The importance of determining chorionicity in twin gestations

A 32-year-old G2P1001 was diagnosed with twins at her initial ultrasound (U/S) examination in her obstetrician's office at 12 weeks' gestation. At her next U/S examination, scheduled at 20 weeks to evaluate fetal anatomy, a dividing membrane was not visualized between the twins, and a monoamniotic gestation was suspected. Maternal-fetal medicine consultation was requested, and a monochorionic-diamniotic gestation was subsequently diagnosed—complicated by severe twin-twin transfusion syndrome (TTTS).

Q How common are twin pregnancies, and how do monochorionic and dichorionic twins arise?

A Based on data from the Centers for Disease Control and Prevention, the number of twins almost doubled between 1980 and 2009, increasing from 18.9 to 33.2 per 1000 births.[1] Since 2005, the increase has slowed to less than 1% per year. As a result, however, twins accounted for fewer than 1 in 53 pregnancies delivered in the United States in 1980 but now make up 1 in 30. Approximately one-third of the increase is due to increasing maternal age at conception, and the remainder is thought to be secondary to the widespread availability and use of assisted reproductive technology.

In a dizygotic twin gestation, fertilization of 2 oocytes by 2 sperm results in a pregnancy that is dichorionic (DC) and diamniotic (DA). In about 25% of monozygotic twin gestations, cleavage of the morula within 4 days of conception will result in "identical twins" that are also DC and DA, with separate placental masses (Figure 1). In most of the remaining 75% of monozygotic twin gestations, cleavage of the more advanced blastocyst between 4 and 8 days after conception results in monochorionic, diamniotic (MC, DA) membranes and a single placental mass (Figure 1).

Cleavage between 8 and 12 days after conception occurs in less than 1% of twins and results in a monochorionic monoamnionic (MC, MA) gestation. Cleavage beyond 12 days after conception, which is fortunately rare, may result in conjoined twins.

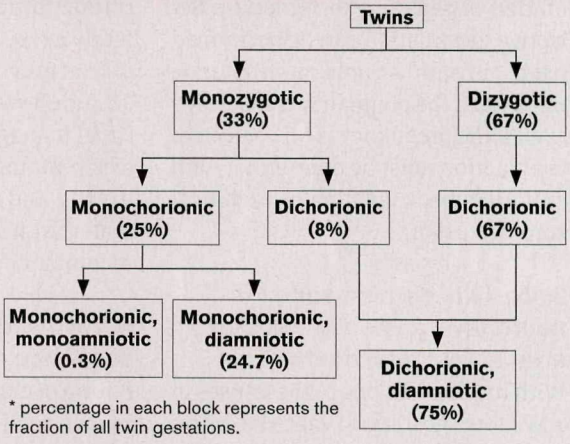
Q Why is it important to determine chorionicity?

A MC twins are associated with increased risks compared with DC twins, and these risks necessitate closer surveillance. In one large twin cohort study, the perinatal mortality rate was found to be more than two-fold increased in MC compared with DC twins.[2] This was predominately influenced by the marked increase in fetal demise in MC twins, 7.6% versus 1.6%. Overall neonatal morbidity was also increased in MC twins compared with their DC counterparts. Several unique complications of MC twins contribute to these differences:

1. Twin-twin transfusion syndrome

Inter-twin vascular anastomoses are present in virtually all MC placentas. An imbalance in flow across the transplacental connections in MC twins can lead to volume and endocrine changes that result in a polyhydramnios/oligohydramnios sequence known as TTTS. This condition complicates 8% to 10% of MC twin gestations and usually presents in the second trimester.[3] TTTS

Figure 1 Breakdown of zygosity and chorionicity in twin gestations*



* percentage in each block represents the fraction of all twin gestations.

accounts for more than one-third of all perinatal deaths in MC pregnancies.[2] In severe cases, the perinatal mortality without treatment is 70% to 100%. Most experts consider fetoscopic laser photocoagulation of placental anastomoses to be the best available approach to treat severe TTTS in continuing pregnancies less than 26 weeks.[3] This procedure has been associated with an overall perinatal survival of 50% to 70% in those with severe disease. Early detection of disease can lead to appropriate treatment and improve perinatal outcomes.[4]

