



1.

Meriki N.^{a,b} · Henry A.^{c-e} · Sanderson J.^c · Majajan A.^c · Wu L.^d · Welsh A.W.^{c-e} **Development of Normal Gestational Ranges for the Right Myocardial Performance Index in the Australian Population with Three Alternative Caliper Placements.** *Fetal Diagn Ther.* 2014;36(4):272-81. doi: 10.1159/000362388. Epub 2014 Nov 8.

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OBJECTIVES: To construct gestational age-adjusted reference ranges for the right fetal modified myocardial performance index (RMPI) in an Australian population and to assess the influence of valve click caliper position on constituent time intervals and the RMPI.

METHODS: A prospective cross-sectional study of RMPI from 235 normal fetuses at 17-38 weeks of gestation was performed. Two Doppler waveforms were obtained: tricuspid and pulmonary valves for 'a' and 'b' readings, respectively. The ultrasound machine settings were: Doppler sweep velocity 15 cm/s, angle of insonation <15°, minimal gain, and wall motion filter 300 Hz. The 'a' and 'b' intervals were measured at three different caliper positions in each fetus: at the beginning of the original valve clicks ('original'), at the beginning of the reflected tricuspid and pulmonary closure clicks ('reflected') and at the peak of valve clicks ('peak'). RMPI was calculated as (a - b)/b. The three readings were obtained and averaged per examination, with intraobserver repeatability assessed by intraclass correlation coefficient (ICC) and 95% CI.

RESULTS: For 'original', 'reflected' and 'peak' RMPI, mean ± SD, ICC (95% CI) were: 0.53 ± 0.10, 0.86 (0.83-0.89); 0.48 ± 0.10, 0.84 (0.81-0.87) and 0.48 ± 0.10, 0.89 (0.87-0.91), respectively. The RMPI increased by approximately 15% as gestation increased and decreased slightly with increasing heart rate.

CONCLUSION: This is the first publication of reference ranges for RMPI based on caliper position. All methods showed good ICC, including the 'peak' method which we have previously

proposed for routine use based on its repeatability and ease of identification when measuring the myocardial performance index.

2.

Eghbalian F¹. **The impact of supine and prone positioning on arterial oxygenation in premature neonates.** *J Neonatal Perinatal Med.* 2014 Jan 1;7(4):273-7. doi: 10.3233/NPM-14814049.

BACKGROUND: Respiratory distress syndrome (RDS) is one of the most important causes of mortality and morbidity in premature newborns. The aim of this study was to determine the effect of body position on oxygen saturation in hospitalized premature infants with RDS.

METHODS: From June 2010 to December 2012, 69 premature infants with RDS were evaluated in an interventional analytic study. Patients had a mean gestational age (\pm SD) of 31.4 (\pm 2.41) weeks (range: 28–35 weeks) with a mean birth weight (\pm SD) of 1446.6 (\pm 218.90) grams (range: 850–2400 grams). Infants were studied both in supine and in prone positions. Oxygen saturation was monitored by trans-cutaneous pulse oximeter and oxygen saturation was continually monitored for 3 hours in each position and mean oxygen saturation was calculated at the end of each 3 hour period. All patients were premature, NPO, oxygen dependent and had RDS. The range of the postnatal age of the studied infants was 24–48 hr.

RESULTS: Means (\pm SD) of oxygen saturation during 3 hours in prone and supine positions were 92.54% (\pm 2.24%) and 91.78% (\pm 2.35%), respectively ($p = 0.001$). Also means (\pm SD) of oxygen saturation at the end of each 3-hours period prone and supine positions were 91.30% (\pm 2.42%) and 90.30% (\pm 3.15%), respectively ($p = 0.006$).

CONCLUSION: These findings suggest that, in premature infants with RDS, oxygen saturation was significantly higher in the prone compared with the supine posture.

3.

Ajetunmobi OM1, Whyte B2, Chalmers J3, Tappin DM4, Wolfson L5, Fleming M6, MacDonald A7, Wood R6, Stockton DL6; Glasgow Centre for Population Health Breastfeeding Project Steering Group. **Breastfeeding is Associated with Reduced Childhood Hospitalization: Evidence from a Scottish Birth Cohort (1997-2009).** *J Pediatr.* 2014 Dec 30. pii: S0022-3476(14)01065-8. doi: 10.1016/j.jpeds.2014.11.013. [Epub ahead of print]

OBJECTIVE: To evaluate the risk of childhood hospitalization associated with infant feeding patterns at 6-8 weeks of age in Scotland.

