The Diagnostics of Fetal Heart Defects in the First and Early Second Trimester – Early Fetal Echocardiography

Examinations of the fetal heart are increasingly being conducted as part of first-trimester screening, either as a sole visualisation of the four-chamber view or a visualisation of the four-chamber view and both ventricular outflow tracts or as a segmental approach as part of complete fetal echocardiography. Alongside anamnestic risks, markers for heart defects that become apparent during a first-trimester screening, such as thickened nuchal translucency, an abnormal blood flow velocity profile in the ductus venosus and the presence of tricuspid valve regurgitation, are indications for an early echocardiogram in this high-risk group. However, heart defects most often occur in fetuses in a low-risk group who display none of the markers mentioned. An increasing number of examiners are therefore also conducting a fetal echocardiogram as part of the detailed first-trimester screening of fetal organs. Up to 80% of severe heart defects can be diagnosed as early as the 12th and 13th weeks of gestation.

Apart from the examiner’s experience and the best possible equipment, prerequisites are a consistent visualisation of all cross-sections and connections following a strict protocol, including transvaginal approach in some cases, and, in very rare cases, during a repeat examination a few days later. Nevertheless, primarily due to the intrauterine development of some heart defects, a further echocardiographic examination should always be carried out in the second trimester, when the detection rate is up to 10% higher.
Introduction

The sonographic first-trimester screening established during the last decades for fetal aneuploidies through measuring nuchal translucency and the associated higher demands on examiners and equipment, particularly in conducting an advanced first-trimester screening including the examination of the nasal bone and the blood flow pattern into the ductus venosus and through the tricuspid valve, have resulted in increasingly more pregnant women undergoing this examination between the 12th+6 weeks of pregnancy on the one hand, and on the other, to an increasing number of examiners dealing with the presentation of fetal anatomy in this stage of pregnancy and trying to diagnose as many non-chromosomal malformations as possible as part of this examination.

Even if the first-trimester screening is initially defined via the risk evaluation for aneuploidies and particularly through the potential reduction of the invasive interventions associated with the risk of miscarriage, and early diagnostics to exclude malformations has only been carried out for fetuses with thicker nuchal translucency, it still offers the possibilities for all fetuses to be examined, even those with normal nuchal translucency thickness.

In many clinics, the sonographic first-trimester screening is now a comprehensive, detailed depiction of the fetal anatomy and does not merely serve the purpose of accurately determining the gestational age, detecting a multiple pregnancy and determining the chorionicity as well as screening for fetal aneuploidies, but rather is performed with the goal of detecting severe fetal anomalies early and potentially weeks before the second-trimester screening, independent of maternal age, anamnestic risk or the thickness of nuchal translucency [1,2].

Similarly to the advanced organ diagnostics and the fetal echocardiogram in the second trimester, the sensitivity and specificity of the first-trimester screening is dependent on the experience of the examiner, the precise representation of the fetal organs in accordance with a protocol, as well as the quality of the ultrasound equipment and often a transvaginal sonogram being carried out in addition to the transabdominal one. This applies in particular when examining the heart of a fetus. The attentiveness of the examiner or the desire for a complete sampling of the fetal organs influence the detection rate of non-chromosomal malformations, which is higher for the same malformations in the group of fetuses with thicker nuchal translucency than in the group with normal nuchal translucency thickness [3].

