Gestational Age at Birth and Outcomes After Neonatal Cardiac Surgery
An Analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database

John M. Costello, MD, MPH; Sara K. Pasquali, MD, MHS; Jeffrey P. Jacobs, MD; Xia He, MS; Kevin D. Hill, MD, MS; David S. Cooper, MD, MPH; Carl L. Backer, MD; Marshall L. Jacobs, MD

Background—Gestational age at birth is a potentially important modifiable risk factor in neonates with congenital heart disease. We evaluated the relationship between gestational age and outcomes in a multicenter cohort of neonates undergoing cardiac surgery, focusing on those born at early term (ie, 37–38 weeks’ gestation).

Methods and Results—Neonates in the Society of Thoracic Surgeons Congenital Heart Surgery Database who underwent cardiac surgery between 2010 and 2011 were included. Multivariable logistic regression was used to evaluate the association of gestational age at birth with in-hospital mortality, postoperative length of stay, and complications, adjusting for other important patient characteristics. Of 4784 included neonates (92 hospitals), 48% were born before 39 weeks’ gestation, including 31% at 37 to 38 weeks. Compared with a 39.5-week gestational age reference level, birth at 37 weeks’ gestational age was associated with higher in-hospital mortality, with an adjusted odds ratio (95% confidence interval) of 1.34 (1.05–1.71; P=0.02). Complication rates were higher and postoperative length of stay was significantly prolonged for those born at 37 and 38 weeks’ gestation (adjusted P<0.01 for all). Late-preterm births (34–36 weeks’ gestation) also had greater mortality and postoperative length of stay (adjusted P≤0.003 for all).

Conclusions—Birth during the early term period of 37 to 38 weeks’ gestation is associated with worse outcomes after neonatal cardiac surgery. These data challenge the commonly held perception that delivery at any time during term gestation is equally safe and appropriate and question the related practice of elective delivery of fetuses with complex congenital heart disease at early term. (*Circulation*. 2014;129:2511-2517.)

Key Words: cardiopulmonary bypass ◼ congenital ◼ congenital heart defects ◼ pediatrics ◼ surgery

Congenital heart defects are the most common birth anomalies, with moderate-to-severe variants occurring in approximately 6 per 1000 live births.1 Patients with critical congenital heart disease, including a variety of anomalies characterized by ductal dependency of either systemic or pulmonary blood flow (including most single-ventricle heart defects), typically undergo cardiac surgery during the first few days of life. In the United States alone, approximately 6000 neonatal cardiac operations are performed annually. Although outcomes have improved recently, certain lesions are still associated with average in-hospital mortality of 10% to 20% or more, and many survivors continue to experience significant morbidity and consume considerable healthcare resources.2-3 Thus, there is a need to examine potentially modifiable risk factors for poor outcomes.

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From the Divisions of Pediatric Cardiology (J.M.C.) and Cardiovascular and Thoracic Surgery (C.L.B.), Ann & Robert H. Lurie Children’s Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, IL; Department of Pediatrics and Communicable Disease, University of Michigan C.S. Mott Children’s Hospital, Ann Arbor, MI (S.K.P.); Department of Surgery, All Children’s Hospital and John Hopkins University, Saint Petersburg, FL (J.P.J.); Duke University Medical Center and Duke Clinical Research Institute, Durham, NC (X.H., K.D.H.); The Heart Institute, Cincinnati Children’s Hospital Medical Center, University of Cincinnati School of Medicine, Cincinnati, OH (D.S.C.); Division of Cardiac Surgery, Department of Surgery, Johns Hopkins School of Medicine, Baltimore, MD (M.L.J.).
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Correspondence to John M. Costello, MD, MPH, Division of Pediatrics, Northwestern University Feinberg School of Medicine, Regenstein Cardiac Care Unit, Ann & Robert H. Lurie Children’s Hospital of Chicago, 225 East Chicago Ave, Box 21, Chicago, IL 60611—2605. E-mail jmcostello@luriechildrens.org
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Gestational age at birth is likely one such risk factor. Births occurring between 37 weeks 0 days and 41 weeks 6 days completed gestation are designated “term,” signifying a period traditionally perceived as a safe window for delivery.4 In neonates and young infants undergoing cardiac surgery, both prematurity and low birth weight are well-established risk factors for poor outcomes.5-7 Thus, fetuses diagnosed prenatally with complex congenital heart disease are often scheduled for elective delivery once term gestation is reached. The majority of such births occur at early term (ie, at 37–38 weeks’ gestational age), in the interest of facilitating care coordination at tertiary care centers.8-12
Recent investigations have explored the relationship between gestational age at term birth and outcome in infants with cardiac disease and have challenged the assumption that early term birth is optimal. However, these investigations have been limited by single-center design and the use of administrative data. Thus, our understanding of the relationship between early term birth and outcome in neonates with complex congenital heart disease is incomplete.

