Growth Disturbances—Risk of Intrauterine Growth Restriction
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence
1. Simon NV, Surosky BA, Shearer DM, Levisky JS. Effect of the pretest probability of intrauterine growth retardation on the predictiveness of sonographic estimated fetal weight in detecting IUGR: a clinical application of Bayes' theorem. *J Clin Ultrasound* 1990; 18(3):145-153.	10	405	Bayes' Theorem: Effect of clinical risk of intrauterine growth restriction (IUGR) on predictiveness of estimated fetal weight by US.	• The greater the risk of IUGR based on clinical findings, the greater the PPV of US for IUGR, but also the greater the likelihood of having a baby with IUGR even when the US estimated fetal weight was normal. • Assessing pre-US clinical risk of IUGR may improve clinical decision-making.	2
2. Skovron ML, Berkowitz GS, Lapinski RH, Kim JM, Chitkara U. Evaluation of early third-trimester ultrasound screening for intrauterine growth retardation. *J Ultrasound Med* 1991; 10(3):153-159.	9	69 of 768 infants were IUGR at birth	Comparative study. Assessment of US fetal biometry to detect IUGR using ROC curve analysis of data at 26-34 weeks.	• Estimated fetal weight and abdominal circumference were equivalently better than femur length/abdominal circumference at predicting IUGR. • Biometry done at 26-34 weeks was less predictive than when done within 2 weeks of delivery.	2
3. Dashe JS, McIntire DD, Lucas MJ, Leveno KJ. Effects of symmetric and asymmetric fetal growth on pregnancy outcomes. *Obstet Gynecol* 2000; 96(3):321-327.	3a	1,364	Retrospective cohort study to assess the prevalence of head circumference to abdomen circumference (HC/AC) asymmetry among small for gestational age (SGA) fetuses, and to determine the likelihood of adverse outcomes among asymmetric and symmetric SGA infants compared with their appropriate for gestational age (AGA) counterparts.	A neonatal outcome composite, including one or more of respiratory distress, intraventricular hemorrhage, sepsis, or neonatal death, was more frequent among asymmetric SGA than AGA infants (14% vs 5%, P=.001). Symmetric SGA infants were not at increased risk of morbidity compared with AGA infants.	2
4. A randomised trial of timed delivery for the compromised preterm fetus: short term outcomes and Bayesian interpretation. *Bjog* 2003; 110(1):27-32.	1	587 babies	Multicenter study. Randomized controlled trial to determine the optimal timing of deliver of preterm growth restricted fetuses.	Immediate vs delayed delivery did not demonstrate a difference in short term survival, but delay decreased the number of cesarean deliveries.	1
5. Thornton JG, Hornbuckle J, Vail A, Spiegelhalter DJ, Levene M. Infant wellbeing at 2 years of age in the Growth Restriction Intervention Trial (GRIT): multicentred randomised controlled trial. *Lancet* 2004; 364(9433):513-520.	1	573 babies	Multicenter study. Randomized controlled trial to determine the long-term outcomes for growth restricted infants delivered immediately vs delayed time interval.	Overall rate of death or disability was 55 (19%) of 290 immediate births, and 44 (16%) of 283 delayed births – they were similar.	1
6. Manning FA. The use of sonography in the evaluation of the high-risk pregnancy. *Radiol Clin North Am* 1990; 28(1):205-216.	12	N/A	Review of the use of biophysical profile (BPP) and its component tests. Use in IUGR is addressed.	• This summarizes Manning's extensive research on the BPP, so it is personal research conclusion rather than literature review opinion. • Pages 213-215, see flowcharts for management of IUGR. • BPP is a mainstay of management of IUGR or suspected IUGR.	4

