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Ultrasound screening for complications in twin pregnancy

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A B S T R A C T

In the decades since the introduction of ultrasound into routine obstetric practice, the advantages of ultrasound have moved beyond the simple ability to identify multiple pregnancies antenatally to the possibility of screening them for fetal anomalies, pre-eclampsia, preterm birth, and the complications specific to monochorionic pregnancies. Screening studies have often excluded twins because physiological differences impact on the validity and sensitivity of the screening tests in routine use in singletons, and therefore, the evidence of screening performance in multiple pregnancy lags behind the evidence from singleton pregnancies. In general, most pregnancy complications are more common in twin pregnancy, but screening tests are less accurate or well validated. In this review article we present the current state of the evidence and avenues for future research relating to the use of ultrasound and screening for complications in twin pregnancies, including the monochorionicity-related pathologies, such as twin–twin transfusion syndrome, selective growth restriction, twin anaemia–polycythaemia sequence and twin reversed arterial perfusion sequence.

1. Introduction

In the decades since the introduction of ultrasound into routine obstetric practice, the advantages have moved beyond the simple ability to identify multiple pregnancies antenatally to the possibility of screening these pregnancies both for the same conditions as those screened for in singleton pregnancies, and for the identification and management of complications specific to twin pregnancies. Screening studies have often excluded twin pregnancies, and physiological differences specific to twin pregnancies impact the validity and sensitivity of widely used screening tests. Twin pregnancies continue to increase in frequency with the increasing use of assisted reproductive technologies and the increase in maternal age, both factors associated with an increasing incidence of multiple gestation [1,2]. In this context, the need for all obstetricians to appreciate the special complications of multiple pregnancies and the differences in interpreting widely used screening tests in twin pregnancies has become clear. According to data from the Office of National Statistics, the incidence of multiple births in the UK was 16 per 1000 total births in 2015 compared to 10 per 1000 in 1980 [1,3]. In the USA the number of twins almost doubled between 1980 and 2009, increasing from 18.9 to 33.2 per 1000 births [4]. Despite the fact that multiple pregnancies constitute <2% of births in the UK, they contribute to 7% of stillbirths, 18% of neonatal deaths and they have six times greater risk of cerebral palsy compared to singleton pregnancies [5]. In this review article we present the current evidence relating to the use of ultrasound and screening for complications in twin pregnancies.

2. Pregnancy dating, chorionicity, and amnionicity

2.1. Dating

Dating in singleton pregnancy using the crown–rump length (CRL) prior to 14 weeks gestation is a well-validated and standard practice. This is complicated in multiple pregnancies by the presence of multiple fetuses, which through natural variation will rarely be identical in size. The operator must then choose whether to use the larger, the smaller, or the mean of the two CRLs to date the pregnancy.

It has been suggested that the smaller CRL is more representative of the true gestational age [6], but using the smaller CRL to date the pregnancy carries the risk of assuming that the larger twin is 'large for dates' rather than identifying the smaller twin as growth-restricted. Using only the larger twin to date the pregnancy leads to a slight overestimation of the true gestational age, whereas the use of the mean or the smaller twin is associated with underestimation

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[7]. The most usual practice, therefore, is to use the larger CRL to date the pregnancy [1,8,9] because this protects against missing a diagnosis of intrauterine growth restriction in the smaller twin.

2.2. Chorionicity

After determining gestation, it is next of greatest importance to determine chorionicity, because the risks associated with dichorionic pregnancies are substantially different from those associated with monochorionic pregnancies. Monochorionic pregnancies are vulnerable to the complications of a shared placental circulation including twin–twin transfusion syndrome (TTTS), twin anaemia–polycythaemia sequence (TAPS), selective fetal growth restriction (sFGR), and twin reversed arterial perfusion (TRAP). In addition, preterm delivery, congenital abnormalities and intrauterine death are all more frequent in monochorionic pregnancies [10]. The risk of intrauterine fetal death is 11.6% in monochorionic pregnancies compared to 5% in dichorionic pregnancies [11]. Moreover, following single intrauterine demise, the risk of intrauterine death and neurological damage is far greater to the surviving twin in a monochorionic than dichorionic twin pregnancy [12]. Identifying chorionicity in the first trimester determines the frequency and type of surveillance that should be planned for the remainder of the pregnancy. Finally, chorionicity must be determined before proceeding with selective fetal reduction, since reduction with intrafetal potassium chloride is only possible in dichorionic pregnancies and monochorionic pregnancies must be managed with cord ligation or radiofrequency ablation to avoid compromising the co-twin through the interdependent placental circulation.

