Critical Congenital Heart Disease in Neonates: Evaluation and Management

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Introduction

Critical congenital heart disease (CHD) is one of the commonest causes of mortality and morbidity in neonates and requires multidisciplinary approach for optimal outcomes. Critical CHD, defined as requiring surgery or catheter based intervention in the first year of life, occurs in approximately 25 percent of those with CHD. According to registry data 3 in 1000 live births will require intervention for heart disease in the first year of life 12. Early evaluation and treatment is necessary to avoid the severe irreversible secondary effects of the heart disease on other organs. With improvements in intensive care and paediatric cardiac surgery, the mortality rates have come down significantly for these heart diseases.

Clinical Presentation

Timing of presentation of the heart disease depends upon the severity of the defect and the physiological effects of the transitional circulation. Common presentations of neonatal CHDs include cyanosis, heart failure including cardiogenic shock, arrhythmias and rarely asymptomatic heart murmurs. Increasingly, neonates with critical CHD are diagnosed by fetal echocardiography. Critical congenital heart lesions may be ductus-dependent. The affected neonate may not be symptomatic at birth because the ductus arteriosus has not yet closed prior to discharge. A review of 10 studies reported that 30 percent of patients with critical CHD were diagnosed after discharge1. The lesions which were not diagnosed prior to discharge were primarily ductus-dependent and included coarctation of the aorta, interrupted aortic arch, aortic stenosis, hypoplastic left heart syndrome (HLHS), and transposition of the great arteries. Nonductal-dependent cyanotic lesions with only mild desaturation or tachypnea initially, such as truncus arteriosus, tetralogy of Fallot, and total anomalous pulmonary venous connection were also missed. Closure of ductus arteriosus can precipitate rapid clinical deterioration with potentially life-threatening consequences (i.e., cyanosis, severe metabolic acidosis, seizures, cardiogenic shock, cardiac arrest, or end-organ injury)1. In a population-based study from the California state-wide death registry, more than half of the 152 neonates with a missed diagnosis of critical CHD at birth died1.

Cyanosis: Cyanosis, usually detected when the concentration of reduced hemoglobin is more 3 g/dl in neonates, is an important sign of CHD. Respiratory disorders, central nervous system disorders and profound polycythemia are more common causes of cyanosis in neonates and need to be distinguished from CHDs.

The normal closure of the ductus arteriosus in the first days of life can precipitate profound cyanosis in the following scenarios:

1. When the ductus arteriosus is the only mechanism of pulmonary blood flow, such as in patients with critically obstructive right heart lesions (eg, critical pulmonary stenosis/atresia).
2. When the ductus arteriosus supplies the majority of systemic circulation in critically obstructive left heart lesions (including HLHS and critical aortic valve stenosis). With ductal closure, these patients will present with decreased peripheral perfusion, cyanosis, metabolic acidosis and shock.
3. When the ductus arteriosus provides mixing between parallel pulmonary and systemic circulations (transposition of the great arteries).

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Nonductal-dependent critical congenital heart defects like total anomalous pulmonary venous connection (TAPVC), truncus arteriosus and tricuspid atresia with increased pulmonary blood flow also present with cyanosis. Lesions such as critical coarctation of the aorta or interrupted arch may exhibit differential cyanosis.

**Heart failure and cardiogenic shock:** Pulmonary venous congestion, resulting in tachypnea and increased work of breathing, can occur when there is a rapid increase in pulmonary blood flow associated with a fall in pulmonary vascular resistance postnatally in conditions such as truncus arteriosus or duc tus arteriosus in premature infants, or pulmonary venous obstruction in TAPVC.

A variety of mechanisms can lead to cardiogenic shock in newborns with ductal-dependent CHD when the ductus arteriosus closes:

1. In left heart obstructive lesions (e.g., HLHS, critical aortic stenosis, coarctation of the aorta, and interrupted aortic arch), systemic perfusion is lost.
2. In right-sided obstructive lesions restricted pulmonary blood flow results in decreased systemic oxygen delivery and metabolic acidosis which may result in shock.
3. In lesions with parallel pulmonary and systemic circulations (e.g., transposition of the great arteries with intact ventricular septum), mixing between the two circulations is decreased, leading to hypoxia and metabolic acidosis, which results in failure and shock.

