

Assessment of Fetal Well-Being
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Signore C, Freeman RK, Spong CY. Antenatal testing-a reevaluation: executive summary of a Eunice Kennedy Shriver National Institute of Child Health and Human Development workshop. <i>Obstet Gynecol.</i> 2009;113(3):687-701.	Review/Other-Dx	N/A	A summary of the discussions at the workshop, including synopses of oral presentations on the epidemiology of stillbirth and fetal neurological injury, fetal physiology, techniques for antenatal monitoring, and maternal and fetal indications for monitoring.	No results stated in abstract.	4
2. ACOG practice bulletin. Antepartum fetal surveillance. Number 9, October 1999 (replaces Technical Bulletin Number 188, January 1994). Clinical management guidelines for obstetrician-gynecologists. <i>Int J Gynaecol Obstet.</i> 2000;68(2):175-185.	Review/Other-Dx	N/A	To review the current indications for and techniques of antepartum fetal surveillance and outline management guidelines for antepartum fetal surveillance, consistent with the best contemporary scientific evidence.	No results stated in abstract.	4
3. Liston R, Sawchuck D, Young D. Fetal health surveillance: antepartum and intrapartum consensus guideline. <i>J Obstet Gynaecol Can.</i> 2007;29(9 Suppl 4):S3-56.	Review/Other-Dx	N/A	To provide new recommendations pertaining to the application and documentation of fetal surveillance in the antepartum and intrapartum period that will decrease the incidence of birth asphyxia while maintaining the lowest possible rate of obstetrical intervention.	A comprehensive review of randomized controlled trials published between January 1996 and March 2007 was undertaken, and MEDLINE and the Cochrane Database were used to search the literature for all new studies on fetal surveillance both antepartum and intrapartum. The level of evidence has been determined using the criteria and classifications of the Canadian Task Force on Preventive Health Care.	4
4. Berkley E, Chauhan SP, Abuhamad A. Doppler assessment of the fetus with intrauterine growth restriction. <i>Am J Obstet Gynecol.</i> 2012;206(4):300-308.	Review/Other-Dx	N/A	To provide evidence-based guidelines for utilization of Doppler studies for fetuses with IUGR.	Summary of randomized and quasirandomized studies indicates that, among high-risk pregnancies with suspected IUGR, the use of umbilical arterial Doppler assessment significantly decreases the likelihood of labor induction, cesarean delivery, and perinatal deaths (1.2% vs 1.7%; RR, 0.71; 95% CI, 0.52–0.98). Antepartum surveillance with Doppler of the UA should be started when the fetus is viable and IUGR is suspected. Although Doppler studies of the ductus venosus, middle cerebral artery and other vessels have some prognostic value for IUGR fetuses, currently there is a lack of randomized trials showing benefit. Thus, Doppler studies of vessels other than the UA, as part of assessment of fetal well-being in pregnancies complicated by IUGR, should be reserved for research protocols.	4

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5. Dugoff L. First- and second-trimester maternal serum markers for aneuploidy and adverse obstetric outcomes. <i>Obstet Gynecol.</i> 2010;115(5):1052-1061.	Review/Other-Dx	N/A	To review the relationships between these maternal serum levels of the first- and second-trimester markers and adverse obstetric outcomes. In addition, potential management strategies and future areas of research are discussed.	Maternal serum levels of the first- and second-trimester markers for aneuploidy have been shown to be associated with adverse obstetric outcomes in the absence of aneuploidy or neural-tube defects. The likelihood of an adverse obstetric outcome increases as the values of the marker become more extreme, and as the number of abnormal markers increases. Although many of the associations between maternal serum markers for aneuploidy and adverse obstetric outcomes are statistically significant, the sensitivity and positive predictive values for the individual outcomes are too low for them to be clinically useful as screening tests. Currently in the United States there is not a uniformly accepted practice for the care of women with abnormal maternal serum markers regarding risk of future obstetric complications. There are no randomized trials assessing any type of intervention or treatment for patients with abnormal serum markers.	4

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6. Moore TR, Piacquadio K. A prospective evaluation of fetal movement screening to reduce the incidence of antepartum fetal death. <i>Am J Obstet Gynecol.</i> 1989;160(5 Pt 1):1075-1080.	Observational-Dx	Control period: 2,519 births; Study period: 1,864 births	To conduct a study of the impact of a fetal movement screening program on perinatal outcome in a population of military dependent women.	During a 7-month control period, 2,519 deliveries occurred, no formal fetal movement assessment was done, and the fetal mortality rate was 8.7 per 1,000 births. A pilot study was conducted to validate a protocol in which the patient was instructed to record the elapsed time required to appreciate 10 fetal movements. The mean time interval was 20.9 ± 18.1 minutes (mean ± SO). Patients in whom 2 hours elapsed without 10 fetal movements (mean + 5 SO) were to report to the delivery unit for further evaluation. During the study period, 1,864 patients were delivered of infants and the fetal mortality rate was 2.1 per 1,000 (x2 = 6.8, P<0.01). During the study period the number of antepartum tests performed increased by 13%. Interventions for fetal compromise prompted by inadequate fetal activity tripled in the study period, resulting in a drop in fetal mortality among patients with decreased movement from 44 to 10 per 1,000.	3
7. Haws RA, Yakoob MY, Soomro T, Menezes EV, Darmstadt GL, Bhutta ZA. Reducing stillbirths: screening and monitoring during pregnancy and labour. <i>BMC Pregnancy Childbirth.</i> 2009;9 Suppl 1:S5.	Meta-analysis	N/A	To review available published evidence for the impact of 14 screening and monitoring interventions in pregnancy on stillbirth, including identification and management of high-risk pregnancies, advanced monitoring techniques, and monitoring of labor.	There was evidence of direct impact of any of these screening procedures and interventions on stillbirth incidence. Observational studies testing some interventions, including fetal movement monitoring and Doppler monitoring, showed some evidence of impact on stillbirths in selected high-risk populations, but require larger rigorous trials to confirm impact. Other interventions, such as amniotic fluid assessment for oligohydramnios, appear predictive of stillbirth risk, but studies are lacking which assess the impact on perinatal mortality of subsequent intervention based on test findings. Few rigorous studies of cardiotocography have reported stillbirth outcomes, but steep declines in stillbirth rates have been observed in high-income settings such as the U.S., where cardiotocography is used in conjunction with Caesarean section for fetal distress.	M

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8. Zelop CM, Javitt MC, Glanc P, et al. ACR Appropriateness Criteria(R) growth disturbances - risk of intrauterine growth restriction. <i>Ultrasound Q.</i> 2013;29(3):147-151.	Review/Other-Dx	N/A	ACR Appropriateness Criteria on growth disturbances-risk of IUGR.	N/A	4
9. Manning FA, Lange IR, Morrison I, Harman CR. Fetal biophysical profile score and the nonstress test: a comparative trial. <i>Obstet Gynecol.</i> 1984;64(3):326-331.	Experimental-Dx	735 patients	To determine the differences in predictive accuracy or perinatal outcome, if any, between the nonstress test and fetal BPP scoring.	Fetal BPP scoring resulted in a significantly higher positive predictive value in regards to low Apgar scores. Sensitivity, specificity, and accuracy, although higher with fetal BPP scoring, did not demonstrate significant differences when compared with the nonstress test. The negative predictive value between the 2 methods was similar. All major anomalies were detected during US scanning, whereas none of these anomalies were detected by heart rate testing alone.	1
10. Manning FA. Dynamic ultrasound-based fetal assessment: the fetal biophysical profile score. <i>Clin Obstet Gynecol.</i> 1995;38(1):26-44.	Review/Other-Dx	N/A	To review dynamic US-based fetal assessment and BPP score.	No results stated in abstract.	4
11. Pinette MG, Blackstone J, Wax JR, Cartin A. Using fetal acoustic stimulation to shorten the biophysical profile. <i>J Clin Ultrasound.</i> 2005;33(5):223-225.	Observational-Dx	870 patients	To determine whether fetal acoustic stimulation can decrease the time required to achieve a reassuring BPP.	A total of 870 patients were enrolled (458 control, 412 with stimulation). The fetal acoustic stimulation group had decreased testing time (3 minutes) and fewer nonreassuring tests (5%). The fetal acoustic stimulation group had fewer studies without breathing, potentially reducing the need for further testing or intervention.	3

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12. Chauhan SP, Doherty DD, Magann EF, Cahanding F, Moreno F, Klausen JH. Amniotic fluid index vs single deepest pocket technique during modified biophysical profile: a randomized clinical trial. <i>Am J Obstet Gynecol.</i> 2004;191(2):661-667; discussion 667-668.	Experimental-Dx	1,080 women	To determine the superior technique, if either, of the AFI vs the single deepest pocket technique in predicting an adverse pregnancy outcome among high-risk patients undergoing antenatal testing.	Between January of 1997 and December of 2001, 1,080 women were randomized with 530 women in the AFI arm, and 558 in the 2 x 1 pocket arm. The maternal demographics and prenatal complications were similar between groups. Significantly more patients were identified as having oligohydramnios using AFI (17%) compared with using 2 x 1 pocket (10%) ($P=.002$). The overall rate of cesarean section for nonreassuring fetal heart rate tracing was 3.8% (30 cases, with 16 cases in the AFI-monitored, and 14 cases in the 2 x 1 pocket-monitored groups, respectively, $P=.608$). Logistic regression analysis showed no difference between the groups with respect to the ability to identify patients who underwent cesarean section for nonreassuring fetal heart rate tracing during labor ($P=.999$). The UA pH <7.1 ($P=.688$) and admission to the newborn intensive care unit were also comparable between groups.	1
13. Acharya G, Wilsgaard T, Berntsen GK, Maltau JM, Kiserud T. Reference ranges for serial measurements of blood velocity and pulsatility index at the intra-abdominal portion, and fetal and placental ends of the umbilical artery. <i>Ultrasound Obstet Gynecol.</i> 2005;26(2):162-169.	Observational-Dx	130 participants with 513 sets of observations	To construct reference ranges for serial measurements of UA blood flow velocity and PI at standardized insonation sites during the second half of pregnancy.	UA blood velocities and PI were higher at the intra-abdominal portion and fetal end than at the placental end. The gestational age-related increase of end-diastolic velocity was greater than the corresponding increase of the peak systolic velocity at all locations. The mean differences (delta values) of UA blood velocities between the fetal and placental ends increased and that of PI decreased with advancing gestational age.	3
14. Figueras F, Fernandez S, Eixarch E, et al. Umbilical artery pulsatility index: reliability at different sampling sites. <i>J Perinat Med.</i> 2006;34(5):409-413.	Observational-Dx	100 singleton pregnancies	To analyze the inter-observer and inter-artery reliability of the UA PI at different sampling sites.	The mean percentage of PI difference between arteries was 15.2%, 14.5% and 22% at the placental end, free-loop and perivesical site, respectively. The Intraclass correlation coefficients at each site were 0.51, 0.59 and 0.67, respectively. Whereas about 20% of cases showed a percentage of PI difference between arteries >20% at free-loop and placental end sites, and at the perivesical site this figure was 45%.	2

