No. 260, June 2011

Ultrasound in Twin Pregnancies

This Clinical Practice Guideline has been prepared by the Diagnostic Imaging Committee, reviewed by the Genetics Committee and the Maternal Fetal Medicine Committee, and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

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Disclosure statements have been received from all members of the committees.

Abstract

Objective: To review the literature with respect to the use of diagnostic ultrasound in the management of twin pregnancies. To make recommendations for the best use of ultrasound in twin pregnancies.

Outcomes: Reduction in perinatal mortality and morbidity and short- and long-term neonatal morbidity in twin pregnancies. Optimization of ultrasound use in twin pregnancies.

Key Words: Ultrasound, twins, antenatal, prematurity, cervix, amniotic fluid

J Obstet Gynaecol Can 2011;33(6):643–656

Evidence: Published literature was retrieved through searches of PubMed and the Cochrane Library in 2008 and 2009 using appropriate controlled vocabulary (e.g., twin, ultrasound, cervix, prematurity) and key words (e.g., acardiac, twin, reversed arterial perfusion, twin-to-twin transfusion syndrome, amniotic fluid). Results were restricted to systematic reviews, randomized control trials/controlled clinical trials, and observational studies. There were no date restrictions. Studies were restricted to those with available English or French abstracts or text. Searches were updated on a regular basis and incorporated into the guideline to September 2009. Grey (unpublished) literature was identified through searching the websites of health technology assessment and health technology assessment-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies.

Values: The evidence collected was reviewed by the Diagnostic Imaging Committee of the Society of Obstetricians and Gynaecologists of Canada, with input from members of the Maternal Fetal Medicine Committee and the Genetics Committee of the SOGC. The recommendations were made according to the guidelines developed by The Canadian Task Force on Preventive Health Care (Table 1).

Benefits, harms, and costs: The benefit expected from this guideline is facilitation and optimization of the use of ultrasound in twin pregnancy.

Summary Statements

1. There are insufficient data to make recommendations on repeat anatomical assessments in twin pregnancies. Therefore, a complete anatomical survey at each scan may not be needed following a complete and normal assessment. (III)
2. There are insufficient data to recommend a routine preterm labour surveillance protocol in terms of frequency, timing, and optimal cervical length thresholds. (II-2)
3. Singleton growth curves currently provide the best predictors of adverse outcome in twins and may be used for evaluating growth abnormalities. (III)
4. It is suggested that growth discordance be defined using either a difference (20 mm) in absolute measurement in abdominal circumference or a difference of 20% in ultrasound-derived estimated fetal weight. (II-2)
5. Although there is insufficient evidence to recommend a specific schedule for ultrasound assessment of twin gestation, most experts recommend serial ultrasound assessment every 2 to 3 weeks, starting at 16 weeks of gestation for monochorionic pregnancies and every 3 to 4 weeks, starting from the anatomy scan (18 to 22 weeks) for dichorionic pregnancies. (II-1)
6. Umbilical artery Doppler may be useful in the surveillance of twin gestations when there are complications involving the placental circulation or fetal hemodynamic physiology. (II-2)
7. Although many methods of evaluating the level of amniotic fluid in twins (deepest vertical pocket, single pocket, amniotic fluid index) have been described, there is not enough evidence to suggest that one method is more predictive than the others of adverse pregnancy outcome. (II-3)
8. Referral to an appropriate high-risk pregnancy centre is indicated when complications unique to twins are suspected on ultrasound. (II-2) These complications include:
    1. Twin-to-twin transfusion syndrome
    2. Monoamniotic twins gestation
    3. Conjoined twins
    4. Twin reversed arterial perfusion sequence
    5. Single fetal death in the second or third trimester
    6. Growth discordance in monochorionic twins.

Recommendations

1. All patients who are suspected to have a twin pregnancy on first trimester physical examination or who are at risk (e.g., pregnancies resulting from assisted reproductive technologies) should have first trimester ultrasound performed. (II-2A)
2. Every attempt should be made to determine and report amnionicity and chorionicity when a twin pregnancy is identified. (II-2A)
3. Although the accuracy in confirmation of gestational age at the first and second trimester is comparable, dating should be done with first trimester ultrasound. (II-2A)
4. Beyond the first trimester, it is suggested that a combination of parameters rather than a single parameter should be used to confirm gestational age. (II-2C)
5. When twin pregnancy is the result of in vitro fertilization, accurate determination of gestational age should be made from the date of embryo transfer. (II-1A)
6. There is insufficient evidence to make a recommendation of which fetus (when discordant for size) to use to date a twin pregnancy. However, to avoid missing a situation of early intrauterine growth restriction in one twin, most experts agree that the clinician may consider dating pregnancy using the larger fetus. (III-C)
7. In twin pregnancies, aneuploidy screening using nuchal transluscency measurements should be offered. (II-2B)
8. Detailed ultrasound examination to screen for fetal anomalies should be offered, preferably between 18 and 22 weeks' gestation, in all twin pregnancies. (II-2B)
9. When ultrasound is used to screen for preterm birth in a twin gestation, endovaginal ultrasound measurement of the cervical length should be performed. (II-2A)
10. Increased fetal surveillance should be considered when there is either growth restriction diagnosed in one twin or significant growth discordance. (II-2A)
11. Umbilical artery Doppler should not be routinely offered in uncomplicated twin pregnancies. (I-E)
12. For defining oligohydramnios and polyhydramnios, the ultrasonographer should use the deepest vertical pocket in either sac: oligohydramnios when < 2 cm and polyhydramnios when > 8 cm. (II-2B)

ABBREVIATIONS

AC	abdominal circumference
CL	cervical length
EFW	estimated fetal weight
IUGR	intrauterine growth restriction
NPV	negative predictive value
NT	nuchal translucency
PPV	positive predictive value
TTTS	twin-to-twin transfusion syndrome