STUDY DESIGN: A retrospective population level study based on the linkage of birth, death, maternity, infant health, child health surveillance, and admission records for children born as single births in Scotland between 1997 and 2009 ($n = 502\ 948$) followed up to March 2012.

Descriptive analyses, Kaplan Meier tests, and Cox regression were used to quantify the association between the mode of infant feeding and risk of childhood hospitalization for respiratory, gastrointestinal, and urinary tract infections, and other common childhood ailments during the study period.

RESULTS: Within the first 6 months of life, there was a greater hazard ratio (HR) of hospitalization for common childhood illnesses among formula-fed infants (HR 1.40; 95% CI 1.35-1.45) and mixed-fed infants (HR 1.18; 95% CI 1.11-1.25) compared with infants exclusively breastfed after adjustment for parental, maternal, and infant health characteristics. Within the first year of life and beyond, a greater relative risk of hospitalization was observed among formula-fed infants for a range of individual illnesses reported in childhood including gastrointestinal, respiratory, and urinary tract infections, otitis media, fever, asthma, diabetes, and dental caries.

CONCLUSIONS: Using linked administrative data, we found greater risks of hospitalization in early childhood for a range of common childhood illnesses among Scottish infants who were not exclusively breastfed at 6-8 weeks of age.

4.

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IMPORTANCE: Hypothermia at 33.5°C for 72 hours for neonatal hypoxic ischemic encephalopathy reduces death or disability to 44% to 55%; longer cooling and deeper cooling are neuroprotective in animal models.

OBJECTIVE: To determine if longer duration cooling (120 hours), deeper cooling (32.0°C), or both are superior to cooling at 33.5°C for 72 hours in neonates who are full-term with moderate or severe hypoxic ischemic encephalopathy.

DESIGN, SETTING, AND PARTICIPANTS: A randomized, 2×2 factorial design clinical trial performed in 18 US centers in the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Neonatal Research Network between October 2010 and November 2013.

INTERVENTIONS: Neonates were assigned to 4 hypothermia groups; 33.5°C for 72 hours, 32.0°C for 72 hours, 33.5°C for 120 hours, and 32.0°C for 120 hours.

MAIN OUTCOMES AND MEASURES: The primary outcome of death or disability at 18 to 22 months is ongoing. The independent data and safety monitoring committee paused the trial to evaluate safety (cardiac arrhythmia, persistent acidosis, major vessel thrombosis and bleeding, and death in the neonatal intensive care unit [NICU]) after the first 50 neonates were enrolled, then after every subsequent 25 neonates. The trial was closed for emerging safety profile and futility analysis after the eighth review with 364 neonates enrolled (of 726 planned). This report focuses on safety and NICU deaths by marginal comparisons of 72 hours' vs 120 hours' duration and 33.5°C depth vs 32.0°C depth (predefined secondary outcomes).

RESULTS: The NICU death rates were 7 of 95 neonates (7%) for the 33.5°C for 72 hours group, 13 of 90 neonates (14%) for the 32.0°C for 72 hours group, 15 of 96 neonates (16%) for the 33.5°C for 120 hours group, and 14 of 83 neonates (17%) for the 32.0°C for 120 hours group. The adjusted risk ratio (RR) for NICU deaths for the 120 hours group vs 72 hours group was 1.37 (95% CI, 0.92-2.04) and for the 32.0°C group vs 33.5°C group was 1.24 (95% CI, 0.69-2.25). Safety outcomes were similar between the 120 hours group vs 72 hours group and the 32.0°C group vs 33.5°C group, except major bleeding occurred among 1% in the 120 hours group vs 3% in the 72 hours group (RR, 0.25 [95% CI, 0.07-0.91]). Futility analysis determined that the probability of detecting a statistically significant benefit for longer cooling, deeper cooling, or both for NICU death was less than 2%.

CONCLUSIONS AND RELEVANCE: Among neonates who were full-term with moderate or severe hypoxic ischemic encephalopathy, longer cooling, deeper cooling, or both compared with hypothermia at 33.5°C for 72 hours did not reduce NICU death. These results have implications for patient care and design of future trials.

Trial Registration clinicaltrials.gov Identifier: NCT01192776

5.

Maignien C, Nguyen A, Dussaux C, Cynober E, Gonzales M, Carbonne B. **Outcome of pregnancy following second- or third-trimester intrauterine fetal death.** *Int J Gynaecol Obstet.* 2014 Dec;127(3):275-8. doi: 10.1016/j.ijgo.2014.06.015. Epub 2014 Jul 30.

OBJECTIVE: To investigate the outcomes of a pregnancy after a second- or third-trimester intrauterine fetal death (IUFD).

