wall defects were detected in the first trimester, with large differences in detection for each of the anomalies (Table 1). Whereas abdominal wall defects, such as omphalocele (six of six cases), gastroschisis (one of one case) and larger defects, such as Cantrell's Pentalogy or limb-body wall complex (one of one case) were all detected in the first trimester, only 33% (one of three) diaphragmatic hernias and none of the esophageal atresias were. In 17% of digestive anomalies an abnormal NT or DV blood flow was observed (Table S1).

Nephrourinary and genital anomalies

The first-trimester detection rate for major urinary anomalies was 25% (10/40) (Table 1). At the upper end of the spectrum, low urinary tract obstruction, appearing as megacystis, achieved a detection rate of 88% (seven of eight), and, at the lower end of the spectrum, cystic kidneys had a detection rate of 25% (one of four) and hydronephrosis had a detection rate of 6% (one of 17). Renal agenesis has not been reported to be detected during the first trimester, probably because of confusion between the kidneys and the adrenal glands. Persistent cloaca, although rare, was detected in the first trimester (one of one case). Only 13% of nephrourinary anomalies were associated with abnormal NT or DV blood flow, particularly cystic kidneys (Table S1). Regarding minor

genito-urinary anomalies, pyelectasis, also known as mild hydronephrosis, was rarely (1%) detected in the first trimester (Table 2). Nephrocalcinosis and minor genital anomalies such as hypospadias, undescended testicle, hydrocele or cystic ovaries were never detected during the first trimester.

Skeletal anomalies

Sixty-nine per cent (11/16) of the major skeletal anomalies were detected in the first trimester, the highest rate being achieved for osteochondrodysplasias (86%; six of seven cases). Limb reduction defects were detected in 57% (four of seven) of the cases, and arthrogryposis in 50% (one of two cases). Among skeletal anomalies, 38% presented with abnormal aneuploidy markers (four cases had both abnormal NT and DV blood flow and two cases had an abnormal NT only), particularly osteochondrodysplasias, and none with an absent NB (Table S1). Minor skeletal anomalies, such as talipes, polydactyly and syndactyly, are more common than major defects, but are rarely detected in the first trimester (9%) (Table 2).

Hydrops and polymalformed fetuses

Fetal hydrops was usually detected during the first-trimester scan, with a detection rate of 89% (eight of nine cases). In contrast, only 31% (four of 13) of the fetuses presenting with two or more major structural anomalies involving different systems (hydrocephalus + omphalocele; hydrops + megacystis; transposition of the great arteries + diaphragmatic hernia; and hypoplastic right heart + hydrops) were detected during the first trimester. Abnormal NT or DV blood flow was observed in 64% of these fetuses (nine of nine had hydrops; seven of 12 were polymalformed) and 8% had an absent NB (Table S1).

Pregnancy outcome

Termination of pregnancy was the option for all women carrying a fetus with a severe CNS structural anomaly (acrania-exencephaly, alobar holoprosencephaly and encephalocele), in some types of cardiac defects (severe defects of the left and right heart), in arthrogryposis, fetal hydrops and in clearly defined cystic hygroma (Table 1). Termination was carried out in more than half of the following anomalies: spina bifida, agenesis of corpus callosum, AV canal, megacystis, osteochondrodysplasias and limb reduction defects, and in polymalformed fetuses. Termination was never carried out for facial clefting, diaphragmatic hernia, esophageal atresia and hydronephrosis (Table 1). Regarding minor anomalies, termination was only performed in one CNS anomaly and in two skeletal anomalies (Table 2).

DISCUSSION

Our study demonstrated that the first-trimester ultrasound performed at 11–14 weeks was able to detect 49% of major structural anomalies in chromosomally normal fetuses in singleton pregnancies. The rates of later diagnosis of these defects in the second and third trimesters, and in the neonatal period, were 30%, 15% and 6%, respectively. In abnormal fetuses the detection rates for abnormal markers were 23% for NT, 17% for DV and 5% for NB. As expected, the highest detection rates were found for acrania, holoprosencephaly, omphalocele, gastroschisis and megacystis. Unexpected rates of 69% for skeletal defects and 57% for cardiac defects were threefold more than the previously reported first-trimester detection rates, and both anomaly systems were associated with the highest rates of abnormal aneuploidy markers – 38% and 52%, respectively – suggesting a role for these markers in improving the early detection of structural anomalies.

The first-trimester detection rate of 49% for major structural anomalies was substantially higher than the 29% obtained in a recent systematic review of all reported series during the 2002–2008 period[2] and similar to the 44% reported in a recent large study[4]. Reported series, however, showed a remarkable variability in detection, given that the rates ranged from 18% to 71%[18–25]. The two main factors accounting for a major part of this variability were differences in the inclusion criteria for anomalies and in the type and length of postnatal follow up. An earlier prenatal diagnosis of major fetal anomalies may result in some advantages in management, such as: (a) the possibility of scheduling additional examinations well before the limits for legal termination; (b) the option for an earlier and safer termination of pregnancy[26]; and (c) earlier reassurance and reduced anxiety. Furthermore, it appears that women prefer earlier screening, when possible[27].

