

Applied Physiology to the Contemporary Management of the Neonate with Hypoplastic Left Heart Syndrome

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The surgical treatment of hypoplastic left heart syndrome is still a challenge. Few selected large volume centers that adopted protocols focused on understanding of post-Norwood pathophysiology have reduced their mortality rates to around 15%. The inherent inefficacy of the parallel circulation in Norwood operation lends itself to problems related to postoperative management of these patients crucially revolving around keeping a balance between systemic blood flow (Qs) and pulmonary blood flow (Qp). This paper describes the physiology of the Norwood principle, the importance of an adequate hemodynamic assessment, to guide the different postoperative management options.

INTRODUCTION

Hypoplastic left heart syndrome (HLHS) constitutes a spectrum of cardiac anomalies that result in underdevelopment of left-sided heart structures. It is characterized by aortic atresia or severe stenosis with hypoplasia or absence of the left ventricle¹. Coarctation of the aorta is usually the most frequent associated anomaly and it may impede retrograde blood flow to a diminutive ascending aorta. Postnatal survival is dependent on the ductus arteriosus patency and shunting at atrial level. The natural history is almost universally lethal in the first month of life².

The past decade experienced enormous improvements in the surgical treatment of HLHS. Several current available surgical alternatives have been extensively explored (Table 1). Although multi-institutional studies³ using intention to treat based analyses have demonstrated higher intermediate term survival for patients entered into heart transplantation⁴, the latter has become less or equally important than the staged palliative surgical approach. Reasons include shortage of available donors, post-transplant morbidity and limited long-term survival^{5,6}. Most importantly, there have been significant

Table 1 – Current surgical alternative options in hypoplastic left heart syndrome

Heart transplantation

Norwood procedure and modifications

- *Cardiopulmonary bypass options*
 - Deep hypothermic circulatory arrest
 - Hypothermic bypass with selective regional perfusion
- *Type of arch reconstruction technique*
 - Patch
 - No patch
- *Source of pulmonary blood flow*
 - Modified Blalock-Taussig shunt
 - Right ventricle to pulmonary artery conduit

Stenting of the arterial duct and banding of the pulmonary arteries

improvements in the surgical palliation, originally described by Norwood in 1983⁷. The progressive decline in the surgical mortality is a result of multidisciplinary protocols incorporated to the practice of pediatric cardiac surgery⁸. Despite the initial prohibitive mortality rates, mastering of surgical and anesthetic techniques and the development of safer cardiopulmonary bypass with adequate myocardial and cerebral protection have made feasible the application of the Norwood principle to HLHS.

Nevertheless, most pediatric heart centers still face poor results in the treatment of this complex malformation. Few selected large volume centers that adopted protocols focused on understanding of post-Norwood physiology have reduced their mortality rates to around 10 to 15%^{9,10}. Greater emphasis is being demanded to achieve the task of further reduction in this figure that, most would agree, can be obtained by addressing the directives listed on Table 2.

This review article describes the physiologic principles that guide the modern surgical treatment of the neonate with HLHS.

KEY WORDS

Congenital left heart lesions, Congenital heart disease, cyanotic, Univentricular heart, Neonate, Postoperative care

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Table 2 – Directives on the surgical treatment of hypoplastic left heart syndrome

- Preoperative stabilization
- Adequate surgical correction
- Better understanding of hemodynamics in postoperative stage I palliation
- Minimizing the inter-procedural attrition
- Protection of Fontan candidacy

BALANCING THE CIRCULATIONS IN THE NORWOOD PHYSIOLOGY: SECRET OF A SUCCESSFUL POSTOPERATIVE MANAGEMENT

Post-Norwood physiology: Why the challenge?

In assessing the flow-dynamics of fluids, combinations of two important physical equations (Poiseuille's law and Ohm's law) provide the variables that are functions of flow as shown on Table 3.

Table 3 – Poiseuille's and Ohm's laws

$$R = \frac{P_i - P_o}{Q} = \frac{8\eta l}{\pi r^4}$$

R = Hydraulic resistance; $P_i - P_o$ = Inflow to outflow pressure differential; Q = Volume flow; η = Viscosity of the fluid; r = Radius of the tube.

It is safe to reiterate the well-understood principle of physics that relates to electric or hydraulic circuits, when two resistances of different values are connected in parallel, being supplied by a single power source, more flow occurs through the lower resistor. Conceptually similar, though in a more complex manner, is a single ventricle supplying two vascular beds of differing resistances connected by a shunt that will eject more blood flow towards the path of least resistance. This poses problems in the post-operative management of Norwood patients because a high resistance in the systemic bed leads to pulmonary over-circulation, having the so-called "steal phenomenon" in the systemic side. Conversely, if there is higher resistance in the pulmonary vascular bed, there will be adequate systemic perfusion but with poorly oxygenated blood. In either case, there will be a situation of circulatory shock due to tissue anaerobism. The inherent inefficacy of the parallel circulation in Norwood operation lends itself to problems related to postoperative management of these patients crucially revolving around keeping a balance between systemic blood flow (Qs) and pulmonary blood flow (Qp).