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7. Tongsong T, Srisomboon J. Amniotic fluid volume as a predictor of fetal distress in intrauterine growth retardation. *Int J Gynaecol Obstet* 1993; 40(2):131-134.	9	242 with IUGR	Prospective study to determine the efficacy of amniotic fluid volume as a predictor of intrapartum fetal distress among pregnancies with IUGR compared with nonstress test.	• Among IUGR pregnancies, amniotic fluid volume was a reliable predictor of intrapartum fetal distress. • Sensitivity 84%, specificity 83%, PPV 37%, NPV 98%. • Amniotic fluid volume was comparable to nonstress test as a predictor.	2
8. Cosmi E, Ambrosini G, D'Antona D, Saccardi C, Mari G. Doppler, cardiotocography, and biophysical profile changes in growth-restricted fetuses. *Obstet Gynecol* 2005; 106(6):1240-1245.	9	145 singleton growth-restricted fetuses	Prospective study to assess from diagnosis to delivery the arterial and venous Doppler's and amniotic fluid indices of fetuses with idiopathic growth restriction.	• In fetuses with idiopathic growth restriction, reverse endiastolic flow is associated with increased risk of perinatal morbidity and mortality. • Venous Doppler's revealing absent or reversed flow in the ductus venous is associated with increased perinatal morbidity abdominal mortality.	2
9. Bewley S, Cooper D, Campbell S. Doppler investigation of uteroplacental blood flow resistance in the second trimester: a screening study for pre-eclampsia and intrauterine growth retardation. *Br J Obstet Gynaecol* 1991; 98(9):871-879.	10	977 unselected pregnancies	Cross-sectional study to access screening value of mid-trimester uteroplacental Doppler scans in normal, unselected pregnancies.	• With averaged resistive index (AVRI) of uterine arteries >95%, overall pregnancy risk was 67%, risk of severe abnormality 25%, but sensitivity was only 13% (all risk) and 21% (for severe risk). • With high AVRI in an individual, risk of complication increases as much as 9.8 times. • Not sufficiently sensitive to use as a routine screening test of unselected pregnancies.	2
10. Newnham JP, Patterson LL, James IR, Diepeveen DA, Reid SE. An evaluation of the efficacy of Doppler flow velocity waveform analysis as a screening test in pregnancy. *Am J Obstet Gynecol* 1990; 162(2):403-410.	10	535 medium-risk pregnancies	Prospective double-blind study to evaluate the efficacy of uterine and umbilical Doppler waveform analysis as a screening test for development of fetal hypoxia and IUGR.	• Uteroplacental systolic to diastolic ratios at 24 weeks was associated with subsequent fetal hypoxia. Sensitivity 24%, specificity 94%, 70% of abnormal tests did not have fetal hypoxia. • Umbilical artery (UA) systolic to diastolic ratio at 24-34 weeks was predictive of IUGR, but only weakly if no hypoxia. • Favors role for uteroplacental and UA Doppler in high-risk pregnancies, but not as a primary screening test for low risk pregnancies.	1

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11. Alfirevic Z, Neilson JP. Doppler ultrasonography in high-risk pregnancies: systematic review with meta-analysis. *Am J Obstet Gynecol* 1995; 172(5):1379-1387.	11	12 randomized controlled trials	Review all available (published and unpublished) randomized controlled trials of Doppler US of the umbilical artery in high-risk pregnancies.	Reduction in the number of antenatal admissions (44%, 95% CI: 28%-57%), inductions of labor (20%, 95% CI: 10%-28%), and cesarean sections for fetal distress (52%, 95% CI: 24%-69%) in the Doppler group and that the clinical action guided by Doppler US reduces the odds of perinatal death by 38% (95% CI: 15%-55%).	1
12. Benson CB, Belville JS, Lentini JF, Saltzman DH, Doubilet PM. Intrauterine growth retardation: diagnosis based on multiple parameters--a prospective study. *Radiology* 1990; 177(2):499-502.	10	39 IUGR 317 normal within 2 wks prior to delivery	Prospective study to test accuracy of a scoring system based on estimated fetal weight, amniotic fluid volume, and maternal blood pressure status to diagnose or exclude third trimester IUGR.	Score identifies 3 groups: • <50: excludes IUGR (3% probability) • 50-60: 13% probability of IUGR (indeterminate). • >60: 74% probability of IUGR (very likely) Scoring works best with accurate dating but is still better than any single parameter for pregnancies without accurate dating.	2
13. Ferrazzi E, Vegni C, Bellotti M, Borboni A, Della Peruta S, Barbera A. Role of umbilical Doppler velocimetry in the biophysical assessment of the growth-retarded fetus. Answers from neonatal morbidity and mortality. *J Ultrasound Med* 1991; 10(6):309-315.	9	85 IUGR fetuses	Comparative study to determine if abnormal umbilical (UA) Doppler pulsatility index (PI) predicts adverse outcome in pregnancies with abnormally low fetal growth, oligohydramnios, and non-reactive heart rate traces. Prospective, blinded study with delivery decisions made without knowledge of Doppler.	• With abnormal UA PI, newborns were delivered earlier, usually for fetal indication, were smaller and more asymmetrical than with normal UA PI. • Newborns between 1500-2500g had more severe although equally infrequent morbid episodes with abnormal UA PI. • Newborns between 1000-1500g had more frequent and more severe morbid episodes with abnormal UA PI. • With abnormal UA PI, biophysical monitoring should be more frequent, preferably on an inpatient basis, and acted upon readily as compared to normal UA PI.	2
14. Lombardi SJ, Rosemond R, Ball R, Entman SS, Boehm FH. Umbilical artery velocimetry as a predictor of adverse outcome in pregnancies complicated by oligohydramnios. *Obstet Gynecol* 1989; 74(3 Pt 1):338-341.	10	22 with subjective oligohydr-amnios	Prospective study to determine the predictive value of Doppler velocimetry in identifying the fetus with oligohydramnios at increased risk of adverse perinatal outcome.	• Group 1–normal UA waveforms: 12/13 had normal perinatal outcome. • Group 2–abnormal UA waveforms: 9/9 had abnormal perinatal outcome. • With oligohydramnios, UA Doppler is a useful discriminator of perinatal risk.	2