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15. Khare M, Paul S, Konje JC. Variation in Doppler indices along the length of the cord from the intraabdominal to the placental insertion. <i>Acta Obstet Gynecol Scand.</i> 2006;85(8):922-928.	Observational-Dx	71 fetuses	To assess the feasibility of obtaining UA Doppler waveforms from the intra-abdominal portion (perivesical) of the umbilical arteries and to compare the indices from this site to those from the free loop of cord placental insertion and abdominal insertion.	Doppler waveforms acceptable for inclusion in the study were obtained in 100% of cases from the free loop site. There were failures to obtain waveforms that met the inclusion criteria in 3 (4%) cases at the placental insertion site, 3 (4.2%) cases at the PVC site, and 12 (16.9%) cases at the abdominal insertion. The 3 indices fell progressively with gestation from the PVC to the placental insertion sites. There were no significant differences between the 2 PVC arteries using nonparametric test of mean difference for related samples using Wilcoxon signed-rank test ($P>0.05$) for all the indices. The relation between the differences at the 2 ends of the cord was fairly consistent across gestation.	3
16. Meher S, Hernandez-Andrade E, Basheer SN, Lees C. Impact of cerebral redistribution on neurodevelopmental outcome in small-for-gestational-age or growth-restricted babies: a systematic review. <i>Ultrasound Obstet Gynecol.</i> 2015;46(4):398-404.	Review/Other-Dx	9 studies	To review systematically the evidence on impact of cerebral redistribution, as assessed by fetal middle cerebral artery Doppler, on neurological outcomes in SGA or growth-restricted fetuses.	The search yielded 1180 possible citations, of which 9 studies were included in the review, with a total of 1198 fetuses. Definitions of SGA and cerebral redistribution were variable, as was study quality. Data could not be synthesized in meta-analyses because of heterogeneity in outcome reporting. Cerebral redistribution was not associated with increased risk of intraventricular hemorrhage in neonates (5 studies; n = 806). When present in preterm fetuses, cerebral redistribution was associated with normal Neonatal Behavioral Assessment Scale (NBAS) scores at 40 weeks (1 study; n = 62) but abnormal psychomotor development at 1 year of age on the Bayley scale (1 study; n = 172). When present in term SGA fetuses, cerebral redistribution was associated with increased risk of motor and state organizational problems on NBAS (2 studies; n = 158), and lower mean percentile scores in communication and problem solving at 2 years of age on the Ages and Stages Questionnaire (1 study; n = 125).	4

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17. DeVore GR. The importance of the cerebroplacental ratio in the evaluation of fetal well-being in SGA and AGA fetuses. <i>Am J Obstet Gynecol.</i> 2015;213(1):5-15.	Review/Other-Dx	8 studies	To review the data from studies in which CPR has been evaluated in fetuses that were appropriate for gestational age and those with SGA to determine whether this test should be considered for integration into clinical practice.	Fetuses with an abnormal CPR that are appropriate for gestational age or have late-onset SGA (>34 weeks of gestation) have a higher incidence of fetal distress in labor requiring emergency cesarean delivery, a lower cord pH, and an increased admission rate to the newborn intensive care unit when compared with fetuses with a normal CPR. Fetuses with early-onset SGA (<34 weeks of gestation) with an abnormal CPR have a higher incidence of the following when compared with fetuses with a normal CPR: (1) lower gestational age at birth, (2) lower mean birthweight, (3) lower birthweight centile, (4) birthweight less than the 10th centile, (5) higher rate of cesarean delivery for fetal distress in labor, (6) higher rate of Apgar scores less than 7 at 5 minutes, (7) an increased rate of neonatal acidosis, (8) an increased rate of newborn intensive care unit admissions, (9) higher rate of adverse neonatal outcome, and (10) a greater incidence of perinatal death. The CPR is also an earlier predictor of adverse outcome than the BPP, UA, or middle cerebral artery.	4
18. Bakalis S, Akolekar R, Gallo DM, Poon LC, Nicolaides KH. Umbilical and fetal middle cerebral artery Doppler at 30-34 weeks' gestation in the prediction of adverse perinatal outcome. <i>Ultrasound Obstet Gynecol.</i> 2015;45(4):409-420.	Observational-Dx	30,780 singleton pregnancies	The objective of this screening study was to investigate the potential value of CPR at 30–34 weeks' gestation in the prediction of adverse perinatal outcome, by examining the relationship between CPR and birth-weight Z-score according to the rates of stillbirth, Cesarean section for fetal distress, umbilical arterial cord blood pH <7.0, umbilical venous cord blood pH <7.1, 5-min Apgar score <7 and admission to neonatal unit or the neonatal intensive care unit.	There was a significant association between CPR and birth-weight Z-score. In addition to maternal characteristics, medical history and obstetric factors, measuring CPR provided a significant contribution to the prediction of arterial cord blood pH ≤7.0, venous cord blood pH ≤7.1 and admission to neonatal unit. The performance of CPR in screening for each adverse outcome was poor, with detection rate of 5%–11% and a false-positive rate of about 5%. In the small subgroup of the population delivering within 2 weeks following assessment, the detection rate improved to 20%–50%, but with a simultaneous increase in false-positive rate to 10%–23%.	3

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19. Khalil AA, Morales-Rosello J, Morlando M, et al. Is fetal cerebroplacental ratio an independent predictor of intrapartum fetal compromise and neonatal unit admission? <i>Am J Obstet Gynecol.</i> 2015;213(1):54 e51-10.	Observational-Dx	8382 singleton pregnancies	To evaluate the association between fetal CPR and intrapartum fetal compromise and admission to the neonatal unit in term pregnancies.	The study cohort included 9772 singleton pregnancies. The rates of operative delivery for presumed fetal compromise and neonatal admission were 17.2% and 3.9%, respectively. Doppler CPR multiples of median was significantly lower in pregnancies requiring operative delivery or admission to neonatal unit for presumed fetal compromise ($P<.01$). On multivariate logistic regression, both CPR multiples of median and birthweight centile were independently associated with the risk of operative delivery for presumed fetal compromise (adjusted OR, 0.67; 95% CI, 0.52–0.87; $P=.003$ and adjusted OR, 0.994; 95% CI, 0.992–0.997; $P<.001$, respectively). The latter associations persisted even after exclusion of SGA cases from the cohort. Multivariate logistic regression also demonstrated that CPR multiples of median was an independent predictor for neonatal unit admission at term (adjusted OR, 0.55; 95% CI, 0.33–0.92; $P=.021$), while birthweight centile was not (adjusted OR, 1.00; 95% CI, 0.99–1.00; $P = .794$). The rates of operative delivery for presumed fetal compromise were significantly higher for appropriate-for-gestational-age fetuses with low CPR multiples of median (22.3%) compared to SGA fetuses with normal CPR multiples of median (17.3%).	4
20. Morales-Rosello J, Khalil A. Fetal cerebral redistribution: a marker of compromise regardless of fetal size. <i>Ultrasound Obstet Gynecol.</i> 2015;46(4):385-388.	Review/Other-Dx	N/A	To explain the rationale to support the role of fetal cerebral redistribution in the identification of fetuses that have failed to reach their growth potential in order to improve identification of adverse outcome at term.	No abstract available.	4

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21. Huhta JC. Fetal congestive heart failure. <i>Semin Fetal Neonatal Med.</i> 2005;10(6):542-552.	Review/Other-Dx	N/A	To present a straightforward method for rapid evaluation of a fetus that may have congestive heart failure.	Fetal echocardiography is used in the diagnosis of many forms of CHD, and in the assessment of the prognosis of cardiac lesions based on their anatomy and presentation in utero. However, the presence of signs of fetal heart failure such as hydrops or valvular regurgitation makes the assessment of prognosis more difficult. A tool for this assessment is the 'CVP score', which combines ultrasonic markers of fetal cardiovascular unwellness based on univariate parameters that have been correlated with perinatal mortality. This profile could become the 'heart failure score' and could potentially be used in much the same way as and in combination with the BPP score.	4
22. Byrne FA, Lee H, Kipps AK, Brook MM, Moon-Grady AJ. Echocardiographic risk stratification of fetuses with sacrococcygeal teratoma and twin-reversed arterial perfusion. <i>Fetal Diagn Ther.</i> 2011;30(4):280-288.	Observational-Dx	19 fetuses (11 sacrococcygeal teratoma, 8 twin-reversed arterial perfusion); 26 detailed fetal echocardiographic studies	To evaluate preintervention echocardiographic parameters of cardiac function in fetuses who survive without hydrops as compared to fetuses who develop hydrops or perinatal death in the setting of sacrococcygeal teratoma and twin-reversed arterial perfusion sequence.	In total, 19 fetuses (11 sacrococcygeal teratoma, 8 twin-reversed arterial perfusion) met the inclusion criteria and 26 detailed fetal echocardiographic studies were reviewed. Outcome was poor in 7 pregnancies (group A) and good in 12 (group B). Group A had worse CVP scores (8.5 vs 10, $P<0.01$) and higher cardiothoracic ratio (0.37 vs 0.30, $P=0.04$). At least 1 of the following was present in each group A fetus: cardiothoracic ratio >0.5 , combined ventricular output >550 mL/min/kg, tricuspid or mitral regurgitation, or mitral valve Z-score >2 . No group B fetus had any of these abnormalities. No fetus in either group had abnormal venous Doppler waveforms at presentation.	4

