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Original Article

Preoperative management of the neonate with critical aortic valvar stenosis*

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Abstract Neonatal critical aortic stenosis is a rare form of CHD that often presents with cardiogenic shock. Although surgical and cardiac catheterisation-based interventions have been successful in alleviating left ventricular outflow tract obstruction, it remains associated with high morbidity and mortality. Critical aortic stenosis results in elevated left ventricular wall stress, which ultimately increases myocardial oxygen consumption and disrupts coronary artery perfusion during diastole, leading to ventricular dysfunction and cardiogenic shock. Critical care management before definitive intervention should be tailored to optimising oxygen delivery and reducing metabolic consumption of the myocardium and peripheral organ systems. This can be accomplished with prostaglandin infusion to maintain system perfusion through patency of the arterial duct, inotropic support, mechanical ventilation, and central nervous system abrogation. Management should also include a multi-specialty medical team including paediatric cardiothoracic surgeons and paediatric cardiologists with expertise in cardiac catheterisation, imaging, and transplantation.

Keywords: Critical aortic stenosis; paediatric critical care; neonate; cardiogenic shock

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CRITICAL AORTIC STENOSIS IS AN UNCOMMON FORM OF CHD presenting in the neonatal period. It is associated with high morbidity and mortality because of its relation with other associated cardiac lesions and its inherent risk of shock and multi-organ dysfunction. Both surgical and cardiac catheterisation approaches have been described regarding the essential intervention of alleviating left ventricle outflow tract obstruction. However, optimal pre-intervention management of such patients is essential to a successful overall outcome. In this review, we describe this neonatal cardiac lesion and discuss preoperative treatment.

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Natural history

As a broad category, aortic valve abnormalities are relatively common, representing 3.5–5% of all congenital heart defects.[1,2] The incidence may be higher, as it is estimated that the bicuspid aortic valves, including those asymptomatic, occur in as many as 2% of the general population.[3] As such, the natural history for both asymptomatic and progressive aortic valve stenosis beyond infancy has been well described. Determining the natural history of critical aortic stenosis is more complicated.

Isolated critical aortic stenosis is relatively rare in comparison with other isolated defects such as ventricular septal defects. It has a high association with other cardiac lesions, including aortic coarctation, left ventricular hypoplasia, endocardial fibroelastosis, mitral valve abnormalities, and ventricular septal defects. Surgical and cardiac catheterisation-based interventions have also improved with time, and therefore natural history studies are era-dependent

similar to other congenital heart lesions. Finally, the diagnosis of critical aortic stenosis has carried both high morbidity and mortality (73 to 90%) in earlier studies making long-term follow-through difficult.[2,4,5]

More recently, in a multi-institutional study conducted from 1994 to 2002, the courses of 320 infants with critical aortic stenosis were examined.[6] Of the patients, 19 (5.9%) died before any intervention for relief of left ventricular obstruction could be performed, whereas 97 patients (30%) died during the study period following a primary intervention, which included primary cardiac transplantation, Norwood palliation, or biventricular repair.

Pathophysiology

The severity of aortic valve disease is a continuum, with hypoplastic left heart syndrome at its most critical end and a non-stenotic, asymptomatic bicuspid aortic valve at the other. Thus, the clinical presentation in those with aortic valve abnormalities is highly variable, ranging from asymptomatic to cardiogenic shock with multi-organ dysfunction.

With progressive aortic stenosis in younger children or adults, the left ventricular pressure during isovolumic contraction exceeds the systolic aortic pressure to bypass valvar obstruction. On the basis of the law of Laplace, left ventricular myocardial wall stress is directly related to the left ventricular pressure and left ventricle cavity diameter and inversely related to the myocardial wall thickness (Wall stress = Pressure × Radius/2 × Wall thickness). Thus, increased left ventricle afterload increases left ventricular wall stress in aortic stenosis.[7] Compensatory mechanisms to maintain normal wall stress include left ventricular myocyte hypertrophy. This preserves normal stroke volume, ejection fraction, and cardiac output, though at the expense of an elevated end-diastolic pressure and increased metabolic demands of the myocardium (Fig 1).

