13. Beyens T, Biarent D, Bouton JM, Demanet H, Viart P, Dessy H, et al. Cardiac surgery with extracorporeal circulation in 23 infants weighing 2500 g or less: short and intermediate term outcome. *Eur J Cardiothorac Surg.* 1998; 14:165-72.
14. Chang AC, Hanley FL, Lock JE, Castaneda AR, Wessel DL. Management and outcome of low birth weight neonates with congenital heart disease. *J Pediatr.* 1994;124:461-6.
15. Williams GD, Cohen RS. Perioperative management of low birth weight infants for open-heart surgery. *Paediatr Anaesth.* 2011;21:538-53.
16. Alkan-Bozkaya T, Turkoglu H, Akcevin A, Paker T, Ozkan-Cerci H, Dindar A, et al. Cardiac surgery of premature and low birthweight newborns: is a change of fate possible? *Artif Organs.* 2010;34:891-7.
17. Charette K, Hirata Y, Bograd A, Mongero L, Chen J, Quaegebeur J, et al. 180 ml and less: cardiopulmonary bypass techniques to minimize hemodilution for neonates and small infants. *Perfusion.* 2007;22:327-31.
18. Gelehrter S, Fifer CG, Armstrong A, Hirsch J, Gajarski R. Outcomes of hypoplastic left heart syndrome in low-birth-weight patients. *Pediatr Cardiol.* 2011;32:1175-81.
19. Weinstein S, Gaynor JW, Bridges ND, Wernovsky G, Montenegro LM, Godinez RI, et al. Early survival of infants weighing 2.5 kilograms or less undergoing first-stage reconstruction for hypoplastic left heart syndrome. *Circulation.* 1999;100:II167-70.
20. Kopf GS, Mello DM. Surgery for congenital heart disease in low-birth weight neonates: a comprehensive statewide Connecticut program to improve outcomes. *Conn Med.* 2003;67:327-32.
21. Reddy VM, McElhinney DB, Sagrado T, Parry AJ, Teitel DF, Hanley FL. Results of 102 cases of complete repair of congenital heart defects in patients weighing 700 to 2500 grams. *J Thorac Cardiovasc Surg.* 1999;117:324-31.
22. Bacha EA, Almodovar M, Wessel DL, Zurakowski D, Mayer JE Jr, Jonas RA, et al. Surgery for coarctation of the aorta in infants weighing less than 2 kg. *Ann Thorac Surg.* 2001;71:1260-4.
23. Haas F, Goldberg CS, Ohye RG, Mosca RS, Bove EL. Primary repair of aortic arch obstruction with ventricular septal defect in preterm and low birth weight infants. *Eur J Cardiothorac Surg.* 2000;17:643-7.
24. Reddy VM. Low birth weight and very low birth weight neonates with congenital heart disease: timing of surgery, reasons for delaying or not delaying surgery. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu.* 2013;16:13-20.
25. Roussin R, Belli E, Bruniaux J, Demontoux S, Touchot A, Planche C, et al. Surgery for transposition of the great arteries in neonates weighing less than 2,000 grams: a consecutive series of 25 patients. *Ann Thorac Surg.* 2007;83: 173-7.
26. Wernovsky G, Rubenstein SD, Spray TL. Cardiac surgery in the low-birth weight neonate: new approaches. *Clin Perinatol.* 2001;28:249-64.
27. Shepard CW, Kochilas LK, Rosengart RM, Brearley AM, Bryant R III, Moller JH, et al. Repair of major congenital cardiac defects in low-birth-weight infants: is delay warranted? *J Thorac Cardiovasc Surg.* 2010;140:1104-9.
28. Cheng HH, Almodovar MC, Laussen PC, Wypij D, Polito A, Brown DW, et al. Outcomes and risk factors for mortality in premature neonates with critical congenital heart disease. *Pediatr Cardiol.* 2011;32:1139-46.
29. Costello JM, Polito A, Brown DW, McElrath TF, Graham DA, Thiagarajan RR, et al. Birth before 39 weeks' gestation is associated with worse outcomes in neonates with heart disease. *Pediatrics.* 2010;126:277-84.
30. Dees E, Lin H, Cotton RB, Graham TP, Dodd DA. Outcome of preterm infants with congenital heart disease. *J Pediatr.* 2000;137:653-9.
31. Numa A, Butt W, Mee RB. Outcome of infants with birthweight 2000 g or less who undergo major cardiac surgery. *J Paediatr Child Health.* 1992;28:318-20.

