Best on Time, Not a Little Early:

Gestational Age and Outcomes for Neonates with Congenital Heart Disease

Running title: Thiagarajan; Neonates with congenital heart disease

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Human gestation lasts 40 weeks from the date of the last menstrual cycle\textsuperscript{1,2}. Neonates born 3
weeks prior (37 weeks gestation) through 2 weeks after 40 weeks of gestation are considered as
being born at “Term”. This classification is based on the presumption that no differences in
neonatal outcomes exist for those born during this 5-week period. Neonates born at or after 37
weeks of gestation, but prior to 39 weeks gestation, are thought to have matured adequately to
allow an uneventful transition to post-natal life. Elective delivery on or after 37 weeks of
gestation is therefore being increasingly utilized for medical (maternal and fetal) and non-
medical reasons\textsuperscript{2-3}. Recent research on gestational age and outcomes has shown that
considerable differences exist in mortality and morbidity for neonates born during that 5-week
time period\textsuperscript{4-9}. These reports also show that otherwise healthy neonates born at Early-Term (37
or 38 weeks) gestation have increased risk of poor outcomes compared with those born later at
Term (39 or 40 weeks) gestation.

Neonates born at Early-Term gestation have been shown to have a higher incidence of
respiratory failure requiring mechanical ventilation, surfactant deficiency and hyaline membrane
disease, transient tachypnea of newborn, need for neonatal intensive care unit admission, low 5
min APGAR scores, and hypoglycemia compared to those born at Term gestation\textsuperscript{2-3,10}. Tita et al
studied the association of Early-Term delivery and a composite neonatal mortality and morbidity
outcome containing neonatal death, respiratory complications, hypoglycemia, sepsis and need for
neonatal intensive care in a cohort of neonates delivered electively by repeat cesarean section
delivery at or after 37 weeks gestation\textsuperscript{7}. Compared to neonates born at 39 weeks gestation, those
born at 37 (adjusted odds ratio for poor outcome: 2.1) and 38 (adjusted odds ratio for poor
outcome: 1.5) weeks gestation had increased odds of the poor outcomes. Other studies have
shown similar results for neonates born electively at Early-Term for non-medical indications.
Some studies have also shown that poorer outcomes for Early-Term deliveries may be more common in those delivered by elective Cesarean section prior to the onset of labor\textsuperscript{2, 7}. Because these concerning findings have been consistent in many investigations, efforts to reduce the rate of elective delivery without medical indications before 39 weeks gestation are underway\textsuperscript{2}.

Early-Term delivery may be needed for certain medical indications including maternal or fetal conditions and in some circumstances early birth may improve neonatal outcomes\textsuperscript{2, 11, 12}. A committee opinion statement from The American College of Obstetrics and Gynecologists and The Society of Maternal–Fetal Medicine in (Number 560 and 561) lists maternal and fetal conditions including fetal congenital malformations where Pre-Term (birth prior to 37 weeks gestation) or Early-Term delivery may be considered\textsuperscript{2, 11}. Several studies have shown that neonates with a prenatal diagnosis of congenital heart disease are born sooner than those without a prenatal diagnosis\textsuperscript{13, 14}. Reasons for early delivery of children with prenatal diagnosis of congenital heart disease are largely unknown. However, one commonly cited reason for elective early delivery of neonates with congenital heart disease is to facilitate better coordination of the complex post-natal care often required by these neonates\textsuperscript{14, 15}. Regardless, it seems that a prenatal diagnosis of congenital heart disease may lead to elective delivery before 39 weeks of gestation, and that these Early-Term neonates may be subject to increased non-cardiac neonatal morbidity similar to those seen with otherwise healthy Early-Term neonates. Indeed, the association of early gestational age and poor outcomes in neonates with congenital heart disease has been shown to true in several recent investigations on this topic\textsuperscript{14, 15}.

In this issue of Circulation, Costello et al. investigate whether Early-Term (37 – 38 completed weeks of gestation) neonates with congenital heart disease had poorer outcomes compared with those born at Term (39 – 40 weeks of gestation)\textsuperscript{16}. These analyses were
conducted using multi-center data from 4,784 neonates with congenital heart disease undergoing cardiac surgery soon after birth during the years 2010 – 2011 and reported to the Society of Thoracic Surgeons Congenital Heart Database from 92 US hospitals performing pediatric cardiac surgery. In this study cohort, prenatal diagnosis was present in 46% of neonates, and these neonates had lower median gestational age compared to those without prenatal diagnosis (38 vs. 39 weeks). Nearly one third (31%) of neonates in this cohort were born at Early-Term. As expected, neonates born at Early-Term had increased post-operative mortality and major post-operative complications and longer length of hospitalization compared to those born at Term. Furthermore, at the end of their hospitalization, fewer Early-Term neonates were discharged home compared with those born at Term, indicating continued need for medical intervention and resource utilization even after hospital discharge in Early-Term neonates.

These data make a compelling argument that the practice of elective delivery of neonates with congenital heart disease at Early-Term should be discouraged. However, a few issues need careful consideration. First, no information is available on reasons for Early-Term delivery in this study cohort. A better understanding of reasons leading to delivery at Early-Term, including whether medical indications were present or absent is essential for the evaluation of the risks and benefits of Early vs. waiting for Term birth. Second, current knowledge on outcomes for Early-Term term neonates with congenital heart disease, including data presented in this manuscript, have focused on evaluating post-surgical outcomes rather than condition at birth or preoperatively. Given that many factors including gestational age can strongly influence post-cardiac surgical mortality, discrimination of risk due Early-Term birth from those imposed by cardiac surgery is difficult. Inclusion of variables that describe pre-operative condition and management strategies can help better understand issues related to Early-Term delivery and help
plan specific therapies and timing of surgical interventions. Finally, postponing delivery until Term in some cardiac lesions may carry increased risk to the fetus\textsuperscript{12, 17}. Thus information on the risk to fetal health by waiting for delivery until 39 or 40 weeks gestation, based on type of lesion, can help identify high-risk congenital heart defects or other patient factors for which Early-Term delivery may be beneficial.

In summary, Costello et al. show that neonates with congenital heart disease delivered at Early-Term face higher odds of post-operative mortality and morbidity compared to those delivered at Term gestation. Based on data from this study and prior investigations, the practice of elective Early-Term delivery in neonates with congenital heart without maternal or fetal indications should be discouraged.

**Conflict of Interest Disclosures:** None

**References:**


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