The purpose of the present study was to examine the association between early term birth and outcomes after neonatal heart surgery across a large multicenter cohort using clinical registry data. Our primary outcome was in-hospital mortality. Postoperative length of stay and complications were examined as secondary outcomes.

### Methods

#### Data Source

The Society of Thoracic Surgeons Congenital Heart Surgery (STS-CHS) Database was used for this study. This database currently represents >85% of all pediatric heart centers in the United States. Perioperative, operative, and outcomes data are collected on all of the patients undergoing pediatric and congenital heart surgery at participating centers using standard definitions (STS-CHS Database data specifications, version 3.0, available at http://www.sts.org/node/518). The Duke Clinical Research Institute serves as the data warehouse and analytic center for all of the STS databases. This study was approved by the Duke University Institutional Review Board with waiver of informed consent and by the STS-CHS Database Access and Publications Committee.

#### Study Population

A variable specifying gestational age stratified by weeks was added to the STS-CHS Database on January 1, 2010. Thus, the potential study population eligible for inclusion consisted of 9936 neonates from 101 STS-CHS centers who underwent a primary cardiovascular operation before 28 days of age from January 1, 2010, through December 31, 2011. We excluded 445 patients who underwent a non-cardiac primary operation. Given the significantly different operative risk involved for various congenital heart defects, we excluded 109 patients whose operation could not be classified into one of the STS-European Association for Cardiothoracic Surgery (EACTS) Mortality Categories (category 1, lowest mortality risk; category 5, highest mortality risk). We also excluded patients undergoing isolated closure of patent ductus arteriosus (n=1702) or permanent/temporary pacemaker operation and those in whom a patent ductus arteriosus operation or pacemaker was the primary procedure (n=93), in addition to those with missing data for key exposure and outcomes variables (n=2804, of which 2012 were excluded for missing gestational age).

#### Outcomes

The primary outcome for this study was in-hospital mortality. Secondary outcomes included the occurrence of at least one of the following major complications: postoperative mechanical circulatory support, renal failure requiring dialysis, neurologic deficit persisting at discharge, stroke, unplanned cardiac reoperation or interventional cardiovascular catheterization during the postoperative time period, and heart block requiring permanent pacemaker. We also assessed the occurrence of one or more of an inclusive list of complications coded in the STS-CHS Database. Of note, complications occurring after discharge from the STS-CHS center are not captured in the database. Postoperative length of stay was also analyzed.