Table 1. Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventive Health Care

Quality of evidence assessment*	Classification of recommendations†
I: Evidence obtained from at least one properly randomized controlled trial	A. There is good evidence to recommend the clinical preventive action
II-1: Evidence from well-designed controlled trials without randomization	B. There is fair evidence to recommend the clinical preventive action
II-2: Evidence from well–designed cohort (prospective or retrospective) or case–control studies, preferably from more than one centre or research group	C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making
II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category	D. There is fair evidence to recommend against the clinical preventive action
	E. There is good evidence to recommend against the clinical preventive action
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

* The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.[100]

† Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the The Canadian Task Force on Preventive Health Care.[100]

INTRODUCTION

This document was originally to be written for multiple pregnancy: twins and higher order multiples. However, since twins make up >98% of all multiple pregnancies, and most published studies in the areas covered by this document are of twins and not higher order multiples, this guideline discusses only twins. As twins and higher order multiples were included in some studies, areas of this document are applicable to higher order multiples (e.g., determination of chorionicity and amnionicity), but others are applicable only to twin pregnancy.

From the first trimester until delivery of the second fetus, the use of ultrasound in the management of twins is both ubiquitous and indispensable. Some of the most common clinical uses are determination of chorionicity, confirmation of gestational age, diagnosis of anomalies and complications, measurement of cervical length, and assessment of growth and amniotic fluid, placental localization, and fetal position for intrapartum management.

Ultrasound is the only safe and reliable method for the diagnosis and assessment of twins, although improved detection of twins by routine sonographic examination has not led to a significant reduction in perinatal mortality. This may be due to lack of standardized protocols for the management of twins rather than the technology itself.[1] In addition, protocols for increased surveillance in twins have not been investigated in a prospective, randomized fashion or stratified according to chorionicity. Established guidelines for the type and frequency of testing are neither evidence-based nor uniformly followed. Nevertheless, despite the lack of level I evidence, virtually all twins are followed routinely with greater fetal surveillance than low-risk singleton fetuses.[2]

SONOGRAPHIC DETERMINATION OF CHORIONICITY AND AMNIONICITY

Early and accurate determination of amnionicity and chorionicity is critical in the antenatal management of twins. Ideally, determination of chorionicity should be done in the first trimester. The management of structural anomalies, screening for and identification of aneuploidy, determination of the etiology of fetal growth and/or fluid discordance, early diagnosis of twin-to-twin transfusion syndrome, and the management of a surviving twin following intrauterine demise are examples of clinical management depending on chorionicity. The high mortality and morbidity of monoamniotic twins is well-documented, and early and intensive monitoring and intervention may improve outcomes.[3–5]

Before 10 weeks' gestation, several sonographic findings can help determine chorionicity. These are (1) the number of observable gestational sacs, (2) the number of amniotic sacs within the chorionic cavity, and (3) the number of yolk sacs.

1. Number of Gestational Sacs

The relationship between the number of gestational sacs and the number of embryonic heartbeats gives strong evidence of chorionicity. Each gestational sac forms its own placenta and chorion. Thus, the presence of 2 gestational sacs implies a dichorionic pregnancy, while a single gestational sac with 2 identified heartbeats implies a monochorionic twin pregnancy.[6]

2. Number of Amniotic Sacs Within the Chorionic Cavity

When diamniotic twins are identified before 10 weeks' gestation, separate and distinct amnions may be visible on ultrasound. The amnion grows outward from the embryonic disk, and before 10 weeks the separate amnions of a diamniotic pregnancy will not have enlarged sufficiently to contact each other and create the inter-twin septum. Each single amnion is extremely thin and delicate and may be very difficult to see on transabdominal scanning; however, endovaginal imaging is often successful in differentiating separate amnions.

3. Number of Yolk Sacs

The number of yolk sacs may help diagnose the amnionicity.[7] When 2 yolk sacs are seen in the extra-embryonal coeloma, the pregnancy will be diamniotic, while a single yolk sac will in most cases indicate monoamniotic twins. A single yolk sac seen when there are dual embryos should prompt a follow-up first trimester scan to definitively assign amnionicity.

After 10 weeks, these sonographic signs are no longer present: gestational sacs are no longer distinctly separable, and the inter-twin membrane is formed. At this stage, a new set of sonographic findings will help determine amnionicity/chorionicity. These findings are (1) fetal genitalia, (2) placental number, (3) chorionic peak sign, and (4) membrane characteristics.

The following order provides a logical sequence to determine chorionicity after 10 weeks of gestation. Of note, step 1 is not routinely used at the 10- to 14-week scan.

1. Sex Discordance

Phenotypic discordance identifies dichorionicity in all but the rarest cases. Concordance of phenotype does not rule out dichorionicity.

2. Number of Distinct Placentas

A single placental mass likely indicates monochorionicity, whereas the presence of 2 distinct, separate placentas identifies dichorionicity. Careful sonographic examination may help distinguish a single placenta from 2 placentas in abutment.

3. Presence or Absence of the Chorionic Peak (also called the twin peak or lambda sign)

This represents a projecting zone of tissue of similar echotexture to the placenta, triangular in cross-section and wider at the chorionic surface of the placenta, extending into, and tapering to a point within, the inter-twin membrane. The twin peak sign most often identifies dichorionicity.[8,9] Monochorionicity can be determined by absence of the twin peak sign.