Bartram et al¹¹ studied 122 patients who underwent Norwood operation between 1980 and 1995 and pointed out mismatched pulmonary to systemic blood flow as the second most common cause of death next only to coronary related reasons. Clinical experience and

simulated models support the idea of balancing (Qp) and (Qs) to sustain aerobic milieu that is best possible with adequate systemic oxygen delivery (DO_2). Barnea et al¹² correlated the DO_2 and the Qp/Qs ratio in a mathematical model of the Norwood physiology. They concluded that the DO_2 increases proportionately to the Qp/Qs up to a certain point (between 0.7 and 1)¹³, when starts to decline.

Unfortunately, the deleterious effects of excessive diastolic run off are not limited to coronary malperfusion. Importantly cerebral, renal and splanchnic circulations face the risk of hypoperfusion. Although roughly the adaptive mechanisms usually do not differ between adults and children, some peculiarities should be examined in the latter, which may have relevant implications over the post-operative recovery. Firstly, the oxygen consumption of the child at rest is higher when compared to the adult¹⁴. Profound hypothermia and total circulatory arrest, which has been employed in the majority of centers in the first stage of Norwood operation, have effects in the relationship between oxygen delivery and consumption. Moreover, the metabolic response to stress is more pronounced in children¹⁵. Oxygen consumption is independent of oxygen delivery in a wide range of situations. For example, during periods of low cardiac output, aerobic metabolism is maintained initially because of higher oxygen extraction rate. However, this later mechanism has a limit, which matches an oxygen extraction rate around 50 to 60%, when lactic acidosis develops^{16,17}. Although not least important, cardiopulmonary bypass may play an aggravating role in this scenario, due to situations of inadequate oxygen delivery, excessive loss of vasomotor tone and altered microcirculation. In addition, regional metabolic requirements may be elevated, closely related to non-homogeneous cooling and re-warming or as a result of failing to provide an adequate oxygen delivery to the tissues. Systemic inflammatory response to cardiopulmonary bypass can be implicated into this issue¹⁸. During pediatric cardiopulmonary bypass, the blood supply to different organs and systems are significantly altered due to redistribution of flow, in hypothermia or normothermia and low-flow or high-flow perfusion¹⁹. Mesenteric hypoperfusion usually is a consequence of these impaired regional blood flow distributions²⁰. The immediate consequences are altered intestinal permeability, bacterial translocation, and passage of endotoxins to the systemic circulation²¹. The activation of cytokines leads to systemic inflammatory response, one of the trigger mechanisms implicated in the development of multiple organ failure.

Important determinants of Qp and Qs are the pulmonary (PVR) and systemic (SVR) vascular resistances, both of which are frequently susceptible to individual variations in response to cardiopulmonary bypass and deep hypothermic circulatory arrest. This makes a fixed and non-individualized management approach to fit the post-operative needs of all Norwood patients an idealist's

dream. Despite the use of best myocardial protection, neonatal heart usually arrives in the postoperative unit with some degree of myocardial depression. A problem that is commonly due to limited reserve of a neonatal, single, volume loaded, morphological right ventricle.

Modified Norwood: Why the change?

The "classic" Norwood procedure consists of atrial septectomy, reconstruction of ascending aorta and aortic arch, creation of unrestricted pulmonary venous return through a large atrial communication and placement of a systemic to pulmonary shunt (Figure 1). The 15-year experience at the Children's Hospital in Philadelphia²² with 840 patients having the stage I Norwood have identified as independent predictors of hospital mortality low birth weight (<2.5 kg), operation performed after 2 weeks of age, associated cardiac anomalies, total support time and ECMO support.