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<p>23. Huhta JC, Paul JJ. Doppler in fetal heart failure. <i>Clin Obstet Gynecol.</i> 2010;53(4):915-929.</p>	<p>Review/Other-Dx</p>	<p>N/A</p>	<p>To present a summary of fetal Doppler and its place in the diagnosis and assessment of prognosis of fetal heart failure.</p>	<p>Fetal echocardiography has progressed to be able to diagnose many forms of CHD and to assess the prognosis of cardiac lesions based on their anatomy and presentation in utero. Fetal echocardiography is for pregnancies at risk of structural, functional, and rhythm-related fetal heart disease. Routine obstetrical US screening is critical in the prenatal detection of fetal heart disease/CHD. With or without CHD, fetal heart dysfunction defined as inadequate tissue perfusion may occur. Perinatal problems other than CHD can also be assessed, such as the effects of noncardiac malformations that affect hemodynamics, that is, twin-twin transfusion. Cardiac rhythm can affect cardiac function and outcome, and prenatal diagnosis can be lifesaving. A tool for the assessment of cardiac function is the CVP Score that combines ultrasonic markers of fetal cardiovascular unwellness based on univariate parameters, which have been correlated with perinatal mortality. This “heart failure score” could potentially be used in much the same way as and in combination with the BPP score.</p>	<p>4</p>

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24. Pruetz JD, Votava-Smith J, Miller DA. Clinical relevance of fetal hemodynamic monitoring: Perinatal implications. <i>Semin Fetal Neonatal Med.</i> 2015;20(4):217-224.	Review/Other-Dx	N/A	To reviews the essential tools and techniques used for hemodynamic monitoring of the fetus and their clinical importance from the obstetricians', perinatologists', neonatologists', and pediatric sub-specialists' perspective.	US evaluation of the fetus using 2D, color Doppler and pulse-wave Doppler techniques form the foundation of antenatal diagnosis of structural anomalies, rhythm abnormalities and altered fetal circulation. Accurate and timely prenatal identification of the fetus at risk is critical for appropriate parental counseling, antenatal diagnostic testing, consideration for fetal intervention, perinatal planning, and coordination of postnatal care delivery. Fetal hemodynamic monitoring and serial assessment are vital to ensuring fetal wellbeing, particularly in the setting of complex congenital anomalies. A complete hemodynamic evaluation of the fetus gives important information on the likelihood of a smooth postnatal transition and contributes to ensuring the best possible outcome for the neonate.	4
25. Awadh AM, Prefumo F, Bland JM, Carvalho JS. Assessment of the intraobserver variability in the measurement of fetal cardiothoracic ratio using ellipse and diameter methods. <i>Ultrasound Obstet Gynecol.</i> 2006;28(1):53-56.	Observational-Dx	200 singleton pregnancies	To assess the variability of fetal heart and thoracic area and circumference measurements using the ellipse and diameter methods at different gestational ages.	For the same method, intraobserver variability was good. Coefficient of variation for all measurements varied between 3%–11%. The ellipse method tended to give larger measurements than did the diameter method, the absolute difference increasing with fetal age. The mean ellipse/diameter ratio was 1.10, 1.04, 1.05 and 1.02 for heart area, thorax area, heart circumference and thorax circumference, respectively. In most cases, intraobserver variability of the thorax measurements was independent of gestational age. In contrast, there was a greater variability of heart measurements with increasing gestational age.	3
26. AIUM practice guideline for the performance of fetal echocardiography. <i>J Ultrasound Med.</i> 2013;32(6):1067-1082.	Review/Other-Dx	N/A	To provide practice guidelines for the performance of fetal echocardiography.	No results stated in abstract.	4

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27. Schneider C, McCrindle BW, Carvalho JS, Hornberger LK, McCarthy KP, Daubeney PE. Development of Z-scores for fetal cardiac dimensions from echocardiography. <i>Ultrasound Obstet Gynecol.</i> 2005;26(6):599-605.	Observational-Dx	130 fetuses	To produce formulae and nomograms allowing computation of Z-scores for fetal cardiac dimensions from knowledge of femur length, biparietal diameter or gestational age using fetal echocardiography.	The relationships between cardiac dimensions and femur length, biparietal diameter, or gestational age were described following natural log transformation. From this analysis, femur length (taken as an expression of fetal size) had the highest correlation to fetal cardiac dimensions. From the developed nomograms, Z-scores of specific fetal cardiac structures could be estimated from knowledge of the femur length, biparietal diameter, or gestational age and echocardiographically derived measurements.	3
28. Figueras F, Benavides A, Del Rio M, et al. Monitoring of fetuses with intrauterine growth restriction: longitudinal changes in ductus venosus and aortic isthmus flow. <i>Ultrasound Obstet Gynecol.</i> 2009;33(1):39-43.	Observational-Dx	162 observational on 46 fetuses	To explore in growth-restricted fetuses the sequence of changes in aortic isthmus and ductus venosus blood flow in relation to other arterial Doppler parameters commonly used to evaluate fetal wellbeing.	A total of 162 observations were performed on 46 fetuses (median, 3; range, 2–10). The median gestational age at inclusion was 28.9 (range, 23.6–33.4) weeks and delivery occurred at a median gestational age of 30.5 (range, 25.9–33.9) weeks. 6 (13%) cases of perinatal mortality occurred. Umbilical and middle cerebral artery Doppler showed an almost linear deterioration throughout monitoring, becoming abnormal on average 24 days and 20 days before delivery, respectively. Aortic isthmus Doppler became abnormal on average 13 days before delivery, while ductus venosus Doppler did so within the last week before delivery.	3
29. Eidem BW, Edwards JM, Cetta F. Quantitative assessment of fetal ventricular function: establishing normal values of the myocardial performance index in the fetus. <i>Echocardiography.</i> 2001;18(1):9-13.	Observational-Dx	125 normal fetuses	To define the myocardial performance index in a group of normal fetuses and compare these data to other published studies of this index.	In normal fetuses, the left ventricular myocardial performance index was 0.36 +/- 0.06 and the right ventricular myocardial performance index was 0.35 +/- 0.05. This was not statistically different from the group of normal children in whom the left ventricular myocardial performance index was 0.35 +/- 0.03 and the right ventricular myocardial performance index was 0.32 +/- 0.03. In addition, no significant change in the fetal myocardial performance index was seen with advancing gestational age.	4

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30. Friedman D, Buyon J, Kim M, Glickstein JS. Fetal cardiac function assessed by Doppler myocardial performance index (Tei Index). <i>Ultrasound Obstet Gynecol.</i> 2003;21(1):33-36.	Review/Other-Dx	N/A	To determine normal values of fetal left ventricular Tei Index in second- and third-trimester fetuses and to compare these to other values reported in the literature.	The normal Tei Index in second- and early third-trimester fetuses (18–31 weeks' gestation) was 0.53 +/- 0.13. The isovolumic contraction time was 43 +/- 14 ms, the ejection time was 173 +/- 16 ms and the isovolumic relaxation time was 48 +/- 13 ms.	4
31. Tsutsumi T, Ishii M, Eto G, Hota M, Kato H. Serial evaluation for myocardial performance in fetuses and neonates using a new Doppler index. <i>Pediatr Int.</i> 1999;41(6):722-727.	Observational-Dx	50 normal fetuses, 35 fetuses with (IUGR, 30 fetuses of diabetic mothers and 20 normal infants	To longitudinally determine the Tei index.	The Tei index of the left ventricle decreased linearly with advancing gestational age during 18–33 weeks and decreased acceleratively with increasing gestational age after 34 weeks. The index of the right ventricle decreased slightly and linearly with advancing gestational age during 18–41 weeks. In neonates, the Tei index of the left and right ventricle increased immediately and transiently after birth and decreased and stabilized after 24 hours of life. From 18 to 26 weeks of gestation, the Tei indices in fetuses with IUGR and of diabetic mothers were not significantly different from controls. However, from 27 to 40 weeks of gestation, the Tei indices in both fetuses with IUGR and of diabetic mothers were significantly greater than controls.	3
32. Glickstein J, Buyon J, Kim M, Friedman D. The fetal Doppler mechanical PR interval: a validation study. <i>Fetal Diagn Ther.</i> 2004;19(1):31-34.	Review/Other-Dx	15 physicians	To evaluate the accuracy of pulsed Doppler-derived fetal PR interval measurements obtained by physicians participating in a multicenter prospective fetal echocardiographic study.	14 of the 15 physicians were considered to have adequate ability to measure the fetal PR interval according to our established criterion. The overall mean difference between the physicians and the central reader's measurements was -0.26 +/- 11.04 ms (P=0.84). In addition, 95% of the observed differences were included in the interval (-2.23 to 21.81), which is well within our clinically acceptable range of +/- 30 ms.	4
33. Van Bergen AH, Cuneo BF, Davis N. Prospective echocardiographic evaluation of atrioventricular conduction in fetuses with maternal Sjogren's antibodies. <i>Am J Obstet Gynecol.</i> 2004;191(3):1014-1018.	Observational-Dx	139 fetal echocardiograms	To evaluate the incidence of 1 degrees and 2 degrees atrioventricular block by measuring Doppler-derived mechanical PR intervals.	139 fetal echocardiograms performed on 59 SSA/SSB-positive pregnant women at 24.3 +/- 5.0 weeks gestation were compared with 150 controls. Mechanical PR intervals of the study group (120.5 +/- 9.8 milliseconds) and controls (120.6 +/- 8.7 milliseconds) were the same but differed significantly from fetuses with 1 degrees and 2 degrees atrioventricular block (191.5 +/- 29.6 milliseconds).	4

