Fetal Transcerebellar Diameter Measurement for Prediction of Gestational Age in Twins

Martin R. Chavez MD

Cande V. Ananth PhD, MPH

Lillian M. Kaminsky MD

John C. Smulian MD, MPH
Lehigh Valley Health Network, john.smulian@lvhn.org

Lami Yeo MD

See next page for additional authors

Published In/Presented At

Chavez, M., Ananth, C., Kaminsky, L., Smulian, J., Yeo, L., & Vintzileos, A. (2006). Fetal transcerebellar diameter measurement for prediction of gestational age in twins. *American Journal Of Obstetrics And Gynecology*, *195*(6), 1596-1600.

American Journal of Obstetrics and Gynecology (2006) **195**, 1596–600

ELSEVIER

American Journal of Obstetrics & Gynecology

www.ajog.org

Fetal transcerebellar diameter measurement for prediction of gestational age in twins

Martin R. Chavez, MD,[a] Cande V. Ananth, PhD, MPH,[b] Lillian M. Kaminsky, MD,[a] John C. Smulian, MD, MPH,[a] Lami Yeo, MD,[a] Anthony M. Vintzileos, MD[a]

Division of Maternal-Fetal Medicine,[a] Division of Epidemiology and Biostatistics,[b] Department of Obstetrics, Gynecology and Reproductive Sciences, UMDNJ-Robert Wood Johnson Medical School/Robert Wood Johnson University Hospital, New Brunswick, NJ

Received for publication November 8, 2005; revised February 27, 2006; accepted March 18, 2006

KEY WORDS
Cerebellum
Twins
Chorionicity
Ultrasound
Gestational age
Nomogram

Objective: This study was undertaken to determine the accuracy of our previously published and prospectively validated institution-specific singleton transcerebellar diameter (TCD) nomogram in the prediction of gestational age (GA) in twin pregnancies. We further evaluated whether the prediction of GA in twin gestations using the singleton TCD nomogram differs between monochorionic and dichorionic twins.

Study design: In our previously published studies, we retrospectively constructed a cross-sectional nomogram using TCD measurements in 24,026 well-dated, singleton fetuses, and prospectively validated the nomogram using 2,597 singleton fetuses. The current study comprised of 1,278 well-dated twins (19.6% monochorionic) seen in our ultrasound unit between August 1994 and May 2003, and the singleton TCD nomogram was validated in these twin gestations. The actual GA was subtracted from the GA predicted by the TCD nomogram and the concordance between actual and predicted GAs was assessed on the basis of the Pearson's correlation coefficient (r). This was performed separately for monochorionic and dichorionic twins.

Results: Concordance between the actual and predicted twin TCD measurements based on our previously published singleton TCD nomogram was high (Pearson's correlation, $r = 0.95$, $P < .0001$). Between 16 and 23 weeks' gestation, the predicted mean GA was within 6 days of actual GA. Between 24 and 30 weeks, the predicted mean GA was within 3 days, and at 32 weeks or more, the predicted mean GA was within 5 days of the actual GA. Prediction of GA based on the singleton TCD nomogram was equally accurate in both monochorionic and dichorionic twin gestations ($P = .686$).

Conclusion: This study demonstrates that our previously validated singleton TCD nomogram is reliable and accurate in twins irrespective of placental chorionicity.

Supported through the "Samuel A. Pasquale, MD" research grant awarded to Dr Chavez by the Department of Obstetrics, Gynecology, and Reproductive Sciences, UMDNJ-Robert Wood Johnson Medical School, NJ. Drs Ananth and Smulian are partly supported through a grant (R01-HD038902) from the National Institutes of Health awarded to Dr Ananth.

Reprints not available from the authors.