The prevalence of congenital heart defects (CHD) is 10 out of 1000 live births, whereby 3–4/1000 babies born alive displayed a major CHD that required cardiological interventions and/or cardiosurgery. Approximately one-third of children with congenital malformations have a heart defect and, despite all the advances made in their treatment, heart defects remain the most significant cause of mortality and morbidity among infants and children. In the last 30 years, as a result of the inclusion of the systematic examination of the four-chamber view and partly also both ventricular outflow tracts in the ultrasound screening examination between the 18th and 24th weeks of pregnancy and the increasingly frequent use of colour Doppler devices, coupled with the intensive training of examiners, a detection rate of 60–80% for major CHDs as well as minor CHD, such as small ventricular septal defects, was achieved in the second trimester. This is advantageous for many of these children, as the knowledge of the existence of a major heart defect enables the precise planning of perinatal treatment in advance. In particularly, those defects benefit considerably from prenatal diagnosis for which a sufficient perfusion of the pulmonary or circulatory system is dependent on the ductus arteriosus and/or the foramen ovale remaining open. Both pre-operative morbidity as well as mortality can be significantly reduced for some major heart defects, as this has been well established for the transposition of the large arteries, the hypoplastic left heart and the coarctatio aortae (aortic coarctation) [4]. Furthermore, it appears that, in some situations, fetuses with severe outflow tract anomalies benefit from interventions controlled by intratherine ultrasound (balloon dilatation of a semilunar valve; opening of a closed or highly restrictive foramen ovale), thereby preventing the rapid development towards the hypoplastic ventricle during pregnancy and so the possibility of a univentricular repair can be reduced or intervention can have a life-saving effect in cases of hydrops [5].

Features of Early Fetal Echocardiography

Although it has been used successfully since the early 1990s [6–8], early fetal echocardiography has only been set up at the relevant centres within the last 10 years and is now used worldwide for risk groups between the 12th and 14th weeks of pregnancy. The huge improvement in ultrasound technology allows this examination to be carried out transabdominally for the majority of fetuses. The global establishment of aneuploidy screenings with the measurement of nuchal translucency (NT measurement) and their expansion to further markers, such as nasal bone, blood flow velocity profile of the ductus venosus (DV) and tricuspid valve regurgitation (TR) has been crucial. It is increasingly being complemented by a comprehensive first-trimester screening of the fetus and its organs, whereby the four-chamber view and, with increasing frequency, both ventricular outflow tracts are already part of the examination protocol. An increasing number of examiners now have sufficient experience with detailed first-trimester screening, including the visualisation of the most important cardiac cross-sections through two-dimensional and colour-coded echocardiography. A further reason for the current rapid spread of detailed early fetal echocardiography is that fetuses with thickened nuchal translucency have an abnormal flow profile in the ductus venosus and, in the presence of a tricuspid valve regurgitation, have increased risk of the presence of a heart defect and the exclusion of which should, in the interests of the parents, if possible take place immediately on detection of one of these abnormalities, and not 8 weeks later in the second trimester. As the majority of fetuses with heart defects have neither a genetic risk nor one of the abnormalities mentioned in the first-trimester screening, some call for a fetal echocardiography to be carried out as standard, as part of the detailed first-trimester screening [1,9].

As this also applies generally to the diagnosis of malformations and to the echocardiogram in particular, their detection rate is dependent on a variety of factors, both in the second trimester, but even more so in the first trimester, due to the extreme difficulty of carrying out a comprehensive examination of the fetal heart [4,10,11]:

1. Time of examination (10th–11th week of pregnancy, 12th–13th week of pregnancy, 14th–15th week of pregnancy) and respective visualisation of the cardiac structures [12–14];
2. Scope of examination – screening by markers only (NT, DV, TR), through the visualisation of the four-chamber view, through the visualisation of the four-chamber view and outflows of both great arteries, or through complete early echocardiography with segmental procedure [1, 2, 4, 11, 13, 16, 17];
3. Use of colour Doppler [4];
4. Equipment quality and use of high frequency transducers (transabdominal and transvaginal) [18];
5. Consistent use of transvaginal echocardiography, in particular in the case of a non-optimal depiction of cardiac structures [7, 8, 12–14, 19];
6. Attentiveness of the examiner: higher detection rates for the same fetal anomalies in groups with noticeable markers (NT, DV, TR) [3];
7. Detection rates for a major CHD vs. a minor CHD and the inconsistent definition of a major CHD vs. a minor CHD [20].

The difficulties of an early examination of the fetal heart have been documented in many studies. Alongside the malformations of the brain and kidneys that are not yet manifest in the first trimester and therefore not visible in a first-trimester examination, heart defects are also one of the severe anomalies to have very low detection rates in all studies without exception – including in the second trimester – due to the particular difficulties experienced when examining this organ. A meta-analysis summarised 36 237 pregnancies that were examined over eight centres from 1993 to 2008 between the 11th and 13th week of pregnancy. The average detection rate for major CHD was 29% (95% CI: 25–33%); the pooled detection rate for major CHD between the 11th and 13th week of pregnancy was only 17% (95% CI: 10–25%) [21].