2. Intrauterine growth restriction

The prevalence of intrauterine growth restriction (IUGR) has been reported to be 26% in DC twins and as high as 46% in MC twins.[5] Monochorionicity increases the overall risk of IUGR in twin pregnancies due to disproportionate placental sharing. In one prospective series, selective IUGR, defined as a birthweight discordance of at least 25% in the absence of TTTS, was reported to complicate about 15% of MC pregnancies and was associated with perinatal mortality of 5% to 10%.[6] Management options range from selective termination to strict antepartum surveillance and consideration of early delivery, depending on the gestational age at diagnosis, severity of growth impairment, and patient preference.

It is particularly important to establish chorionicity prior to consideration of selective termination. Selective termination can be performed using intracardiac potassium chloride injection if the pregnancy is DC. However, if the pregnancy is MC, selective termination must be done either with radiofrequency ablation or umbilical cord occlusion.

3. Co-twin demise and neurodevelopmental morbidity after single fetal death

With the death of one of the fetuses in a MC twin gestation, vascular intraplacental connections may place the co-twin at significant perinatal risk. In a recent meta-analysis, death of 1 twin was associated with co-twin demise in 15% of MC gestations and 3% of DC gestations.[7] Similarly, the incidence of neurologic morbidity following death of a co-twin was 26% in MC gestations, compared with 2% in DC gestations. Previously thought to be related to the passage of thromboplastin-like substances after the death of the twin, the more widely accepted theory is that acute hypotension in the initial dying fetus results in a "sink" phenomenon.[8] Acute exsanguination of the normal co-twin results in its death or survival with neurologic sequelae. Thus, immediate or emergent delivery confers no advantage to the surviving fetus after the death of its co-twin in a MC twin gestation.

4. Monoamniotic twins

Although MA twins comprise only 0.3% of twin pregnancies (Figure 1), they are at particularly high risk. Historically, MA twins have been associated with perinatal mortality in up to 80% of cases, primarily related to umbilical cord entanglement.[9] Even in recent series, the perinatal mortality rate is approximately 15%. In an effort to avoid fetal demise, a number of authors have discussed the role of inpatient management as early as 24 to 28 weeks, with steroid administration for fetal lung maturity, daily fetal surveillance, serial assessment of fetal growth, and delivery between 32 and 34 weeks.[9-11] However, the optimal management of these pregnancies remains to be delineated definitively, and co-management with a maternal-fetal medicine specialist is recommended.

5. Twin anemia-polycythemia sequence

A form of chronic fetofetal transfusion known as twin anemia-polycythemia sequence (TAPS) may occur spontaneously in up to 5% of MC twin pregnancies and is also a recognized complication of incomplete laser treatment for TTTS.[12] Significant hemoglobin differences in the fetuses can be identified by finding an elevated middle cerebral artery peak systolic velocity, indicating severe fetal anemia in 1 twin, or by the presence of fetal hydrops in the absence of oligohydramnios-polyhydramnios sequence.

Extreme cases of TAPS can progress to fetal death. Suggested treatment options include laser photocoagulation, intrauterine blood transfusion, selective termination, and early delivery, but there is inadequate literature to guide the optimal approach.

These complications highlight the need to properly establish chorionicity so that management of the pregnancy and antenatal surveillance can be planned appropriately.[13] The American Institute of Ultrasound in Medicine in conjunction with the American College of Radiology and the American College of Obstetricians and Gynecologists recommend that amnionicity and chorionicity should be documented for all multiple gestations when possible.[14, 15] The British, Australian and New Zealand, Canadian, and French Colleges of Obstetrics and Gynecology have made similar recommendations.[16-19]

How is chorionicity determined sonographically?

Chorionicity is most reliably established sonographically early in gestation.