#### Analysis

Summary statistics were reported as count (percentage) or median with 25th to 75th percentiles, as appropriate. The Wilcoxon rank-sum test was used to compare gestational age at birth for patients with and without a prenatal diagnosis of congenital heart disease. Because it is known that both treatment and outcomes may vary across centers, our analytic approach to evaluate the relationship between gestational age and outcome was chosen specifically to account for confounding by center, and conditional logistic regression models stratified by center were used for our primary outcome variable. Results were adjusted for known factors associated with outcome in this population, including STS-EACTS Mortality Category of the primary procedure, age and weight at surgery, sex, and the presence of any STS preoperative risk factor or any noncardiac anatomic or genetic abnormality/syndrome. Both unadjusted and adjusted odds ratios and 95% confidence intervals are presented using models that account for center differences. In modeling the trend between event risk and gestational age, natural cubic spline transformation was applied to the gestational age variable in weeks, allowing the models to accommodate a nonlinear relationship between the outcomes and gestational age. The knots (where the trend is allowed to change, subjecting to mathematical conditions ensuring smoothness) were chosen without knowledge of the clinical outcomes and on the basis of the distribution of gestational age. The knots used in all of the models were 36.5, 38.5, and 40.5 weeks. We chose 39.5 weeks as the referent level of gestational age on the basis of an empirical analysis of the study data and that available in previous studies. For the postoperative length-of-stay outcome, negative binomial models using the canonical log-link function were fitted with indicator variables for centers and other covariates as noted above, thereby generating estimated ratios of median postoperative length of stay between 2 gestational age values. To facilitate the interpretation of the ratios of length of stay, we calculated the extra days of stay associated with gestational age by multiplying the population median length of stay by (ratio −1).

We evaluated the missing data mechanism and determined that a missing-at-random assumption was implausible for gestational age, because the event of not having the variable recorded was likely associated with greater gestational age values even after conditioning on variables collected by the STS-CHS Database. In light of this, the multiple imputation approach was not adopted. We instead performed a complete case analysis, because this approach is known to produce unbiased estimates under the assumption that the regression model is correctly specified and that missingness depends on covariates but not the outcomes. SAS/STAT software version 9.2 (SAS Institute Inc, Cary, NC) and R version 2.14 (R Foundation for Statistical Computing, Vienna, Austria) were used to perform the analyses. A P<0.05 was considered statistically significant.

### Results

#### Study Population

The study population included 4784 neonates who underwent cardiac operations at 92 institutions. Preoperative characteristics and operative variables are displayed in Table 1. The median gestational age at birth was 39 weeks (25th to 75th percentile, 37–39 weeks). Median gestational age in those with a prenatal diagnosis of congenital heart disease was 38 weeks (25th to 75th percentile, 37–39 weeks) and in those without a prenatal diagnosis was 39 weeks (25th to 75th percentile, 37–40 weeks; P<0.001). Of note, 48% of study patients were born before 39 weeks’ gestation, including 31% at 37 to 38 weeks’ gestation. Age at surgery was similar for patients born at 39 to 40 weeks’ gestational age when compared with patients born at 37 to 38 weeks (median, 7 days; 25th to 75th percentile, 4–12 days for both groups). Patients born at earlier gestational ages underwent surgery at progressively older ages (median age at surgery, 8 days for 34–36 weeks and 13 days for ≤34 weeks). Given the small number of study patients born at the extremes of gestational age (n=154 patients born at ≤33 weeks’ gestational age at birth; n=14 patients born at...
In-Hospital Mortality

Overall in-hospital mortality was 9.9% (474 of 4784). Unadjusted mortality rates by week of gestational age at birth are shown in Table 2. In-hospital mortality was 7.3% at 39 to 40 weeks, 9.0% at 38 weeks, and 13.2% at 37 weeks. Adjusted mortality data are shown in Table 2 and Figure 1. When compared with the 39.5-week referent level, adjusted odds of mortality were significantly higher for patients born at 37 weeks’ gestation. Birth during the late preterm period of 34 to 36 weeks’ gestation also had greater adjusted mortality.

Postoperative Complications

Of 4784 study patients, at least 1 postoperative complication occurred in 67.9% (n=3247), and at least 1 major postoperative complication occurred in 19.0% (n=911). When compared with a 39.5-week referent level, patients born at 37 and 38 weeks’ gestation had greater adjusted odds of developing 1 or more postoperative complications of any type, and those born at 37 weeks had greater adjusted odds of developing 1 or more major postoperative complications (Table 3).