Very poor results were also shown by a large Swedish study which investigated and compared the efficiency of diagnostics to exclude malformations in the first and second trimesters without a strict investigation protocol between 1999 and 2002 [22]. The detection rate for heart defects was particularly bad in both groups, whereby only the four-chamber view was to be depicted in both groups; an inadequate image of the four-chamber view was accepted in the early group, insofar as the nuchal translucency was normal; a fetal echocardiogram was only conducted for fetuses with a nuchal translucency over 3.5 mm. The poor detection rates for major heart defects were not significantly different in each group and amounted to 11% (7/61) and 15% (9/60) respectively; finally, the heart of only one fetus was recognised as abnormal in the early examination as a result of dextrocardia, and for three other fetuses, the severe heart defect was first detected in the second (5% before 22nd week of pregnancy) or third trimester [22].

Considerably higher detection rates for non-chromosomal anomalies were found in sonographic first-trimester screenings that followed strict investigation guidelines, which were carried out at centres and by examiners that already have a lot of experience in first-trimester screening as part of aneuploidy screening. Many more malformations were able to be diagnosed for both time intervals in a prospective cohort study at two large British centres with investigators certified by the Fetal Medicine Foundation U.K. for both the first- and second-trimester ultrasound examinations [23]. After excluding fetuses with aneuploidy (0.7%), 488/44,859 (1.1%) of euploid fetuses had a severe anomaly, 213 (43.6%) of which were diagnosed as early as the first-trimester screening between the 11th and 13th weeks of pregnancy; anomalies were detected in a further 262 out of 42,643 (626/488, 53.7%) fetuses between the 14th and 18th weeks of pregnancy. Certain anomalies, such as atracrania/anencephaly, alo-
time and, on the other hand, the cardiac cross-sections can be ade-
quately depicted in almost all cases by means of transabdominal
sonography, meaning that an additional transvaginal examina-
tion is not required. In the 13th week of pregnancy, all cardiac
structures can generally be visualised transabdominally in the
segmental approach, and a transvaginal examination with a
transducer or a delayed second examination is only necessary
for very few fetuses.

The colour Doppler is of particular importance in the early
echocardiogram, as it is frequently indispensable in locating ves-
sels; the B-scan and colour Doppler complement each other, as
the optimum angle for depicting a vessel in the B-scan is 90°,
but is 0° in the colour Doppler, and so, for example, when the fe-
tus is in a particular position, the aorta can be depicted well in
the B-scan, but the truncus pulmonalis can only be depicted us-
ing colour Doppler. Due to their small size, hypoplastic arteries
are primarily only recognised by a colour Doppler echocardi-
ogram if there is an obstruction of the semilunar valve. In the pres-
ence of abnormalities, advantage should always be attempted to be
taken of the better resolution of a higher frequency transvagi-
nal or transabdominal ultrasound [6–8, 10, 12, 13, 18], which can
considerably increase diagnostic accuracy in the depiction of
smaller atrioventricular septal defects and ventricular septal de-
fects, whether isolated or as part of a tetralogy of Fallot or a dou-
ble outlet right ventricle. Examinations in the 14th and 15th
weeks of pregnancy enable an even better visualisation of the
cardiac structures and should be carried out to differentiate ab-
normal findings in an echocardiogram in the previous weeks or
in the case of any other abnormalities that would indicate an
echocardiogram [4, 24]. The three-dimensional echocardiogram
using STIC (spatio-temporal image correlation) technology can
generate good volumes with high frequency vaginal transducers,
but is inferior in the diagnosis and differentiation of heart defects
in the first trimester due to its lower resolution in two-dimen-
sional echocardiography [30]. In any case, discussion will con-
inue in future as to whether, in the case of the complete replace-
ment of the first-trimester aneuploidy screening with the analy-
sis of cell-free fetal DNA in the mother’s blood, it would be sensi-
tive to carry out the first-trimester screening and the echocar-
diogram between the 13th and 15th weeks of pregnancy, as some
working groups have long been proposing [8, 31].