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15. Rochelson B, Bracero LA, Porte J, Farmakides G. Diagnosis of intrauterine growth retardation as a two-step process with morphometric ultrasound and Doppler umbilical artery velocimetry. *J Reprod Med* 1992; 37(11):925-929.	9	40 small-for-gestational-age (SGA) fetuses within 3 wks of delivery	Compare morphometry and UA Doppler separately and together to predict small fetuses and adverse outcomes.	• SGA accuracy: 65% by US, 92% by US and abnormal UA Doppler. • Adverse outcome: 62% with abnormal UA Doppler vs 14% with normal UA Doppler.	2
16. Tyrrell SN, Lilford RJ, Macdonald HN, Nelson EJ, Porter J, Gupta JK. Randomized comparison of routine vs highly selective use of Doppler ultrasound and biophysical scoring to investigate high risk pregnancies. *Br J Obstet Gynaecol* 1990; 97(10):909-916.	1	500 at high risk for IUGR or stillbirth	Randomized trial to compare routine with highly selective use of uterine and UA Doppler and biophysical profile (BPP) in high risk pregnancies to check for improved outcomes and/or iatrogenic preterm delivery.	• 902 BPP and Doppler assessments in the 250 study patients but only 12 in 250 controls. • Persistently abnormal BPP was always associated with absence of end diastolic flow. • No statistically significant difference between study and control groups in gestational age at induction of labor or in intervention rate. • Statistically significant lower frequency of depressed 5-minute Apgar scores in study group. • Statistically significant increased rate of serious neonatal morbidity in the control group.	1
17. James DK, Parker MJ, Smoleniec JS. Comprehensive fetal assessment with three ultrasonographic characteristics. *Am J Obstet Gynecol* 1992; 166(5):1486-1495.	15	103 fetuses at risk for chronic fetal asphyxia	Order and time scale for development of abnormalities of UA Doppler, abdominal circumference, BPP, and what is the short term outcome with abnormalities of these parameters in fetuses at risk of chronic asphyxia.	• Order of deterioration, but with very variable time scale: UA Doppler first, then abdominal circumference, and finally BPP. • Normal tests, abnormal UA Doppler alone, or abnormal abdominal circumference alone all had excellent prognosis. • Worst prognosis occurred with all three tests abnormal (28 fetuses). • Avoid intervention for normal tests or abnormal UA Doppler only or abnormal abdominal circumference only. • Consider deliver at ≥34 wks with abnormal UA Doppler and abdominal circumference before abnormal BPP. • Implement specific measures to prevent necrotizing enterocolitis in newborns in which all three prenatal parameters were abnormal.	2

