Risk of late-preterm stillbirth and neonatal morbidity for monochorionic and dichorionic twins

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OBJECTIVE: The purpose of this study was to determine the prospective risk of intrauterine fetal death (IUFD) at ≥34 weeks' gestation for monochorionic and dichorionic twins receiving intensive antenatal fetal surveillance. The secondary objective was to calculate the incidence of prematurity-related neonatal morbidity/mortality rates that have been stratified by gestational week and chorionicity.

STUDY DESIGN: A retrospective cohort study of all twins at ≥34 weeks' gestation who were delivered at the Medical University of South Carolina (1987-2010) was performed. Twins were cared for in a long-standing Twin Clinic with standardized treatment and surveillance protocols and supervised by a consistent Maternal-Fetal Medicine specialist. Gestational age—specific fetal/neonatal mortality rates and composite neonatal morbidity rates were compared by chorionicity. A generalized linear mixed model was used to identify variables that were associated with increased composite neonatal morbidity.

RESULTS: Among 768 twin gestations (601 dichorionic and 167 monochorionic), only 1 dichorionic IUFD occurred. The prospective risk of IUFD at ≥34 weeks' gestation was 0.17% for dichorionic twins and 0% for monochorionic twins. Composite neonatal morbidity decreased with each gestational week ($P < .0001$). Morbidity was increased by white race, gestational diabetes mellitus, and elective indication for delivery. The nadir of composite neonatal morbidity occurred at 36/0-36/6 weeks' gestation for monochorionic twins and 37/0-37/6 weeks' gestation for dichorionic twins.

CONCLUSION: Our data do not support concern for an increased risk of stillbirth in uncomplicated intensively monitored monochorionic twins at ≥34 weeks' gestation. However, our data do show significantly increased rates of neonatal morbidity in late preterm monochorionic twins that cannot be justified by a corresponding reduction in the risk of stillbirth. We believe that our data support delivery of uncomplicated monochorionic twins at 37 weeks' gestation.

Key words: delivery timing, dichorionic twins, monochorionic twins, stillbirth

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The frequency of twin gestations has risen dramatically over the past 30 years, increasing by >60% between 1980 and 2006 and now represents almost 4% of all live births.[1]

Monochorionic twin gestations experience rates of stillbirth that are higher than either singleton or dichorionic twin gestations.[2-4] This increased stillbirth rate is attributed primarily to placental vascular complications such as twin-twin transfusion syndrome.[3,4] Other contributors include increased risks of congenital malformations, selective growth restriction, maternal obstetric complications, and co-twin death because of intravascular shunting after a single intrauterine death.[4]

Recently, concerns have been raised that even "apparently uncomplicated" monochorionic twins are at increased risk for fetal death. Third-trimester stillbirth rates as high as 4.3% have been reported.[5] Subsequent cohort studies, however, have reported a lower stillbirth risk in late pregnancy.[6-9] A recent metaanalysis described an almost 4-fold increased risk of stillbirth for "apparently uncomplicated" monochorionic twins.[10]

In February 2011, the National Institutes of Health (NIH) and Society for Maternal-Fetal Medicine collaborated to publish expert consensus-based recommendations on the optimal timing of delivery for high-risk pregnancies.[11] For uncomplicated dichorionic twins, delivery at 38 weeks' gestation was recommended. Uncomplicated monochorionic twins, however, had less specific recommendations for delivery at 34-37 weeks' gestation. This broad interval reflects the uncertainty over the possible greater risk of late stillbirth even for "apparently uncomplicated" monochorionic twins.

The purpose of this investigation was to review a large cohort of twin gestations cared for at a single institution in a

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specialized, antenatal Twin Clinic since 1987. The primary objective was to determine the prospective risk for stillbirth among continuing monochorionic and dichorionic twin gestations in the late preterm and early term gestational age time periods. Second, we determined the gestational age-specific neonatal morbidity and mortality rates for monochorionic and dichorionic twins. These data will help better define the optimal balance between the risk of stillbirth and the neonatal morbidity that is associated with elective preterm delivery of monochorionic and dichorionic twins.

Materials and Methods

This retrospective cohort study examined all dichorionic and monochorionic twins at ≥34 weeks' gestation who were delivered at the Medical University of South Carolina (MUSC) from 1987-2010. After institutional review board approval (IRB #00012449; 9/13/2011), subjects were identified, and maternal/neonatal variables were obtained from the Perinatal Information Network System (PINS) database. PINS is an institutional research quality database with multiple edits and audits to ensure accuracy. PINS was complemented by a second database that was created specifically for the Twin Clinic and is maintained by a certified nurse-midwife who is involved in the care of those patients. Specific maternal variables including gestational age, indication for delivery, and chorionicity were confirmed by individual review of each maternal medical record.

