Anomalies of the placenta and umbilical cord in twin gestations

Corinne Hubinont, MD, PhD; Liesbeth Lewi, MD, PhD; Pierre Bernard, MD; Etienne Marbaix, MD, PhD; Frédéric Debiève, MD, PhD; Eric Jauniaux, MD, PhD

The frequency of twin gestations has increased over the last few decades, mainly due to maternal age at childbearing, and the use of assisted reproductive technologies. Twins are at higher risk of aneuploidy, structural anomalies, and placental abnormalities. Some of the placental and umbilical cord abnormalities found in twin gestations are nonspecific and can be found in singleton gestations (ie, placenta previa, placental abruption, single umbilical artery, velamentous cord insertion, vasa previa, etc). However, other anomalies are unique to twin gestations, and are mainly associated with monochorionic twins—these include intraplacental anastomosis and cord entanglement. Most of these conditions can be diagnosed with ultrasound. An accurate and early diagnosis is important in the management of twin gestations. Determination of chorionicity, amnionicity, and the identification of placental anomalies are key issues for the adequate management of twin pregnancies. Pathologic placental examination after delivery can help in assessing the presence of placental and umbilical cord abnormalities, as well as providing information about chorionicity and gaining insight into the potential mechanisms of disease affecting twin gestations.

Key words: chorionicity, cord entanglement, discordant growth, fetal placental ratio, intertwin septum, multiple gestation, twin to twin transfusion syndrome, vascular anastomosis, zygosity

With the development of new assisted reproductive techniques (ART) in the late 1970s, multiple gestation pregnancy rates have increased markedly around the world. In the United States, the rate of twin pregnancies has stabilized at 32 per 1000 births in 2006.[1] The latest Centers for Disease Control and Prevention report on ART surveillance indicates that 43% of ART-conceived infants in 2011 in the United States were twins.[2]

Twinning is associated with higher incidence of perinatal risks for both mothers and fetuses compared to singleton pregnancies. The main risks are early and late miscarriage, pre-eclampsia, antepartum bleeding, postpartum hemorrhage, preterm delivery, intrauterine growth restriction (IUGR), and stillbirths.[1-5] Twins are also more prone to birth asphyxia, hyaline membrane disease, respiratory disorders, seizures, and long-term developmental morbidity.[1-5] Prematurity and its complications is the single most important cause of perinatal morbidity and mortality in multiple pregnancies.[6] Overall, perinatal mortality rates are reported to be 4-fold higher for twins than for singletons.[1,3,5] Most of these complications are directly or indirectly associated with placental or umbilical cord disorders.[5]

Twin pregnancies are obviously at higher risks for birth defects than singleton due to the development of 2 fetuses instead of 1.[1,5,8] Cohort studies have suggested that in vitro fertilization (IVF) could be associated with higher incidence of birth defects.[7,8] However, the lack of information on the etiology of the infertility, chorionicity, maternal preexisting medical conditions, parental smoking status, and social environments in most studies hampers the interpretation of the corresponding data.[7] A recent large Australian cohort study showed that the increased risk of birth defects associated with IVF is no longer significant after adjustment for parental factors.[8] However, placenta previa and velamentous cord insertion (VCI) are more common in singleton IVF than in spontaneous pregnancies suggesting the incidence of placental and cord anomalies can be influenced by the mode of conception.[4,7]

Development, position, and vascularity abnormalities of the placenta and the umbilical cord can impact significantly perinatal morbidity and mortality. The aim of this review is to provide an outline of these anomalies associated with the twinning process and discuss the corresponding pathophysiology and diagnostic features. Most of these pathologies can be diagnosed in utero by routine ultrasound examination and should be an integral part of prenatal investigations in twins.[4,5,9] For a better understanding of the pathogenesis, it is essential to confirm the prenatal diagnosis with a detailed histopathological placenta examination at birth. Placental and cord pathologies are traditionally divided into primary or

From the Departments of Obstetrics (Drs Hubinont, Bernard, and Debiève) and Pathology (Dr Marbaix), Saint Luc University Hospital, Université de Louvain, Brussels, Belgium; Department of Obstetrics, University Hospitals, Department of Development and Regeneration, Katholieke Universiteit Leuven, Leuven, Belgium (Dr Lewi); and Institute for Women's Health, University College London Medical School, London, United Kingdom (Dr Jauniaux).

Received May 6, 2015; revised June 24, 2015; accepted June 25, 2015.

Drs Hubinont, Bernard, and Debiève are supported by the charity Fetus for Life.

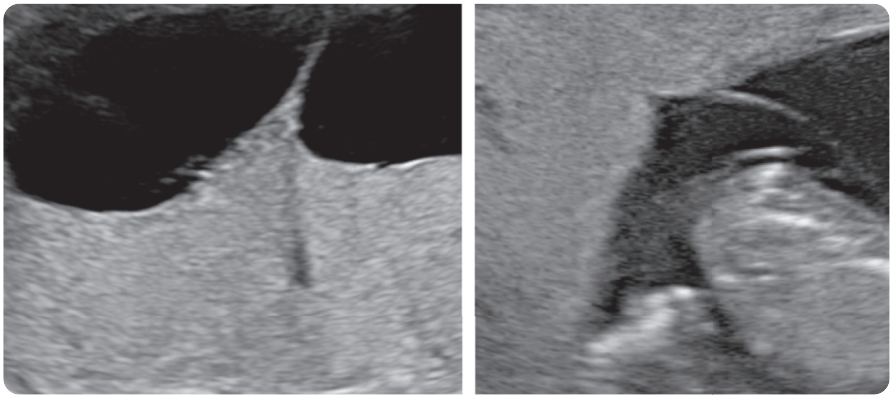
The authors report no conflict of interest.