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34. Alfirevic Z, Stampalija T, Gyte GM. Fetal and umbilical Doppler ultrasound in normal pregnancy. <i>Cochrane Database Syst Rev.</i> 2010(8):CD001450.	Review/Other-Dx	5 trials with 14,185 women	To assess the effects on obstetric practice and pregnancy outcome of routine fetal and umbilical Doppler US in unselected and low-risk pregnancies.	5 trials involving 14,185 women were included. The methodological quality of the trials was generally unclear because of insufficient data included in the reports. Routine fetal and umbilical Doppler US examination in low-risk or unselected populations did not result in increased antenatal, obstetric and neonatal interventions, and no overall differences were detected for substantive short term clinical outcomes such as perinatal mortality. There is no available evidence to assess the effect on substantive long term outcomes such as childhood neurodevelopment and no data to assess maternal outcomes, particularly psychological effects.	4
35. Miller DA, Rabello YA, Paul RH. The modified biophysical profile: antepartum testing in the 1990s. <i>Am J Obstet Gynecol.</i> 1996;174(3):812-817.	Observational-Dx	15,482 women	To determine the false-negative and false-positive rates of antepartum testing by use of the modified BPP.	The false-negative rate of the antepartum testing protocol was 0.8 per 1,000 women tested. 60% of those delivered because of an abnormal antepartum test had no evidence of short-term or long-term fetal compromise. False-positive test results led to preterm delivery in 1.5% of those tested before term.	4
36. Bricker L, Neilson JP. Routine doppler ultrasound in pregnancy. <i>Cochrane Database Syst Rev.</i> 2000(2):CD001450.	Review/Other-Dx	5 trials with 14,338 women	To assess the effects on obstetric practice and pregnancy outcome of routine Doppler US in unselected and low risk pregnancies.	5 trials were included which recruited 14,338 women. The methodological quality of the trials was generally good. Based on existing evidence, routine Doppler US examination in low risk or unselected populations did not result in increased antenatal, obstetric and neonatal interventions, and no overall differences were detected for substantive short term clinical outcomes such as perinatal mortality. There is no available evidence to assess the effect on substantive long term outcomes such as childhood neurodevelopment. There is no available evidence to assess maternal outcomes, particularly psychological effects. In 2 studies there were unexpected findings suggesting possible harmful effects, but the explanation for this is not clear, and further evaluation regarding the safety of Doppler US is required.	4

* See Last Page for Key

Assessment of Fetal Well-Being
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
37. Manning FA, Morrison I, Harman CR, Lange IR, Menticoglou S. Fetal assessment based on fetal biophysical profile scoring: experience in 19,221 referred high-risk pregnancies. II. An analysis of false-negative fetal deaths. <i>Am J Obstet Gynecol.</i> 1987;157(4 Pt 1):880-884.	Review/Other-Dx	44,828 fetal BPP scores	To catalog all false-negative fetal deaths by number and associated etiologic factors and to calculate the probability of a fetal death within 1 week of a last normal fetal BPP score.	The incidence of false-negative fetal death, which is defined as stillbirth unrelated to major anomaly or alloimmunization occurring after a last normal fetal biophysical score, was determined in 19,221 referred high-risk pregnancies. The calculated rate of fetal death after a last normal test was 0.726/1000 (14 deaths), which remained relatively constant despite a progressive increase in tests and patients studied.	4
38. Fox NS, Rebarber A, Silverstein M, Roman AS, Klauser CK, Saltzman DH. The effectiveness of antepartum surveillance in reducing the risk of stillbirth in patients with advanced maternal age. <i>Eur J Obstet Gynecol Reprod Biol.</i> 2013;170(2):387-390.	Review/Other-Dx	4,469 patients	To estimate the effectiveness of antepartum surveillance and delivery at 41 weeks in reducing the risk of stillbirth in advanced maternal age patients.	4,469 patients met the inclusion criteria: 1,541 (34.5%) were advanced maternal age and 2,928 (65.5%) were non-advanced maternal age. Using our advanced maternal age protocol for surveillance and timing of delivery, the incidence of stillbirth was similar to the non-advanced maternal age population (stillbirth ≥ 20 weeks: 3.9 per 1,000 vs 3.4 per 1,000, $P=0.799$; stillbirth ≥ 36 weeks: 1.4 per 1,000 vs 1.1 per 1000, $P=0.773$). When looking at women age <35 , age 35–39, and age ≥ 40 , the incidence of stillbirth ≥ 20 weeks and ≥ 36 weeks did not increase across the 3 groups. Our findings were similar when we excluded all patients with other indications for antepartum surveillance.	4

**Assessment of Fetal Well-Being
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
39. Lalor JG, Fawole B, Alfirevic Z, Devane D. Biophysical profile for fetal assessment in high risk pregnancies. <i>Cochrane Database Syst Rev.</i> 2008(1):CD000038.	Meta-analysis	5 trials; 2,974 women	To assess the effects of the BPP when compared with conventional monitoring on pregnancy outcome in high-risk pregnancies.	We included 5 trials, involving 2,974 women. Most trials were not of high quality. Although the overall incidence of adverse outcomes was low, available evidence from randomized controlled trials does not support the use of BPP as a test of fetal wellbeing in high-risk pregnancies. We found no significant differences between the groups in perinatal deaths (RR 1.33, 95% CI, 0.60 to 2.98) or in Apgar score >7 at 5 minutes (RR 1.27, 95% CI, 0.85 to 1.92). Combined data from the 2 high-quality trials suggest an increased risk of caesarean section in the BPP group RR 1.60, 95% CI 1.05 to 2.44, n = 280, interaction test $P=0.03$. However, the number of participating women was relatively small (n = 280). Therefore, additional evidence is required in order to be definitive regarding the efficacy of this test in high-risk pregnancies. Furthermore, the impact of the BPP on other interventions, length of hospitalization, serious short-term and long-term neonatal morbidity and parental satisfaction requires further evaluation.	M
40. Magann EF, Doherty DA, Field K, Chauhan SP, Muffley PE, Morrison JC. Biophysical profile with amniotic fluid volume assessments. <i>Obstet Gynecol.</i> 2004;104(1):5-10.	Observational-Dx	AFI used 273 pregnancies and single deepest pocket in 264 pregnancies	To compare the AFI with the single deepest pocket technique along with the other components of the BPP in predicting an adverse pregnancy outcome.	The AFI was used in 273 pregnancies and the single deepest pocket in 264. The AFI significantly increased the number of pregnancies labeled as oligohydramnios, 102 women (38%) compared with 46 women (17%; $P<.001$), OR = 2.84, 95% CI, 1.90–4.25 in the single deepest pocket group. There was no difference in the number of women with oligohydramnios in the AFI group, 16/102 (16%), undergoing a cesarean delivery for fetal intolerance of labor compared with the single deepest pocket group, 6/46 (13%; $P=.676$). More women with normal fluid by the AFI method (AFI >5), 20/170 (12%), underwent a cesarean delivery for fetal distress than the women with normal fluid by the single deepest pocket technique (2 cm x 1 cm pocket present) group, 12/218 (6%; $P=.037$, OR = 2.22, 95% CI, 1.05–4.70).	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
41. Nabhan AF, Abdelmoula YA. Amniotic fluid index versus single deepest vertical pocket: a meta-analysis of randomized controlled trials. <i>Int J Gynaecol Obstet.</i> 2009;104(3):184-188.	Meta-analysis	4 trials (3,125 women)	To compare the use of the AFI with the single deepest vertical pocket measurement, during antepartum fetal surveillance, in preventing adverse pregnancy outcome.	4 trials (3,125 women) met the inclusion criteria. When the AFI was used, significantly more cases of oligohydramnios were diagnosed (RR 2.33, 95% CI, 1.67–3.24), and more women had inductions of labor (RR 2.10, 95% CI, 1.60–2.76) and cesarean delivery for fetal distress (RR 1.45, 95% CI, 1.07–1.97). There is no evidence that 1 method is superior to the other in the prevention of poor peripartum outcomes, including: admission to a neonatal intensive care unit; an UA pH of <7.1; the presence of meconium; an Apgar score of <7 at 5 minutes; or cesarean delivery.	M
42. Voxman EG, Tran S, Wing DA. Low amniotic fluid index as a predictor of adverse perinatal outcome. <i>J Perinatol.</i> 2002;22(4):282-285.	Observational- Dx	779 women	To determine whether an antepartum AFI of 5.0 cm or less is a predictor of adverse perinatal outcome.	An AFI of ≤ 5.0 cm was significantly associated with an abnormal antepartum fetal heart rate tracing but not with cesarean delivery, meconium-stained fluid, Apgar <7, or neonatal intensive care unit admission. Subjects with an AFI of ≤ 5.0 cm had a higher rate of cesarean for fetal distress, but this did not reach statistical significance. Receiver-operator curves produced no diagnostic cutoff values for AFI or largest pocket and prediction of any of the chosen parameters.	4
43. Rossi AC, Prefumo F. Perinatal outcomes of isolated oligohydramnios at term and post-term pregnancy: a systematic review of literature with meta-analysis. <i>Eur J Obstet Gynecol Reprod Biol.</i> 2013;169(2):149-154.	Meta-analysis	4 articles	To review outcomes of term and post-term pregnancies with isolated oligohydramnios vs normal amniotic fluid at labor assessment.	4 articles provided 679 (17.2%) cases with isolated oligohydramnios and 3,264 (82.8%) with normal amniotic fluid. Obstetric interventions occurred more frequently in the isolated oligohydramnios than normal amniotic fluid group (isolated oligohydramnios: 89/679, 13% vs normal; amniotic fluid: 166/3354, 5%; OR: 2.30; 95% CI: 1.00–5.29). Meta-analysis did not show differences with regard to meconium, Apgar, pH, SGA, neonatal intensive care unit and perinatal death.	M