Exclusion criteria included gestational age <34 weeks, monoamnionicity, aneuploidy, fetal anomalies that require prolonged hospitalization or immediate surgery, co-twin death at <34 weeks' gestation, or unknown chorionicity. Chorionicity was assigned prenatally by ultrasound assessment of the placental number, thickness of the dividing membrane, the presence or absence of a "twin-peak" sign, and fetal gender in all patients. After delivery, the assignment of chorionicity was confirmed in all cases by inspection of the placentas and membranes. Chorionicity was further confirmed by individual review of placental pathologic findings, which were available in 70% of patients. Gestational age was determined by the patient's last menstrual period or date of fertilization in cases of assisted reproduction. When the menstrual dating was unknown or discordant with first or early second-trimester ultrasound measurements, the ultrasound-based dating criteria were used.

Twin gestations were cared for through a specialized Twin Clinic staffed by obstetrics-gynecology residents and a consistent, dedicated certified nurse-midwife. The Twin Clinic was directed by a single Maternal-Fetal Medicine physician. Twin gestations have been managed in a standardized fashion following protocols that were established by the supervising Maternal-Fetal Medicine specialist. Since the inception of the Twin Clinic, third-trimester fetal surveillance has included ultrasonographic surveillance of fetal growth, growth discordance, and amniotic fluid volumes at least every 4 weeks. Since 2005, monochorionic twins have undergone ultrasound surveillance at least every 3 weeks. Umbilical artery Doppler assessment was not used routinely for ultrasonographic fetal assessment. It was used selectively to further evaluate fetuses who are suspected of having an estimated fetal weight <10th percentile, an abdominal circumference <5th percentile, growth discordance >20%, a deepest vertical pocket <2 cm, or suspected twin-twin transfusion syndrome. Weekly nonstress testing has been initiated routinely at 32 weeks' gestation for monochorionic twins and 34 weeks' gestation for dichorionic twins, unless earlier surveillance was indicated. All twins were seen on a weekly basis after 34 weeks' gestation. Timing of delivery for uncomplicated dichorionic and monochorionic twins was recommended at 38 and at 37 weeks' gestation, respectively (Figure 1). For twins with maternal or fetal complications, there was a liberal policy of delivery at any time after 35 weeks' gestation (Figure 2).

The primary outcomes in this study were stillbirth and composite neonatal morbidity/mortality rates, stratified by gestational age and chorionicity. *Stillbirths* were defined as an intrauterine fetal death (IUFD) between 34 weeks' gestation and delivery. Composite neonatal morbidity was composed of transient tachypnea of the newborn infant, respiratory distress syndrome, continuous positive air pressure ventilation or oxygen requirement outside of the delivery room, sepsis or sepsis work-up, necrotizing enterocolitis, any grade intraventricular hemorrhage, phototherapy, or neonatal death. Neonatal death was the death of a liveborn infant by 28 days of life. These diagnoses were extracted from PINS and represented the final discharge diagnoses assigned by the Neonatology attending staff.

Statistical analysis was performed with SAS software (version 9.2; SAS Institute, Cary NC) and SPSS software (version 12.0; SPSS Inc, Chicago IL). Subjects were segregated initially by chorionicity (dichorionic vs monochorionic). A univariate analysis was performed comparing continuous and categoric demographic and outcome variables. Continuous variables were compared with the Mann-Whitney *U* test; χ^2 or Fisher exact test were used for categoric variables. To determine which variables were associated with a higher risk of stillbirth or composite neonatal morbidity/mortality rates, a generalized linear mixed model analysis was used. This model was used in preference to a standard logistic regression model because the outcomes of each twin were not independent of the co-twin. The prospective risks of IUFD for both monochorionic and dichorionic twins were calculated as the number of stillbirths during or after a given week-long gestational period divided by the total number of ongoing pregnancies at the start of the time period.[5,6] Gestational age–specific prospective risks of perinatal death were calculated with the use of the concept of "fetuses at risk."[9,12-15] This calculation is performed by dividing the number of stillbirths and neonatal deaths during any given week by the number of fetuses remaining in utero, and thus "at risk," at the beginning of that week. These risks were calculated weekly from 34 to ≥39 weeks' gestation, and the monochorionic and dichorionic twin outcomes were compared.