Markers for the Presence of a Heart Defect

Heart defects are some of the anomalies that accompany tran-
sient markers during the late-early and early-second trimester,
which are evaluated as part of the aneuploidy screening. thick-
ened nuchal translucency, abnormal blood flow pattern in the
ductus venosus as well as the presence of a tricuspid valve regur-
gitation are markers not only for aneuploidies with and without
heart defects, but also for heart defects in euploid fetuses. The risk
of the existence of a heart defect in euploid fetuses increases exponen-
tially with the thickness of nuchal translucency (NT). A meta-
analysis of 10 studies with 192 922 euploid fetuses with a
thicker NT showed that the prevalence of a major CHD was 1.5%
for a thickness of between 2.5 mm and 3.4 mm (95th – 99th per-
centiles), 3.3% in the case of a NT of 3.5–4.4 mm, 5.5% for a NT of
4.5–5.4 mm, 15% for an NT of 5.5–6.6 mm and 19% for an NT be-
tween 6.5 mm and 8.4 mm [32]. In comparison with a normal
prevalence of 8/1000 live births, the risk of a heart defect in the
2.5 mm to 3.4 mm nuchal thickness group increases 2.5-fold,
with a 10-fold increase in risk in the group with an NT above
3.5 mm [32]. The individual heart defects do not appear to differ
with regard to nuchal thickness [33].

In any case, nuchal thickness, the blood flow velocity profile in
the ductus venosus and the presence of a tricuspid valve regurgi-
tation are not independent markers, as they are all influenced by
changes in haemodynamics. Slight haemodynamic changes in the
case of heart defects and other illnesses and a delayed develop-
ment of myocardial diastolic and systolic function are primarily
manifested in the first trimester, as diastolic function, in particu-
lar the compliance of the heart, and systolic function are still low
and, due to the high placentional resistance, the cardiac afterload is
still high. In the second trimester, in the case of considerably bet-
ter diastolic and systolic cardiac function and considerably lower
heart defects afterload, the higher pulsatility of the blood flow velocity
profile of the duc tus venosus only occurs in the case of severe
right heart obstruction [34]. The thickness of the nuchal translu-
cency, pulsatility in the blood flow pattern of the ductus venosus
and the presence of a tricuspid valve regurgitation therefore cor-
relate with one another [15, 35–39]. Abnormal blood flow pat-
terns were found in 20–40% of fetuses with thicker nuchal trans-
lucency, while their prevalence is only 2–3% in fetuses with nor-
mal nuchal translucency thickness [35, 38, 40]. Furthermore, the
thickness of the nuchal translucency correlates with the fre-
quency of an abnormal blood flow pattern in the duc tus venosus
and a tricuspid valve regurgitation. All three markers for heart
defects are also only transiently visible at the time of the first-tri-
imester screening.

The connection between these markers and the presence of a
heart defect implies that a thicker nuchal translucency, an abnor-
mal flow velocity profile in the ductus venosus and a tricuspid
valve regurgitation represent indications for an echocardiog-
ographic examination. The presence of one or more of these
markers is by far the most frequent indication for early
echocardiography. Furthermore, this connection also offers the
possibility to conduct a screening for heart defects as part of
the first-trimester screening using these indirect markers, which are
considerably easier and more common than the presentation of
the four-chamber view, outflow tracts and major arteries. The
potential of this approach has been examined in many investiga-
tions in recent years, particularly considering the still low detec-
tion rates for heart defects even in the second trimester [4]. A re-
cently published meta-analysis of 20 studies, which were pub-
lished between 1999 and 2012, covers 205 232 fetuses with nor-
mal karyotype [41], 537 of which had a major heart defect. The
analysis showed major differences in the respective detection
rates of the individual studies, even for apparently similar study
designs. Overall, the sensitivity and specificity of an NT above
the 95th percentile (corresponding to an/NT of 2.5 mm) were 44.4%
(95% CI: 39.5–49.5) and 94.5% (95% CI: 94.4–94.6), and, for an
NT above the 99th percentile, 19.5% (95% CI: 15.9–23.5) and
99.1% (95% CI: 99.1–99.2) respectively; the results were similar
when only studies in which the investigators were certified by
the Fetal Medicine Foundation UK were considered; the sensi-
tivity and specificity of an NT above the 95th percentile (cor-
responding to an NT of 2.5 mm) were 45.6% (95% CI: 39.6–51.7)
and 94.7% (95% CI: 94.6–94.9), and, for an NT above the 99th
percentile, 21.0% (95% CI: 16.5–26.1) and 99.2% (95% CI: 99.2–99.3)
respectively [41].