Cardiogenic shock must be differentiated from other causes of shock, such as sepsis and metabolic disorders.

**Asymptomatic murmurs:** Pathological murmurs appear at characteristic ages. Stenotic and regurgitant valvar murmurs tend to appear shortly after birth whereas shunt lesions produce murmurs after two to four weeks. Physiological murmurs are present in as high as 70% of neonates and need to be distinguished from pathological murmurs.

**Abnormal rhythm:** Presence of brady or tachyarrhythmias during prenatal evaluation or postnatally may give a clue to the presence of CHDs. Tachyarrhythmias may give a clue to the presence of Ebstein's anomaly, ventricular inversion, hypertrophic cardiomyopathy and rhabdomyomas. Complete heart block may indicate the presence of maternal lupus and associated neonatal dilated cardiomyopathy.

**Prenatal diagnosis:** The sensitivity of prenatal screening with echocardiography for severe heart diseases is good, though coarctation of aorta and TAPVC may be missed.

**Clues from evaluation of the Neonate:**

**Precordial activity** - Dextrocardia is often associated with complex CHD. In addition cardiac enlargement in a newborn with respiratory symptoms is more suggestive of cardiac than pulmonary disease.

**Split Second Heart Sound (S2)** - Although an audible split S2 reduces the likelihood of severe CHD, the newborn's rapid heart rate often makes it challenging to detect S2 splitting. Splitting is audible in 80 percent of normal newborns by 48 hours of age, when the heart rate is less than 150 beats per minute. As an infant's heart is positioned more horizontally, splitting may be easier to hear along the mid to lower sternal border than in children or adults. A single second heart sound occurs with aortic atresia, pulmonary atresia, truncus arteriosus and conditions with severe pulmonary hypertension.

**Other heart sounds** - The following additional heart sounds may be associated with cardiac abnormalities.

- Early systolic clicks, which occur with semilunar valve stenosis and truncus arteriosus.
- Mid-systolic click with Ebstein's anomaly of the tricuspid valve.
- S3 gallop from ventricular dysfunction.

**Murmurs:** Though pathological murmurs indicate the presence of heart disease absence of murmurs does not rule out critical CHD. The following factors may account for the absence of a murmur:

- The velocity of turbulent blood flow may not be high enough to generate a murmur. This typically occurs in HLHS, simple transposition of the great arteries, TAPVCs, pulmonary atresia, and cardiomyopathy.
- Decreased ventricular function can limit the generation of a murmur. As an example, if the left ventricular myocardium cannot generate enough contraction to create sufficient flow across a critically obstructed aortic valve, a murmur of aortic stenosis will not be heard.
- Elevated pulmonary resistance may limit flow.

**Peripheral arterial pulses** - Though the diagnosis of coarctation of the aorta and other aortic arch obstructions is strongly suggested in an infant with decreased or absent pulses in the lower extremities with strong upper extremity pulses, the absence of the same does not rule these disorders.

**Extracardiac abnormalities** - Extracardiac abnormalities are frequently detected in children with CHD. Skeletal abnormalities, especially those of the hand and arm, are often associated with cardiac malformations. CHD may be a component of many specific syndromes and chromosomal disorders. In a review of the population-based surveillance data from the Metropolitan Atlanta Congenital Defects Program, 12.3 percent of infants with CHD had a chromosomal abnormality. In a Danish population-based study, chromosomal defects were detected in 7 percent of patients with CHD, and extracardiac anomalies in 22 percent.
Pulse oximetry screening: Data have shown that universal neonatal screening with pulse oximetry improves the identification of patients with critical CHD compared with physical examination alone. In a 2012 meta-analysis of 13 studies with data from 229,421 newborn infants, the overall sensitivity of pulse oximetry for detection of critical CHD was 76.5 percent (95% CI 67.7-83.5) and specificity was 99.9 percent (95% CI 99.7-99.9). All the studies in the analysis used a cutoff SpO2 threshold of < 95 percent. The overall false-positive rate was 0.14 percent (95% CI 0.06-0.33).