4. Inter-Twin Membrane Characteristics

The membrane of a dichorionic pregnancy consists of 2 layers of amnion and 2 layers of chorion. It is thicker and more reflective than the monochorionic diamniotic membrane. A membrane thickness of >2 mm identifies dichorionicity with a positive predictive value of 95% and monochorionicity with a positive predictive value of 90% for a membrane thickness ≤ 2 mm.[10] In the second trimester, the number of membranes may be counted, and if there are >2, then dichorionicity is strongly suggested.[11]

If a membrane is not detected, careful evaluation to diagnose or exclude the possibility of monochorionic monoamniotic twinning is warranted. When an inter-twin membrane is not visualized, possibilities include monoamniotic twinning, presence of a twin with complete oligohydramnios (stuck twin), or a diamniotic twin pregnancy in which the membrane is present but not seen owing to its thinness and orientation to the transducer. The most definitive sonographic finding in the diagnosis of monoamniotic twins is the demonstration of cord entanglement from the placental or umbilical origin. Colour Doppler may facilitate identification of this finding. Entanglement of limbs or observation of a limb circumscribing the other is suggestive of monoamnionicity. Failure to find the membrane between the 2 cord insertions in the placenta strongly supports monoamnionicity. The use of transvaginal ultrasound is often a helpful adjunct to transabdominal scanning in identifying the membrane.

Accuracy is improved when the assessment of chorionicity is undertaken before 14 weeks' gestation rather than after 14 weeks. Stenhouse et al.[8] in a study of 131 twin pregnancies found the sensitivity after 14 weeks was 77% for monochorionicity (10/13) and 90% for dichorionicity (26/29); before 14 weeks, accuracy was 99% for both groups (98/99 overall, 21 of 22 for monochorionics) combined.

The twin peak sign alone in the second trimester can accurately identify the chorionicity in many cases, but that may not be sufficient to guide clinical management in

all cases.[9,12] Scardo et al.[12] in their second trimester study found that the twin peak alone may not be sufficiently accurate. With a composite of second trimester ultrasound markers (number of placentas, fetal phenotype, membrane thickness, and twin peak sign), the sensitivity for correct identification of monochorionic pregnancies is reported at 91.7% with 97.3% specificity.[12] In the second trimester, the twin peak sign becomes more difficult to visualize, and it disappears in about 7% of dichorionic pregnancies at 16 to 20 weeks. Therefore, the absence of the twin peak sign in the second or third trimester cannot exclude dichorionicity.[12,13]

Recommendations

1. All patients who are suspected to have a twin pregnancy on first trimester physical examination or who are at risk (e.g., pregnancies resulting from assisted reproductive technologies) should have first trimester ultrasound performed. (II-2A)
2. Every attempt should be made to determine and report amnionicity and chorionicity when a twin pregnancy is identified. (II-2A)

DETERMINING GESTATIONAL AGE IN TWIN PREGNANCIES

The accurate confirmation of gestational age using ultrasound is essential to pregnancy management. It necessitates determining whether there is a high probability that the measurements of the fetus are appropriate for the estimated gestational age. Early studies of the reliability of ultrasound to confirm gestational age used menstrual dating in women with regular cycles; however, menstrual dating is fraught with biological variability. More recently, studies of this nature were done in IVF pregnancies, for which conception date is known precisely, but it is unclear whether this will work as well with natural conceptions. The literature on gestational age confirmation is also not specific to multiple pregnancies, and in general these studies were a mixture of singletons, twins, and triplets, with the vast majority of subjects being singleton.[14–17] Studies assessing the benefits of confirmation of gestational age by ultrasound have been published,[18] but with singleton not twin pregnancies. A comprehensive and critical review of this topic is well beyond the scope of this document.

The first trimester is generally considered to be the ideal time to confirm or establish accurate gestational age dating, and it is statistically superior to second trimester dating. However, in 2 dating studies using twins, the difference in accuracy compared with IVF could be considered clinically insignificant (underestimate 1 day from IVF dating) with both first (11 to 14 weeks) and second (18 to 22 weeks) trimester ultrasound estimates being very accurate in relation to conceptual age by IVF.[15,19] Hence, in twins, although there is expert consensus that first trimester ultrasound dating is preferable, second trimester dating is also acceptable and accurate.

The best parameter or parameters to use for the most accurate dating vary according to the gestational age. Many studies show that singleton dating formulas work equally well with twins, hence studies in this area are usually a mixture of singletons and multiples.[14–17] In the first trimester, crown–rump length provides appropriate gestational dating within 5 to 7 days.[15–17] First trimester crown–rump length and second trimester biparietal diameter provide gestational age with an error of plus or minus 7 days and are very similar in accuracy.[16] In the second trimester, different combinations of each parameter demonstrate slight differences in accuracy, with the best estimate using a combination of head circumference, abdominal circumference, and femur length.[14] Some centres use an average of all parameters, equally weighted, or use mathematical formulas that give different significance to each parameter used. There are more than 30 different formulas in the literature, using different combinations of parameters.[14] In general, about 95% of gestational age estimates in the first and second trimester will be within 5 to 7 days of the "true" gestational age, regardless of the parameter or parameters used.[14,16,17]

In twin pregnancies, modest size discordance is common. Several studies have cited the need to use the larger twin for dating purposes to minimize the chance of missing a fetus that might present with IUGR.[16,19] Some studies have based the estimated gestational age on the mean of the fetuses.[14] Salomon et al.[20] recently suggested that if the inter-twin crown–rump length discrepancy was less than the 95th percentile, according to their charts, the biometry of the smaller fetus was the more correlative with the conception date of IVF pregnancies.[20] However, the majority of centres, largely on the basis of expert opinion, use the larger of the 2 fetuses to date a pregnancy, erring on the side of overestimation of gestational age and lessening the chance of missing IUGR in the smaller twin.