0002-9378/$ - see front matter © 2006 Mosby, Inc. All rights reserved.
doi:10.1016/j.ajog.2006.03.062

Clinical dating criteria has retained importance, and the value of ultrasound biometry for dating has been repeatedly demonstrated.[1,2] Fetal transcerebellar diameter (TCD) measurements have proven to be among the most reliable. However, appropriate biometry to evaluate twin pregnancies has been largely unexplored.[3-6] This is especially important given the variability in growth and size experienced by twins.[7,8] Previous studies that applied singleton TCD nomogram measurements to twins for prediction of gestational age (GA) have led to mixed results.[3,4,9] Unfortunately, these studies did not use nomograms that were created using rigorous statistical methodology and/or adequate study size.[1,2] In addition, none of the previously developed nomograms, to the best of our knowledge, were ever prospectively validated. Several studies[10-13] have also shown twin fetal biometric parameters and perinatal outcomes among twins to vary considerably by placental chorionicity. Whether the TCD is affected by placental chorionicity in twin gestations remains unknown.

We undertook this study to determine whether our previously constructed and validated TCD nomogram derived from singleton pregnancies would offer an accurate prediction of GA both in monochorionic and dichorionic twin gestations.

Material and methods

This Institutional Review Board-approved study was based on ultrasound assessments of pregnant women evaluated at the University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, New Brunswick, NJ. Our ultrasound unit serves as a tertiary referral center that performs ultrasound examinations on routine and referred complicated pregnancies. The study population consisted of twin gestations that had ultrasound in our unit between 14 and 38 weeks from August 1994 to May 2003. Indications for ultrasound included fetal viability, dating, targeted or routine anatomic surveys, genetic sonography, and follow-up growth. Only pregnancies whose menstrual estimate of GA was confirmed by ultrasound at 20 weeks or less were included. For fetuses with multiple TCD measurements at different GAs, only the last TCD examination was used for this study. Chorionicity was assigned early by ultrasound characteristics of membranes (thickness, number of layers, and T vs peak sign), placental number, fetal sex, and/or pregnancy history.

Transverse views of the fetal intracranial anatomy were obtained for each fetus by using high-resolution ultrasound equipment (Ultramark-9, HDI-3000, HDI-5000 ATL-Philips Medical Systems, NA, Bothell, WA; Aloka 5500, Wallingford, CT; and GE Voluson Expert, Fairfield, CT). TCD diameter measurements were obtained prospectively by placing the ultrasound machine on screen calipers at the outer margins of the cerebellum. This information was then recorded at the time of examination into a reporting database OBserver version 5.2.08 (Vision Chips, Inc, Laguna Hills, CA), and Crystal Reports Developer (edition version 11.0.0.895; Business Objects Americas, Inc, San Jose, CA) was used to extract the data from the reporting system.

In our previous study, cross-sectional TCD nomogram was constructed by using recorded singleton TCD measurements.[1,2] A single measurement was used for each patient. For fetuses with multiple TCD measurements at different GAs, only the last TCD examination was used in the nomogram construction. We previously documented that the interobserver and intraobserver variability of TCD in both second and third trimesters were superior (interobserver variability was $\leq$3.6%; intraobserver variability $\leq$3.8%).[1,2] These same criteria as in the previous study were used for the current study on twin gestations.

Statistical analysis

The methodology for deriving the TCD nomogram (n = 24,026) and validation (n = 2,597) in singleton gestations has been reported previously.[1,2] Briefly the nomogram was based on a third-degree polynomial regression. Equations were derived by modeling the mean and SD based on the following fitted linear regression model. The regression equations for the mean and variability (SD) of the nomogram for the prediction of GA based on TCD were as follows:

$$GA_{mean} = 8.119 + 4.244\,(TCD) + 1.113\,(TCD^2) - 0.169\,(TCD^3) \quad (1)$$

$$GA_{SD} = 1.713 - 1.304\,(TCD) + 0.567\,(TCD^2) - 0.067\,(TCD^3) \quad (2)$$

Regression equations 1 and 2 were subsequently combined by using the relationship mean $\pm$ z (SD), from which the 5th, 10th, 50th, 90th, and 95th percentiles were derived, where z is the standard normal deviate, and SD the standard deviation. The standard normal deviate, z, were $\pm$1.96 for the 5th and 95th percentiles; $\pm$1.28 for the 10th and 90th percentiles; and zero for the 50th percentile.