In a large multicenter prospective Chinese study of 122,738 newborn infants born between 2011 and 2012, the sensitivity for detecting critical CHD was greatest when the combination of pulse oximetry plus clinical assessment (93 percent) compared with either pulse oximetry alone (84 percent) or clinical assessment alone (77 percent). In this cohort, the false-positive rate for pulse oximetry alone was 0.3 percent (394 of 120,561 patients).

AAP, AHA, and ACC screening approach: The AAP, AHA, and ACC endorse the following strategy of universal newborn screening based on a review of the available literature that included the previously discussed prospective studies:

- Timing – Screening should not be performed until after 24 hours of life or as late as possible if early discharge is planned.
- Instrumentation – The screening should be performed using a motion-tolerant pulse oximeter. Either disposable or reusable probes can be used. Reusable probes reduce the cost of screening, but must be appropriately cleaned to minimize the risk of infection.
- Probe placement – Screening is recommended in the right hand (preductal) and either foot (postductal). Screening at both locations can occur simultaneously or in direct sequence.
- Personnel – Screening is performed by qualified and trained personnel.
- A positive screening test includes fulfilling one of the following three criterions:
  - Single SpO2 measurement <90 percent
  - SpO2 measurement <95 percent in both upper and lower extremities on three occasions, each separated by one hour
  - SpO2 difference >3 percent between the upper and lower extremities

Hyperoxia test: Performed on neonates to determine whether cyanosis is due to lung disease or CHD. Requires measurement of arterial PaO2 for diagnosis; pulse oximetry cannot be used for this purpose.

Test is performed by administering 100 % oxygen for >10 min
- PaO2 > 150 mmHg (passed hyperoxia test): pulmonary disease likely
- PaO2 < 100 mmHg or rise by < 30 mmHg (failed hyperoxia test): cardiac cause (R-L shunt) likely
- Values between 100 and 150 mmHg or even beyond 150 mm Hg can be present in structural heart diseases with complete admixture and increased pulmonary blood flow including HLHS and total anomalous pulmonary venous return.

- Pulmonary disease with a massive intrapulmonary shunt may have a failed hyperoxia test.

Clues from chest roentgenogram and electrocardiogram: In addition to cardiomegaly, visceral and cardiac situs, sidedness of the arch, decreased or increased pulmonary blood flow and pulmonary venous hypertension can be inferred from a chest x-ray. Electrocardiograms should be interpreted in the light of gestational and postnatal age and proper lead placement. Abnormal rhythms and ventricular dominance give clues to specific heart defects.

General measures for stabilisation
1. Vascular access can be established reliably in the first two weeks of life through the umbilical route for volume resuscitation, medications and monitoring.
2. Care should be taken to replenish intravascular volume before institution of inotropic support and anesthesia if present should be corrected.
3. Neonates who present with shock and who fail a hyperoxia test should be considered to have a ductus-dependant circulation until proved otherwise and prostaglandin E1 (PGE1) should be started even before an anatomic diagnosis.
4. Deterioration on PGE1 may be a sign of TAPVC, HLHS or mitral atresia with restrictive PFO or TGA with intact IVS and restrictive PFO and warrant urgent echocardiogram.
5. During echocardiography, temperature and hemodynamic instability are common in sick neonates with critical CHDs and require close monitoring by medical staff.
6. Apnea can develop in about 10 – 12 % of neonates requiring high dose prostaglandin and require intubation and ventilation, particularly if planned for transport to another center.

Lesion-specific care
1. Duct dependant systemic circulation (Critical aortic stenosis, coarctation of aorta, interrupted aortic arch, HLHS):

These infants most commonly present with clinical signs of systemic hyperperfusion, with acidosis and hypotension, with signs of end-organ impairment.
Peripheral pulses are often globally reduced; if there is obstruction within the aortic arch, the femoral pulses will be weaker than the right brachial pulse, or may be absent. In these infants, resuscitation should aim to optimise systemic oxygen delivery and prevent metabolic acidosis, which can be the cause of increased operative mortality.