Before 14 weeks

Evidence of 2 distinct gestational sacs on transvaginal ultrasound (TVU) performed before 10 weeks' gestation suggests dichorionicity (Figure 2). Determination of amnionicity is thought to be less accurate before 10 weeks, due to a delay in the sonographic

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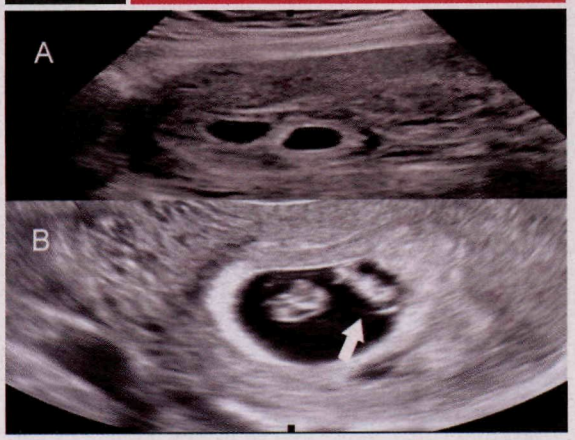
Figure 2 Sonographic evidence of chorionicity at 7-9 weeks



A: Two distinct gestational sacs noted by TVU at 7-9 weeks' gestation consistent with a DC gestation. B: What appears to be a single gestational sac by TVU at 7-9 weeks' gestation consistent with a MC gestation. The small arrow points to 1 of the amnions that is barely visible.

appearance of the thin diamniotic membrane that is often not appreciated in the monochorionic gestation. In such cases, confirmation of the presence of an intervening membrane should be undertaken at a later U/S to exclude a MA twin gestation.

Between 10 and 14 weeks, visualization of the interface between the placenta and the intervening twin membrane is an important determination of chorionicity (Figure 3).[20] A lambda sign (also known as a twin peak sign) is the triangular projection of placental tissue into the base of the intertwin membrane. It represents the chorionic villi between the 2 layers of chorion at its origins from the placenta. The presence of either a lambda sign or 2 separate placentas indicates a DC placentation with a sensitivity of 97% and a specificity of 100%.

The lambda sign tends to disappear with advancing gestational age due to regression of the chorion frondosum to form the chorion leave, and therefore it becomes less useful.[20] When present, the lambda sign indicates dichorionicity, but its absence does not always exclude it. A T sign has been used to describe the U/S visualization of the attachment of the intervening twin membrane to the placenta in cases of MC gestation. When combined with the presence of a single placental mass, it has a sensitivity of 100% and a specificity of 98% for monochorionicity.

At or after 14 weeks

Discordance of fetal gender by U/S has a positive predictive value that approaches 100% for predicting dichorionicity. However, only 55% of all twins are discordant for gender.[21] On rare occasions, post-zygotic disjunction in MC twins can result in a female fetus with 45XO karyotype and a normal male co-twin.[22] Visualization of 2 separate placental masses can also be used to confirm dichorionicity; however, this finding is usually present in only about one-third of twin gestations. Both the presence of a thin bridge of placental tissue between 2 dominant placental masses and the presence of a succenturiate placental lobe can be seen in a MC gestation thereby limiting this parameter as a useful diagnostic tool.

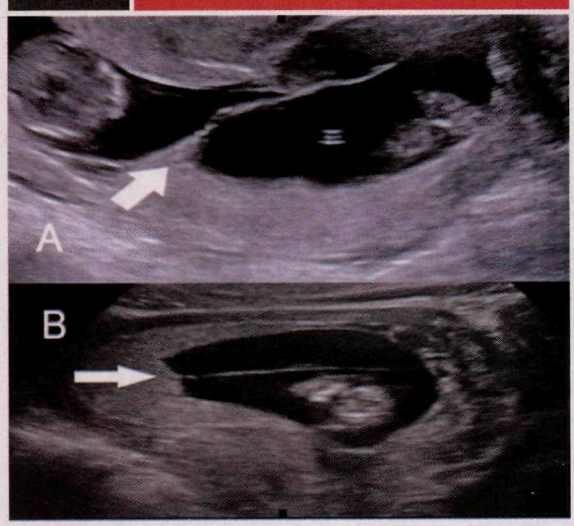
Infrequently, the thickness of the intertwin membrane may be helpful in the determination of chorionicity. In a recent study, a threshold of 2 mm had 90% sensitivity and 76% specificity for determination of MCDA membranes using standard 2-dimensional sonography, and sensitivity was further improved using 3-dimensional sonography.[23]

How does knowledge of chorionicity affect U/S surveillance in twin gestations?