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
44. Ohana O, Holcberg G, Sergienko R, Sheiner E. Risk factors for intrauterine fetal death (1988-2009). <i>J Matern Fetal Neonatal Med.</i> 2011;24(9):1079-1083.	Review/Other-Dx	1,694 intrauterine fetal death cases	To determine risk factors for intrauterine fetal death.	During the study period, out of 228,239 singleton births, 1,694 intrauterine fetal death cases were recorded (7.4 per 1,000 births). The following independent risk factors were identified in the logistic regression executed: Oligohydramnios (OR 2.6, 95% CI, 2.1-3.2, $P < 0.001$), polyhydramnios (OR 1.8, 95% CI, 1.4-2.2, $P < 0.001$), previous adverse perinatal outcome (OR 1.7, 95% CI, 1.5-2.1, $P < 0.001$), congenital malformations (OR 2.0, 95% CI, 1.8-2.3, $P < 0.001$), true knot of cord (OR 3.7, 95% CI, 2.8-4.9, $P < 0.001$), meconium stained amniotic fluid (OR 2.7, 95% CI, 2.3-3.0, $P < 0.001$), placental abruption (OR 2.9, 95% CI, 2.4-3.5, $P < 0.001$), advanced maternal age (OR 1.03, 95% CI, 1.02-1.04, $P < 0.001$), and hypertensive disorders (OR 1.24, 95% CI, 1.0-1.4, $P = 0.026$). Jewish ethnicity (vs Bedouin - OR 0.64, 95% CI, 0.57-0.72, $P < 0.001$), gestational diabetes (OR 0.7, 95% CI, 0.5-0.8, $P = 0.001$), previous cesarean section (OR 0.8, 95% CI, 0.7-0.97, $P = 0.019$), and recurrent abortions (OR 0.8, 95% CI, 0.6-0.9, $P = 0.011$) were negatively associated with intrauterine fetal death.	4
45. Casey BM, McIntire DD, Bloom SL, et al. Pregnancy outcomes after antepartum diagnosis of oligohydramnios at or beyond 34 weeks' gestation. <i>Am J Obstet Gynecol.</i> 2000;182(4):909-912.	Review/Other-Dx	6,423 pregnancies	To assess whether antepartum oligohydramnios is associated with adverse perinatal outcomes.	In our analysis of 6,423 pregnancies, 147 (2.3%) were complicated by oligohydramnios. This complication was associated with increased labor induction (42% vs 18%; $P < .001$), stillbirth (1.4% vs 0.3%; $P < .03$), nonreassuring fetal heart rate (48% vs 39%; $P < .03$), admission to the neonatal intensive care nursery (7% vs 2%; $P < .001$), meconium aspiration syndrome (1% vs 0.1%; $P < .001$), and neonatal death (5% vs 0.3%; $P < .001$).	4

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
46. Mazor M, Ghezzi F, Maymon E, et al. Polyhydramnios is an independent risk factor for perinatal mortality and intrapartum morbidity in preterm delivery. <i>Eur J Obstet Gynecol Reprod Biol.</i> 1996;70(1):41-47.	Observational-Dx	4,211 patients	To investigate the clinical significance of polyhydramnios as a predictor of perinatal death and intrapartum morbidity in patients with preterm delivery.	The prevalence of polyhydramnios among women who delivered preterm was 5% (210/4211) including and 3.7% (142/3818) excluding the cases of congenital malformations, respectively. Polyhydramnios was associated with a higher rate of diabetes, large for gestational age neonates, fetal malpresentation at delivery, previous perinatal death and with a lower Apgar score at 1 and 5 minutes. Polyhydramnios was an independent predictor of perinatal mortality and intrapartum morbidity. When adjusted for well recognized risk factors for perinatal mortality and intrapartum morbidity (eg, diabetes, severe pregnancy induced hypertension, multiparity, congenital malformation, previous perinatal death, low gestational age at delivery), the presence of polyhydramnios significantly increased the rate of perinatal mortality (OR 5.8; 95% CI, 3.68–9.11) and of intrapartum morbidity (OR 2.8; 95% CI, 1.94–4.03).	4
47. Pilliod RA, Page JM, Burwick RM, Kaimal AJ, Cheng YW, Caughey AB. The risk of fetal death in nonanomalous pregnancies affected by polyhydramnios. <i>Am J Obstet Gynecol.</i> 2015;213(3):410 e411-416.	Observational-Dx	1,850,951 pregnancies	To evaluate the ongoing risk of intrauterine fetal demise in nonanomalous pregnancies affected by polyhydramnios.	The risk of intrauterine fetal demise in pregnancies affected by polyhydramnios was greater at every gestational age compared with unaffected pregnancies. The intrauterine fetal demise risk in pregnancies affected by polyhydramnios was more than 7 times higher than unaffected pregnancies at 37 weeks at a rate of 18.0 (95% CI, 9.0–32.6) vs 2.4 (95% CI, 2.0–2.5) and was 11-fold higher by 40 weeks' gestational age at a rate of 66.3 (95% CI, 10.8–68.6) vs 6.0 (95% CI, 5.1–6.3) in unaffected pregnancies. When adjusted for multiple confounding variables, the presence of polyhydramnios remained associated with an increased odds of intrauterine fetal demise in nonanomalous singleton pregnancies, with an adjusted OR of 5.5 (95% CI, 4.1–7.6).	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
48. Pri-Paz S, Khalek N, Fuchs KM, Simpson LL. Maximal amniotic fluid index as a prognostic factor in pregnancies complicated by polyhydramnios. <i>Ultrasound Obstet Gynecol.</i> 2012;39(6):648-653.	Review/Other-Dx	524 singleton pregnancies	To evaluate the association between the maximal AFI and the frequency of specific adverse outcomes.	Higher AFI was associated with a statistically significant increase in the frequency of adverse pregnancy outcomes. The most severe form of polyhydramnios, as based on the maximal AFI (≥ 35 cm; n = 67), was associated with the highest rates of prenatally diagnosed congenital anomalies (79%), preterm delivery (46%), SGA neonate (16%), aneuploidy (13%) and perinatal mortality (27%). No significant association between degree of polyhydramnios and adverse outcome was demonstrated in cases of idiopathic polyhydramnios (n = 253).	4
49. Gonzalez JM, Stamilio DM, Ural S, Macones GA, Odibo AO. Relationship between abnormal fetal testing and adverse perinatal outcomes in intrauterine growth restriction. <i>Am J Obstet Gynecol.</i> 2007;196(5):e48-51.	Observational-Dx	151 singleton pregnancies	To compare the efficacy of nonstress test, BPP, or abnormal Dopplers in predicting adverse perinatal outcomes in IUGR.	151 singleton pregnancies with IUGR met the inclusion criteria. On bivariate analysis significant variables associated with adverse outcomes were as follows: history of chronic hypertension, corticosteroid administration, and gestational age of delivery. These were adjusted by using logistic regression. The positive predictive values of abnormal Doppler for respiratory distress syndrome and the composite of adverse outcomes were 36% and 42% respectively. Of the testing modalities compared, only abnormal Doppler significantly predicted respiratory distress syndrome and the composite of adverse outcome.	3

**Assessment of Fetal Well-Being
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
50. Baschat AA, Weiner CP. Umbilical artery doppler screening for detection of the small fetus in need of antepartum surveillance. <i>Am J Obstet Gynecol.</i> 2000;182(1 Pt 1):154-158.	Observational-Dx	308 fetuses	To test the hypothesis that UA Doppler velocimetry identifies fetuses who are SGA and in need of antenatal surveillance.	Only the UA systolic/diastolic ratio predicted perinatal outcome in the group of fetuses who were presumed to be SGA. Those 138 fetuses with elevated UA systolic/diastolic ratios had lower UA and vein pH values at birth (artery, 7.23 +/- 0.08 vs 7.25 +/- 0.1; $P < .02$; vein, 7.31 +/- 0.01 vs 7.34 +/- 0.09; $P = .01$), an increased likelihood of fetal distress consistent with chronic hypoxemia (26.3% vs 8.6%; $P < .0001$), more admissions to the neonatal intensive care unit (40.7% vs 30.7%; $P < .005$), and a higher incidence of respiratory distress (66% vs 27.3%; $P < .03$). However, it is important that no fetus with a normal Doppler flow measurement was delivered with a metabolic acidemia associated with chronic hypoxemia. Further, the likelihood of a false-positive diagnosis of IUGR was increased in the group with a normal UA Doppler resistance.	4
51. Hugo EJ, Odendaal HJ, Grove D. Evaluation of the use of umbilical artery Doppler flow studies and outcome of pregnancies at a secondary hospital. <i>J Matern Fetal Neonatal Med.</i> 2007;20(3):233-239.	Review/Other-Dx	572 singleton pregnancies	To investigate the use of a personal computer-based, continuous-wave Doppler machine by a trained midwife at a secondary hospital to assess UA flow velocity waveforms in referred women.	A total of 572 singleton pregnancies were followed up. Significantly more infants were SGA when the resistance index was $>P95$ (55.6%) than those between $P75$ and $P95$ (41.2%) or $<P75$ (27.2%). Perinatal mortality rates were 13.2, 39.1 and 41.7 for women with RIs $<P75$, $P75-95$ and $>P95$, respectively.	4