Therefore, there is no absolute consensus on the optimal method to determine gestational age in twin pregnancies. Most academic centres use the estimated gestational age based on a known last menstrual period, corrected for a regular cycle length if the initial ultrasound falls within an accepted range of days. If the fetal biometry does not agree, new gestational age estimates can be established with an anticipated accuracy of 5 to 7 days. Further study in this area appears to be warranted.

Recommendations

3. Although the accuracy in confirmation of gestational age at the first and second trimester is comparable, dating should be done with first trimester ultrasound. (II-2A)
4. Beyond the first trimester, it is suggested that a combination of parameters rather than a single parameter should be used to confirm gestational age. (II-2C)
5. When twin pregnancy is the result of in vitro fertilization, accurate determination of gestational age should be made from the date of embryo transfer. (II-1A)
6. There is insufficient evidence to make recommendation of which fetus (when discordant for size) to use to date a twin pregnancy. However, to avoid missing a situation of early intrauterine growth restriction in one twin, most experts agree that the clinician may consider dating pregnancy using the larger fetus. (III-C)

SCREENING FOR ANOMALIES IN TWIN PREGNANCIES

Aneuploidy Screening in First Trimester

The literature on aneuploidy screening in twins is relatively scant, consisting of small studies with < 10 abnormal fetuses.[21–24] Conclusions are inconsistent, and much larger studies are required to provide definitive answers.

Nuchal transluscency and maternal age in twins

In 1996, Sebire and colleagues[22] evaluated NT in 448 twin pregnancies (both dichorionic and monochorionic). A total of 7.3% of fetuses had an elevated NT above the 95th percentile. In 88.4% of twin pregnancies, both fetuses had a normal NT. An elevated NT was seen in one fetus in 8.7% and in both fetuses in 2.9%. Seven of 8 Down syndrome fetuses were detected with an overall sensitivity of 88%, which is comparable with the singleton detection rate. The screen positive rate was higher in monochorionic twins at 8.4% than in dichorionic twins at 5.4%.[22] In a small study of monochorionic twins, Vandecruys et al.[24] suggested that the best performance was achieved using the average NT, rather than the larger or smaller NT measured within a twin pair. Using the average NT resulted in an estimated 100% sensitivity for a 4.2% false-positive rate. It would appear that NT in conjunction with maternal age has the potential to reach the standard of 75% sensitivity for a 5% screen positive rate proposed by the SOGC in 2007[25]; however, larger studies are needed to verify this.

NT may also be useful in the early detection or prediction of TTTS. One study suggests that an increased NT in monochorionic twins may be an early manifestation of TTTS. An NT threshold at the 95th percentile had a positive and negative predictive value of 43% and 91%, respectively.[26]

Recommendation

7. In twin pregnancies, aneuploidy screening using nuchal transluscency measurements should be offered. (II-2B)

Aneuploidy Screening in the Second Trimester

The use of genetic sonograms to detect Down syndrome in the second trimester has been well studied in singleton pregnancies. A detailed scan is performed with a number of soft markers of Down syndrome, and if there are abnormal findings, a fetus-specific risk is calculated according to the soft marker detected. In twins, the singleton genetic sonogram principles are applied to individual fetuses, and prenatal diagnosis is offered if sufficient risk exists.[27] However, there is very little, if any, information to estimate the efficacy of this approach in twins. Typically, in mixed population studies, the data in twin pregnancies are combined with the singleton data, and abstraction of efficacy specific to twins is impossible.[28] In one study, soft marker discordance was sought for in twin sets discordant for Down syndrome. Of the markers studied, nuchal translucency thickness was found to correctly identify 5 of 9 Down syndrome cases, with the other markers being significantly less efficacious.[29] Therefore, although there may be some utility of second trimester ultrasound in screening for Down syndrome in twins, its efficacy is uncertain.

Congenital Malformations

Congenital anomalies are 1.2 to 2 times more common in twin gestation.[30] In dizygotic twins the rate per fetus is the same as in singletons, whereas in monozygotic twins the rate is 2 to 3 times higher.[31] The most common structural abnormalities are cardiac anomalies, neural tube and brain defects, facial clefts, and gastrointestinal and anterior abdominal wall defects. Apart from structural defects, which also occur in singletons, there are 3 types of congenital anomalies unique to twin pregnancies.[30]

1. Midline structural defects, believed to be a consequence of the twinning process, exemplified by conjoined twins.
2. Malformations resulting from vascular events as a consequence of placental anastomoses, leading to hypotension and/or ischemia. This can happen to

Table 2. Risk of spontaneous preterm birth (< 32 to 33 weeks) given various CL thresholds

Author	Prevalence	N	CL (mm)	GA (weeks)	Sensitivity	Specitivity %	PPV %	NPV %
Goldenberg et al.[34]	8.8%	147	≤ 25	24	53.8	85.8	26.9	95.0
Skentou et al.[35]	7.8%	434	≤ 25	22 to 24	35.3	91.8	26.7	94.3
Vayssiere et al.[36]	5.4%	251	≤ 25	21 to 23	38	97	38	96
Sperling et al.[37]	6.0%	383	≤ 20	23	21.4	96.4	27.8	95.4
Guzman et al.[38]	9.2%	131	≤ 20	21 to 24	42.0	85	22.0	94

a surviving twin after the demise of the other twin. Anomalies seen as consequence of such events include microcephaly, periventricular leukomalacia, hydrocephalus, intestinal atresia, renal dysplasia, and limb amputation.