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18. Morris JM, Trudinger BJ. Sonographic evaluation of intrauterine growth retardation. *Curr Opin Radiol* 1992; 4(2):102-110.	12	N/A	Review of the sonographic evaluation of IUGR.	• Not all small fetuses are the result of growth failure. Fetal behavioral characteristics and selective use of Doppler US may help identify the fetus at risk. • It is not practical to screen the entire pregnant population for IUGR. Use historic and clinical data to select a population at risk. • For sonographically small fetuses, UA Doppler is the best indicator of increased risk of morbidity. • Once a fetus is established as at risk, close assessment of fetal growth and behavior. (BPP or component tests) is needed. • Goal is optimal timing of delivery, ie, the point at which extrauterine survival, free of significant handicaps, is less hazardous than the in utero environment.	4
19. Dubinsky T, Lau M, Powell F, et al. Predicting poor neonatal outcome: a comparative study of noninvasive antenatal testing methods. *AJR Am J Roentgenol* 1997; 168(3):827-831.	9	97	Prospective cohort study to compare amniotic fluid indexes, umbilical cord arterial Doppler waveforms, nonstress tests, and BPPs for predicting poor neonatal outcomes in fetuses who are SGA.	Sensitivities for predicting poor outcome were as follows: cord Doppler imaging, 64%; low amniotic fluid volume (oligohydramnios), 32%; BPP, 18%; and nonstress test, 14%.	2
20. Ott WJ. Intrauterine growth restriction and Doppler ultrasonography. *J Ultrasound Med* 2000; 19(10):661-665; quiz 667.	9	578	Retrospective study of singleton fetuses to clarify the difference between the fetus that is SGA and the fetus with true IGUR.	UA Doppler blood flow studies were a better predictor of neonatal outcome than estimated fetal weight.	2
21. Rizzo G, Capponi A, Talone PE, Arduini D, Romanini C. Doppler indices from inferior vena cava and ductus venous in predicting pH and oxygen tension in umbilical blood at cordocentesis in growth-retarded fetuses. *Ultrasound Obstet Gynecol* 1996; 7(6):401-410.	10	209 normally grown fetuses and 89 growth-retarded fetuses	To assess the value of Doppler indices calculated from the inferior vena cava and ductus venous in the identification of acidemia and hypoxemia as determined by pH and gas analysis of fetal blood obtained by cordocentesis in growth-retarded fetuses.	The pre-load index in the inferior vena cava was the best explanatory variable for acidemia (chi 2 = 48.33; P≤0.001). Hypoxemia was predicted less well by venous indices. Systolic to diastolic ratio in the ductus venous (chi 2 = 9.46; P≤0.005).	2
22. Baschat AA, Cosmi E, Bilardo CM, et al. Predictors of neonatal outcome in early-onset placental dysfunction. *Obstet Gynecol* 2007; 109(2 Pt 1):253-261.	9	604 growth restricted fetuses less than 33 weeks gestation	Prospective multicenter study to evaluate relationships between Doppler abnormalities and perinatal outcomes	• Gestational age was the most significant predictor of survival and intact survival. • Birth weight greater than 600 grams, ductus venous Doppler and cord artery ph predicted neonatal mortality. • Ductus venous Doppler alone predicted intact survival.	2

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23. Snijders RJ, Sherrod C, Gosden CM, Nicolaides KH. Fetal growth retardation: associated malformations and chromosomal abnormalities. *Am J Obstet Gynecol* 1993; 168(2):547-555.	3b	458 IUGR fetuses	To determine the incidence and pattern of chromosomal abnormalities determined by fetal blood sampling among fetus with IUGR at 17-39 weeks.	• 369 normal karyotype. 89 (19%) abnormal • <26 weeks, triploidy most common • >26 weeks, trisomy 18 most common • 96% of chromosomally abnormal fetuses had multisystem fetal defects characteristic for the abnormal karyotype • Compared to IUGR fetuses with normal karyotype, aneuploid cases had higher head circumference to abdominal circumference ratio, higher incidence of normal or high amniotic fluid, and of normal uterine or UA wave forms or both.	2

Evidence Table Key

Study Type Key

Numbers 1-7 are for studies of therapies while numbers 8-15 are used to describe studies of diagnostics.

1. Randomized Controlled Trial — Treatment
2. Controlled Trial
3. Observation Study
    a. Cohort
    b. Cross-sectional
    c. Case-control
4. Clinical Series
5. Case reviews
6. Anecdotes
7. Reviews
8. Randomized Controlled Trial — Diagnostic
9. Comparative Assessment
10. Clinical Assessment
11. Quantitative Review
12. Qualitative Review
13. Descriptive Study
14. Case Report
15. Other (Described in text)

Strength of Evidence Key

- Category 1 - The conclusions of the study are valid and strongly supported by study design, analysis and results.
- Category 2 - The conclusions of the study are likely valid, but study design does not permit certainty.
- Category 3 - The conclusions of the study may be valid but the evidence supporting the conclusions is inconclusive or equivocal.
- Category 4 - The conclusions of the study may not be valid because the evidence may not be reliable given the study design or analysis.