**Assessment of Fetal Well-Being
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
52. Alfrevic Z, Stampalija T, Gyte GM. Fetal and umbilical Doppler ultrasound in high-risk pregnancies. <i>Cochrane Database Syst Rev.</i> 2010(1):CD007529.	Meta-analysis	18 completed studies involving just over 10,000 women	To assess the effects of Doppler US used to assess fetal well-being in high-risk pregnancies on obstetric care and fetal outcomes.	18 completed studies involving just over 10,000 women were included. The trials were generally of unclear quality with some evidence of possible publication bias. The use of Doppler US in high-risk pregnancy was associated a reduction in perinatal deaths (RR 0.71, 95% CI, 0.52 to 0.98, 16 studies, 10,225 babies, 1.2% vs 1.7 %, numbers needed to treat = 203; 95% CI, 103 to 4,352). There were also fewer inductions of labor (average RR 0.89, 95% CI, 0.80 to 0.99, 10 studies, 5,633 women, random effects) and fewer caesarean sections (RR 0.90, 95% CI, 0.84 to 0.97, 14 studies, 7,918 women). No difference was found in operative vaginal births (RR 0.95, 95% CI, 0.80 to 1.14, 4 studies, 2,813 women) nor in Apgar scores <7 at 5 minutes (RR 0.92, 95% CI, 0.69 to 1.24, 7 studies, 6,321 babies).	M

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
53. Grivell RM, Wong L, Bhatia V. Regimens of fetal surveillance for impaired fetal growth. <i>Cochrane Database Syst Rev.</i> 2009(1):CD007113.	Review/Other-Dx	1 trial of 167 women and their babies	To assess the effects of antenatal fetal surveillance regimens on important perinatal and maternal outcomes.	1 trial of 167 women and their babies was included. This trial was a pilot study recruiting alongside another study, therefore a separate sample size was not calculated. The trial compared a twice-weekly surveillance regimen (BPP, nonstress tests, UA and middle cerebral artery Doppler and uterine artery Doppler) with the same regimen applied fortnightly (both groups had growth assessed fortnightly). There were insufficient data to assess this review's primary infant outcome of composite perinatal mortality and serious morbidity (although there were no perinatal deaths) and no difference was seen in the primary maternal outcome of emergency caesarean section for fetal distress. In keeping with the more frequent monitoring, mean gestational age at birth was 4 days less for the twice-weekly surveillance group compared with the fortnightly surveillance group. Women in the twice-weekly surveillance group were 25% more likely to have induction of labor than those in the fortnightly surveillance group. The risk ratio was 1.25 (95% CI, 1.04 to 1.50).	4
54. McCowan LM, Harding JE, Roberts AB, Barker SE, Ford C, Stewart AW. A pilot randomized controlled trial of two regimens of fetal surveillance for small-for-gestational-age fetuses with normal results of umbilical artery doppler velocimetry. <i>Am J Obstet Gynecol.</i> 2000;182(1 Pt 1):81-86.	Observational-Dx	167 patients	To determine whether the frequency of fetal surveillance could be safely reduced from twice weekly to fortnightly in the case of SGA fetuses with normal results of UA Doppler velocimetry studies.	85 women were randomly assigned to undergo twice-weekly fetal surveillance and 82 were randomly assigned to undergo fortnightly fetal surveillance. Those randomly assigned to twice-weekly surveillance were delivered 4 days earlier (264 vs 268 days; $P=.04$) and were more likely to have labor induced ($n = 70, 82\%$, vs $n = 54, 66\%$; $P=.02$) than those randomly assigned to fortnightly surveillance. 54 babies (23%) were admitted to the neonatal nursery, but there were no differences in neonatal morbidity between the groups.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
55. Hack KE, Kaandorp JJ, Derks JB, Elias SG, Pistorius L, Visser GH. The value of umbilical artery Doppler velocimetry in the antenatal surveillance of uncomplicated monochorionic twin pregnancies. <i>Ultrasound Obstet Gynecol.</i> 2008;31(6):662-668.	Observational-Dx	67 monochorionic twin pregnancies	To investigate the predictive value of abnormal UA Doppler findings on outcome in uncomplicated monochorionic twin pregnancies.	Mortality rates were similar in the normal and abnormal Doppler groups. Using both group definitions, total neonatal morbidity was higher in the abnormal Doppler group; this was significant at >32 weeks' gestation, and was due to lower birth weight and earlier gestational age at delivery. There was no mortality at ≥36 weeks in the abnormal Doppler group, but there were 4 perinatal deaths in the normal Doppler group. Gestational age at delivery was significantly lower when 1 or more abnormal Doppler findings had been present (median, 34 + 1 weeks vs 36 + 3 weeks) and infants with abnormal Doppler findings weighed on average 261 g (95% CI, 21–502 g) less than those with normal findings.	3
56. Westergaard HB, Langhoff-Roos J, Lingman G, Marsal K, Kreiner S. A critical appraisal of the use of umbilical artery Doppler ultrasound in high-risk pregnancies: use of meta-analyses in evidence-based obstetrics. <i>Ultrasound Obstet Gynecol.</i> 2001;17(6):466-476.	Meta-analysis	13 studies	To reanalyze randomized controlled trials on the use of UA Doppler velocimetry in high-risk pregnancies and determine which high-risk pregnancies benefit from the use of Doppler velocimetry.	The 'well-defined studies' had a more uniform study design as compared to the 'general risk studies' and they showed a significant reduction in antenatal admissions (OR, 0.56; 95% CI, 0.43–0.72), inductions of labor (0.78; 0.63–0.96), elective deliveries (inductions of labor and elective Cesarean sections) (0.73; 0.61–0.88) and Cesarean sections (0.78; 0.65–0.94). By perinatal audit it was found that more perinatal deaths in the 'well-defined studies' were potentially avoidable by use of Doppler velocimetry ($P < 0.0005$) and the rate of avoidable perinatal deaths was higher among controls (50%) than cases (20%) in this group.	M
57. Pessel C, Merriam A, Vani K, et al. Do Doppler studies enhance surveillance of uncomplicated monochorionic diamniotic twins? <i>J Ultrasound Med.</i> 2015;34(4):569-575.	Observational-Dx	96 Patients	To determine whether isolated abnormal Doppler indices before 28 weeks predict adverse pregnancy outcomes in uncomplicated monochorionic diamniotic twins.	96 patients were included, with 22 (22.9%) having isolated Doppler abnormalities before 28 weeks. The incidence of the primary outcome did not differ between groups (36.4% vs 28.4%; $P = .47$). The abnormal Doppler group underwent a greater number of US examinations (15 vs 10; $P = .001$) and more antenatal admissions for fetal concerns (50.0% vs 12.2%; $P < .001$).	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
58. Wieczorek A, Hernandez-Robles J, Ewing L, Leshko J, Luther S, Huhta J. Prediction of outcome of fetal congenital heart disease using a cardiovascular profile score. <i>Ultrasound Obstet Gynecol.</i> 2008;31(3):284-288.	Observational-Dx	131 singleton pregnancies	To assess the value of the CVP score in evaluating the condition and in maintaining surveillance of fetuses with CHD.	Fetuses with a final CVP score ≤ 7 were statistically significantly more likely to suffer mortality than were fetuses with a final CVP score ≥ 8 (87.5% vs 15.2% mortality; $P < 0.0001$, chi square = 24.5). Significance was maintained after controlling for birth weight, lag time between the final examination and delivery and the dichotomized 5-min Apgar score (OR, 22.3; $P = 0.024$). For low Apgar score and mortality, the CVP score had low sensitivity (0.25 and 0.27, respectively) but high specificity (0.98 and 0.99, respectively). The presence of hydrops and severe cardiomegaly were statistically significantly associated with mortality ($P < 0.05$).	4
59. Makikallio K, Rasanen J, Makikallio T, Vuolteenaho O, Huhta JC. Human fetal cardiovascular profile score and neonatal outcome in intrauterine growth restriction. <i>Ultrasound Obstet Gynecol.</i> 2008;31(1):48-54.	Observational-Dx	75 fetuses	To determine whether low CVP score has prognostic value for predicting neonatal mortality and severe morbidity in human fetuses with growth restriction.	During the neonatal period, 6/75 neonates died and 2 had cerebral palsy (Group 1, $n = 8$). Compared with the fetuses discharged home from hospital (Group 2, $n = 67$), those in Group 1 were delivered at an earlier gestational age (28 (range, 24–35) weeks vs 35 (range, 26–40) weeks, $P < 0.01$) and had lower CVP scores (4 (range, 2–6) vs 9 (range, 5–10), $P < 0.0001$). All CVP subscale scores were lower ($P < 0.01$) in Group 1 than in Group 2 fetuses. Gestational age-adjusted hazard ratios (95% CIs) for adverse neonatal outcome were highest for cardiomegaly (13.9 (1.7–114.3), $P = 0.014$), monophasic atrioventricular filling pattern or holosystolic tricuspid regurgitation (9.5 (2.3–38.4), $P = 0.002$) and atrial pulsations in the umbilical vein 7.7 (1.4–41.2), $P = 0.017$).	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>60. Friedman DM, Kim MY, Copel JA, et al. Utility of cardiac monitoring in fetuses at risk for congenital heart block: the PR Interval and Dexamethasone Evaluation (PRIDE) prospective study. <i>Circulation</i>. 2008;117(4):485-493.</p>	<p>Observational-Dx</p>	<p>95 patients</p>	<p>To determine the earliest noninvasive echocardiographic marker of atrioventricular nodal and/or myocardial injury.</p>	<p>The protocol included fetal echocardiograms performed weekly from 16 to 26 weeks' gestation and biweekly from 26 to 34 weeks. Pulse rate intervals >150 ms were considered prolonged, consistent with first-degree block. 92 fetuses had normal pulse rate intervals. Neonatal lupus developed in 10 cases; 4 were neonatal lupus rash only. 3 fetuses had third-degree block; none had a preceding abnormal pulse rate interval, although in 2 fetuses >1 week elapsed between echocardiographic evaluations. Tricuspid regurgitation preceded third-degree block in 1 fetus, and an atrial echodensity preceded block in a second. 2 fetuses had pulse rate intervals >150 ms. Both were detected at or before 22 weeks, and each reversed within 1 week with 4 mg dexamethasone. The electrocardiogram of 1 additional newborn revealed a prolonged pulse rate interval persistent at 3 years despite normal intervals throughout gestation. No first-degree block developed after a normal electrocardiogram at birth. Heart block occurred in 3/16 pregnancies (19%) in mothers with a previous child with congenital heart block and in 3/74 pregnancies (4%) in mothers without a previous child with congenital heart block or rash ($P=0.067$).</p>	<p>3</p>

