

EDITORIAL COMMENT

Neonatal Tetralogy Staged Versus Complete Repair



Is it Time to Rethink Neonatal Tetralogy?*

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Since Aldo Castaneda first reported infant and neonatal repair of tetralogy of Fallot (TOF) in 1977 (1), the general age for elective repair in North America has decreased to under 1 year of age (2). For those needing intervention in the neonatal period, the ideal approach has remained a topic of discussion influenced by regional history and institutional experience. Some institutions favor primary repair, whereas others favor staged repair with an initial palliation of a Blalock-Taussig (BT) shunt (2), a right ventricular outflow procedure (3), or more recently, transcatheter palliation (4-8).

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In this issue of the *Journal*, Savla et al. (9) utilize 11 years of a large administrative dataset to provide insight regarding those requiring intervention in the first 30 days of life. The 2-year Kaplan Meier survival is sobering. For the 1,032 neonates who received primary repair, the 2-year survival was 77%. Those undergoing a staged repair (n = 1,331) had an 84% survival, with the hazard ratio favoring staged repair (hazard ratio: 1.51; 95% confidence interval: 1.05 to 2.06; p = 0.024). In both groups, patient loss continued beyond the intervention phase. The operative mortality data are

validated by, and essentially matched, that seen in the Society of Thoracic Surgeon data: 7% for repair and 6% for a BT shunt (2). Furthermore, the analysis by Savla et al. (9) adjusts for patient factors, including prematurity, weight, and genetic syndromes; pre-treatment acuity, including need for ventilation or prostaglandin infusion; and institutional factors, including surgical volume and preferences. A propensity score model is utilized to control for pre-operative variables and hospital-specific characteristics, and a causal mediation analysis was used to determine if mortalities were related to surgical approach or post-operative factors. Cardiac complications were more than doubled in the repair group and had a mediating effect on repaired mortality of 78% at 2 years. Finally, subgroup analyses did not show a difference in mortality for patients who received BT shunts versus complete repairs, nor were mortality differences detected in patients who did or did not receive conduits within the complete repair group.

Given the limitations of an administrative dataset, this data is not likely to change an institutions' preference or bias to their primary approach of managing the symptomatic neonate. The differences in outcomes are not statistically explained by shunt versus repair or conduit repair versus no conduit repair. However, this data may influence decision making in those who are perceived to be at higher risk. The challenge is to reliably identify those that are likely to: 1) have a cardiac complication (a mediator of mortality in this study); or 2) to fail the institutions' preferred strategy. Thus, future studies will need to delineate additional risk factors, such as pulmonary valve and artery architecture—something not possible in an administrative dataset.

At a high level, there are 2 goals for TOF therapy: 1) prevention of early death through establishment of a reliable source of adequate pulmonary blood flow;

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and 2) maintenance of long-term cardiac health. Before the advance of interventional techniques, reliable and adequate pulmonary blood flow was established through primary repair or palliative surgical procedures. With evolving technology, prevention of early cyanotic death can now be achieved with catheter-based techniques (4-8). Although it is unclear which transcatheter or surgical palliations might have been performed in the 315 staged patients that did not receive a BT shunt, their inclusion in the staged group led to a statistically improved survival compared with those receiving repair. Certainly, the types, quality, and application of catheter-based therapy have evolved significantly during the time frame of the study (2004 to 2015).

For example, right ventricular outflow tract (RVOT) stenting has been shown to relieve cyanosis and allow for elective repair outside of the newborn period in those with TOF pulmonary stenosis and even valvar pulmonary atresia (4,6). This strategy was used by the group in Toronto to manage high-risk neonates defined by small pulmonary arteries (Nakata <100), birth weight <2.5 kg, and multiple comorbidities (4). Pulmonary artery growth was substantial. Mortality was not eliminated, but did shift away from operative-related death. Repair was then safely performed at an age of 6 months.

A 2018 multicenter study, which looked at 106 patent ductus arteriosus (PDA) stents and 251 BT shunts for varying diagnoses having ductal-dependent blood flow, showed that patients with PDA stents had one-half of the intensive care unit length of stay and about 20% larger pulmonary arteries (7). Survival between groups was similar. The stent group had higher unplanned reintervention, but appeared to have fewer cardiac-specific complications. Ductal stents hold promise as a less-invasive

means of establishing adequate and reliable pulmonary blood flow in the neonate—especially in neonates with tetralogy and pulmonary atresia.

Regardless of transcatheter approach, there are associated pitfalls. PDA stenting is not uniformly applicable due to certain technical issues with ductal variation. PDA stents have diastolic flow. RVOT stents that cross the pulmonary valve preclude valve preservation. There may be some patients that might otherwise have had preservation of a borderline valve that subsequently required a transannular patch due to the presence of a stent in the RVOT. All transcatheter procedures utilize off-label devices. Surgeons, interventionalists, and engineers will need to collaborate to establish new purpose-built devices that are more effective.

The data presented by Savla et al. (9) should provide the impetus for us to seek to do better with this patient population. Intuitively, initial less-invasive approaches are favorable, and early small series and small multicenter studies are promising. That said, the majority of patients did well. A broader application of transcatheter initial palliation would warrant a judicious approach. Further risk stratification may provide a plausible rationale for more institutions to test these newer interventional techniques in the highest-risk patients. Perhaps the success with high-risk interventional aortic valve implantation is a harbinger of what is to come for higher-risk symptomatic neonates who have TOF (10).

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