2.2.1. Dichorionic diamniotic vs monochorionic diamniotic

The signs available to determine chorionicity vary according to gestation; in general, the diagnosis is more accurate the earlier in pregnancy the twins are assessed (Table 1, Fig. 1). Ultrasound accuracy at <14 weeks has been reported at 99%, but the sensitivity for monochorionicity falls to only 77% after 14 weeks gestation [13]. Pitfalls in the assessment of chorionicity include the possibility that monochorionic placentas may be bilobar and thus appear as two distinct masses, the rare occurrence of dizygotic monochorionic pregnancies, and the disappearance of the chorionic peak (the “lambda sign”) at later gestations. Both chorionicity and amnionicity should be determined and documented before 14 weeks gestation.

2.2.2. Monochorionic diamniotic vs monochorionic monoamniotic

The absence of the inter-twin membrane (monoamniotic) is best confirmed by transvaginal scan. Another useful finding is the demonstration of cord entanglement, which is almost universal in monoamniotic twin pregnancies, using colour and pulsed-wave Doppler ultrasound. Using pulsed-wave Doppler, two distinct arterial waveform patterns with different heart rates are seen within the same sampling gate. The presence of two yolk sacs in early pregnancy suggests diamniotic twin pregnancy.

3. Screening for aneuploidy and structural abnormalities

3.1. Aneuploidy screening

Dizygotic pregnancies have two fetal chromosomal arrangements and two fetuses at risk of aneuploidy. The risk of aneuploidy affecting one or both fetuses is therefore higher than the risk of aneuploidy affecting a singleton pregnancy, with the estimated age-related risk of a 33-year-old carrying a dizygotic pregnancy being equivalent to that of a 35-year-old woman with a singleton pregnancy [14]. National guidelines recommend assigning a risk ‘per fetus’ in dizygotic pregnancies, whereas monozygotic pregnancies are assumed by virtue of their common embryological origin to have a risk equivalent to the age-adjusted risk for an equivalent singleton pregnancy [1,8,15]. In fact, the observed incidence of Down syndrome has been found to be lower, most significantly so in monozygotic pregnancies, where the observed-to-expected ratio is only 33.6% [16]. The reasons for this finding, consistent over a number of studies [17], are undetermined but could include higher rates of pregnancy loss obscuring the true incidence of Down syndrome. This could also explain the finding of lower risk in monochorionic pregnancies, where the fragility of the pregnancy is greater and pregnancy loss rates are higher than in dichorionic pregnancies. Although the risk of aneuploidy seems to be affected by zygosity, it is not possible at present to determine zygosity clinically; therefore counselling prior to screening tests must take into account that as many as 20% of dichorionic pregnancies will be monozygotic.

The combined screening test (nuchal translucency (NT), maternal serum β-human chorionic gonadotrophin, and pregnancy-associated plasma protein-A) is the first-line screening test for singleton pregnancies in the UK, whereas the quadruple serum screening is available to women presenting after 14 weeks. In singletons, the combined test has a reported detection rate for trisomy 21 of up to 90% for a 5% false-positive rate [18]. In twin pregnancies, the detection rate is reported to be 72–100% for a false-positive rate of 5% [19]. The incorporation of the NT into the combined test allows a fetus-specific risk to be assigned in dichorionic pregnancies. Since monochorionic twins share a karyotype, the risk calculated takes into account a mean of the NT measurements and a per-pregnancy risk is given [20]. When offering diagnostic testing, it is important to consider that the procedure-related risks to the pregnancy are greater in twin pregnancy, and understanding the pretest probability of an adverse diagnosis is necessary to inform patient decision-making [21].

3.2. Non-invasive prenatal testing in twins

Cell-free fetal DNA testing has recently been introduced into practice for aneuploidy screening in singleton pregnancies; detection rates have been excellent (>99% for trisomy 21 with a false-positive rate of <0.1%) [22]. Since twins have been thought to be associated both with an increased risk of aneuploidy and with greater risks during diagnostic testing, the advantages of non-

Table 1
Ultrasound indicators of chorionicity.

Gestation visible	Dichorionic, diamniotic	Monochorionic, diamniotic	Monochorionic, monoamniotic
<10 weeks	Two yolk sacs	Two yolk sacs	Single yolk sac
	Two amniotic sacs	Two amniotic sacs	Single amniotic sac
	Two gestational sacs	Two gestational sacs	Single gestational sac
Up to 16–20 weeks	Chorionic peak “lambda sign”	“T sign”	No inter-twin membrane visible
From 14 to 16 weeks	Discordant fetal sex	Concordant fetal sex is expected	Concordant fetal sex is expected
Throughout pregnancy	Distinct placental masses	Single placental mass	Single placental mass

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