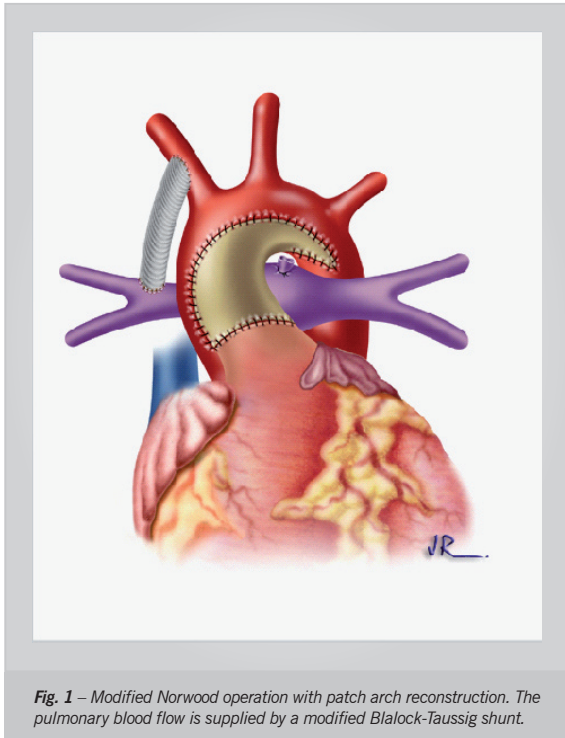


Fig. 1 – Modified Norwood operation with patch arch reconstruction. The pulmonary blood flow is supplied by a modified Blalock-Taussig shunt.

Various groups^{23,24} have identified smaller size of the ascending aorta (less than 2.5mm) as a significant risk factor for mortality and therefore focused on arriving at the best surgical option to deal with the long and small ascending aorta. In general, three methods of aortic arch reconstruction have been described. The Norwood procedure and its modifications⁷ and the Lamberti modification²³ involve the use of a homograft patch to augment the aortic arch. In the Lamberti modification, the proximal aorta and pulmonary artery are transected, and an end-to-end anastomosis is created between the proximal neo-aorta and the augmented proximal arch. Either technique requires placement of an adequate

patch that must extend distally beyond ductal tissue. Care must be taken to avoid placing excessive patch material, as this is thought to contribute to early and late arch obstruction, reportedly as high as 20% to 25%^{24,25}. The third method is direct anastomosis without the use of a homograft augmentation patch as described by Fraser and Mee²⁶, which by report has a low incidence of late arch obstruction⁹. However, using similar techniques without prosthetic patch material, Ishino et al²⁵ at Birmingham Children's Hospital (UK) described in 1999 an incidence of aortic arch obstruction of 23% in 120 patients. This figure is identical to the incidences of arch obstruction in other studies²⁷⁻²⁹. Concern over left pulmonary artery and left bronchial compression by the no-patch technique has been raised, but the problem has not been recognized clinically as occurring with an increased frequency compared with patch repair techniques⁹.

Until recently, most of the arch reconstructions required an obligatory period of deep hypothermic circulatory arrest. Several studies^{30,31} evaluating the effects of prolonged circulatory arrest clearly demonstrated long-term neurologic sequelae³², and acute deleterious effects on kidneys, liver and intestines due to extended periods of cold global ischemia. More importantly, deep hypothermic circulatory arrest has been reported to cause an increase in pulmonary vascular resistance³³⁻³⁵ postoperatively. In addition, Tweddell and coworkers³⁶ found that systemic vascular resistance was also elevated after the Norwood procedure using deep hypothermic circulatory arrest. Moreover, Tokunaga and coworkers³⁷ demonstrated that sympathetic nerve activity and systemic vascular resistance significantly increased immediately after deep hypothermic circulatory arrest in an animal model.

Imoto and colleagues^{38,39} firstly described the technique of selective regional perfusion through cannulation of the shunt in order to provide antegrade cerebral perfusion, completely avoiding deep hypothermic circulatory arrest. The procedure can be performed with deep hypothermic low-flow⁴⁰ or moderate hypothermia, high-flow and low-resistance perfusion⁴¹. Pigula and colleagues⁴² added cannulation of the descending aorta to maintain lower-body perfusion. Although no randomized studies supporting the benefits of regional perfusion are available, clinical observations suggest earlier return of renal function and less hemodynamic instability in regionally perfused patients. Although some studies^{42,43} have provided objective evidence of improved cerebral metabolic activity, there has not been any favorable impact on survival with the use of selective regional perfusion, and experience is still too early to evaluate long-term neurologic outcome.