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
61. Van Mieghem T, Hodges R, Jaeggi E, Ryan G. Functional echocardiography in the fetus with non-cardiac disease. <i>Prenat Diagn.</i> 2014;34(1):23-32.	Review/Other-Dx	N/A	To describe the hemodynamic changes observed in fetuses with extra cardiac conditions such as IUGR, tumors, twin-twin transfusion syndrome, congenital infections, and in fetuses of mothers with diabetes.	In most fetuses with mild extra cardiac disease, the alterations in fetal cardiac function remain subclinical. Cardiac function assessment has however helped us to achieve a better understanding of the pathophysiology of these diseases. In fetuses at the more severe end of the disease spectrum, functional echocardiography may help in guiding clinical decision-making regarding the need for either delivery or fetal therapy. The growth-restricted fetus represents a special indication for routine cardiac function assessment, as in utero hemodynamic changes may help optimize the timing of delivery. Moreover, in IUGR, the altered hemodynamics causes cardiovascular remodeling, which can result in an increased risk of postnatal cardiovascular disease.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>62. Baschat AA, Gembruch U, Harman CR. The sequence of changes in Doppler and biophysical parameters as severe fetal growth restriction worsens. <i>Ultrasound Obstet Gynecol.</i> 2001;18(6):571-577.</p>	<p>Observational-Dx</p>	<p>236 patients</p>	<p>To test the hypothesis that hemodynamic changes depicted by Doppler precede deteriorating BPP score in severe IUGR.</p>	<p>44/236 IUGR fetuses (18.6%) required delivery for abnormal BPP scoring. The median gestational age at entry was 25 weeks and 1 day and at delivery was 29 weeks and 6 days. The median interval between examinations was 1.5 days and the majority had daily testing in the week prior to delivery. Between first examination and delivery, significant deterioration was observed for Doppler criteria (chi-square, $P < 0.001$) and biophysical parameters (Fisher's exact, $P = 0.02$) predominantly confined to the week prior to delivery/stillbirth. Doppler variables changed first. In 42 fetuses (95.5%), 1 or more vascular beds deteriorated, accelerating especially in the UA and ductus venosus at a median of 4 days before BPP scoring deteriorated. 2 to 3 days before delivery, fetal breathing movement began to decline. The next day, amniotic fluid volume began to drop. Composite BPP score dropped abruptly on the day of delivery, with loss of fetal movement and tone. 3 principal patterns of Doppler deterioration were observed: (i) worsening UA PI, advent of brain sparing and venous deterioration (n = 32, 72.7%); (ii) abnormal precordial venous flows, advent of brain sparing (n = 6, 13.6%); and (iii) abnormal ductus venosus only (n = 4, 9.1%). In the majority (31, 70.5%), Doppler deterioration was complete 24 hours before BPP score decline. In the remainder (11, 25%), Doppler deterioration and BPP score $< 6/10$ were simultaneous.</p>	<p>3</p>

**Assessment of Fetal Well-Being
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
63. Baschat AA, Galan HL, Bhide A, et al. Doppler and biophysical assessment in growth restricted fetuses: distribution of test results. <i>Ultrasound Obstet Gynecol.</i> 2006;27(1):41-47.	Observational-Dx	328 IUGR fetuses	To examine the relationship between Doppler US and biophysical test results in IUGR fetuses.	Abnormal UA Doppler results alone were observed in 109 fetuses (33.2%), brain sparing in 87 (26.5%) and an abnormal ductus venosus in 132 (40.2%). The BPP scoring was normal in 158 (48.2%), equivocal in 68 (20.7%) and abnormal in 102 (31.1%). Both testing modalities stratified patients into groups with comparable acid-base disturbance and perinatal outcome. Of the 9 possible test combinations the largest subgroups were: abnormal UA alone/normal BPP scoring (n = 69; 21%) and abnormal ductus venosus Doppler/abnormal BPP scoring (n = 62; 18.9%). Assessment of compromise by both testing modalities was concordant in 146 (44.5%) cases. In 182 fetuses with discordant results the BPP scoring grade was better in 115 (63.2%, $P < 0.0001$). Marked disagreement of test abnormality was present in 57 (17.4%) fetuses. Of these, abnormal venous Doppler in the presence of a normal BPP scoring constituted the largest group (Chi-square $P < 0.002$). Stratification was not significantly different in patients delivered prior to 32 weeks' gestation.	3
64. Gerber S, Hohlfeld P, Viquerat F, Tolsa JF, Vial Y. Intrauterine growth restriction and absent or reverse end-diastolic blood flow in umbilical artery (Doppler class II or III): A retrospective study of short- and long-term fetal morbidity and mortality. <i>Eur J Obstet Gynecol Reprod Biol.</i> 2006;126(1):20-26.	Observational-Dx	69 IUGR fetuses	To study the short- and long-term morbidity and mortality among these children associated with our defined management.	In Group 1, stillbirth was observed after a mean delay of 6.3 days. Group 2 delivered at an average of 31.6 weeks and 2 died in the neonatal period (6%). In Group 3 after a mean delay of 8 days, average gestational age at delivery was 31.7 weeks; 2 intra uterine and 4 perinatal deaths were observed (22%). Long-term follow-up revealed no sequelae in 25/31 (81%) and 15/18 (83%), and major handicap occurred in 1 (3%) and 2 patients (11%), respectively, for Groups 2 and 3.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
65. Mandruzzato GP, Bogatti P, Fischer L, Gigli C. The clinical significance of absent or reverse end-diastolic flow in the fetal aorta and umbilical artery. <i>Ultrasound Obstet Gynecol.</i> 1991;1(3):192-196.	Review/Other-Dx	32 fetuses	To report the clinical management of pregnancies showing absence of end-diastolic flow and/or reverse flow in the fetal aorta and/or UA.	Reverse flow was observed in 11 cases and absence of end-diastolic flow in 21 cases. The 2 groups are considered separately. No significant difference was found in the mean gestational age at delivery. However, a highly significant difference was found in the mean birth weight and perinatal mortality rate. All the cases of perinatal mortality were encountered in the group presenting with reverse flow (mortality rate, 63.6%). All the live fetuses were delivered by Cesarean section and no neonatal mortality was observed in this group. 2 cases of handicap were observed, 1 in each group. In our experience, reverse flow indicates the necessity for immediate delivery if no other clinical contraindications are present. Absence of end-diastolic flow can be observed for longer periods without adverse outcome. Absence of end-diastolic flow always precedes the appearance of fetal distress.	4
66. Figueras F, Cruz-Martinez R, Sanz-Cortes M, et al. Neurobehavioral outcomes in preterm, growth-restricted infants with and without prenatal advanced signs of brain-sparing. <i>Ultrasound Obstet Gynecol.</i> 2011;38(3):288-294.	Observational-Dx	126 preterm newborns (64 controls and 62 IUGR)	To evaluate the neurobehavioral outcomes of preterm infants with IUGR, with and without prenatal advanced brain-sparing.	A total of 126 preterm newborns (64 controls and 62 IUGR) were included. Among IUGR fetuses, the proportion of abnormal middle cerebral artery Doppler parameters was 53%. Compared with appropriate-for-gestational age infants, newborns in the IUGR subgroup with abnormal middle cerebral artery Doppler had significantly lower neurobehavioral scores in the areas of habituation, motor system, social-interactive and attention. Similarly, the proportion of infants with abnormal neurobehavioral scores was significantly higher in the IUGR subgroup with abnormal middle cerebral artery Doppler parameters in the areas of habituation, social-interactive, motor system and attention.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
67. Turan OM, Turan S, Berg C, et al. Duration of persistent abnormal ductus venosus flow and its impact on perinatal outcome in fetal growth restriction. <i>Ultrasound Obstet Gynecol.</i> 2011;38(3):295-302.	Observational- Dx	177 patients	To study if the duration of individual Doppler abnormalities is an independent predictor of adverse outcome in fetal growth restriction caused by placental dysfunction.	177 study participants underwent a total of 1,069 examinations. The duration of an absent/reversed a-wave in the ductus venosus reversed a-wave was significantly higher in stillbirths (median, 6 days) compared with intact survivors and those with major morbidity (median, 0 days for both; $P=0.006$ and $P=0.001$, respectively). Duration of brain sparing was also longer in stillbirth cases compared with intact survivors (median, 19 days vs 9 days, $P=0.02$). Stepwise multinomial logistic regression showed that gestational age at delivery was a significant codeterminant of outcome for all arterial Doppler abnormalities when the ductus venosus a-wave was antegrade. However, when present, the duration of ductus venosus reversed a-wave was the only contributor to stillbirth (probability of stillbirth = $1/(1 + \exp - (\text{interval to delivery} \times 1.03 - 2.28))$, $r^2 = 0.73$). Receiver-operating characteristics curve statistics showed that a ductus venosus reversed a-wave for >7 days predicted stillbirth (100% sensitivity, 80% specificity, likelihood ratio = 5.0, $P<0.0001$). In contrast, neither neonatal death nor neonatal morbidity was predicted by the days of persistent ductus venosus reversed a-wave.	4

