

Congenital Anomalies of the Cardiovascular System

Human development is a complex and intricate process. Despite a range of external variables and uncontrollable influences experienced throughout development, the human body commonly prevails, successfully developing as genetically programmed. However, occasional dysfunction during development can present as a phenotypically observable anomaly. When these anomalies present in the cardiovascular system, disastrous consequences ensue. Critical analysis of the etiology, pathophysiology, management and prognosis of two common congenital heart defects, Tetralogy of Fallot and hypoplastic left heart syndrome, elucidates the dangers associated with dysfunctional development within the cardiovascular system.

Thorough deconstruction of a medical condition requires investigation of epidemiology, etiology, pathophysiology, diagnosis, management, and prognosis. This review aims to elucidate these components in an effort to increase awareness and understanding of two prevalent cardiac developmental abnormalities, Tetralogy of Fallot and hypoplastic left heart syndrome. While this narrow focus only investigates two congenital cardiac anomalies, congenital heart defects present as a common and detrimental developmental disorder across the world. An estimated ten percent of all live births present with congenital heart defects. Of more concern, despite modern advances in surgical and medical interventions, these congenital heart defects commonly result in residual hemodynamic and electroconductive deficiencies after treatment (Wang, et al., 2019). Increased interest from the clinical and academic

community is necessary to enhance outcomes and opportunities in this disadvantaged population.

The cardiovascular system is prone to a wide range of developmental abnormalities. The Tetralogy of Fallot proves one of the most common cardiovascular congenital anomalies, affecting every five in ten thousand live births, and accounting for seven to ten percent of all congenital cardiovascular defects. Unfortunately, this multifaceted congenital anomaly can prove quite serious. The Tetralogy of Fallot is characterized by pulmonary stenosis, an interventricular septal defect, right ventricular hypertrophy, and an overriding aorta. The development of these four simultaneous anomalies are multifactorial. Contemporary research has identified several casual links and potentially impactful correlations. For example, Tetralogy of Fallot has been associated with maternal conditions and behaviors, such as untreated diabetes, phenylketonuria, and excess ingestion of retinoic acid. However, genetic abnormalities have been identified as well, including microdeletions of chromosome 22q11.2, JAG1/NOTCH2 mutations, and Alagille syndrome (Diaz-Frias & Guillaume, 2018). Nonetheless, despite identification of causal links and correlative associations, the direct etiology of Tetralogy of Fallot has not been confirmed. Thankfully, understanding of pathogenesis is more thoroughly understood.

The underlying etiology of the Tetralogy of Fallot remains under investigated. However, pathophysiology has been deconstructed through clinical models and animal studies. Contemporary paradigms suggest the congenital anomaly begins to develop around the twentieth day of gestation. At this time, the conus arteriosus, which forms the superior anterior region of the right ventricle, divides unequally. In turn, a small

infundibulum and a membranous interventricular septal defect are created from the irregular division. The presence of these two irregularities disrupts the lateral folding and looping mechanisms that result in the morphology of the four chambered heart. The disruption of folding and differentiation, due to malformed conus arteriosus development, cultivates an aortic orifice directly positioned over the persistent interventricular septal defect. This abnormal pathway results in an intracardiac shunt of blood from the right to left chamber, diminishing oxygenation. Simultaneously, the proximal positioning of the displaced aorta predisposes the pulmonary trunk to stenosis. The culmination of increased resistance in the pulmonary trunk, backflow through the interventricular septal defect, and decreased oxygenation, increases demand on the right ventricle, resulting in right ventricular hypertrophy (Winn & Hutchins, 1973). Consequentially, the four features defining the Tetralogy of Fallot are created.

Roughly three to five percent of births in the United States display the Tetralogy of Fallot. A significant prevalence, coupled with an early gestational development, allows early for identification. Most cases are discovered prenatal ultrasound and are confirmed via prenatal echocardiograms. However, some cases are not discovered until after birth (Widyastuti, 2015). While echocardiograms present as the gold standard for diagnosis, traditional chest radiographs also elucidate the underlying pathology. A boot-shaped heart sign is readily identifiable in the majority of patients (Figure 1). This pathognomonic sign is created by an upward pointing cardiac apex, resulting from right ventricular hypertrophy, and a narrowed pulmonary artery, due to hypoplastic development and stenosis (Haider, 2008). Severity of cardiac disruption is variable in this population. However, immediate intervention is always indicated.

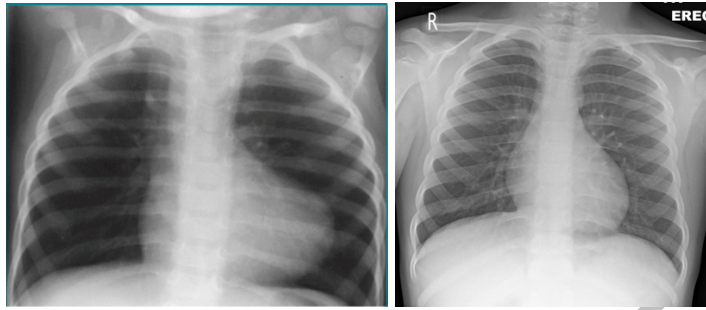


Figure 1: Traditional Chest X-Ray displaying the boot-shaped heart sign associated with Tetralogy of Fallot (Left). The upward pointing cardiac apex and narrowed pulmonary artery is not present under normal conditions (right).