Although the aforementioned modifications were important contributions, many other technical changes have been introduced to achieve a balance circulation during the early postoperative period, since it is a major determinant in the immediate and the inter-procedural survival. Those modifications have focused on limiting pulmonary blood flow (smaller, longer shunts or shunt

banding) and improving systemic blood flow⁴⁴. The systemic to pulmonary artery shunt size is a very important factor that affects distribution of flow between two parallel circulations, compromising the coronary blood flow during the diastole⁴⁵. Positron emission tomographic studies⁴⁶ of coronary blood flow quantification in infants after repair of their congenital cardiac defects demonstrated less coronary reserve as compared to adults. Specifically after the Norwood procedure, there is higher resting coronary flow but a lower indexed coronary blood flow to the systemic ventricle than those after a biventricular repair. This is related to the increased energy requirements of the systemic ventricle demanded to pump through both systemic and pulmonary beds. Qualitative analysis of coronary blood flow⁴⁷ using trans-esophageal echocardiography and Doppler flowmetry described coronary flow abnormalities after Norwood operation, when the predominant flow occurs during the systole. Recent attempts to further eliminate the deleterious effects of systemic arterial source of pulmonary blood, by use of a non-valved right ventricle to pulmonary artery conduit is an addition to the surgical armamentarium. The latter will be addressed as a different section, since it represents an important contribution that changed the postoperative hemodynamics and its management protocols.

Prior to discussing various management themes, it is mandatory to be in contact with advances in techniques employed to guide therapy in these neonates.

HEMODYNAMIC ASSESSMENT IN HLHS

Clinical parameters, widely used on a routine basis, were demonstrated to be non-predictive of major adverse events after pediatric cardiac surgery, especially in neonates. The definition of a reliable marker of tissue hypoperfusion has been extremely difficult to be accomplished. Reasons for that rely on limitations of invasive monitoring imposed by patient weight, and certain anatomic features, such as atrial septal defects that can interfere in the accurate measurement of cardiac output, mixed venous oxygen saturation and oxygen delivery and consumption. In addition, few studies^{48,49} evaluated or included indicators of systemic oxygen delivery in the postoperative management of patients following the Norwood procedure.

Individually, none of the parameters obtained in blood gas analysis are considered important in terms of estimating hemodynamic status. On the other hand, combined parameters can estimate indirectly the oxygen delivery and tissue perfusion⁵⁰. Oxygen arterial saturation greater than 80% was proposed to be indicative of pulmonary overcirculation and consequently of systemic hypoperfusion, but did not show reliability in some clinical studies⁵¹.

The mixed venous oxygen saturation (SvO_2) is generally accepted as an indicator of adequacy of cardiac output and has a strong association with lactic acidosis in intensive care patients⁵². Considering a stable arterial

content of oxygen and an adequate cellular metabolism, SvO_2 higher than 60% means adequate cardiac output. The main advantages of its determination are the capacity in determining both the oxygen delivery and consumption. However, several factors interfere with its values other than the cardiac output, such as the hemoglobin value, arterial oxygen saturation, and the metabolic rate. Since SvO_2 represents the mixture of all venous return blood from the organism, the best sampling site should be the pulmonary artery⁵³. Nevertheless, that is not an ideal site in congenital heart malformations with septal defects, since every left to right shunt may lead to inaccuracy. Others^{54,55} have validated the SvO_2 determination in the superior vena cava, close to the right atrium junction. Recently, small oxymetric catheters that are suitable for use in neonates have been developed and safely used. The acquirement of this technology proved to be beneficial in the determination of systemic oxygen delivery after the Norwood procedure⁵⁶, with a favorable impact on morbidity and mortality⁴⁸. The therapeutic management is guided by the oxymetric data and aimed at achieving adequate systemic oxygen delivery defined as a SvO_2 greater than 50%, with a pulmonary to systemic flow ratio nearing unity.

The arteriovenous oxygen content difference ($AVDO_2$) is another parameter that can be used as a marker of tissue perfusion⁵⁷, and it has been considered as indicative of a balanced circulation when its values were less than or equal to 5 ml/dl.

Although the identification of lactic acidosis has been suggested as a clinically useful indicator of decreased oxygen delivery, it predictably lags the period of inadequate tissue oxygen delivery. Several studies⁵⁸⁻⁶¹ examined the prognostic value of blood lactate after congenital heart operations and they have found conflicting results, but agreed in the power of its serial determination⁶². Rossi and coworkers⁶² postulate that elevated lactate levels might represent previous hemodynamic compromise, during or before operation, sometimes associated with liver dysfunction. Uncomplicated survivors of Norwood procedure have an elevated lactic acid level in the early postoperative period⁶¹. Furthermore, abrupt life-threatening decreases in the systemic oxygen delivery can occur and lead to death before lactic acid becomes elevated.