Two fundamental principles underlie the resuscitation of these infants. Firstly, ductal patency (to provide systemic blood flow) is vital for early survival; thus all patients in whom this diagnosis is suspected should be started on prostaglandin infusion at a rate appropriate to maintain ductal patency. Apnea secondary to prostaglandin infusion is a relatively common indication for intubation in these patients, but not necessarily an indication to reduce the dose and never an indication to stop the infusion. Secondly, when ductal patency has been established, attention must be directed to the balance between systemic and pulmonary blood flows. In these patients, the systemic, myocardial, and pulmonary circulations are in parallel and in constant dynamic competition with one another. In short, increases in pulmonary blood flow lead to reductions in systemic and myocardial blood flow, with continuing signs of poor peripheral perfusion, metabolic acidosis, oliguria, and myocardial dysfunction. Pulmonary over-circulation should be pre-emptively managed by using measures that restrict pulmonary blood flow, in order to allow adequate perfusion of the systemic and myocardial vascular beds.

In summary:

(1) Prostaglandin infusion must be started at a rate sufficient to maintain ductal patency.

(2) Ventilatory parameters should be adjusted to manipulate the pulmonary vascular resistance to avoid pulmonary over-circulation, so as to maintain a pulmonary to systemic blood flow ratio of about 1:1. This goal can usually be achieved by applying a modest level of positive end expiratory pressure (4–6 cm H2O), ventilating in room air, and adjusting inspiratory pressures, rate, or tidal volumes to achieve an arterial CO2 tension of 5–6 kPa and a systemic saturation of 75–85%, avoiding respiratory alkalosis.

(3) Systemic venous saturations are the best indicators of peripheral tissue perfusion and should be maintained at around 40–50%.

(3) Improving total cardiac output and oxygen delivery are more important than increasing FiO2. If signs of low cardiac output persist, the patient should be reassessed to ensure that the prostaglandin infusion is adequate and intravascular volume is satisfactory. Anemia should be corrected; sedation and muscle paralysis may help. If the systemic blood pressure allows, a low dose nitroprusside infusion may improve metabolic acidosis. Otherwise, a low dose inotrope infusion may be of benefit in arresting the vicious cycle of metabolic acidosis and worsening ventricular function. In general, high dose inotrope infusions should be avoided because they may increase systemic vascular resistance, thus forcing more blood into the lungs and worsening the pulmonary to systemic blood flow distribution.

(4) Balloon atrial septostomy will help in the presence of a restrictive patent foramen ovale.

(5) Early surgical correction should be planned once metabolic acidosis and end-organ dysfunction improve.

II. Duct dependant pulmonary circulation
(Critical pulmonary stenosis, pulmonary atresia with intact IVS, Tricuspid atresia, single ventricle physiology and TOF with severe RVOT obstruction, Ebsteins anomaly with critical pulmonary stenosis):

In this group of conditions providing a stable source of pulmonary blood flow is the principal objective. Though PGE, can act as a temporary stabilising measure, interventional (balloon pulmonary valvotomy, ductus arteriosus stenting, pulmonary valve perforation) or surgical management (systemic to pulmonary artery shunt) will be needed after correction of metabolic acidosis.

- In pulmonary atresia with intact IVS, presence of RV dependant coronary circulation should be looked for, as in the presence of the same decompression of RV is contraindicated. Shunt surgeries will be the treatment of choice.

- In Ebstein anomaly, the presence of associated accessory pathway mediated tachycardia may complicate management. Measures to decrease pulmonary vascular resistance and hence improve antegrade pulmonary flow (high FiO2, nitric oxide and hyperventilation to induce mild respiratory alkalosis) may be useful in some neonates. Pulmonary hypoplasia in severe Ebstein anomaly (due to dilated right heart in utero) may not respond to the above measures and may have a high mortality.

III. Lack of intercirculatory mixing
(Transposition of great arteries):

Neonates with TGA and intact IVS need intermixing between the parallel pulmonary and systemic circulations for survival. Initial management of such neonates aims at ensuring adequate intermixing and maximizing the mixed venous systemic saturation (an index of systemic perfusion). Children who do not respond to intravenous prostaglandin infusion usually have a restrictive foramen ovale and/or severe pulmonary hypertension.