Concordance between the actual for each of the twin fetuses and the predicted TCD were based on calculating the Pearson's (linear) correlation coefficient. We further estimated the difference between the actual and predicted GAs based on the predicted TCD measurements for each fetus.

Results

Between August 1994 and May 2003, there were 1430 twin gestations identified from our data. We excluded 152 subjects because of incorrect dating. After exclusions, there were 1278 twin pregnancies available for analysis, of which 19.6% (n = 250) were monochorionic.

Table I Maternal characteristics

	Total	Placental chorionicity		
		Monochorionic	Dichorionic	*P* value*
Number of pregnancies	1,278	250	1,028	—
Maternal age (y)†	30.9 ± 6.4	31.3 ± 6.6	30.8 ± 6.2	.001
Parity‡	1 (0-6)	1 (0-5)	1 (0-6)	.053
Gravidity‡	2 (1-13)	2 (1-8)	2 (1-13)	.001

Difference in maternal age was assessed based on the Student *t* test, and those of parity and gravidity based on Wilcoxon test.

* *P* values correspond to difference in maternal characteristics between monochorionic and dichorionic twin gestations.

† Data are expressed as mean (SD).

‡ Data are expressed as median (range).

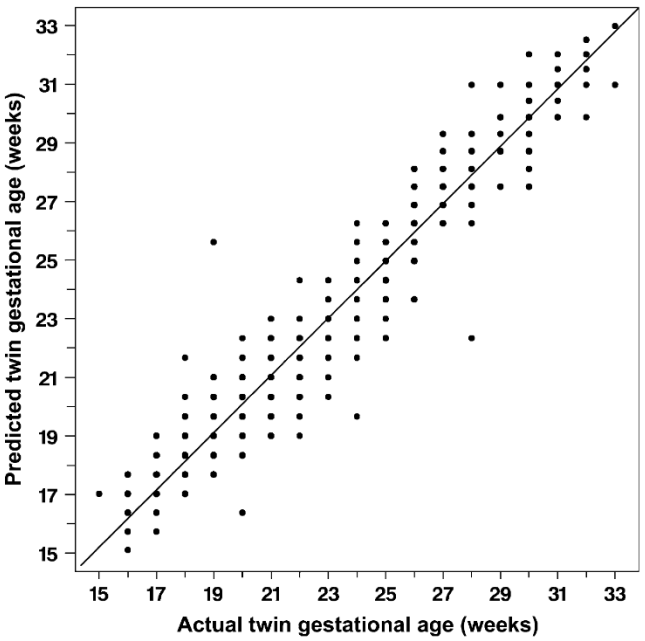

Figure Actual-to-predicted GA based on the TCD nomogram in singleton gestations (Pearson's correlation coefficient 0.96; $P < .0001$; $R^2 = 92.2\%$).

Table II Concordance between the actual and predicted GA throughout gestation based on TCD measurements

TCD measurement in twins (cm)	GA		
	Actual mean	Predicted mean	Mean difference (SD)
1.6	16 wk, 5 d	16 wk, 0 d	−5 d (3)
1.8	18 wk, 4 d	17 wk, 5 d	−6 d (2)
2.0	19 wk, 5 d	19 wk, 4 d	−1 d (1)
2.2	20 wk, 5 d	21 wk, 3 d	+5 d (2)
2.4	22 wk, 5 d	23 wk, 0 d	+2 d (2)
2.6	24 wk, 3 d	24 wk, 0 d	−3 d (1)
2.8	25 wk, 1 d	25 wk, 0 d	−1 d (1)
3.0	26 wk, 1 d	26 wk, 3 d	+2 d (1)
3.2	27 wk, 5 d	28 wk, 0 d	+2 d (2)
3.4	28 wk, 5 d	29 wk, 0 d	+2 d (1)
3.6	30 wk, 2 d	30 wk, 0 d	−2 d (1)
3.8	31 wk, 0 d	31 wk, 0 d	−0 d (0)
4.0	31 wk, 3 d	32 wk, 0 d	−5 d (3)
4.2	33 wk, 0 d	33 wk, 0 d	0 d (0)

Mean (SD) for actual and predicted GAs were 20.8 (3.2) and 20.8 (3.1) wks, respectively.