Postoperative Length of Stay

The median postoperative hospital length of stay for all of the study patients was 16 days (25th to 75th percentile, 9–34 days). When compared with a 39.5-week referent level, patients born at 34 to 38 weeks’ gestation had a longer adjusted duration of postoperative length of stay (Figure 2). Differences in estimated extra days of postoperative hospitalization and ratios of medians of postoperative length of stay between gestational age groups are shown in Table 4. Of the 4310 patients who survived to hospital discharge, those born at 39 to 40 weeks were less likely to be discharged to another acute or chronic care center (4.0%) compared with those born at 37 to 38 weeks (5.5%), 34 to 36 weeks (6.4%), or <34 weeks (18.9%; 3 degree-of-freedom $\chi^2$ test $P<0.001$). This observation likely has a differential influence on length-of-stay data and capture of complications.

Discussion

In neonates undergoing cardiac surgery, we found that outcomes were worse in patients born during the early term.
period of 37 to 38 weeks’ completed gestation. When compared with a 39.5-week referent group, risk-adjusted in-hospital mortality was significantly higher for patients born at 37 weeks’ gestation. Early term neonates also had higher rates of postoperative complications and prolonged length of stay. Consistent with previous studies, we also found that birth during the late preterm period of 34 to 36 weeks’ gestation was associated with worse outcomes.

Prematurity was formally defined in the 1960s by an American Academy of Pediatrics committee as birth before 37 weeks’ completed gestation.19 It has long been known that premature neonates, including those with heart defects, are at risk for adverse outcomes.7 When compared with term infants with congenital heart disease, those born prematurely have an ≥2-fold greater risk of in-hospital mortality.5,20 The findings reported in our study and others suggest that gestational age, when analyzed as an ordinal variable, may provide more granularity and additional inferences relative to analyses on the basis of a binary determination of prematurity.

Two previous studies have examined the association between gestational age at term and outcomes in patients with heart disease. In an investigation of 971 neonates with critical congenital heart disease, those born at 37 to 38 weeks’ gestation had 2.3-fold greater adjusted odds of in-hospital mortality when compared with a referent group born at 39 to 40 weeks.13 That study involved robust risk adjustment but was limited by its single-center design and failure to account for any postnatal deaths that occurred before interhospital transfer to the study center. In a study examining National Health Statistics-linked birth-death files of 14.9-million infants born in the United States, the infant mortality rate attributable to congenital heart disease increased in a linear fashion with decreasing gestational age before 39 weeks.14 That study captured all postnatal mortalities regardless of referral to a tertiary care center, but risk adjustment was limited by the use of an administrative data set. The design of the present study overcame several of these limitations. The multicenter cohort of patients captured by the STS-CHS Database makes our findings highly generalizable, and the use of rich clinical registry data allowed for more comprehensive risk adjustment. Importantly, we were able to adjust for weight at the time of surgery, a potential source of confounding when assessing the relationship between gestational age and outcomes.6,21

Our findings are consistent with those reported in recent observational studies involving infants without cardiac or

<table>
<thead>
<tr>
<th>Table 3. Data for Complications by Week of Gestational Age at Birth</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gestational Age, wk</strong></td>
</tr>
<tr>
<td>-------------------------</td>
</tr>
<tr>
<td>Any complication</td>
</tr>
<tr>
<td>34.0</td>
</tr>
<tr>
<td>35.0</td>
</tr>
<tr>
<td>36.0</td>
</tr>
<tr>
<td>37.0</td>
</tr>
<tr>
<td>38.0</td>
</tr>
<tr>
<td>39.5</td>
</tr>
<tr>
<td>41.0</td>
</tr>
<tr>
<td>Major complication</td>
</tr>
<tr>
<td>34.0</td>
</tr>
<tr>
<td>35.0</td>
</tr>
<tr>
<td>36.0</td>
</tr>
<tr>
<td>37.0</td>
</tr>
<tr>
<td>38.0</td>
</tr>
<tr>
<td>39.5</td>
</tr>
<tr>
<td>41.0</td>
</tr>
</tbody>
</table>

Unadjusted values were estimated by models that included a center variable but did not include other patient level risk factors. CI indicates confidence interval; and OR, odds ratio.