Coronary perfusion relies on the ratio of the diastolic perfusion time index to the systolic perfusion time index. In the presence of aortic stenosis, progressive left ventricular hypertrophy and elevation of left ventricular end-diastolic pressure can lead to the risk of myocardial ischaemia owing to an imbalance between coronary blood flow and oxygen demand, especially during times of increased needs such as exercise (Fig 2).

The immature neonatal myocardium has inherent differences in comparison with that of older children and adults. Incomplete development of contractile proteins, the sarcoplasmic reticulum, and overall calcium metabolism causes poor systolic and diastolic function reserve with stress. Instead of modifying stroke volume, the neonatal myocardium relies on increasing heart rate to maintain cardiac output.[8] Neonatal myocardium is poorly equipped to tolerate acute elevations in left ventricular afterload, as occurs in critical aortic stenosis following birth. The resultant increase in left ventricular systolic pressure greatly increases left ventricular wall stress. Acute increases in afterload may induce acute ventricular dilation as opposed to compensatory ventricular hypertrophy, also increasing wall stress and left ventricular end-diastolic pressure. Myocardial oxygen consumption is increased. As neonatal cardiac output is highly dependent on heart rate, less time per cardiac cycle is devoted to diastolic coronary artery perfusion in the failing neonatal heart. A cycle ensues, and cardiogenic shock with multi-organ dysfunction rapidly occurs unless the obstruction is alleviated.

Consideration of the diagnosis of critical aortic stenosis should occur in the neonate who exhibits signs of congestive heart failure and/or low cardiac output or left ventricular dysfunction when: patency of the arterial duct is required for maintenance of systemic perfusion, inotropic support is required for maintenance of systemic perfusion, and/or respiratory insufficiency or failure is present. Importantly, an elevated gradient across a stenotic aortic valve is not essential to this definition. A left ventricle with severe dysfunction may not generate a significant gradient across a severely stenotic aortic valve.

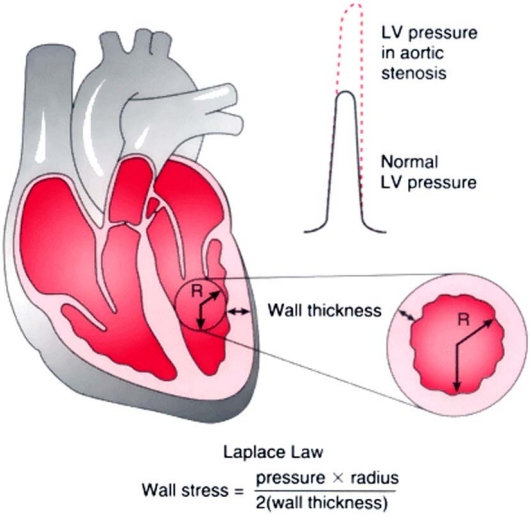

Figure 1.
Pathophysiology of aortic stenosis. The formula for left ventricle wall stress is derived from the law of Laplace. As demonstrated in the figure inset, left ventricular systolic pressure is greatly increased in the presence of aortic stenosis in comparison with the normal left ventricular systolic pressure. Wall stress is directly proportional to left ventricular pressure. In progressive aortic stenosis, compensatory left ventricular hypertrophy may regulate such increases in wall stress, as wall stress is inversely proportional to ventricular wall thickness (reprinted with permission from Opie[7]).