Although evidence for the optimal surveillance of twin gestations is limited, it is prudent to develop a management plan based on risk assessment related to chorionicity. All women with a twin pregnancy should be offered U/S examination at 10 to 13 weeks' gestation to assess chorionicity, viability, crown-rump length, and nuchal translucency.[3] Regardless of chorionicity, an anatomical assessment should be performed at 18 to 20 weeks' gestation. Fundal height is not expected to reliably detect growth abnormalities in multiple gestations, and for this reason, serial sonographic assessment is recommended. DC twins should undergo sonography approximately every 4 weeks to assess fetal growth.

In MC, DA twins, sonography as often as every 2 weeks has been proposed to monitor for the development

Figure 3 Sonographic evidence of chorionicity at 10-14 weeks



A: Lambda sign indicative of dichorionic gestation. B: T sign indicative of a MC gestation.

of TTTS.[3,24,25] The serial sonographic evaluations should include at least the maximal vertical pocket of amniotic fluid in each sac, and the presence of the bladder in each fetus.[3] Limited sonography may be alternated every 2 weeks with serial growth assessments. In addition, the prevalence of cardiac anomalies is increased in MC twins, and screening for congenital heart disease is warranted.[3] If the estimated fetal weight is below the tenth percentile, umbilical artery Doppler studies should be considered.[24] In 2 retrospective series of MC twins, U/S examinations performed every 2 weeks were more likely to result in the early detection of TTTS as compared with traditional monthly assessment.[25,26]

Conclusions

- Chorionicity should be routinely assessed in twin gestations, as early as possible in pregnancy, and ideally by 10 to 13 weeks.
- MC twins are at increased risk of specific complications, including TTTS, selective IUGR, severe perinatal morbidity and mortality after the death of a co-twin, monoamnionicity and subsequent cord entanglement, and TAPS.
- In DC twins, U/S examinations approximately every 4 weeks should be considered to assess fetal growth.
- In MC twins, limited U/S examinations every 2 weeks should be considered, beginning at 16 weeks, with evaluation of fetal growth at about 4-week intervals. COG

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REFERENCES

1. Martin JA, Hamilton BE, Osterman MJK. *Three decades of twin births in the United States, 1980-2009. NCHS Data Brief, No. 80.* Hyattsville, MD: National Center for Health Statistics; 2012.

2. Hack KE, Derks JB, Elias SG, et al. Increased perinatal mortality and morbidity in monochorionic versus dichorionic twin pregnancies: clinical implications of a large Dutch cohort study. *BJOG.* 2008;115(1):58-67.

3. Society for Maternal-Fetal Medicine (SMFM); Simpson LL. Twin-twin transfusion syndrome. *Am J Obstet Gynecol.* 2013;208(1):3-18.

4. Huber A, Diehl W, Bregenzer T, Hackelöer BJ, Hecher K. Stage-related outcome in twin-twin transfusion syndrome treated by fetoscopic laser coagulation. *Obstet Gynecol.* 2006;108(2):333-337.

5. Chauhan SP, Shields D, Parker D, Sanderson M, Scardo JA, Magann EF. Detecting fetal growth restriction or discordant growth in twin gestations stratified by placental chorionicity. *J Reprod Med.* 2004;49(4):279-284.

6. Lewi L, Jani J, Blickstein I, et al. The outcome of monochorionic diamniotic twin gestations in the era of invasive fetal therapy: a prospective cohort study. *Am J Obstet Gynecol.* 2008;199(5):514.e1-514.e8.

7. Hillman SC, Morris RK, Kilby MD. Co-twin prognosis after single fetal death: a systematic review and meta-analysis. *Obstet Gynecol.* 2011;118(4):928-940.