Neonates suffering from undiagnosed Tetralogy of Fallot commonly present with mild to moderate cyanosis, dependent upon the severity of hemodynamic disruption. In severe cases, a lack of oxygenation, and a limited pulmonary blood flow, induce respiratory arrest. Regardless of severity, this congenital anomaly is surgically corrected to extend lifespan into adulthood. The ventral septal defect is repaired using a transannular patch, preventing backflow. This is achieved through ventriculotomy or atriotomy, with similar degrees of success. Additionally, the pulmonary artery is either bypassed, expanded via balloon dilation, or enlarged through stenting. Perioperative mortality has been reduced to roughly three percent, with average lifespans exceeding forty years of age. However, despite advancements in therapeutic interventions, residual effects remain. Additional stenting or dilation is a common necessity in the aging cohort. Moreover, arrhythmia is a common complication, contributing to an increased risk of sudden cardiac arrest. Renin-angiotensin-aldosterone system inhibitors are commonly prescribed for chronic maintenance. However, pharmacological management is only mildly effective. Despite advancements in therapeutic techniques,

lifespan pales in comparison to healthy peers (Van der Ven, 2019). Further research is necessary to identify more successful intervention strategies and enhance outcomes for this vulnerable population. Unfortunately, Tetralogy of Fallot is not the only cardiac anomaly posing significant risks for survival.

Hypoplastic left heart syndrome presents as an additional congenital heart defect with a high risk of mortality. Hypoplastic left heart syndrome presents as a rare congenital anomaly, in which the left atria and ventricle are severely underdeveloped. As aforementioned, cardiac anomalies can impose dangerous consequences, and hypoplastic left heart syndrome is no different. Even with advancements in medical intervention, roughly one in three newborns fail to survive. Investigation of pathophysiology and treatment expose the need for improved interventions.

Hypoplastic left heart syndrome begins developing during gestation. This flow defect is suspected to originate due to genetic abnormalities, as a hereditary correlations have been identified in epidemiological research. However, further research is required to elucidate etiological origins (Liu, et al., 2017). While the initiating cause is underexplored, pathophysiology is well developed. Hypoplastic left heart syndrome is initiated by aortic valve stenosis or atresia, left ventricular outflow obstruction, and mitral valves stenosis or atresia. With inadequate ejection from the left atrium and ventricle, the fetus depends on a patent ductus arteriosus to circulate oxygenated blood. However, chronic dependence on the patent ductus arteriosus results in further hypoplasia of the left ventricle and atria, while inducing hypertrophy in the right ventricle. This hemodynamic irregularity results in backflow and increased pulmonary pressure,

ultimately leading to cyanosis (Gobergs, Salputra & Lubuau, 2016). This aberrant anatomy requires immediate intervention.

Hypoplastic left heart syndrome is not clinically observable until after the second trimester, as the left side of the heart often appears adequately developed until this time. However, echocardiograms during screening procedures during the third trimester commonly identify this congenital defect, with computer tomography confirming the defects existence. Perinatal intervention is often entertained, with pulmonary trunk anastomosis, reconstruction of the ascending aorta, and systemic-to-pulmonary arterial shunting presenting as common perinatal interventions. However, clinical research suggests these strategies only mildly improve outcomes. Ultimately, corrective surgery, addressing valve dysfunction, or total heart transplant is required within six months of birth to avoid a fatal outcome (Tworetzky, et al., 2001). Traditional radiographs expose consequences of untreated hypoplastic left heart syndrome.

Hypoplastic left heart syndrome induces cyanosis. In turn, radiographic features display common features of hypoxemia and congestive heart failure (Bardo, et al., 2001). Pulmonary vasculature displays reorganization, while the right ventricle and atria display hypertrophy (Figure 2). If left untreated, hypoplastic left heart syndrome is fatal. However, even with treatment, survival rates remain bleak. Only thirty-nine percent of patients survive after fifteen years (Mahle, et al., 2000). Further research is necessary to identify early intervention strategies and bolster overall outcomes.

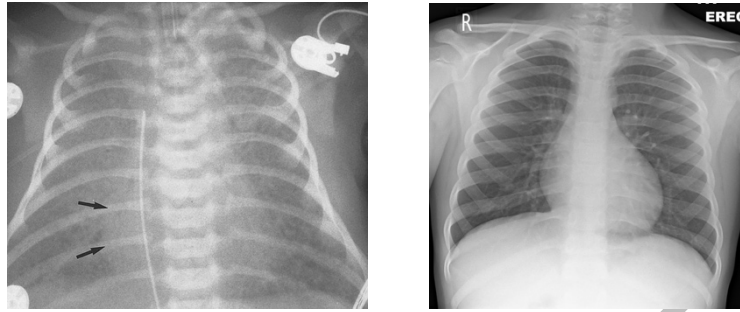


Figure 2: Traditional chest radiograph of hypoplastic left heart syndrome displaying right sided hypertrophy, left sided hypotrophy, and pulmonary reorganization (left) compared to normal anatomy (right).

decades. However, long term survival rates remain bleak. Critical analysis of Tetralogy of Fallot and Hypoplastic left heart syndrome display this reality. Further research is necessary to enhance outcomes and improve lifespan in this population.

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