EDITORIAL COMMENTARY

Timing is even more important than we thought! The effect of gestational age versus body weight on outcomes of neonatal heart surgery

Osman O. Al-Radi, MD, MSc, FRCSC

See related article on pages 2499-506.

The outcomes of heart surgery for neonates have improved dramatically over the last few decades. Significant incremental improvements in our understanding of the pathophysiology, as well as surgical techniques and perioperative care, have contributed to this positive change.

From the Department of Surgery, King Abdulaziz University, Jeddah, Saudi Arabia.

Disclosures: Author has nothing to disclose with regard to commercial support.

Received for publication Sept 25, 2014; accepted for publication Sept 26, 2014; available ahead of print Oct 22, 2014.

Address for reprints: Osman O. Al-Radi, MD, MSc, FRCSC, Department of Surgery, PO Box 80215, Building 10, room 1027, Jeddah, Makkah Province 21589, Saudi Arabia (E-mail: oradi@kau.edu.sa).

J Thorac Cardiovasc Surg 2014;148:2506-7

0022-5223/\$36.00

Copyright © 2014 by The American Association for Thoracic Surgery

<http://dx.doi.org/10.1016/j.jtcvs.2014.09.107>

However, both low body weight and prematurity are still recognized predictors of adverse outcomes in these patients.^{1,2} It is somewhat challenging to differentiate which of the 2 factors has more predictive power because the 2 factors are correlated and there is significant variability in how these 2 seemingly simple measures are recorded and reported in databases and in the literature. The size of the child undergoing surgery is reported in variable forms including body weight, body surface area, or less frequently birth weight. There is even more variability in the reporting of prematurity. The spectrum includes reporting gestational age in weeks (mostly not including added days), a binary designation as premature at a certain cutoff point, or no reporting on prematurity whatsoever.

This differentiation between weight and prematurity is probably important. Theoretically, body weight is a technical challenge that can be overcome by improvements

in cardiopulmonary bypass, surgical instrumentation and techniques, and attention to minimizing unnecessary harm. On the other hand, prematurity is a physiologic challenge. Immature cardiac, pulmonary, neuronal, and hepatic tissues are probably more sensitive to surgical injury and more prone to dysfunction. Prematurity, however, may be a potentially modifiable risk factor. This leads to the question: why are many of the children with significant congenital heart disease born prematurely? One clue comes from studies that show that neonates with a prenatal diagnosis of congenital heart disease are born sooner than those without a prenatal diagnosis. Facilitation of tertiary care and transport is commonly cited as a reason for early delivery of neonates with complex lesions.³ This is justified by the definition of term delivery, which has historically been birth between 37 weeks 0 days to 41 weeks 6 days from the first day of the last menstrual cycle. Birth at any time in this 5-week period was believed to be equally safe. This is now officially history.

In April 2013, a joint statement from the American College of Obstetricians and Gynecologists (ACOG), and the Society for Maternal-Fetal Medicine (SMFM) recommended limiting early term delivery if not otherwise medically indicated.⁴ This was based on an increasing body of evidence suggesting that there is a significant difference in hard clinical outcomes including mortality between neonates born in the early term period and those born in the late term period.^{5,6} The definition of term pregnancy has consequently been revised to include more granularity. The National Institute of Child Health and Human Development, ACOG, SMFM, the World Health Organization, and other relevant bodies have jointly recommended redefining term pregnancy. Birth between 37 weeks 0 days and 38 weeks 6 days is designated as early term. Birth between 39 weeks 0 days and 40 weeks 6 days is designated as full term. Birth between 41 weeks 0 days and 41 weeks 6 days is designated as late term. These bodies have also recommended that nonmedically indicated delivery should not be undertaken before 39 weeks of gestation.⁷