Further, it was shown that, in the case of fetuses with thicker nu-
chal translucency, through the combination of thicker nuchal
translucency and an abnormal flow pattern in the ductus veno-
sus and/or the presence of tricuspid valve regurgitation, the detection rates for heart defects was increased for euploid fetuses. In a meta-analysis (9 studies of fetuses with thicker NT [n = 2908] and 7 studies of fetuses with normal NT [n = 47610]), in the case of thicker NT, the sensitivity of the abnormal ductus venosus flow pattern was 83%, the specificity was 80%, positive LH 4.4, negative LR 0.2 with a false positive rate of 20%; in fetuses with normal NT, the sensitivity was 19%, specificity 96%, positive LH 5.0, negative LR 0.8 with a false positive rate of 4% [42].

A large study of 44,456 euploid fetuses with 85 major heart defects showed that an NT in the ≥95th percentile would only have identified 30 (35%) (false positive rate: 4.8%) of heart defects, an NT in the ≥95th percentile or presence of a tricuspid valve regurgitation would have identified 43% (false positive rate: 5.9%) and an NT in the ≥95th percentile or presence of a tricuspid valve regurgitation or an abnormal ductus venosus flow pattern would have identified 57.6% (false positive rate: 8.0%) [37]. In a fixed false positive rate of 5%, only 35% of heart defects would be detected through thicker NT (NT ≥95th percentile), 45% would have been detected as a result of NT and ductus venosus flow pattern, 49% through NT and tricuspid valve regurgitation and 54% through NT and ductus venosus and tricuspid valve regurgitation [37].

A study from a centre in Barcelona showed similar results; here, over an eight-year period (2002–2009), 13,773 single pregnancies with a crown-rump length of between 43 mm and 90 mm, corresponding to the 11th + 0 to 14th + 4 weeks of pregnancy, as well as the blood flow pattern in the ductus venosus were measured [21]. The aim of the study was to use the ductus venosus blood flow not as a secondary marker in fetuses with thicker nuchal translucency as in other studies [42], but rather as a second marker alongside nuchal translucency thickness, as an earlier study of this group had shown that the additional evaluation of the ductus venosus blood flow profile can increase the sensitivity of the nuchal translucency thickness (NT >99th percentile) for heart defects in euploid fetuses by 11%, from 29% to 40% [40]. In another group, 12.5% of euploid fetuses with normal nuchal translucency, in which a heart defect was later detected, showed an abnormal flow velocity profile in the ductus venosus, as, however, did 4.3% of healthy fetuses also [39]. 12,799 normal fetuses were compared with the 37 euploid fetuses with major heart defects (in total, 760 fetuses had chromosomal or non-chromosomal anomalies). Of the 37 fetuses, 40% had an NT ≥95th percentile, 27% had an NT >99th percentile and 47% had an absent or reverse flow in the ductus venosus during atrial contraction. With the combination of an NT >99th percentile and an abnormal flow profile in the ductus venosus (absent or reverse flow during atrial contraction) as a selection criterion, 47% of fetuses with heart defects and 2.7% of normal fetuses would have undergone a fetal echocardiogram [21].