8. Cleary-Goldman J, D'Alton M. Management of single fetal demise in a multiple gestation. *Obstet Gynecol Surv.* 2004;59(4):285-298.

9. Baxi LV, Walsh CA. Monoamniotic twins in contemporary practice: a single-center study of perinatal outcomes. *J Matern Fetal Neonatal Med.* 2010;23(6):506-510.

10. DeFalco LM, Sciscione AC, Megerian G, et al. Inpatient versus outpatient management of monoamniotic twins and outcomes. *Am J Perinatol.* 2006;23(4):205-211.

11. Ezra Y, Shveiky D, Ophir E, et al. Intensive management and early delivery reduce antenatal mortality in monoamniotic twin pregnancies. *Acta Obstet Gynecol Scand.* 2005;84(5):432-435.

12. Slaghekke F, Kist WJ, Oepkes D, et al. Twin anemia-polycythemia sequence: diagnostic criteria, classification, perinatal management and outcome. *Fetal Diagn Ther.* 2010;27(4):181-190.

13. Moise KJ Jr, Johnson A. There is NO diagnosis of twins. *Am J Obstet Gynecol.* 2010;203(1):1-2.

14. *AIUM Practice Guideline for the Performance of Obstetric Ultrasound Examinations.* Laurel, MD: American Institute of Ultrasound in Medicine; 2007.

15. American College of Obstetricians and Gynecologists. ACOG practice bulletin no. 101: ultrasonography in pregnancy. *Obstet Gynecol.* 2009; 113(2 pt 1):451-461. Reaffirmed 2011.

16. Royal College of Obstetricians and Gynaecologists. Management of monochorionic twin pregnancy. Green-top guideline no. 51. 2008.

17. Royal Australian and New Zealand College of Obstetricians and Gynaecologists. Management of monochorionic twin pregnancy. C-Obs 42. 2011.

18. Morin L, Lim K. Ultrasound in twin pregnancies. *J Obstet Gynaecol Can.* 2011;33(6):643-656.

19. Vayssière C, Benoist G, Blondel B, et al; French College of Gynaecologists and Obstetricians. Twin pregnancies: guidelines for clinical practice from the French College of Gynaecologists and Obstetricians (CNGOF). *Eur J Obstet Gynecol Reprod Biol.* 2011;156(1):12-17.

20. Carroll SG, Soothill PW, Abdel-Fattah SA, Porter H, Montague I, Kyle PM. Prediction of chorionicity in twin pregnancies at 10-14 weeks of gestation. *BJOG.* 2002;109(2):182-186.

21. Shetty A, Smith AP. The sonographic diagnosis of chorionicity. *Prenat Diagn.* 2005;25(9):735-739.

22. Zech NH, Wisser J, Natalucci G, Riegel M, Baumer A, Schinzel A. Monochorionic-diamniotic twins discordant in gender from a naturally conceived pregnancy through postzygotic sex chromosome loss in a 47,XXY zygote. *Prenat Diagn.* 2008;28(8):759-763.

23. Senat MV, Quarello E, Levaillant JM, Buonumano A, Boulvain M, Frydman R. Determining chorionicity in twin gestations: three-dimensional (3D) multiplanar sonographic measurement of intra-amniotic membrane thickness. *Ultrasound Obstet Gynecol.* 2006;28(5):665-669.

24. Society for Maternal-Fetal Medicine. Berkley E, Chauhan SP, Abuhamad A. Doppler assessment of the fetus with intrauterine growth restriction. *Am J Obstet* Gynecol. 2012;206(4):300-308. Erratum in: Am J Obstet Gynecol. 2012;206(6):508.

25. Carver A, Haeri S, Moldenhauer J, Wolfe HM, Goodnight W. Monochorionic diamniotic twin pregnancy: timing and duration of sonographic surveillance for detection of twin-twin transfusion syndrome. *J Ultrasound Med.* 2011;30(3):297-301.

26. Thorson HL, Ramaeker DM, Emery SP. Optimal interval for ultrasound surveillance in monochorionic twin gestations. *Obstet Gynecol.* 2011;117(1):131-135.