3. Defects or deformities from intrauterine crowding: foot deformities, hip dislocation, and skull asymmetry

Edwards et al.[32] evaluated the accuracy of antenatal ultrasound in the detection of fetal anomalies in 245 twins managed in a specialized multiples clinic. The prevalence of anomalies was 4.9%. In this study, antepartum ultrasound detected 88% of anomalies; ultrasound for the detection of congenital anomalies in twins therefore appears to be effective.[32]

Twin pregnancies will be scanned multiple times during pregnancy, predominantly to assess fetal growth. There are no data to determine whether formal reassessment of fetal anatomy at each scan is of significant value in anomaly detection in twins. Only one study of singleton pregnancies[33] found that routine repeat anatomy scanning in the early third trimester resulted in further diagnosis of anomalies. In the second trimester, a major anomaly was detected in 0.36% of scanned fetuses, and anatomical reassessment in the third trimester resulted in further diagnosis in 0.22% of the fetuses previous assessed as "normal." The anomalies detected were predominantly lesions that may develop late in pregnancy and that would not be detectable in the mid-second trimester. Given the number of ultrasound examinations per twin pregnancy and the rising rates of multiple gestations, the resource implications of a policy of repeated anatomical evaluation are significant. There are insufficient data to make a recommendation on how often repeat anatomical survey should be done in twin pregnancies.

Ultrasound scanning for fetal anomalies in twins is clearly justifiable and best performed between 18 and 22 weeks' gestation. A management plan necessitates knowledge of chorionicity and consideration of the risk to the unaffected fetus.

Summary Statement

1. There are insufficient data to make recommendations on repeat anatomical assessments in twin pregnancies. Therefore, a complete anatomical survey at each scan may not be needed following a complete and normal assessment. (III)

Recommendation

8. Detailed ultrasound examination to screen for fetal anomalies should be offered, preferably between 18 and 22 weeks' gestation, in all twin pregnancies. (II-2B)

SCREENING FOR PRETERM BIRTH

Preterm birth is a major cause of mortality and morbidity in twin pregnancies. Sonographic assessment of the cervical length can identify twins at significantly elevated risk of preterm delivery. A number of studies have shown that cervical length can help identify those twins that may be at either increased or reduced risk of early delivery. Most of these studies include both monochorionic and dichorionic pregnancies, and differentiation on that basis is not known. Studies varied with respect to the cervical length threshold chosen, the gestational age at which the cervical length assessment was performed, and the definition of preterm birth. Tables 2 and 3 show information from studies that were similar with respect to these 3 variables. None of the studies included patients who had a cerclage, and all studies employed transvaginal ultrasound.

The studies listed in Table 2 show that a finding of a certain cervical length measured between 21 and 24 weeks correlates highly with preterm birth at < 32 to 33 weeks. The results are fairly consistent in that the risk of preterm birth is increased 3- to 5-fold from baseline prevalence. The absolute PPV ranges from 22% to 38 %. Notably, the negative predictive values are quite high and consistent across these studies: 94% to 96%.

Table 3 shows studies that attempted to define a threshold at which the likelihood of delivery prior to 34 to 35 weeks is low. The results are more variable than those shown in

Table 3. Probability of exceeding 34 to 35 weeks given CL > 35 mm

Author	Definition threshold weeks	Prevalence of threshold %	N	CL (mm)	GA at scan weeks	Sensitivity %	Specificity %	PPV %
Soriano et al.[39]	> 35	79.5	44	> 35	18 to 24	88.5	88.9	96.7
Sperling et al.[37]	> 34	87	383	> 35	23	62.8	54	90.1
Yang et al.[40]	> 35	76.9	65	> 35	18 to 26	90	93.3	97.6
Vayssiere et al.[36]	> 35	85.3	225	> 30	21 to 23	90	27.3	87.8

GA: gestational age

Table 2. Given a CL > 35 mm measured around the mid-second trimester, the probability of reaching 34 to 35 weeks is quite high (88% to 98%).

Cervical length decreases with increasing gestational age, and those who deliver preterm have a cervical shortening rate greater than those who do not. Fujita et al.,[41] in a study of 144 twin pregnancies delivering after 34 weeks, demonstrated a cervical length decrease of 0.8 mm/week. Bergelin et al.[42] found that the median rate of cervical shortening in women who delivered at term was 1.8 mm per week compared with a rate of 2.9 mm/week for those who delivered preterm. Gibson et al.[43] found that a rate of cervical shortening > 2.5 mm/week predicted preterm delivery (positive likelihood ratio of 10.8). Thus, it is clear that progressive shortening greater than expected may indicate a higher risk of preterm labour.

However, application to clinical practice is less clear. The 95% confidence interval of inter- and intraobserver variability (intraobserver repeatability coefficient of approximately ± 6 mm and the interobserver limits of agreement was approximately ± 10 mm)[44] is quite large relative to the reported rates of cervical change. Observed changes may simply be observer variability unless the interobservation interval is quite long. There is also no proven intervention in this scenario. Thus, the optimal protocol for serial CL evaluation in twins is unclear.

In women with signs and symptoms of preterm labour between 23 and 33 weeks, CL was a better predictor of preterm delivery than funnelling and digital examination.[45] Fuchs et al.[46] found that among twin pregnancies that presented in preterm labour, the longer the CL, the less likely it was that delivery would occur within 1 week. At a cervical length of > 25 mm, there were no deliveries (0/21) that occurred within a week, whereas when cervical lengths were ≤ 15 mm, the rate of delivery was 44% (18 of 32).

Summary Statement

2. There are insufficient data to recommend a routine preterm labour surveillance protocol in terms of frequency, timing, and optimal cervical length thresholds. (II-2)

Recommendation

9. When ultrasound is used to screen for preterm birth in a twin gestation, endovaginal ultrasound measurement of the cervical length should be performed. (II-2A)

ASSESSMENT OF FETAL GROWTH

The growth of twins is not significantly different from the growth of singletons in the first and second trimesters. However, there is disagreement regarding the rate of fetal growth in the third trimester in uncomplicated twin pregnancies. Most studies have described slower fetal growth after 30 to 32 weeks' gestation.[47–50] The slower growth rate in twins has been attributed to placental crowding and more frequent anomalous umbilical cord insertion.