*Data show exact binomial confidence intervals.
other birth defects. In such patients, a U-shaped relationship exists between gestational age at term birth and outcomes, with a nadir for adverse results at 39 to 40 weeks. In these studies, seemingly healthy infants born at early term have consistently higher rates of mortality, neonatal intensive care admission, and other morbidities commonly associated with prematurity. Although our study and those noted above were not designed to establish causality, maturational differences in multiple organ systems are likely contributory to the adverse outcomes experience by patients born at early term. When compared with infants without birth defects who undergo elective delivery at 39 to 40 weeks’ gestation, those born at early term are much more likely to require mechanical ventilation, to have respiratory distress syndrome requiring surfactant, to develop hypoglycemia, and to develop sepsis. Subtle but important developmental changes in the respiratory system occur in late gestation, including pathways critical to surfactant production, nitric oxide and surfactant production, as well as fetal lung fluid clearance. Incomplete maturation of energy stores, enzyme function, and immunity may also be causal in the observed outcomes.

A number of studies have identified an association between a prenatal diagnosis of congenital heart disease and earlier delivery. This finding may be explained in part by the fact that mothers expecting a fetus with congenital heart disease often undergo frequent fetal monitoring in late gestation, such as serial fetal nonstress tests and biophysical profiles, with the potential that the results of such testing are false positives far more often that true positives. Physician and maternal anxiety could also be a factor. Further study of the relationship between prenatal diagnosis and earlier delivery is warranted.

When considering our findings and the cumulative body of literature examining the relationship between gestational age and outcomes in neonates with or without cardiac disease, the take-home message is consistent and clear. Delivery at 39 to 40 weeks’ gestation is associated with the lowest rates of early morbidity and mortality. Some evidence suggests that neurodevelopmental outcomes may also be more favorable in infants born at 39 to 40 weeks’ gestational age who undergo cardiac surgery. There are several important inferences from these data. The relatively common practice of scheduled, elective delivery of neonates with a prenatal diagnosis of congenital heart disease at 37 to 38 weeks’ gestation requires re-evaluation. In selected cases, there may be compelling fetal or maternal indications for earlier delivery (eg, hydrops fetalis or pre-eclampsia). However, our data and others suggest that scheduling the elective delivery of a fetus with congenital heart disease before 39 weeks’ gestational age should generally be avoided. Such scheduled deliveries are often motivated by a desire to achieve a controlled birth near a congenital heart center. The perceived convenience of having a set delivery date for the parents, extended families, and the multiple clinician subspecialists involved in the care of these neonates may be contributory. It is important to recognize that the elimination of elective early term deliveries could potentially lead to the spontaneous delivery of more infants with critical congenital heart disease at hospitals remotely located from a congenital heart center. This issue could be largely overcome by anticipatory relocation of the expectant mother closer to the pediatric heart center during late gestation to await the onset of labor. Further evaluation of such strategies is necessary. The information provided by this study and others may also be useful for counseling parents and referring clinicians. Finally,

### Table 4. Unadjusted Postoperative Days, Estimated Extra Postoperative Days, and Ratios of Medians of Postoperative Days of Hospitalization by Week of Gestation at Birth