The use of intracardiac lines inserted before weaning from cardiopulmonary bypass has an importance in estimating circulating blood volume, ventricular function and may serve as a guide to the diagnosis of residual problems in the postoperative period. Moreover, the benefit of its real time determination may encourage further assessment with bidimensional echocardiography or cardiac catheterization. Besides the diagnosis of residual defects responsible for deteriorated postoperative recovery, echocardiography has a fundamental role on the quantitative and qualitative evaluation of global and regional ventricular function and the presence

of pericardial effusions. Analyzing specifically the postoperative period of Norwood procedure, some clinical situations and anatomic features deserve special attention during the echocardiographic evaluation. Presence of new onset or worsening of tricuspid regurgitation might be early indicators of ventricular dysfunction. The persistence of poor oxygenation should lead to the suspicion of small pulmonary arteries or signs of obstruction or stenosis in the systemic to pulmonary artery shunt. A restrictive atrial septal defect may cause low cardiac output, with persistently elevated left atrial pressures. The presence of residual arch obstruction is another factor that may compromise the cardiac output, and lead to systemic hypoperfusion. Obstruction of left pulmonary artery or left main stem bronchus may be associated with some types of aortic arch reconstruction procedures.

POSTOPERATIVE MANAGEMENT OPTION

Currently there are two schools of thought to achieve this precise balance after the Norwood procedure. It is important to understand that those schools are not static and usually intertwined, in different protocols, according to the institution. The first, primarily uses maneuvers to either manipulate Qp by reduction of minute ventilation and inhalation of hypoxic and/or hypercarbic gas mixtures. The second manipulates Qs by infusions of systemic vasodilators.

Qp manipulation

PVR - The effect of acidosis, hypoxia and hypercarbia on pulmonary vasculature has been well understood. Inducing permissive respiratory acidosis to effectively control Qp and its positive effects on the outcome of hypoplastic left heart patients has been recognized since 1986. Methods have evolved since then. In the initial period, the aim was to reduce alveolar minute ventilation and increase dead space, leading to carbon dioxide retention. This could be done by reducing respiratory rate, tidal volume or both with high positive end-expiratory pressures and room air inspired oxygen fraction. The almost instantaneous reduction of pulmonary blood flow was an advantage that was utilized by centers striving to improve results in postoperative Norwood cases. On the other hand, some drawbacks of this management have been identified. These hypoventilatory methods led to decreased functional residual capacity, micro-atelectasis and intrapulmonary shunting in the neonate⁶³ resulting in ventilation-perfusion mismatch, pulmonary venous desaturation and hypoxia. Obviously, deprivation of oxygen is undesirable in the normal course of recovery after cardiopulmonary bypass and circulatory arrest.

Therefore, other ways to induce respiratory acidosis were explored. Increasing the fraction of carbon dioxide (CO₂) in the inspired gas was suggested as the alternative method^{64,65} when the mechanical variables of ventilation (respiratory rate, tidal volume and positive end expiratory

pressure) are set free from control of PCO₂. The advantage of this technique was to achieve elevated PVR without adversely effecting DO₂. Addition of higher amounts of CO₂ (delivered level of 1-2% or 8-30 mmHg) in the inspired gas is aimed to maintain the paCO₂ in the range of 45-50 mmHg⁶⁶. Although attractive, this strategy was used in combination with increased minute ventilation^{63,67-69}. Theoretically, the increase in minute ventilation would lead to an additional increase in PVR because of a raised mean airway pressure⁷⁰. The simultaneous downside of CO₂ washout and resultant hypocapnic alkalosis, by higher minute ventilation could be countered by inspired CO₂. Bradley et al⁷¹ concluded that the inspired CO₂ could improve DO₂ effectively, only if the minute ventilation is kept constant. Hypercarbia poses yet another advantage towards reduction of Qp:Qs ratio in that its systemic vasodilatory effect may increase and redistribute total cardiac output favorably.

However, experimental studies⁷² showed that the concentrations of CO₂ required in the inspired gas to achieve statistically significant elevation of PVR was extremely high (80-95 mmHg). It was also demonstrated that there is a significant PVR elevation, when the inspired O₂ concentration is reduced. Hence, the logical next step using this principle was to reduce the oxygen content in the breathing gas mixture to less than 21%. This was achieved by addition of nitrogen in the inspired gas. The hypoxic or sub ambient gas therapy was successfully used, keeping the inspired oxygen fraction in the 14 to 20% range^{73,74}.

This protocol should be especially beneficial in some clinical instances such as low birth weight neonates with unusually high PVR, unresponsive to hypoxic gas mixture⁷⁵. Adversely, these effects were more prominent in pre-bypass settings in reducing Qp as compared to post-bypass scenario after Norwood repair.

On the other hand, recent studies⁷⁶ have shown that high levels of fraction of inspired oxygen can in fact improve mixed venous oxygen saturation and systemic oxygen delivery. Bradley et al⁷⁶ postulate that protocols aimed at minimizing the FiO₂ and carefully controlling ventilation may not be warranted.

