CHAPTER 9

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Targeted ultrasound examination provides the possibility to diagnose a variety of structural malformations of the fetus. Nowadays, screening for congenital anomalies is offered as standard obstetric care by ultrasound examination around 20 weeks’ gestation in most Western countries. A prenatal diagnosis of a congenital heart defect (CHD), may lead to changes in obstetric management and allows for optimal neonatal care which may improve the neonatal outcome. CHD are still amongst the most commonly overlooked lesions in prenatal screening. CHD are the most common congenital defects in neonates, occurring in 6-8/1000 live births. One third of these (2-3/1000) are severe CHD, commonly defined as being potentially life threatening and requiring surgery in the first year of life. Severe CHD are the leading cause of non-infectious neonatal mortality in at term born neonates. The goal of this thesis was to gain insight in the performance of second trimester standard anomaly screening in detecting CHD and to evaluate the influence of a prenatal diagnosis on the outcome.

First, in Chapter 2, a systematic review was performed, to evaluate the performance of second trimester screening by ultrasound in detecting CHD internationally. A meta-analysis was performed on the detection rates of CHD in low risk or general populations. Analysis were performed differentiated per specific diagnosis, since CHD are very heterogeneous in anatomy, severity and prognosis. A separate analysis was performed for isolated CHD, meaning the CHD being the only congenital defect present, without any genetic or extracardiac structural anomaly. Unfortunately, very few studies report on isolated CHD. Detection rates higher than 90% were found for univentricular defects and heterotaxy cases. Defects like coarctation of the aorta and transposition of the great arteries were detected less frequently. We found that the prenatal detection rate of a CHD generally is correlated with the severity of the heart defect.

A large retrospective and partly prospective cohort study was performed in a large region in the Netherlands to evaluate the performance of prenatal screening by ultrasound, including more than 1900 cases of fetuses/neonates with CHD born between 2002 and 2012.

In Chapter 3, we evaluated the effect of the introduction of the national second trimester screening program in the Netherlands in 2007 on the prenatal detection rates of CHD. Cases were divided into two groups: before and after the introduction of screening. The prenatal detection rate increased from 35.8 to 59.7% after the introduction of screening and of isolated CHD from 22.8 to 44.2%. The highest detection rates were found in the hypoplastic left heart syndrome, other univentricular defects and complex defects with atrial isomerism (>93%). Since the introduction of screening, the ‘late’ referrals
(after 24 weeks of gestation) to a tertiary centre decreased by 24.3%. Of the CHD cases identified on prenatal scan without any extracardiac structural anomalies 10.9% had an aneuploidy. In the total cohort 2.0% had a 22q11 deletion. Other genetic syndromes (e.g. CHARGE, Williams, Holt–Oram syndrome) were diagnosed in 3.9% of the total cohort. Termination of pregnancy is performed in about 50% of all the prenatally diagnosed cases and in about 30% of the prenatally diagnosed cases with isolated CHD. Colleagues from Belgium complemented the Dutch screening program with the high detection rates in a published reply on the study. In a reaction from our side we elaborated on why we think the Dutch screening program has these high detection rates. Essentially the prenatal screening in the Netherlands is centrally organised, with a uniform protocol, training, regulations and close quality monitoring.

Transposition of the great arteries (TGA) is one of the most common cyanotic CHDs, with an incidence of 0.2–0.3 per 1000 live births. Simple TGA is rarely associated with chromosomal or extracardiac anomalies. The condition is generally well tolerated by the fetus, but life-threatening cyanotic complications occur shortly after birth. Chapter 4 focuses on the prenatal detection of TGA, as well as the effect of prenatal detection on pre- and postsurgical mortality and morbidity. Of all cases (n=144), 26.4% were diagnosed prenatally, the detection rate was 41.0% after introduction of the second trimester anomaly scan. First-year mortality was significantly lower in cases with a prenatal diagnosis of TGA than in those without (0.0% vs 11.4%, respectively). Presurgical mortality (4.9%) only occurred in undetected simple TGA cases. Closure of the duct before treatment, renal dysfunction and hypoxia occurred significantly more often in the group without a prenatal diagnosis.

When a fetal CHD is suspected in a second trimester anomaly scan, the patient is referred to a tertiary center where fetal echocardiography is performed. In Chapter 5 the accuracy of fetal echocardiography in diagnosing CHD is examined. All cases with CHD that were referred prenatally to the three tertiary centers in the study region between 2002 and 2012 were included (n=708). Prenatal and postnatal diagnoses were compared and the degree of agreement was classified as ‘correct’ (anatomy correct and the postnatal diagnosis led to a similar outcome as expected), ‘discrepant’ (anatomical discrepancies present but the severity and prognosis of the defect were diagnosed correctly) or ‘no similarity’ (the pre- and postnatal diagnoses differed completely).

The prenatal diagnosis was correct in 82.1% of cases and discrepancies were present in 9.9%; however, these did not result in a different outcome. In 8.1% there was no similarity between prenatal and postnatal diagnoses. Disagreement between pre- and postnatal diagnoses occurred significantly more frequently in cases that presented
with a normal four-chamber view than in those with an abnormal four-chamber view (5.5% vs 1.9%). Incorrect identification of the outflow tracts and incorrect differentiation between unbalanced atrioventricular septal defect and hypoplastic left heart syndrome were relatively commonly encountered. In many cases with disagreement, trisomy 21, an extracardiac anomaly or a high maternal body mass index was present.

With the increasing prenatal detection rates of CHD, obstetricians are more frequently faced with pregnancies complicated by a fetal CHD. Congenital anomalies in general are associated with preterm birth and fetal demise. The aim in Chapter 6 was to gain insight into the incidence of preterm birth and fetal demise in singleton pregnancies with fetuses with isolated CHD. In this analysis fetuses and infants from singleton pregnancies diagnosed with severe isolated CHD, born in the study region between 2002 and 2012, were included. All cases in the CHD cohort were assessed for preterm birth or fetal demise. The proportions of preterm birth and fetal demise were compared to a control group (all births in the study region in 2010 (PRN data)) and odds ratios were calculated.

The proportion of preterm births in the CHD cohort (n=1013) was 9.1% compared to 5.6% in the control group, with an odds ratio of 1.7. The preterm birth started spontaneously in 49.5% and 38.4% were induced. In 15 cases fetal demise occurred (1.5%), compared to 0.7% in the control group, odds ratio 2.0.

In Chapter 7 a prenatally diagnosed CHD case is presented with unexpected postnatal complications. Persistence of the left superior vena cava (LSVC) in the absence of the right superior vena cava (RSVC) in a fetus with otherwise normal cardiac anatomy is usually not predictive of postnatal complications. This case report shows that cardiac anomalies that were assumed to be fairly innocuous can have an unexpected outcome.

In Chapter 8 all the findings in this thesis are discussed and suggestions to improve the prenatal screening program and detection rates are postulated in order to achieve a reduction of mortality and morbidity of the affected infants.