The American Congress of Obstetricians and Gynecologists technical bulletin on assessment of growth[51] suggests that centres should use growth tables derived from twin gestations. However, most studies of twin growth curves are derived from a small sample size that includes pregnancies with adverse outcomes and do not take into account chorionicity, race, or gender. The argument in favour of using twin growth charts is that it likely prevents the over-diagnosis of IUGR in normally grown twins (which would result in an increase in iatrogenic preterm delivery). A large cohort study[52] comparing the outcome of twins and singletons, taking into account chorionicity and fetal growth centiles, demonstrated that twins with growth restriction (defined using singleton growth curves) were not protected from perinatal loss; growth restricted monochorionic twins were, in fact, at increased risk of perinatal mortality. Therefore, although it is suggested that the twin growth curve pattern starts to decelerate from 32 weeks' gestation, IUGR twins defined according to the singleton growth curve have worse outcomes than those defined as appropriately grown using the same curve. Thus, the literature still suggests that the use of biometry charts from singletons in the follow-up of twin pregnancy provide good predictors of adverse perinatal outcome.[52] Further investigation in this area using twin growth charts is warranted.

Determination of fetal growth discordance is important, because studies have shown an association with increased mortality and morbidity when there are significant differences in birthweight.[53–58] Therefore, detection of antenatal growth discordance by ultrasound is useful in identifying twins that may require increased surveillance to prevent higher fetal/neonatal complications. Confounding factors in studies of twin growth discordance include chorionicity, gestational age at delivery, and growth restriction relative to expected birth weight, as well as suboptimal sample size. Growth discordance has been defined in several ways, with the most common being the difference in estimated fetal weight derived by ultrasound biometry.[59] Another method uses absolute differences in abdominal circumference.[59] Both methods have their strengths and weaknesses.

Birthweight discordance is defined by the following formula, using the larger of the twins as the denominator.

$$\frac{\text{EFW larger twin} - \text{EFW smaller twin}}{\text{EFW largest twin}} \times 100\%$$

There is no single definition of growth discordance in twins. Clinically significant birthweight threshold definitions in the literature (based on morbidity and mortality in the postnatal population) range from 15%[54] to 30%.[57,60] The largest (more than 250 000 cases) and most recent postnatal study[55] (which also corrected for IUGR) found statistically significant odds ratios of neonatal mortality for the smaller fetus at 25% birthweight discordance and for the larger fetus at 30% birth weight discordance.

Study findings have not been consistent with respect to the accuracy of ultrasound to diagnose discordance.[61–69] This may be due to the error associated with all of the ultrasound-derived estimated fetal weight formulas. The SOGC consensus statement on twin gestations[59] suggests using an EFW discordance of >20%. Given the relative imprecision of EFW formulas (none of which were determined from pure twin populations) and the desire to have a high index of suspicion, adopting a 20% threshold is a reasonable option.

Another definition of significant growth discordance includes abdominal circumference measurement differences of >20 mm. A large study by Caravello et al.[66] compared the use of AC difference and ultrasound EFW difference to predict true birthweight discordance. This study was of twins delivered between the mid-second trimester and term. Other studies were not all concordant in term of definitions. The range of sensitivities for IUGR was 43% to 83% and 33% to 93% for AC and EFW, respectively. The range of specificities for appropriate for gestational age was 68% to 91% versus 81% to 98% for AC and EFW, respectively.[66] Studies that directly compared the 2, showed them to be equally efficacious compared with estimated fetal weight formulas.[66,67] Regardless of growth curves used, increased fetal surveillance is indicated when abdominal circumference and/or EFW of one or both twins is <10th percentile or when growth discordance is identified.[19,70–72]

Summary Statements

3. Singleton growth curves currently provide the best predictors of adverse outcome in twins and may be used for evaluating growth abnormalities. (III)
4. It is suggested that growth discordance be defined using either a difference (20 mm) in absolute measurement in abdominal circumference or a difference of 20% in ultrasound derived estimated fetal weight. (II-2)

FETAL SURVEILLANCE

There are few published studies indicating how frequently routine reassessment should be done in twin pregnancies. Giles et al.[73] in a secondary analysis of their randomized trial (all twins) reported fewer fetal deaths than expected in their routine surveillance group: 11.4/1000 live births (9/1000 live births in the Doppler group) compared with historical control subjects (85.7/1000). In that study, twins had repeat biometry scans at 30 and 35 weeks after a normal 25-week scan. Thus routine surveillance of twin pregnancies every 5 weeks appears to be beneficial. Whether more frequent surveillance would improve the results further remains to be seen; however, it is suggested that more frequent surveillance will result in significantly higher false-positive rates for IUGR.[74]

In current practice, the frequency of ultrasound evaluation in twin pregnancies is determined according to chorionicity and growth pattern. In general, when monochorionic twin pregnancies are identified, ultrasound scans are scheduled every 2 to 3 weeks, starting at 16 to 18 weeks, to better ascertain early evidence of TTTS.[59] For all twin pregnancies, the anomaly screening scan should be scheduled at 18 to 22 weeks. Most tertiary care centres routinely assess fetal growth every 2 to 4 weeks, depending on chorionicity, largely on the basis of expert opinion.[59] Monochorionic twins are scanned more frequently to allow for earlier diagnosis of TTTS and/or growth restriction or discordance, which have greater implications for the non-affected twin than they do in dichorionic pregnancies. Some specialized centres or clinics perform growth scans more frequently than every

2 weeks in uncomplicated monochorionic twin pregnancies, but there is little evidence beyond expert opinion to support this practice. Some centres advocate scanning dichorionic twins every 3 weeks in the third trimester, since the growth rate slows down after 30 to 32 weeks.