METHODS: A prospective observational study was conducted at Trousseau Hospital (Paris, France) between 1996 and 2011. The first ongoing pregnancy in women who had had a previous IUFD was monitored. Management of their treatment was according to a standardized protocol. Recurrence of fetal death was the main outcome criterion.

RESULTS: The subsequent pregnancies of 87 women who had experienced at least one previous IUFD were followed up. The cause of previous IUFD was placental in 50 (57%) women, unknown in 19 (22%), adnexal in 12 (14%), metabolic in 2 (2%), and malformative in 4 (5%). Three (3%) participants had another stillbirth. Overall, obstetric complications occurred in 34 (39%) pregnancies (including 22 [25%] preterm births, 5 [6%] small for gestational age, and 6 [7%] maternal vascular complications). Obstetric complications were significantly more common among women whose previous stillbirth had been due to placental causes than among those affected by other causes ($P=0.02$).

CONCLUSION: Most pregnancies after IUFD resulted in a live birth; however, adverse obstetric outcomes were more common when the previous stillbirth was due to placental causes.

6.

Baer RJ, Norton ME, Shaw GM, et al. **Risk of selected structural abnormalities in infants after increased nuchal translucency measurement.** *Am J Obstet Gynecol.* 2014 Dec;211(6):675.e1-19. doi: 10.1016/j.ajog.2014.06.025. Epub 2014 Jun 17.

OBJECTIVE: We sought to examine the association between increased first-trimester fetal nuchal translucency (NT) measurement and major noncardiac structural birth defects in euploid infants.

STUDY DESIGN: Included were 75,899 singleton infants without aneuploidy or critical congenital heart defects born in California in 2009 through 2010 with NT measured between 11-14 weeks of gestation. Logistic binomial regression was employed to estimate relative risks (RRs) and 95% confidence intervals (CIs) for occurrence of birth defects in infants with an increased NT measurement (by percentile at crown-rump length [CRL] and by ≥ 3.5 mm compared to those with measurements < 90 th percentile for CRL).

RESULTS: When considered by CRL adjusted percentile and by measurement ≥ 3.5 mm, infants with a NT ≥ 95 th percentile were at risk of having ≥ 1 major structural birth defects (any defect, RR, 1.6; 95% CI, 1.3–1.9; multiple defects, RR, 2.1; 95% CI, 1.3–3.4). Infants with a NT measurement ≥ 95 th percentile were at particularly high risk for pulmonary, gastrointestinal, genitourinary, and musculoskeletal anomalies (RR, 1.6–2.7; 95% CI, 1.1–5.4).

CONCLUSION: Our findings demonstrate that risks of major pulmonary, gastrointestinal, genitourinary, and musculoskeletal structural birth defects exist for NT measurements ≥ 95 th percentile. The ≥ 3 -fold risks were observed for congenital hydrocephalus; agenesis, hypoplasia, and dysplasia of the lung; atresia and stenosis of the small intestine; osteodystrophies; and diaphragm anomalies.

7.

Pasquini L., Masini G., Gaini C., Franchi C., Trotta M., Dani C., and Di Tommaso M. **The utility of infection screening in isolated mild ventriculomegaly: an observational retrospective study on 141 fetuses.** *Prenat Diagn.* 2014 Dec;34(13):1295-300. doi: 10.1002/pd.4470. Epub 2014 Aug 22.

OBJECTIVE: The aim of this study was to evaluate the utility of screening for infections in case of isolated mild ventriculomegaly (imVM).

METHODS: We retrospectively reviewed 141 cases of imVM. Screening for infections including TORCH, parvovirus B19, and syphilis was carried out in all cases. Follow-up ultrasound, fetal karyotype, and magnetic resonance imaging (MRI) were offered. Postnatal follow-up was obtained from pediatricians, medical records, parents, and postmortem reports in cases of termination of pregnancy or stillbirth.

RESULTS: The imVM was bilateral in 70 fetuses and unilateral in 71 and regressed during pregnancy in 66.6% of cases. Associated anomalies were observed in 15 cases with follow-up ultrasound and in seven cases with MRI. Fetal karyotype was abnormal in one fetus (47, XXY). Maternal IgM for parvovirus B19 resulted positive in 4.6% of cases, and one neonate was infected without any fetal/neonatal adverse consequence. Recent cytomegalovirus infection was documented in 4.4% of cases. Only in one case the infection was transmitted to the fetus; after 3 years, the child has good neuromotor development but has severe hearing impairment.

CONCLUSIONS: When this diagnosis occurs, tests could be limited to cytomegalovirus and parvovirus B19, whereas a complete TORCH screening is probably not necessary.

8.