Hematocrit - Increasing viscosity of blood creates inherent resistance to flow according to Poiseuille's law. This effect is exponentially pronounced with hematocrit values higher than 45% and more evident in high-flow than in low-flow conditions⁷⁷. Some authors have included this strategy routinely in the post-operative management⁹.

Qs manipulation

It has been demonstrated⁴⁸ that neonates after the Norwood procedure maintain a higher baseline level of SVR that is also subject to abrupt fluctuations, regardless of cardiopulmonary bypass strategy employed. The minute-to-minute control of systemic vascular resistance

is an amalgam of the influences of the autonomic nervous system by changing the total cross-sectional area of the systemic vascular bed and the local metabolic factors. From the aortic to the venous side, greatest resistance is exerted at the arteriolar level (60%), followed by capillaries & small veins (15% each) and large and mid-sized arteries (10%)⁷⁸.

The rationale of the use of vasodilators is justified initially by common consequences of cardiopulmonary bypass, such as pulmonary endothelial swelling, interstitial lung edema and microatelectasis, which already keeps the PVR high and further elevations would be unnecessary. In addition, unrecognized pulmonary venous desaturation occurs early after Norwood operation^{76,79}. Moreover, it is thought that further reduction in alveolar oxygen availability only impairs even more the pulmonary venous saturation, thus hampering DO_2 .

Reduction in SVR has been achieved by an arteriolar dilator (sodium nitroprusside), an alpha-receptor antagonist (phenoxybenzamine) or chlorpromazine or an inodilator (milrinone). Nitroprusside is a mixed, arterial and venous, vasodilator with nitric oxide related mechanism of action. It has a short half-life and it is easily reversible. The disadvantage of sodium nitroprusside is that it does not tackle the frequent and abrupt changes in SVR.

Phenoxybenzamine blocks irreversibly and non-competitively alpha-adrenergic receptors, leading to more prolonged vasodilatation. Phenoxybenzamine has been advocated by most centers performing neonatal surgery at the onset of CPB. Usually, it can be titrated with the mean arterial pressures, although some groups have advocated continuous infusion of the same in the post-operative period^{56,80,81}. Use of phenoxybenzamine after the Norwood procedure improves DO_2 and induces fixed and balanced Qp:Qs ratio. In this setting any increase in mean arterial pressure with afterload reduction promoted by phenoxybenzamine, reflects in better SvO_2 . Therefore, no steps need to be taken to reduce FiO_2 or manipulate mechanical ventilation. Problems related to excessive vasodilation with the use of phenoxybenzamine have been reported⁸², which can be countered with judicious use of vasoconstrictors like nor-epinephrine and vasopressin.

Chlorpromazine⁸³, a phenothiazine neuroleptic drug with significant alpha blocking capabilities has also been successfully used. Choice of inotropic agents has drifted from those having vasoconstrictive properties towards those with vasodilatory properties. In order to reduce the range for pulmonary vascular resistance to fluctuate, pulmonary vasculature can be dilated maximally at weaning from cardiopulmonary bypass with inhaled nitric oxide and high concentration of inspired oxygen as potent pulmonary vasodilators⁸⁴. Under this condition, pulmonary blood flow is dependent on systemic to pulmonary shunt adjustments. This completely distinct approach was proposed by Nakano et al⁴¹, which simply taper inhaled nitrous oxide and inspired oxygen fraction as arterial oxygen saturation improved, with continuous infusion of chlorpromazine to keep SVR low. Frequent ventilator manipulation is rarely required.

RIGHT VENTRICLE TO PULMONARY ARTERY CONDUIT: THE DEFINITIVE SOLUTION?

The right ventricle to pulmonary artery (RV-PA) conduit to reestablish pulmonary blood supply in stage I palliation for HLHS was firstly introduced by Norwood in 1981⁸⁵. At that time, shunts were excessively large and all patients died either from pulmonary overcirculation or from right ventricular failure. Kishimoto et al⁸⁶ revived the initial concept using a xenopericardial valved conduit, which was replaced later by Sano et al⁸⁷ that used a 4 or 5 mm nonvalved PTFE (Figure 2) conduit. Their initial experience with 19 consecutive patients achieved an excellent 89% hospital survival. More importantly, placing the pulmonary and systemic circulations in parallel resulted in a more predictable postoperative recovery. The pulmonary bed was neither anymore subjected to nor dependent on diastolic flow, and there should be less change in pulmonary blood flow with pulmonary hypertensive crisis or during resuscitation in the presence of low cardiac output or after a cardiac arrest. No particular Qp and/or Qs manipulation were required postoperatively, maintaining adequate blood oxygenation and higher diastolic pressures^{88,89}. Excellent hemodynamics provided by this technique was particularly beneficial for low birth weight infants, a subset known to be of higher hospital mortality, usually due to pulmonary overcirculation even with the smallest 3 mm Blalock-Taussig shunt.