It is certainly necessary for fetuses with the markers mentioned to undergo a fetal echocardiogram. However, the false positive rates for the respective markers are very high, and their positive predicted values are too low for them to be suitable for a general screening for heart defects. For the prenatal detection of heart defects, it appears more sensible and realistic to integrate the direct visualisation of the cardiac structures and cross-sections into the protocol of ultrasound screening examinations in the second semester, and further into the future, into the first-trimester screening as well.

Early Echocardiogram as Part of the Detailed First-Trimester Screening

It has been already shown that in experienced hands and with modern ultrasound equipment a majority of major [8,13] and up to 65% of all heart defects [13] were able to be diagnosed by the end of the first trimester and beginning of the second trimester. A further analysis of the Lübeck data between 1992 and 2007 revealed that 66/77 of heart defects (3521 fetuses examined) were detected between the 11th + 0 and 13th + 6 weeks of pregnancy, a further 9.1% in the second trimester, 2.6% in the third trimester and 2.6% postnatally [29]. Nowadays, a comprehensive echocardiogram is increasingly being carried out as part of sonographic examination of all fetal organs at prenatal medical centres, not only in the case of relevant risk (genetic, markers in first-trimester screening), but for all pregnant women as part of a detailed first-trimester screening [1,2,9]. Becker et al. [1] recently showed that the majority of severe, non-chromosomal anomalies (72/94; 76.6%) arose in fetuses with “normal” NT and this could be diagnosed prenatally by means of a sonogram through the combination of a detailed first- and second-trimester screening, respectively in combination with an echocardiogram. The detection rates for severe anomalies during the first-trimester screening were 58.6% (65/111 cases) in the group with “normal” NT, 62.2% (23/37) in the group with chromosomal anomalies and 56.8% (42/74) in the group with non-chromosomal anomalies. Up to the 24th + 0 week of pregnancy, a further 24 anomalies were discovered in the group with “normal” NT, of which were aneuploidies. With “normal” NT, the detection rate by the 24th + 0 week of pregnancy was 80.2% (89/111) and 87.4% (97/111) by birth. In 14 cases, aneuploidies (5 cases) and severe malformations (9 cases) were only diagnosed postnatally [1]. The authors requested that all pregnant women, regardless of the thickness of the fetal nuchal translucency, should be offered these examinations, and justified this in terms of ethics [1]. In a recently published study conducted at two large centres in Romania and Greece, 5472 fetuses were examined by a few very experienced examiners over 27 consecutive months (between January 2010 and March 2012) between the 12 + 0 and 13 + 6 weeks of pregnancy as part of an advance aneuploidy screening, a detailed organ diagnostic test including early echocardiography with appropriate, modern ultrasound machines [2]. A strict investigation protocol was executed for this. The duration of the examinations was between 18 and 52 minutes (average: 34 minutes), with between 24 and 62 images (average: 36 images) being saved per examination. In the case of an incomplete depiction of the fetal organs or cross-sections, the examination was carried out after a short break and/or a few days later; an additional transvaginal sonogram was necessary for 480 (7.80%) of fetuses, either as a result of an unfavourable fetal position (5.59%) or due to maternal factors, such as adipsomy, myoma, abdominal scars or retroverted uterus (2.21%). The prevalence of fetal anomalies was 3.0% (165/5472 cases). The detection rate for all non-chromosomal fetal anomalies was 40.6% (67/165 cases). The anomalies were divided in accordance with the RCOG’s definition: “major (lethal or severe) anomalies: incompatible with life or associated with possible survival but severe immediate or long-term morbidity; moderate and minor anomalies: short or long-term morbidity of minor or moderate severity”. The prevalence of major (lethal and severe) anomalies amounted to 1.39% (76/5472), 76% (58/76) of these were discovered at the first-trimester screening, i.e. 1.06% (58/5472) of the fetuses examined. An addi-
Gembruch U et al. The Diagnostics of severe heart defect between the first and second examinations; the early echocardiogram, the cardiac changes developed into a fetus and, for a further 6 fetuses with anomalies detected in the early echocardiogram in 6 out of 12 cases, the fetal cardiologist confirmed the diagnosis, but in one case his diagnosis was slightly different and in 3 of the 26 cases which had been detected in the early echocardiogram, the heart defects developed progressively [9]. In both studies, the authors came to the conclusion that the early fetal echocardiogram is feasible and that most severe heart defects can be diagnosed by examiners well-versed in prenatal diagnostics; the appearance of some heart defects can change progressively until the second trimester, particularly semilunar valve stenosis and coarctatio aortae [9,17].