<table>
<thead>
<tr>
<th>Gestational Age, wk</th>
<th>Observed</th>
<th>Unadjusted Extra Days (95% CI)</th>
<th>Unadjusted Ratio (95% CI)</th>
<th>P Value</th>
<th>Adjusted Extra Days (95% CI)</th>
<th>Adjusted ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>34.0</td>
<td>19.0 (10.0-42.5)</td>
<td>7.7 (5.7-9.8)</td>
<td>1.48 (1.36-1.61)</td>
<td>&lt;0.001</td>
<td>6.1 (4.4-8.0)</td>
<td>1.38 (1.27-1.50)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>35.0</td>
<td>24.0 (12.0-44.0)</td>
<td>6.2 (4.6-8.0)</td>
<td>1.39 (1.29-1.50)</td>
<td>&lt;0.001</td>
<td>4.8 (3.4-6.4)</td>
<td>1.30 (1.21-1.40)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>36.0</td>
<td>18.0 (10.0-37.0)</td>
<td>5.0 (3.7-6.4)</td>
<td>1.31 (1.23-1.40)</td>
<td>&lt;0.001</td>
<td>3.7 (2.5-4.9)</td>
<td>1.23 (1.16-1.31)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>37.0</td>
<td>18.5 (10.0-35.0)</td>
<td>3.9 (2.8-5.1)</td>
<td>1.24 (1.18-1.32)</td>
<td>&lt;0.001</td>
<td>2.6 (1.7-3.6)</td>
<td>1.16 (1.10-1.23)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>38.0</td>
<td>18.0 (9.0-35.0)</td>
<td>2.7 (1.7-3.7)</td>
<td>1.17 (1.11-1.23)</td>
<td>&lt;0.001</td>
<td>1.6 (0.7-2.5)</td>
<td>1.10 (1.05-1.15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>39.5</td>
<td>15.0 (8.0-29.0)</td>
<td>Reference level</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>41.0</td>
<td>13.5 (8.0-25.3)</td>
<td>-0.9 (-2.3 to -0.5)</td>
<td>0.94 (0.86-1.03)</td>
<td>0.20</td>
<td>-0.2 (-1.5 to -1.2)</td>
<td>0.99 (0.91-1.08)</td>
<td>0.80</td>
</tr>
</tbody>
</table>

Unadjusted values were estimated by models that included a center variable but did not include other patient level risk factors. CI indicates confidence interval; and LOS, length of stay.

*Data were reported as median (interquartile range).

†Unadjusted extra days were calculated by multiplying the population median postoperative length of stay (16 days) by the ratio of medians – 1.
when conducting outcomes research, the analysis of gestational age as a continuous or ordinal variable may be more powerful and clinically relevant when compared with the binary variable of prematurity.

The strengths of this study lie in the multicenter patient population, which makes the findings highly generalizable. Limitations of this study are primarily related to the nature of the STS-CHS Database. Importantly, obstetric factors that may have influenced the timing of birth, such as the onset of natural labor, scheduled elective delivery, or the existence of maternal or fetal indications for delivery, were not available in the database. Similarly, perinatal details, such as method of delivery, were not available. Thus, it is possible that confounding by factors related to fetal well-being in utero may have influenced the observed outcomes. However, previous studies have found that elective deliveries are commonly scheduled at early term for fetuses with complex congenital heart disease, and our collective experience indicates that the medical indications cited for some unscheduled early term deliveries are rather soft. As would be expected, the rates of noncardiac risk factors, including chromosomal anomalies/syndromes and noncardiac congenital anatomic abnormalities, were slightly higher in the late preterm and early term patient groups (data not shown). However, the multivariable models were adjusted for these and other preoperative risk factors. This study was not designed to determine the ideal timing of cardiac surgery for neonates born at earlier gestational ages. For such patients, it is unknown whether a strategy of early surgery is superior to a strategy of medical management and nutritional support while awaiting growth and maturity. However, the multivariable models were adjusted for age at surgery, and thus our results are independent of any associations related to this variable. The STS-CHS Database also does not include fetuses that die in utero or any postnatal deaths that occur before a cardiac surgical procedure at an STS center. Finally, the database primarily captures complications specific to congenital heart surgery and not those medical complications more generally associated with prematurity. The observation that complication rates did not progressively increase with earlier gestational age at birth is counterintuitive but is likely explained by both this issue and other aspects of the study design. Premature neonates with complex cardiac defects who underwent preoperative medical management for >28 days before surgery were excluded from this study on the basis of nonneonatal age at surgery. In addition, postoperative complications occurring after transfer to another institution from the center where the cardiac operation was performed were not captured in the STS-CHS Database, and such transfers were more common in patients born at earlier gestational ages.