Eighty-five percent of the women in our sample were white, 10% were black, and 5% women of "other" race/ethnicity, and approximately 45% of the women were nulliparous. The mean maternal age was 30 years with a median parity of 2 prior pregnancies (Table I).

Concordance between actual and predicted GA using the singleton TCD nomogram was high (Figure; Pearson's correlation, $r = 0.96$, $P < .0001$; $R^2 = 92.2\%$). The Pearson's correlation coefficients for the concordance between the actual and predicted GAs in monochorionic and dichorionic twins were 0.95 and 0.96, respectively ($P < .0001$). Between 16 and 23 weeks' gestation, the mean predicted GA ranged within 1 to 6 days of actual GA. Between 24 and 30 weeks, the mean predicted GA was within 3 days, and at 31 weeks or greater, the mean predicted GA was within 5 days of the actual GA (Table II). In addition, there was no difference on the basis of chorionicity in GA prediction by using our singleton TCD nomogram with greater than 98% of TCD predicted GA within 3 days of actual GA, regardless of chorionicity (Table III).

Comment

The number of twin pregnancies has been increasing in the United States and in other western countries.[14-17] Accurate gestational dating is of paramount importance and the cornerstone for management of pregnancies, especially those carrying twins and higher-order multiples. Tools to date pregnancies especially at later GA should be simple to use. Our study corroborates those of Goldstein et al[3,4] and shows that 1 nomogram derived from

Table III Accuracy of TCD measurements in predicting GA in twins

Actual-to-expected GA (d)	Total (%) (n = 1278)	Placental chorionicity (%)	
		Monochorionic (n = 250)	Dichorionic (n = 1028)
0	41.3	37.3	42.3
±1	88.2	84.1	89.2
±2	98.1	95.6	98.7
±3	99.6	98.4	99.9
±4	99.7	98.8	99.9
±5	99.8	99.2	100.0
±6	100.0	100.0	100.0

singletons for TCD can effectively be used in twin gestations for accurate prediction of GA. These studies collectively provide convincing data and resolve the question of the need for separate nomograms for multiple gestations or based on chorionicity.

Although our study and Goldstein et al[3,4] previously published work concur, we also established that chorionicity does not alter the accuracy of dating by using TCD measurements. In addition, we described the accuracy of actual-to-expected GA that could be obtained. Our study also had the advantage of a larger sample size and used robust statistical methodology for fetal nomogram construction that has been published and tested by Altman and Chitty.[18,19]

Accurate and easily reproducible ultrasound fetal biometry parameter for gestational dating is clinically important for the optimal obstetric management of pregnancies, especially in determining timing of a variety of gestational tests, assessing adequacy of growth, and timing of delivery. The ability to predict GA within 5 to 6 days in the second and third trimesters for twins provides a solid foundation for planning clinical management. The robustness of the singleton nomograms is a testament to using sound statistical methodology for the construction and validation of clinically useful fetal biometric parameters. However, from a biologic perspective, it confirms that the cerebellar size is relatively unaffected by fetal number. This is in contrast to several other biometric parameters, especially abdominal circumference, which may be relatively smaller in twins.[9]

The current study is based on large number of well-dated twin gestations. The analysis is based on robust statistical methodology and provides reassurance that the TCD is unaffected in twin gestations, regardless of chorionicity—an observation that was previously confirmed in singleton gestations. Given that the study is from a single institution, whether these findings apply in other patient settings and populations remains unknown. Another limitation of the study is regarding the accurate assignment of placental chorionicity with pathology confirmation.

The results of this and previously published studies on TCD from our institution are encouraging.[1,2] However, it is likely that additional small improvements in accurate gestational dating can be achieved by incorporating the results of TCD with some combination of other fetal biometric parameters, including head circumference, biparietal diameter, and femur length. Nevertheless, the best combination of biometry remains to be determined. Until the results of these studies become available, based on the encouraging results of this and previous studies,[1,2] we recommend that TCD be used as an important ultrasound biometric parameter in both singleton and twins (regardless of chorionicity) for prediction of GA.