The RV-PA conduit became worldwide popular and its results were considered reproducible⁸⁸⁻⁹¹, consistently

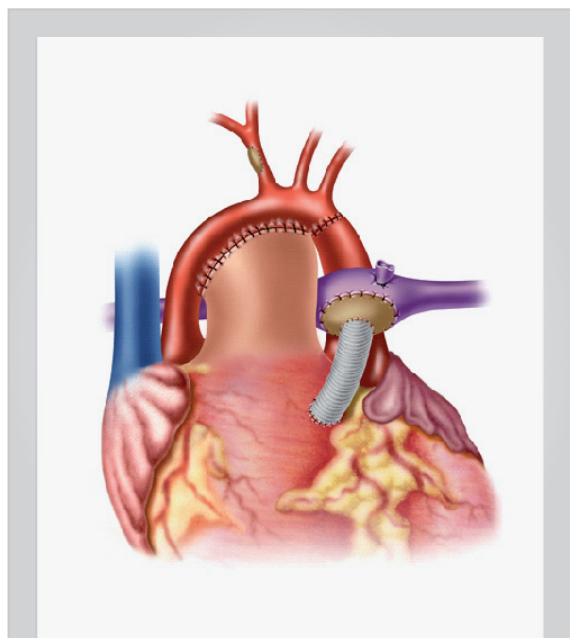


Fig. 2 – Modified Norwood operation without patch arch reconstruction. Neo-aorta is formed by the remnant hypoplastic ascending aorta with coronary ostia, the pulmonary trunk and descending aorta distal to arterial duct. A non valved right ventricle to pulmonary artery conduit is the only source of pulmonary blood flow.



improving the mortality rates after the first stage palliation in many centers^{87,90,92}. However, highly experienced centers^{88,91,93} on the modified Norwood have not shown a favorable impact on hospital survival.

Several nonrandomized studies⁸⁸⁻⁹⁴ have compared the RV-PA conduit and the modified Blalock-Taussig shunt as the source of pulmonary blood flow. Hemodynamic evidences of those studies are summarized in Table 4. In spite of more predictable hemodynamics in the RV-PA conduit group, there were no significant differences in length of intensive care stay, duration of ventilatory support, inotropic use^{88,91,93,95} and systemic oxygen delivery⁹³.

The RV-PA conduit has potential limitations that need to be further investigated. The effects of a right ventriculotomy are of a great concern, in terms of ventricular failure and trigger of arrhythmias. Current evidences do not support this concept, since ventricular function (dp/dt) during catheterization at 5 months follow-up showed better performance in the RV-PA conduit group, comparing to BT shunt^{90,96}. Moreover, preliminary systolic ventricular performance by strain Doppler echocardiography suggested a better early ventricular function with the RV-PA conduit group⁹⁵. These findings were attributed to reduced right ventricular overload because of lower Qp:Qs, as well as improved coronary perfusion due to higher diastolic pressures⁸⁹.

Another potential problem is related to the degree of flow reversal in the nonvalved conduit. Nonetheless, free pulmonary regurgitation seems to be well tolerated over the short term. Likewise every other prosthetic tube in pediatric cardiac surgery, it becomes obstructed with time, particularly within 3 months after surgery. That obligates an earlier second stage, which may be favorable in terms of reducing the interprocedural attrition. At this stage, pulmonary resistance is higher. On the contrary, pulmonary artery growth has been controversially^{87,89,90,97,98} shown to be as good as with the BT shunt, despite a lower Qp:Qs. Usually, the RV-PA conduit was left open in order to provide an extra source of pulmonary blood flow. Outcomes after the second stage performed earlier support the idea that

the pulmonary blood flow is lower, but enough^{90,94} to provide good oxygenation without important ventricular loading. That concept is supported by similar outcomes in patients submitted to early (3 months) second stage after the modified Norwood procedure⁹⁹, but expected more prolonged postoperative recovery. However, Malec et al⁹⁴ haven't found any need for earlier second stage with the RV-PA conduit, since the lower Qp:Qs ratio ensured good condition for the development of the pulmonary vasculature (more centrally located shunt and pulsatility of forward flow from the pumping ventricle).

STENTING OF THE ARTERIAL DUCT AND BANDING OF THE PULMONARY ARTERIES

Stenting the arterial duct in combination with pulmonary artery banding and, if necessary, atrial septotomy offers a different approach to palliation of HLHS¹⁰⁰. Neoaortic reconstruction and establishment of a bi-directional cavopulmonary connection can then be performed during a single operation¹⁰¹. Moreover, in selected hypoplastic left ventricles, in which left ventricular growth can be observed foremost during the postnatal follow-up, the surgical decision made immediately after birth would result in a single ventricle palliation, although in the same patient biventricular repair may have been provided a few months later. In this context, despite multiple left heart obstructive lesions, a biventricular repair is thought to be preferable when possible.