Kritzer S, Magner K, Warshak R. **Increasing Maternal Body Mass Index and the Accuracy of Sonographic Estimation of Fetal Weight Near Delivery.** *J Ultrasound Med.* 2014 Dec;33(12):2173-9. doi: 10.7863/ultra.33.12.2173.

OBJECTIVES: To evaluate whether an increasing body mass index (BMI) influences the accuracy of sonographic estimation of fetal weight.

METHODS: We performed a retrospective cohort study of singleton deliveries over a 2-year period in a single institution. Patients were included if they had a fetal weight estimation within 2

weeks of delivery. The Δ estimated fetal weight (EFW) was calculated by subtracting the sonographic EFW from the birth weight and compared among our study groups, which were based on the maternal BMI class. We also compared the absolute percentage error of estimation, rate of substantial error greater than 20%, rate of underestimation, and ability to predict fetal weight greater than 4000 g. Post hoc power analysis determined that our study group of 1200 patients allowed for an α of .05 and β of .90.

RESULTS: We included 1177 women in our analysis. The median Δ EFW varied between study groups: 137, 202, 157, 200, and 189 g, respectively, in normal-weight, overweight, and obese classes 1, 2, and 3 ($P = .01$). The median percentage error of estimation between study groups varied between 5.0% in normal-weight women and 7.1% in class 2 obese women ($P = .05$). The rate of substantial error was similar between study groups and varied between 2.7% in class 1 obese women and 4.3% in normal-weight and class 2 obese women. Linear regression analysis showed a weak association between maternal BMI and Δ EFW ($R^2 = 0.005$; $r = 0.069$).

CONCLUSIONS: The absolute Δ EFW was lower in normal-weight women; however, the percentage error of the EFW was similar between women of varying BMI classifications, as was the rate of substantial error and the rate of underestimation of the EFW.

9.

Abramovici A¹, Gandley R, Clifton R, Leveno K, Myatt L, Wapner R, Thorp J Jr, Mercer B, Peaceman A, Samuels P, Sciscione A, Harper M, Saade G, Sorokin Y; the Eunice Kennedy Shriver National Institute of Child Health Human Development Maternal-Fetal Medicine Units Network. **Prenatal vitamin C and E supplementation in smokers is associated with reduced placental abruption and preterm birth: a secondary analysis.** *BJOG*. 2014 Dec 17. doi: 10.1111/1471-0528.13201. [Epub ahead of print]

OBJECTIVE: Smoking and pre-eclampsia (PE) are associated with increases in preterm birth, placental abruption and low birthweight. We evaluated the relationship between prenatal vitamin C and E (C/E) supplementation and perinatal outcomes by maternal self-reported smoking status focusing on outcomes known to be impacted by maternal smoking.

DESIGN/SETTING/POPULATION: A secondary analysis of a multi-centre trial of vitamin C/E supplementation starting at 9-16 weeks in low-risk nulliparous women with singleton gestations.

METHODS: We examined the effect of vitamin C/E by smoking status at randomisation using the Breslow-Day test for interaction.

MAIN OUTCOME MEASURES: The trial's primary outcomes were PE and a composite outcome of pregnancy-associated hypertension (PAH) with serious adverse outcomes. Perinatal outcomes included preterm birth and abruption.

RESULTS: There were no differences in baseline characteristics within subgroups (smokers versus nonsmokers) by vitamin supplementation status. The effect of prenatal vitamin C/E on the risk of PE ($P = 0.66$) or PAH composite outcome ($P = 0.86$) did not differ by smoking status. Vitamin C/E was protective for placental abruption in smokers (relative risk [RR] 0.09; 95% CI 0.00-0.87], but not in nonsmokers (RR 0.92; 95% CI 0.52-1.62) ($P = 0.01$), and for preterm birth in smokers (RR 0.76; 95% CI 0.58-0.99) but not in nonsmokers (RR 1.03; 95% CI 0.90-1.17) ($P = 0.046$).

CONCLUSION: In this cohort of women, smoking was not associated with a reduction in PE or the composite outcome of PAH. Vitamin C/E supplementation appears to be associated with a reduction in placental abruption and preterm birth among smokers.

10.

Yang EY, Davies LM, Buchanan P, Kling C, Banyard DA, Ramones T. **Spontaneous onset of labor, not route of delivery, is associated with prolonged length of stay in babies with gastroschisis.** *J Pediatr Surg.* 2014 Dec;49(12):1776-81. doi: 10.1016/j.jpedsurg.2014.09.021. Epub 2014 Oct 12.

BACKGROUND/PURPOSE: We studied obstetric delivery practices for fetal gastroschisis and correlated this with neonatal outcomes. Our objectives were to identify changes in delivery practices over time and to determine if these changes resulted in improved neonatal outcomes.