- If balloon atrial septostomy is not successful in improving the SaO2 and end tidal CO2 levels,
measures to decrease pulmonary vascular resistance as mentioned earlier should be ensured.
- While measures to decrease pulmonary vascular resistance are instituted, manoeuvres to prevent and treat metabolic acidosis like decreasing whole body oxygen consumption (muscle relaxants, sedation, mechanical ventilation) and improving oxygen delivery (ensuring adequate intravascular volume, inotropes, correction of anemia) should be started.

IV. Lesions with complete intracardiac mixing and no pulmonary stenosis:
This group of conditions includes truncus arteriosus, TAPVC and single ventricular physiology lesions. In the first two conditions after general stabilisation measures, emergency surgery should be the treatment option.
- Single ventricle physiology lesions are frequently associated with heterotaxy syndromes and complex extracardiac lesions and hence need evaluation for the same.
- Pulse oximetry screening is particularly useful in this group of disorders as they may be missed by clinical evaluation; the optimal age for 1st stage palliation for single ventricle disorders with no pulmonary stenosis (PA banding) is 6-8 weeks.

V. Severe left ventricular dysfunction in newborns:
- Abnormal left coronary artery from pulmonary artery (ALCAPA) can present with severe LV dysfunction and heart failure in 1st few weeks of life. The presence of q waves in leads I and aVL gives a clue to the presence of this disorder. Echocardiography demonstrates the abnormal coronary artery in almost all cases. Diagnosis of this condition is an indication for surgical correction.
- Myocarditis due to intrauterine viral infections (coxackie, rubella and varicella most commonly) can present with severe LV dysfunction and heart failure. The presence of associated hepatitis and CNS involvement will give a clue to the diagnosis; treatment is symptomatic.
- In infants born to mothers with connective tissue disorders, maternal antibody induced LV dysfunction can present with heart failure commonly associated with abnormalities of atrio-ventricular conduction.

VI. Left to right shunt lesions:
Except for patent ductus arteriosus (PDA) in preterm children, most of the left to right shunt lesions present with asymptomatic murmur. Worsening respiratory distress with CO2 retention and short systolic murmur in preterm child indicates the presence of a PDA. Bounding peripheral pulses, hyperdynamic precordium and cardiomegaly can also be seen. Most of these children respond to fluid restriction, diuretics and medical closure of ductus arteriosus with indomethacin, ibuprofen and recently paracetamol.

VII. Miscellaneous disorders:
- Transient myocardial ischemia: Perinatal asphyxia can result in transient myocardial dysfunction with atrio-ventricular valve regurgitation and elevation of cardiac enzymes; this usually resolves spontaneously with supportive care.
- Hypertrophic cardiomyopathy (genetic forms and in infants born to diabetic mothers) can present with heart failure in neonates. While the former has a grim prognosis, the later usually resolves within 6 months with supportive care.

Conclusion
At present, resources and distribution of expertise do not generally allow access to rapid postnatal diagnosis in symptomatic neonates with suspected CHD. Antenatal detection rates for CHD are low (with considerable lesion-specific and geographic variation). Most cases of congenital cardiac abnormalities are unexpected. We must therefore have a high index of suspicion for including CHD (or arrhythmia) in the differential diagnosis of a neonate with cyanosis or shock in the first minutes, hours, or days of extrauterine life. Early discussion with a cardiac center and institution of appropriate treatment in suspected cases may avoid the pursuit of other less likely diagnoses, the treatments for which may worsen the clinical situation.

References


List of abbreviations

| ACC | American College of Cardiology |
| AHA | American Heart Association |
| ALCAPA | Abnormal left coronary artery from pulmonary artery |
| AAP | American Academy of Pediatrics |
| CHD | Congenital Heart Disease |
| CNS | Central Nervous System |
| HLHS | Hypoplastic Left Heart Syndrome |
| IVS | Interventricular Septum |
| LV | Left Ventricle |
| PA | Pulmonary Artery |
| PDA | Patent Ductus Arteriosus |
| PFO | Patent Foramen Ovale |
| RV | Right Ventricle |
| RVOT | Right Ventricular Outflow Tract |
| TAPVC | Total anomalous pulmonary venous connection |
| TGA | Transposition of great arteries |
| TOF | Tetralogy of Fallot |