Corresponding author: Corinne Hubinont, MD, PhD. corinne.hubinont@uclouvain.be

0002-9378/$36.00

http://dx.doi.org/10.1016/j.ajog.2015.06.054

FIGURE 1
Ultrasound chorionicity diagnosis



Ultrasound of intertwin membranes at level of placental insertion in dichorionic-diamniotic twins with fused placentas showing lambda sign (*left*) and in monochorionic-monoamniotic pregnancy showing T sign (*right*).

Hubinont. Placental and cord disorders in twin gestations. Am J Obstet Gynecol 2015.

congenital anomalies such as tumors and secondary anomalies such as thrombosis. For the purpose of our review, we have analyzed these anomalies according their specific and nonspecific association with twin pregnancies.

Zygosity vs chorionicity

Zygosity and chorionicity are distinct entities. A dichorionic (DC)-diamniotic (DA) placenta can be found in both monozygotic (MZ) and dizygotic twins whereas a single or monochorionic (MC) placenta mass is mainly associated with MZ twins.[10] Zygosity or twins classification based on a double or a single fertilization cannot be predicted in DC similar gender twins.[11] The low incidence of MZ twinning is constant worldwide and seems independent of environmental factors.[1,2] However, ART and mainly IVF increase both the incidence of MZ but also MC twins.[3,4]

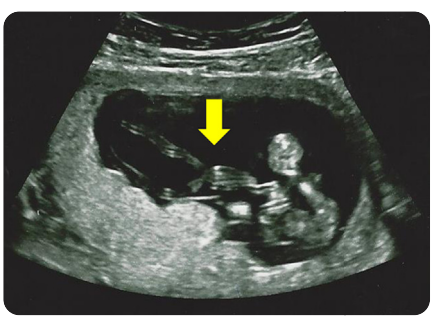
Zygosity is generally established postnatally using genetic tests on umbilical cord blood. Quantitative fluorescent polymerase chain reaction amplification of microsatellite markers has been performed antenatally on fetal/placental cells obtained from amniocentesis or chorionic villous sampling for scientific purposes.[12] Noninvasive prenatal determination of twin zygosity using maternal plasma free fetal DNA sequencing similar to that used for the aneuploidy testing has recently been reported.[13]

Independently of the conception mode, the fetal, placental, and cord anomalies risk depends mainly on the chorionicity and amnionicity in twins.[1,4,5,14] Overall, perinatal mortality is around 11% in MC twins compared to 5.0% in DC twins.[1,5,14] Monoamniotic (MA) twins are rare (1% of MZ twins) but associated with the highest morbidity and mortality rate of all different types of twinning.[9,15,16] An early determination of chorionicity and amnionicity is therefore essential to optimize the management pathways in twin pregnancies.[17-20] The optimal window to determine chorionicity in twins with 98% accuracy is at 7-9 weeks of gestation.[18] Accuracy may be higher for DC twins than MC twins and is related to the gestational age at which the sonographic appearance of the amniotic sac develops.

Ultrasound examination of twin pregnancies at 10-14 weeks of gestation predicts chorionicity with a high degree of accuracy using a combination of the number of placentas, lambda and T signs, and intertwin membrane thickness.[17-19] Two distinct placental masses and different fetal gender indicate DC. When only 1 placental mass is visible on ultrasound, the presence of a lambda sign at the insertion of the intertwin membranes is an accurate predictor for DC whereas T sign is the most reliable indicator of MC (Figure 1).[17-20] Measurements of the intertwin membrane thickness and membrane layer count are associated with a lower sensitivity and specificity than the ultrasound features used earlier in pregnancy but can be useful to determine chorionicity during the second trimester of pregnancy when the insertion of the intertwin is less clear.[20]

MA is determined by the absence of a dividing membrane between the amniotic sacs.[11,15,17] MA should be suspected at 10-14 weeks in the presence of a single amniotic sac and closely inserted umbilical cords (Figure 2). The number of yolk sacs is not always an accurate sonographic sign of amnionicity.[21,22]

FIGURE 2
Ultrasound of monochorionic monoamniotic twin pregnancy



First-trimester ultrasound of monochorionic-monoamniotic twin pregnancy showing single sac and twisted umbilical cords or Y sign (*arrow*).

Hubinont. Placental and cord disorders in twin gestations. Am J Obstet Gynecol 2015.

Twin-specific anomalies of the placenta and umbilical cord

Placental vascular anastomoses

Nearly all MC placentas have vascular connections or anastomoses between the 2 umbilical-placental circulations.[23-28] Postdelivery placental examination injections studies have shown that they are located either superficially on the fetal surface or more deeply inside the placental mass[24-27] (Figure 3). Three different types of anastomoses have