Reddy and colleagues,⁸ in 1 of the studies on which these recommendations were based, found that the infant mortality rate in babies born at 37 weeks was more than double that in babies born at 39 weeks (relative risk [RR], 2.3; 95% confidence interval [CI], 2.1-2.6). Even babies born at 38 weeks had significantly higher infant mortality compared with those born at 39 weeks (RR, 1.4; 95% CI, 1.3-1.5). Costello and colleagues² reported similar findings in neonates undergoing surgery for congenital heart disease. The unadjusted odds ratio (OR) for perioperative death was 1.8 (95% CI, 1.4-2.2) for birth at 37 weeks of gestation and OR 1.4 (95% CI, 1.2-1.8) for birth at 38 weeks of gestation compared with 39 weeks of gestation. Even after adjustment for body weight and risk category of the

surgical procedure, these differences were statistically significant. In this issue of the *Journal of Thoracic and Cardiovascular Surgery*, Kalfa and colleagues⁹ present a single high-volume center experience with surgery for congenital heart disease in patients weighing less than 2.5 kg. Two of their findings are interesting. First, and relevant to this discussion, they found that gestational age was the only independent significant predictor of perioperative death, with an OR of 0.83 (*P* value, .037). This can be interpreted as an improvement of 17% relative risk of death for every week of gestation closer to full term. In this analysis, procedural risk category, biventricular versus univentricular pathway, and usual versus delayed timing of surgery were not predictive of perioperative mortality. The other interesting finding was that biventricular repair in patients who were less than 2.5 kg carried a risk of perioperative death of 9.8% versus 2.2% in patients who weighed more than 2.5 kg (*P* value .02), whereas there was no significant difference based on weight in patients who had univentricular repairs; the risk was about 10% in each group.

In congenital heart surgery, the clinical decision makers have learned to consider and control the timing of surgery and intervention carefully to obtain optimal outcomes. In lesions for which intervention is indicated during the neonatal period, avoiding elective preterm and early term birth is an extension of this consideration and control of timing of intervention. It may prove to be a very important decision in a program to improve outcomes of neonatal cardiac surgery.

References

1. Cruzon CL, Milford-Beland S, Li JS, O'Brien SM, Jacobs JP, Jacobs ML, et al. Cardiac surgery in infants with low birth weight is associated with increased mortality: analysis of the Society of Thoracic Surgeons Congenital Heart Database. *J Thorac Cardiovasc Surg*. 2008;135:546-51.
2. Costello JM, Pasquali SK, Jacobs JP, He X, Hill KD, Cooper DS, et al. Gestational age at birth and outcomes after neonatal cardiac surgery: an analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database. *Circulation*. 2014;129:2511-7.
3. Thiagarajan RR. Best on time, not a little early: gestational age and outcomes for neonates with congenital heart disease. *Circulation*. 2014;129:2495-6.
4. Committee Opinion. Nonmedically indicated early-term deliveries. *Obstet Gynecol*. 2013;121:911-5.
5. Consortium on Safe Labour, Hibbard JU, Wilkins I, Sun L, Gregory K, Haberman S, et al. Respiratory morbidity in late preterm births. *JAMA*. 2010;304:419-25.
6. Tita AT, Landon MB, Spong CY, Lai Y, Leveno KJ, Varner MW, et al. Timing of elective repeat cesarean delivery at term and neonatal outcomes. *N Engl J Med*. 2009;360:111-20.
7. Spong CY. Defining "term" pregnancy: recommendations from the Defining "Term" Pregnancy Workgroup. *JAMA*. 2013;309:2445-6.
8. Reddy UM, Ko CW, Raju TN, Willinger M. Delivery indications at late-preterm gestation and infant mortality rates in the United States. *Pediatrics*. 2009;124:234-40.
9. Kalfa D, Krishnamurthy G, Duchon J, Najjar M, Levasseur S, Chai P, et al. Outcomes of cardiac surgery in patients weighing <2.5 kg: Effect of patient-dependent and independent variables. *J Thorac Cardiovasc Surg*. 2014;148:2499-506.