**Assessment of Fetal Well-Being
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
68. Del Rio M, Martinez JM, Figueras F, et al. Doppler assessment of the aortic isthmus and perinatal outcome in preterm fetuses with severe intrauterine growth restriction. <i>Ultrasound Obstet Gynecol.</i> 2008;31(1):41-47.	Observational-Dx	51 fetuses	To evaluate the characteristics and association with perinatal outcome of the aortic isthmus (AoI) circulation as assessed by Doppler imaging in preterm growth-restricted fetuses with placental insufficiency.	Adverse perinatal outcome was significantly associated with an increased aortic isthmus-PI (area under the curve 0.77; 95% CI, 0.63–0.92; $P<0.005$). A significant correlation ($P<0.001$) was found between retrograde blood flow in the aortic isthmus and adverse perinatal outcome, the overall perinatal mortality being higher in the retrograde group (70% vs 4.8%, $P<0.001$). In 4/5 (80%) fetuses the reversal of flow in the aortic isthmus preceded that in the ductus venosus by 24-48 hours aortic isthmus-peak systolic velocity and aortic isthmus-time-averaged maximum velocity were <5(th) centile in 40/51 (78%) and 48/51 (94%) cases, respectively, whereas aortic isthmus-PI was >95(th) centile in 21/51 (41%) cases.	3

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
69. Turan S, Turan OM, Berg C, et al. Computerized fetal heart rate analysis, Doppler ultrasound and biophysical profile score in the prediction of acid-base status of growth-restricted fetuses. <i>Ultrasound Obstet Gynecol.</i> 2007;30(5):750-756.	Observational-Dx	58 patients	To investigate the performance of non-stress test, computerized fetal heart rate analysis, BPP scoring and arterial and venous Doppler US investigation in the prediction of acid-base status in fetal growth restriction.	56/58 patients (96.6%) received complete assessment of all variables. All were delivered by pre-labor Cesarean section at a median gestational age of 30 + 6 weeks. The UA PI was negatively correlated with the computerized fetal heart rate analysis short-term variation (Pearson correlation - 0.29, $P < 0.05$). The ductus venosus PI was negatively correlated with the pH (Pearson correlation - 0.30, $P < 0.02$). The computerized fetal heart rate analysis mean minute variation and pH were not significantly correlated (Pearson correlation 0.13, $P = 0.34$). Umbilical vein pulsations identified the highest proportion of neonates with a low birth pH (9/17, 53%), the highest number of false positives among patients with an abnormal BPP scoring, abnormal DV Doppler and a short-term variation < 3.5 ms, and also stratified false negatives among patients with an equivocal or normal BPP scoring. Abnormal ductus venosus Doppler correctly identified false positives among patients with an abnormal BPP scoring. Computerized fetal heart rate analysis reduced the rate of an equivocal BPP scoring from 16% to 7.1% when substituted for the traditional non-stress test. Elevated ductus venosus Doppler index and umbilical venous pulsations predicted a low pH with 73% sensitivity and 90% specificity ($P = 0.008$).	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
70. Schwarze A, Gembruch U, Krapp M, Katalinic A, Germer U, Axt-Fliedner R. Qualitative venous Doppler flow waveform analysis in preterm intrauterine growth-restricted fetuses with ARED flow in the umbilical artery--correlation with short-term outcome. <i>Ultrasound Obstet Gynecol.</i> 2005;25(6):573-579.	Observational-Dx	74 fetuses	To examine the significance of severe Doppler waveform abnormalities in the ductus venosus and the umbilical vein for the prediction of adverse outcomes in very preterm growth-restricted fetuses with absent or reversed end-diastolic flow in the UA at 24–34 weeks of gestation.	12 (16.2%) perinatal deaths, of which 8 were stillbirths (10.8%), and 2 (2.7%) neonatal deaths occurred among 74 fetuses. Logistic regression analysis confirmed that abnormal ductus venosus Doppler waveforms ($R^2 = 0.57, P < 0.001$) together with gestational age at delivery ($R^2 = 0.57, P < 0.001$) showed the strongest association with perinatal death, whereas only gestational age was significantly related to neonatal death ($R^2 = 0.67, P < 0.05$). Abnormal ductus venosus Doppler waveforms ($R^2 = 0.86, P < 0.001$) and gestational age ($R^2 = 0.49, P < 0.05$) were strongly associated with adverse outcome (including stillbirth, perinatal death or neonatal death). Abnormal venous Doppler flow patterns performed better in the prediction of fetal or perinatal demise than did absent or reversed end-diastolic flow or brain sparing.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
71. Ferrazzi E, Bozzo M, Rigano S, et al. Temporal sequence of abnormal Doppler changes in the peripheral and central circulatory systems of the severely growth-restricted fetus. <i>Ultrasound Obstet Gynecol.</i> 2002;19(2):140-146.	Observational-Dx	26 patients	To identify the temporal sequence of abnormal Doppler changes in the fetal circulation in a subset of early and severely growth-restricted fetuses.	Mean gestational age and newborn weight at delivery were 29 (standard deviation, 2) weeks and 818 (standard deviation, 150) g, respectively. The sequence of Doppler velocimetric changes was described by onset time cumulative curves that showed 2 time-related events. First, for each vessel there was a progressive increase in the percent of fetuses developing a Doppler abnormality. Second, severely growth-restricted fetuses followed a progressive sequence of acquiring Doppler abnormalities which were categorized into 'early' and 'late' Doppler changes. Early changes occurred in peripheral vessels (umbilical and middle cerebral arteries; 50% of patients affected 15–16 days prior to delivery). Late changes included UA reverse flow, and abnormal changes in the ductus venosus, aortic and pulmonary outflow tracts (50% of patients affected 4-5 days prior to delivery). The time interval between the occurrence of early and late changes was significantly different ($P<0.0001$) and late changes were significantly associated with perinatal death ($P<0.01$).	3
72. Unterscheider J, Daly S, Geary MP, et al. Predictable progressive Doppler deterioration in IUGR: does it really exist? <i>Am J Obstet Gynecol.</i> 2013;209(6):539 e531-537.	Observational-Dx	1,116 nonanomalous fetuses	To study Doppler changes in multiple vessels including UA, middle cerebral artery, ductus venosus, aortic isthmus, and myocardial performance index and to establish whether a predictable progressive sequence of Doppler deterioration exists at the level of the individual fetus and to determine any added benefit in applying these Doppler assessments in IUGR informing surveillance intervals and timing of delivery. Optimal surveillance of fetuses with an estimated fetal weight less than the 10th centile.	Our study of 1116 nonanomalous fetuses comprised 7769 individual Doppler data points. 511 patients (46%) had an abnormal UA, 300 (27%) had an abnormal middle cerebral artery, and 129 (11%) had an abnormal ductus venosus Doppler. The classic pattern from abnormal UA to middle cerebral artery to ductus venosus existed but no more frequently than any of the other potential pattern. Doppler interrogation of the UA and middle cerebral artery remains the most useful and practical tool in identifying fetuses at risk of adverse perinatal outcome, capturing 88% of all adverse outcomes.	3

**Assessment of Fetal Well-Being
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
73. Hecher K, Bilardo CM, Stigter RH, et al. Monitoring of fetuses with intrauterine growth restriction: a longitudinal study. <i>Ultrasound Obstet Gynecol.</i> 2001;18(6):564-570.	Observational-Dx	110 singleton pregnancies	To describe the time sequence of changes in fetal monitoring variables in IUGR and to correlate these findings with fetal outcome at delivery.	93 (60 in Group 1 and 33 in Group 2) fetuses had at least 3 data sets (median, 4; range, 3–27) and had the last measurements taken within 24 hours of delivery or intrauterine death. The percentage of abnormal test results and the degree of abnormality were higher in Group 1 compared to Group 2. AFI and UA PI were the first variables to become abnormal, followed by the middle cerebral artery, aorta, short-term variation, ductus venosus and inferior vena cava. In Group 1, short-term variation and ductus venosus PI showed mirror images of each other in their trend over time. Perinatal mortality was significantly higher if both variables were abnormal compared to only 1 or neither being abnormal (13/33 (39%) vs 4/60 (7%); $P=0.0002$; Fisher's exact test).	3
74. Morris JM, Thompson K, Smithey J, et al. The usefulness of ultrasound assessment of amniotic fluid in predicting adverse outcome in prolonged pregnancy: a prospective blinded observational study. <i>BJOG.</i> 2003;110(11):989-994.	Observational-Dx	1,584 pregnant women	To determine whether a single US scan at or beyond 40 weeks of gestation to detect a single deepest pool of amniotic fluid <2 cm and AFI <5 cm is clinically useful in the prediction of subsequent adverse pregnancy outcome.	An AFI <5 cm but not a single deepest pool <2 cm was significantly associated with birth asphyxia or meconium aspiration. An AFI <5 cm was also significantly associated with caesarean section for fetal distress in labor, a cord arterial pH <7 at delivery and low Apgar scores. Despite there being a statistically significant association with adverse outcomes the sensitivity of AFI was low at 28.6%, 12% and 11.5% for major adverse outcome, fetal distress in labor or admission to the neonatal unit, respectively.	2

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
 - a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
 - b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
 - c) the study is an expert opinion or consensus document.
- M = Meta-analysis

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

AFI = Amniotic fluid index

BPP = Biophysical profile

CHD = Congenital heart disease

CI = Confidence interval

CPR = Cerebroplacental ratio

CVP = Cardiovascular profile

IUGR = Intrauterine growth restriction

OR = Odds ratio

PI = Pulsatility index

RR= Relative risk

SGA = Small-for-gestational-age

UA = Umbilical artery

US = Ultrasound