Grobman and Parilla[75] found that in twins (of all types) the positive predictive value of a sonogram for a growth abnormality at birth significantly decreased if the 20- to 24-week sonogram was normal. Furthermore, in gestations with normal growth at 20 to 24 weeks a mean of 10.3 (± 3.9) weeks elapsed before a growth abnormality was subsequently detected.[75] This suggests that some routine growth scans may be of very limited benefit while increasing the false positive rate. Increased surveillance is warranted when one or both fetuses show growth restriction or discordance. In these circumstances, serial growth scans every 2 to 3 weeks (or more frequently in monochorionic twins) and fetal surveillance testing are indicated as for singleton (Doppler, non-stress test, and/or biophysical profile).

Summary Statements

5. Although there is insufficient evidence to recommend a specific schedule for ultrasound assessment of twin gestation, most experts recommend serial ultrasound assessment every 2 to 3 weeks, starting at 16 weeks of gestation for monochorionic pregnancies and every 3 to 4 weeks, starting from the anatomy scan (18 to 22 weeks) for dichorionic pregnancies. (II-1)

Recommendation

10. Increased fetal surveillance should be considered when there is either growth restriction diagnosed in one twin or significant growth discordance. (II-2A)

USE OF UMBILICAL ARTERY DOPPLER VELOCIMETRY IN TWINS

Because inequality of the 2 fetal-placental circulations can cause inter-twin differences in growth, umbilical artery Doppler velocimetry may improve the detection of IUGR or fetal growth discordance.[65] The largest trial of Doppler assessment of twin pregnancy (n = 526) compared routine biometric ultrasound assessment to routine assessment plus umbilical artery Doppler velocimetry in a randomized fashion at 25, 30, and 35 weeks' gestation.[73] There were no differences between groups in any antenatal, intrapartum, or neonatal outcome; there were fewer unexplained fetal deaths in the Doppler group, but this was not statistically significant. Unfortunately, this study was limited by insufficient power and because monochorionic pregnancies were not analyzed separately. The available data do not show a clear benefit of Doppler velocimetry over the use of ultrasound alone; therefore, routine use of Doppler velocimetry in twin gestations cannot be recommended at this time.

Of note, in uncomplicated monochorionic twins, uterine artery waveform abnormalities may be common, and they reflect retrograde transmission of arterio-arterial interference patterns in the presence of large arterio-arterial anastomosis rather than fetal compromise.[76,77]

Summary Statement

6. Umbilical artery Doppler may be useful in the surveillance of twin gestations when there are complications involving the placental circulation or fetal hemodynamic physiology. (II-2)

Recommendation

11. Umbilical artery Doppler should not be routinely offered in uncomplicated twin pregnancies. (I-E)

ASSESSMENT OF AMNIOTIC FLUID

Currently available evidence[78–81] is insufficient to make a formal recommendation on the best method of amniotic fluid assessment in twins. Outcome-based studies are lacking. Identification of the inter-twin membrane is vital in order to determine the fluid space around each fetus. Accepted methods for fluid estimation include subjective assessment, deepest vertical pocket, modified amniotic fluid index and 2-dimensional pockets. Another method is to ascertain the presence of fluid, caudal and rostral, and determine to which fetus it belongs and subjectively estimate if normal. When amniotic fluid volume appears reduced or increased, the vertical measurement of the largest pocket in each sac is taken. The condition is defined as oligohydramnios when the deepest vertical pocket < 2 cm and as polyhydramnios when the deepest vertical pocket is > 8 cm. These definitions correspond approximately to the 2.5th percentile and 95th percentile across all gestational ages.[82] This is also a common criterion used in defining TTTS, and for these reasons, this may be the clinically useful method for assessing amniotic fluid in twins.[83]

Summary Statements

7. Although many methods of evaluating the level of amniotic fluid in twins (deepest vertical pocket, single pocket, amniotic fluid index) have been described, there is not enough evidence to suggest that one method is more predictive than the others of adverse pregnancy outcome. (II-3)

Recommendation

12. For defining oligohydramnios and polyhydramnios, the ultrasonographer should use the deepest vertical pocket in either sac: oligohydramnios when < 2 cm and polyhydramnios when > 8 cm. (II-2B)

Diagnosis of Twin-To-Twin Transfusion Syndrome

Prenatal diagnosis of twin-to-twin transfusion syndrome is made on the basis of specific ultrasound criteria. Monochorionic twins with an oligohydramnios-polyhydramnios sequence and the presence of a large fetal bladder in the polyhydramnios twin and a small or absent fetal bladder in the oligohydramnios twin are consistent with TTTS. Discordance in fetal size with the larger twin in the polyhydramnios sac is often seen but is not essential to the diagnosis. A pathognomonic sign for the diagnosis of TTTS is the appearance of the donor as the stuck twin contained within the collapsed inter-twin membrane because of anhydramnios. Doppler studies are also part of the diagnostic evaluation. Absent or low end diastolic flow in the umbilical artery of the donor and decreased ventricular function depicted by tricuspid regurgitation, reversal of A wave in ductus venosus, and/or cardiac chamber enlargement in the recipient are seen in more advanced stages of TTTS. Currently, the Quintero classification method[83] is used to stage and determine the management plan for TTTS.

Stage 1 oligo-polyhydramnios sequence

Stage 2 absent bladder in the donor

Stage 3 abnormal fetal vascular Doppler studies

Stage 4 hydrops of one fetus

Stage 5 death of one fetus

In the absence of oligo-polyhydramnios sequence, the diagnosis of TTTS should be entertained with caution when fetal growth discordance is seen in the presence of velamentous cord insertion, 2 vessel cord, or unequal placental partition.