METHODS: After IRB approval, maternal and neonatal records from 219 gastroschisis births between 1990 and 2008 were reviewed. Obstetrical data and neonatal data were collected. Univariate comparisons were made between maternal delivery variables and neonatal outcomes. Significant and clinically relevant obstetrical variables were combined for multivariate linear regression modeling.

RESULTS: The practice of elective cesarean delivery (ELCS) shifted to spontaneous vaginal delivery (sVD) over time ($p < 0.001$). Babies born by sVD had longer hospitalization than those born by ELCS (median 36.0 vs 21.6 days, $p < 0.05$). Gestational age (GA) and birth weight were similar between groups. Babies born by induced VD (iVD) had short hospitalization (median 22.5 days). A linear regression model demonstrated that spontaneous onset of labor (SOL) and GA were independently related to LOS.

CONCLUSIONS: Over nearly two decades, delivery of gastroschisis babies shifted from ELCS to sVD, a practice associated with a significantly longer LOS. Regression models suggest that shorter LOS could be achieved if elective delivery modes are utilized prior to SOL.

11.

Crimmins S¹, Desai A¹, Block-Abraham D¹, Berg C², Gembruch U², Baschat AA³. **A comparison of Doppler and biophysical findings between liveborn and stillborn growth-**

restricted fetuses. Am J Obstet Gynecol. 2014 Dec;211(6):669.e1-10. doi: 10.1016/j.ajog.2014.06.022. Epub 2014 Jun 12.

OBJECTIVE: The purpose of this study was to evaluate the surveillance characteristics that precede stillbirth in growth-restricted fetuses that receive integrated Doppler and biophysical profile scoring (BPS).

STUDY DESIGN: Nine hundred eighty-seven singleton pregnancies that were complicated by fetal growth restriction had multivessel Doppler scans (umbilical and middle cerebral arteries [MCA], ductus venosus, and umbilical vein) and BPS. Surveillance findings were compared between live births and stillbirths.

RESULTS: Forty-seven stillbirths occurred in 2 clusters, 37 at <34 weeks of gestation and 10 thereafter. Before 34 weeks of gestation, stillbirths had parallel escalation of umbilical artery and ductus venosus Doppler findings followed by abnormal BPS. At ≥ 34 weeks of gestation, only a decline in MCA pulsatility index was observed, and 75% of stillbirths were unanticipated by the BPS.

CONCLUSION: Before 34 weeks of gestation, multivessel Doppler abnormality anticipates an abnormal BPS and subsequent stillbirth. After 34 weeks of gestation, stillbirths occur after MCA brain-sparing in a shorter interval than predicted by a normal BPS. Recognition of these differences in clinical behavior requires consideration for the planning of monitoring intervals in preterm and term fetal growth restriction.

12.

Lusk LA¹, Brown EG², Overcash RT³, Grogan TR⁴, Keller RL⁵, Kim JH⁶, Poulain FR⁷, Shew SB⁸, Uy C⁹, DeUgarte DA¹⁰; University of California Fetal Consortium. **Multi-institutional practice patterns and outcomes in uncomplicated gastroschisis: A report from the University of California Fetal Consortium (UCfC).** J Pediatr Surg. 2014 Dec;49(12):1782-6. doi: 10.1016/j.jpedsurg.2014.09.018. Epub 2014 Nov 14.

BACKGROUND/PURPOSE: Gastroschisis is a resource-intensive birth defect without consensus regarding optimal surgical and medical management. We sought to determine best-practice guidelines by examining differences in multi-institutional practices and outcomes.

METHODS: Site-specific practice patterns were queried, and infant–maternal chart review was retrospectively performed for gastroschisis infants treated at 5 UCfC institutions (2007–2012). The primary outcome was length of stay. Univariate analysis was done to assess variation practices and outcomes by site. Multivariate models were constructed with site as an instrumental variable and with sites grouped by silo practice pattern adjusting for confounding factors.

RESULTS: Of 191 gastroschisis infants, 164 infants were uncomplicated. Among uncomplicated patients, there were no deaths and only one case of necrotizing enterocolitis. Bivariate analysis revealed significant differences in practices and outcomes by site. Despite wide variations in practice patterns, there were no major differences in outcome among sites or by silo practice, after adjusting for confounding factors.

CONCLUSIONS: Wide variability exists in institutional practice patterns for infants with gastroschisis, but poor outcomes were not associated with expeditious silo or primary closure, avoidance of routine paralysis, or limited central line and antibiotic durations. Development of clinical pathways incorporating these practices may help standardize care and reduce health care costs.