In neonates who undergo cardiac surgery, optimal early outcomes are associated with delivery at 39 to 40 weeks’ gestation. These data challenge the commonly held perception that delivery at any time during term gestation is equally safe and appropriate and question the related practice of elective delivery of fetuses with complex congenital heart disease at early term. In the absence of fetal or maternal indications for earlier delivery, the potential advantages and risks of scheduling the elective delivery of fetuses with congenital heart disease before 39 weeks’ gestation should be carefully considered. Further study of interventions designed to optimize timing of delivery is also needed to evaluate whether such initiatives are associated with improved outcomes.

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Disclosures

None.

References


**CLINICAL PERSPECTIVE**

Gestational age at birth is a potentially important modifiable risk factor in neonates with congenital heart disease. Using data from 4784 neonates in the Society of Thoracic Surgeons Congenital Heart Surgery Database, we evaluated the relationship between gestational age and outcomes, focusing on those infants born at early term (ie, 37–38 weeks’ gestation). We found that, when compared with a 39.5-week gestational age reference level, birth at 37 weeks’ gestational age was associated with a higher adjusted odds of in-hospital mortality. Patients born at early term had higher complication rates and prolonged postoperative length of stay. Consistent with previous studies, we confirmed that late-preterm births (ie, 34–36 weeks’ gestation) also had greater mortality and postoperative length of stay. We concluded that birth during the early term period of 37 to 38 weeks’ gestation is associated with worse outcomes after neonatal cardiac surgery. These findings are consistent with associations that have recently been identified between birth at early term and outcomes in neonates without birth defects. These data challenge the commonly held perception that delivery at any time during term gestation is equally safe and appropriate and require that we question the related practice of elective delivery of fetuses with complex congenital heart disease at early term.
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Supplemental Table S-1. Adjusted odds of in-hospital mortality by week of gestation at birth, stratified by cardiopulmonary bypass vs. non-cardiopulmonary bypass cases, and by lower complexity (STS-EACTS 1-3) vs. higher complexity (STS-EACTS 4-5) operations.

<table>
<thead>
<tr>
<th>Gestational Age</th>
<th>Overall</th>
<th>CPB</th>
<th>Non-CPB</th>
<th>STS-EACTS 1-3</th>
<th>STS-EACTS 4-5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raw mortality rate</td>
<td>9.9% (474/4784)</td>
<td>10.8% (363/3348)</td>
<td>7.7% (111/1436)</td>
<td>4.4% (72/1654)</td>
<td>12.8% (402/3130)</td>
</tr>
<tr>
<td>34</td>
<td>1.83 (1.26, 2.66)</td>
<td>0.002</td>
<td>1.63 (1.08, 2.46)</td>
<td>0.02</td>
<td>2.19 (1.02, 4.67)</td>
</tr>
<tr>
<td>35</td>
<td>1.70 (1.22, 2.37)</td>
<td>0.002</td>
<td>1.52 (1.05, 2.19)</td>
<td>0.03</td>
<td>1.91 (0.96, 3.79)</td>
</tr>
<tr>
<td>36</td>
<td>1.53 (1.15, 2.03)</td>
<td>0.003</td>
<td>1.40 (1.02, 1.92)</td>
<td>0.04</td>
<td>1.57 (0.85, 2.91)</td>
</tr>
<tr>
<td>37</td>
<td>1.34 (1.05, 1.71)</td>
<td>0.019</td>
<td>1.29 (0.97, 1.71)</td>
<td>0.08</td>
<td>1.22 (0.67, 2.22)</td>
</tr>
<tr>
<td>38</td>
<td>1.16 (0.93, 1.45)</td>
<td>0.19</td>
<td>1.17 (0.89, 1.53)</td>
<td>0.25</td>
<td>0.97 (0.55, 1.72)</td>
</tr>
<tr>
<td>39.5</td>
<td>Referent level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>41</td>
<td>1.18 (0.86, 1.62)</td>
<td>0.32</td>
<td>0.96 (0.63, 1.47)</td>
<td>0.87</td>
<td>2.39 (0.90, 6.32)</td>
</tr>
</tbody>
</table>

CPB, cardiopulmonary bypass; CI, confidence interval; OR, odds ratio; STS-EACTS, Society of Thoracic Surgeons-European Association of Cardiovascular Surgeons.