Michel-Behnke et al¹⁰² adopted this strategy in 20 patients. Based on their initial experience, they advocate that a newborn with HLHS admitted with prostaglandin E1 infusion with a wide open duct, no ductal narrowing and unrestricted atrial septal defect would be considered for bilateral banding within the first 3 to 5 postnatal days. If a pulmonary run off in consequence of a decrease in pulmonary vascular resistance is observed, this procedure should be performed earlier. Ductal stenting, as well as re-evaluation of the effectiveness of the pulmonary banding would be performed 2 to 3 days before hospital discharge. Then, the prostaglandin infusion is discontinued about 2 hours before catheterization to achieve a smaller and

Table 4 – Advantages and disadvantages of the modified Blalock-Taussig (BT) shunt in comparison with the right ventricle to pulmonary artery (RV-PA) conduit during the modified Norwood procedure

BT shunt	RV-PA conduit
<ul style="list-style-type: none"> Advantages <ul style="list-style-type: none"> Better pulmonary artery growth* Better midterm oxygenation Disadvantages <ul style="list-style-type: none"> Diastolic runoff^{61,65,89} Higher Qp:Qs 	<ul style="list-style-type: none"> Advantages <ul style="list-style-type: none"> Higher diastolic blood pressure^{87,88,90-94} Lower pulse pressure⁹⁴ Better coronary perfusion⁸⁹ Disadvantages <ul style="list-style-type: none"> Lower pulmonary blood flow⁹⁰ Early or progressive hypoxemia^{87,94} Ventricular dysfunction** Ventricular arrhythmias**
<p>* <i>controversial</i>^{87,90,91,94,97,98}; ** <i>potential</i>.</p>	

narrower duct, facilitating stent placement and preventing stent dislocation.

A newborn with a restrictive foramen ovale would be catheterized before bilateral banding is provided. In case of any narrowing within the duct, a stent would be placed before the atrial septotomy. Arch reconstruction and bi-directional cavopulmonary connection were performed 3.5 to 6 months later. Bigger structures often allow avoidance of deep hypothermic circulatory arrest by means of cerebral perfusion through the innominate artery. Bidirectional cavopulmonary connection enables unloading the single right ventricle at earlier stage, establishing serial instead of parallel pulmonary and systemic circulations. The postoperative recovery was usually managed with arterial and venous vasodilators and low dose phosphodiesterase inhibitor. The early success rate of this approach was 90%. Additionally, it provided extended waiting periods for heart transplantation in selected 10% of these patients, in which Norwood pathway was not the preferred choice. This minimizes the development of severe pulmonary hypertension before the transplant, extends safely the waiting time of listed patients and improves the ease of subsequent transplant management¹⁰³.

However, this technique deserves further investigation with longer follow-up. Potential issues include interprocedural deaths due to heart failure or pulmonary hypertension. Close follow-up is necessary to detect restrictive atrial septal defect, narrowing of the duct, or compromised pulmonary blood flow. In addition, the development of significant aortic coarctation may compromise retrograde blood flow and coronary perfusion.

CONCLUSIONS

The surgical treatment of hypoplastic left heart syndrome is still a challenge. Heart transplantation is a viable alternative to this problem¹⁰⁴, and it is influenced by institutional preferences and donor availability. Continued impairment of right ventricular function, severe tricuspid regurgitation or coronary fistulae leaves heart transplantation as the treatment of choice. Progressive improvements have been achieved in the surgical palliation, mainly based on the refined application of physiology principles. The balance between systemic and pulmonary circulations is the keystone in the successful postoperative management of the modified Norwood procedure. The current literature strongly supports this concept, electing mixed venous oxygen saturation as the best guide of adequate tissue perfusion. The management options vary among several institutions. Both PVR as well SVR manipulations are welcomed, and sometimes should be used in combination. Although dealing with the complex interaction of two circulations in parallel is manageable in most of the cases, sometimes requires excessive teamwork and experience. New technical modifications, such as the right ventricle to pulmonary artery conduit, have been incorporated to surgery in order to lessen the postoperative complications, supporting the idea of a more "physiologic" pathway. The impact of the ventriculotomy on ventricular systolic, diastolic, and electrical function as well as atrioventricular valve function remains to be determined. Current data was not enough to determine any long-term survival benefit. Only the future will tell us the best way to treat hypoplastic left heart syndrome.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported

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