Six structural anomalies were expected to be detected in more than two thirds of the cases during the first trimester: acrania-exencephaly, alobar holoprosencephaly, omphalocele, gastroschisis, megacystis and hydrops[14,28]. In our series, acrania (17/17 cases), holoprosencephaly (three out of three cases), omphalocele (six out of six cases) and gastroschisis (one out of one case) were always detected early. Omphalocele and megacystis, although easily diagnosed in the first trimester, can be a transient finding in chromosomally normal fetuses[29]. Recently, it has been described that the vast majority (83%) of omphaloceles containing only bowel and observed at 11–13 weeks, resolve by 20 weeks[30]. Moderate megacystis (7–15-mm bladder length) seen in normal-karyotype fetuses deserves further evaluation given that it is associated with a 90% chance of resolution and a favorable prognosis[30,31].

Cystic hygroma is a well-established entity in the second trimester, but it is a confusing finding in the first trimester because the distinction between cystic hygroma and an increased NT is rather subjective, as shown by frequencies varying from 0% (0/29)[18] to 33% (10/30)[25] in reported series. The latter show higher early overall detection rates, as all hygromas are considered to be diagnosed in the first trimester. In our series, a clearly

defined cystic hygroma was seen in three fetuses, accounting for 3% of the first-trimester anomalies, and it was diagnosed when a large cystic cavity was observed, rather than thin septations that are invariably present in all large NT. First-trimester fetal hydrops has been described to be frequently associated with chromosomal anomalies[32], but it is also the third most frequently detected structural anomaly in first-trimester chromosomally normal fetuses.

In our series, four further anomalies achieved first-trimester detection rates above 66%, in contrast to previous series: left heart defects (100%), osteochondrodysplasias (86%), AV canal (80%) and right heart defects (71%). Initially, detection of cardiac defects was poor during the first-trimester sonogram[33], with a detection rate of 26% in the most recently reported first-trimester screening series[4], but increased up to 57% (25/44) in our series. Besides a better early ultrasound visualization of cardiac structures, a reason for this improvement was the role of aneuploidy sonographic markers, such as NT and DV blood flow, which can also signal cardiac defects in euploid fetuses. It is well established that a third of fetuses with a cardiac defect present with an increased NT[34]. We previously reported that an early fetal echocardiogram performed because of an abnormal flow in the DV was able to detect an extra 11% of cardiac defects in fetuses with a normal NT[10,35]. In the present series, 52% (23/44) of fetuses with cardiac defects presented with an increased NT above the 99th percentile or abnormal DV flow, both markers having the same importance (seven with isolated abnormal DV blood flow, seven with isolated increased NT and nine with both abnormal markers). Our 36% rate of increased NT in cardiac anomalies was similar to the 28% rate found in a recently reported large series[4]. In contrast, only four of such fetuses had an absent NB.

Major skeletal anomalies were the second anomaly group showing a clear improvement, the detection rate increasing from 16% in a previous review[2] to 69%. Coincidentally, this group also showed the second-highest rate (38%) for abnormal markers. It has already been reported that most of the lethal skeletal dysplasias might present with an increased NT[4,36]. Particularly among osteochondrodysplasias, 57% (four of seven cases) presented with both abnormal NT and DV blood flow, and an extra 14% (one of seven) had an abnormal NT only. An absent NB was not observed in skeletal dysplasias. In limb-reduction defects, the reason for improvement was that the four limbs were routinely checked together with both hands and feet in each scan. Other structural anomalies potentially associated with an increased NT are diaphragmatic hernia and bilateral talipes[4,20,37,38].

Some weaknesses of our study should be pointed out. The first is the mixed study population, which included routine prenatal patients together with those referred because of an increased NT, a positive screen for aneuploidy, or even for a suspected structural anomaly. Although it is well known that it is easier to detect anomalies in a high-risk population, such as fetuses with increased NT, referrals accounted for only 13% of the study population and for 23% of the abnormal fetuses. The second weakness was the fact that these first-trimester ultrasound scans were performed by highly trained individuals using top-quality equipment at a tertiary center, and that less-experienced clinicians may not be able to replicate our results. The third weakness is that some pregnancies had their second- and third-trimester scans performed in another center. Another limitation is that early fetal echocardiography during the last decade has usually been performed at 14–16 weeks and therefore some cardiac defects detected in the first trimester were ultimately diagnosed in the 16th week. And, finally, the poor detection of minor abnormalities also deserves attention, although this was not the main goal of the fetal anatomic survey.

To conclude, a fetal anatomic survey carried out during the 11–14-week scan can detect half of the major structural anomalies present in chromosomally normal pregnancies. A major improvement was observed in the early detection of cardiac defects and skeletal anomalies, which were the anomalies with the highest rates of abnormal NT and DV blood flow.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Table S1 Rates of abnormal markers (nuchal translucency, ductus venosus flow and nasal bone) in each type of major structural defect