References

1. Chavez MR, Ananth CV, Smulian JC, Yeo L, Oyelese Y, Vintzileos AM. Fetal transcerebellar diameter measurement with particular emphasis in the third trimester: a reliable predictor of gestational age. Am J Obstet Gynecol 2004;191:979-94.
2. Chavez MR, Ananth CV, Smulian JC, Lashley S, Kontopoulos EV, Vintzileos AM. Fetal transcerebellar diameter nomogram in singleton gestations with special emphasis in the third trimester: a comparison with previously published nomograms. Am J Obstet Gynecol 2003;189:1021-102.
3. Goldstein I, Reece EA. Cerebellar growth in normal and growth-restricted fetuses of multiple gestations. Am J Obstet Gynecol 1995;173:1343-8.
4. Goldstein I, Reece EA, Tamir A. Cerebellar growth in normal fetuses of multiple gestations. J Matern Fetal Neonatal Med 2002;11:188-91.
5. Shimizu T, Gaudette S, Nimrod C. Transverse cerebellar diameter in twin gestations. Am J Obstet Gynecol 1992;167:1004-8.
6. Lettieri L, Vintzileos AM, Rodis JF, Egan JF, Wolf EJ, McLean DA. Transverse cerebellar diameter measurements in twin pregnancies and the effect of intrauterine growth retardation. Am J Obstet Gynecol 1992;167:982-5.
7. Sherer DM, Divon MY. Fetal growth in multifetal gestation. Clin Obstet Gynecol 1997;40:764-70.
8. Reece EA, Yarkoni S, Abdalla M, Gabrielli S, Holford T, O'Connor TZ, et al. A prospective longitudinal study of growth in twin gestations compared with growth in singleton pregnancies. I: the fetal head. J Ultrasound Med 1991;10:439-43.
9. Campbell WA, Vintzileos AM, Rodis JF, Turner GW, Egan JF, Nardi DA. Use of the transverse cerebellar diameter/abdominal circumference ratio in pregnancies at risk for intrauterine growth retardation. J Clin Ultrasound 1994;22:497-502.
10. Ananth CV, Vintzileos AM, Shen-Schwarz S, Smulian JC, Lai YL. Standards of birth weight in twin gestations stratified by placental chorionicity. Obstet Gynecol 1998;91:917-24.
11. Carroll SG, Tyfield L, Reeve L, Porter H, Soothill P, Kyle PM. Is zygosity or chorionicity the main determinant of fetal outcome in twin pregnancies? Am J Obstet Gynecol 2005;193:757-61.
12. Dube J, Dodds L, Armson BA. Does chorionicity or zygosity predict adverse perinatal outcomes in twins? Am J Obstet Gynecol 2002;186:579-83.
13. Hatkar PA, Bhide AG. Perinatal outcome of twins in relation to chorionicity. J Postgrad Med 1999;45:33-7.
14. Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Menacker F, Munson ML. Births: final data for 2003. Natl Vital Stat Rep 2005;54:1-116.
15. Smulian JC, Ananth CV, Kinzler WL, Kontopoulos E, Vintzileos AM. Twin deliveries in the United States over three

decades: an age-period-cohort analysis. Obstet Gynecol 2004;104: 278-85.
16. Ananth CV, Joseph KS, Kinzler WL. The influence of obstetric intervention on trends in twin stillbirths: United States, 1989-99. J Matern Fetal Neonatal Med 2004;15:380-7.
17. Joseph KS, Marcoux S, Ohlsson A, Liu S, Allen AC, Kramer MS, et al; Fetal and Infant Heath Study Group of the Canadian Perinatal Surveillance System. Changes in stillbirth and infant mortality associated with increases in preterm birth among twins. Pediatrics 2001;108:1055-61.
18. Altmam DG, Chitty LS. Charts for fetal size, 1: methodology. BJOG 1994;101:29-34.
19. Altman DG, Chitty LS. New charts for ultrasound dating of pregnancy. Ultrasound Obstet Gynecol 1997;10:174-91.