DIAGNOSIS OF RARE OBSTETRICAL COMPLICATIONS UNIQUE TO TWINS

Monoamnionicity

This occurs in approximately 1% of all monozygotic twin pregnancies. These pregnancies are at elevated risk of fetal death because of cord entanglement. Early series reported double survival in only 46% to 65% until 30 to 32 weeks' gestation.[84,85] More recent series reported improved double perinatal survival of 92% when accurate prenatal diagnosis, serial sonography, and antenatal testing were done.[86] Thus early identification is important in the management of these pregnancies.

First trimester ultrasound can predict virtually all cases of monoamniotic twins. Other sonographic indicators include the presence of a single yolk sac and detection of cord entanglement.[87] In the second trimester, the diagnosis of monoamnionicity is made on the basis of the following second trimester ultrasound criteria: (1) single shared placenta, (2) fetal phenotype concordance, (3) absence of inter-twin membrane, (4) adequate amniotic fluid surrounding both fetuses, and (5) free movement of both twins within the uterine cavity.

Twin Reversed Arterial Perfusion Syndrome

Also known as acardiac twinning, twin reversed arterial perfusion syndrome occurs in 1 in 35 000 deliveries, 1 in 100 monozyotic twins, and 1 in 30 monozygotic triplets.[88] These pregnancies have a 90% risk of preterm birth and a 30% risk of congestive heart failure in the normal twin (also called pump twin).[89] Diagnosis of acardiac twins is made when one monochorionic twin has the absence of cardiac pulsation along with poor definition of fetal parts. Definitive diagnosis is established with colour Doppler demonstrating reversal of blood flow within the abnormal fetus. Blood-flow pattern reveals a paradoxical direction of arterial flow towards rather than away from the acardiac twin and retrograde flow in the acardiac twin's abdominal aorta. Differential diagnosis includes intrauterine fetal demise or an abnormal monochorionic twin, or placental tumours.

After the diagnosis of twin reversed arterial perfusion syndrome sequence is made, fetal hemodynamic function should be assessed by fetal echocardiography; hydrops in the pump twin being a poor prognostic feature. In addition, estimation of the weight ratio of the acardiac to the pump twin should be established. In a 1990 study, Moore et al.[89] found that when the weight of the acardiac twin was ≥ 70% of the weight of the normal pump twin, the incidence of preterm birth, polyhydramnios, and fetal hydrops was 90%, 40%, and 30%, respectively. When the ratio was < 70%, the rates were 70%, 30%, and 10%.[89] When the weight ratio was < 50% the complication rates were 18%, 0%, and 35% compared with 44%, 25%, and 94% when > 50%.[92] The overall perinatal mortality was 55% in this untreated cohort.[89] A multitude of treatment options have been described in the literature, and the optimal method depends on gestational age and centre experience. In a review of all reported cases of minimally invasive therapies, Tan et al.[88] reported an overall pump twin survival of 74%. Two recent series reviewed the use of radio frequency ablation and reported pump twin survival rate of around 90%.[90,91] However, in one small case series of untreated, antenatally diagnosed acardiac twins, the perinatal survival of the pump twin was 90%, with 40% demonstrating spontaneous cessation of flow in the acardiac

twin over time.[92] Because of the complexity of these cases and the possible management options, including expectant management,[92,93] referral to a tertiary care unit is indicated.

Conjoined Twins

The incidence of conjoined twins varies between 1 in 50 000 and 1 in 100 000 births.[94,95] The diagnosis can be made by ultrasound examination in the first trimester. If the embryo appears bifid, follow-up imaging should be performed to confirm the diagnosis. Other clues to the diagnosis include the inability to separate the fetal bodies and skin contours, lack of a separating membrane between the twins, the presence of more than 3 vessels in the umbilical cord, heads remaining at the same level and body plane, extremities in unusual proximity, and failure of the fetuses to change their relative positions over time. Of all conjoined twins, only those who are omphalopagus have a reasonable chance of survival.[96]

Single Fetal Death

It is estimated that only 50% of twin pregnancies identified in the first trimester will result in 2 live born infants.[97] When the demise occurs early in pregnancy, the prognosis for the surviving fetus is excellent.[98,99]

Demise of one fetus occurs in 2% to 5% of twin pregnancies during the second and third trimesters. The occurrence of single fetal death is 3-fold to 4-fold higher in monochorionic twins than in dichorionic twins. It is also more common in high-order multiples, complicating 14% to 17% of triplet pregnancies. The loss of a fetus in a twin gestation has been associated with adverse outcomes for the surviving fetus. The greatest risk to the surviving fetus, regardless of chorionicity, is preterm delivery and the associated complications of prematurity. Overall, 50% to 80% of surviving twins are born preterm, most often because of preterm labour. In monochorionic twins, multi-organ damage in the surviving twin can occur. Ischemic injury, which is thought to occur at the time of the demise, has been documented in the spleen, kidney, gastrointestinal tract, skin, and brain of the surviving twin. Up to 20% of surviving fetuses in monochorionic twin pregnancies may experience neurologic injury, such as multicystic encephalomalacia. These abnormalities may not be diagnosed by ultrasound until much later in pregnancy, far removed from the ischemic event. Immediate delivery may not prevent the development of such complications.

In dichorionic twin pregnancies, the risk of major perinatal morbidity or mortality to the surviving twin appears to be negligible, apart from the risk related to preterm delivery.

Summary Statement

8. Referral to an appropriate high-risk pregnancy centre is indicated when complications unique to twins are suspected on ultrasound. (II-2) These complications include:
   1. Twin-to-twin transfusion syndrome
   2. Monoamniotic twins gestations
   3. Conjoined twins
   4. Twin reversed arterial perfusion sequence
   5. Single fetal death in the second or third trimester
   6. Growth discordance in monochorionic twins.

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