Features of Heart Defects to be Diagnosed in the First Trimester

The small size of the fetal heart in the first trimester limits the detectability of smaller, cardiac structural defects despite the use of higher frequency ultrasound, as a result of the relatively poorer detail resolution in the two-dimensional image in particular, but also in the colour Doppler image in comparison with the second-trimester screening. This is particularly the case for the frequent, small ventricular septal defects in the trabecular and outlet part of the interventricular septum; the interventricular shunts for these defects, which lead to their discovery in the second trimester [43,44], are not currently detectable using colour Doppler. Other heart defects change cardiac structures as the pregnancy progresses further, meaning that they are detectable in the four-chamber view; this is particularly true for aortic and pulmonary valve obstructions, which are present in the first trimester and can also be detected through colour Doppler, but which could lead to abnormalities in the ventricle (myocardial hypertrophy, dilatation, hypoplasia, endocardial fibroelastosis) as the pregnancy progresses, depending on the severity of the obstruction [5,8,45]. The changes are similar in those leading to a narrow left ventricle and right heart dominance in the event of a severe obstruction in the first trimester in the context of aortic coarctation, with a normal four-chamber view potentially being seen until birth in the case of light obstruction [46]. Changes in...
an Ebstein’s anomaly are also frequently not manifested until the second trimester, although the frequently associated severe tricuspid valve insufficiency can also be detected in as early as the first trimester [47]. However, fetuses with very severe tricuspid valve insufficiencies in the case of Ebstein’s anomaly (Fig. 1a and b) and tricuspid valve dysplasia, discovered in the first trimester, can die in utero. It is particularly common for fetuses to die quickly after the first trimester with a tetralogy of Fallot with absent pulmonary valve syndrome and open ductus arteriosus (Fig. 2a and b), as the massive backflow due to pulmonary insufficiency in the event of an existing ventricular septal defect leads to an enormous overload in both ventricles [48]. The progress of severe stenosis affecting both semilunar valves can be similar. More frequently depicted and ultimately to be diagnosed in the first and the second trimester are atroventricular septal defect (Fig. 3a and b), tricuspid valve atresia, major ventricular septal defect, pulmonary and aortic atresia on the basis of the absence of the visualisation of one of the two major arteries and their hypoplasia with reverse flow in the colour Doppler, the hypoplastic left heart in the case of a pulmonary atresia with intact ventricular septum and malpositioning of the major arteries, such as double outlet ventricle and transposition of the major arteries (Fig. 4), truncus arteriosus communis and the tetralogy of Fallot (Fig. 5), although here the overriding of the aorta and their increase in size in the case of smaller ventricular septal defects is not as clear and easy to detect in the first trimester as in the second [16]. Even more complex anomalies occurring in heterotaxy syndrome with vena azygos continuity of the inferior vena cava can be detected, as can the presence of a left persistent superior vena cava and of anomalies in the aortic arch, such as a right aortic arch and an arteria lusoria [49]. Cardiomyopathies and heart tumours normally first appear in the second half of pregnancy [8].

**Conclusion for Clinical Practice**

The majority of major heart defects can be diagnosed through a detailed examination of the fetal heart as part of a fetal echocardiogram in the 12th and 13th weeks of pregnancy. A re-
requirement for this is the segmental approach with the visualisation of all connections and the required cross-sections, as well as the use of the transvaginal echocardiogram in the case of inadequate visualisation, and the repetition of the examination after a short time interval if applicable. Besides anamnestic risk, a thickened nuchal translucency, the increased pulsatility of the blood flow pattern in the ductus venosus as well as the presence of a tricuspid valve regurgitation are significant markers for the presence of a heart defect.

**Conflict of Interest**

None.

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