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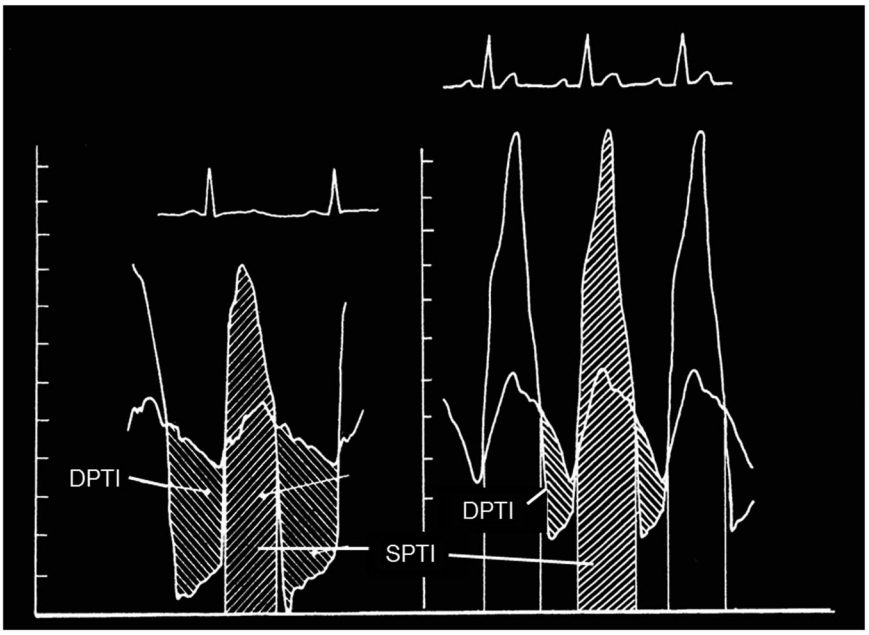

Figure 2.
Diastolic perfusion time index in aortic stenosis. Coronary perfusion relies on the ratio between the diastolic perfusion time index (DPTI) and the systolic perfusion time index (SPTI) in the heart with aortic stenosis (left diagram). During stress such as exercise, left ventricular pressure greatly increases as does the heart rate (right diagram). The diastolic perfusion time index decreases, impairing the DPTI/SPTI ratio.

Preoperative management

Neonates presenting with critical aortic stenosis will demonstrate variable degrees of cardiac output and organ dysfunction. Thus, optimisation of critical care management is essential to the success of the determined intervention for left ventricular outflow tract alleviation. In concordance with the aforementioned pathophysiological mechanisms of disease, critical care management centres on improving oxygen delivery to the cardiac and systemic organs, while decreasing metabolic demands of the same. Monitoring of these infants should include measurement of central venous pressure, mean arterial blood pressure, end-tidal carbon dioxide concentration, and urine output. Judicious laboratory evaluation should also occur, including evaluations of gas exchange, acid–base status, and end-organ function. Quantification of tissue capillary and venous oxygen saturation using near-infrared spectroscopy provides real-time estimation of cerebral and somatic perfusion status, enabling continuous analysis and titration of medical management.[9]

Prostaglandin E1

Adequate systemic perfusion can be sustained through patency of the arterial duct; thus, prostaglandin infusion is a cornerstone of preoperative management in critical aortic stenosis. In the presence of an atrial septal defect, this may alleviate in decompression of the left ventricle as well. Contributions of this right-to-left shunt will depend on the relative resistances between the pulmonary and systemic circulations, on the presence of aortic coarctation, on the degree of antegrade blood flow through the aortic valve, and based on systole and diastole.[10,11]

Doppler investigations of infants with aortic stenosis have demonstrated patency of the arterial duct maintains right-to-left flow, and systemic perfusion, during systole.[11] In the situation of poor antegrade flow through the aortic valve, this shunt would allow retrograde circulation of the transverse aortic arch and cerebral vasculature.

During diastole, ductus arteriosus flow is determined by the relative resistances between the pulmonary and systemic vascular beds (Fig 3). As pulmonary vascular resistance decreases, systemic circulation can decrease owing to increased right-to-left shunting. Resultant detriments would be increased pulmonary blood flow leading to decreased lung compliance and decreased coronary blood flow from diastolic hypotension. Decreasing the prostaglandin administration infusion rate may mitigate these potentially harmful effects.

Inotropic and vasoactive support

Neonates presenting with cardiogenic shock should have prompt institution of inotropic and vasoactive support after optimisation of volume status has occurred. No clear recommendations regarding the modality of inotropic support exist. In a neonatal

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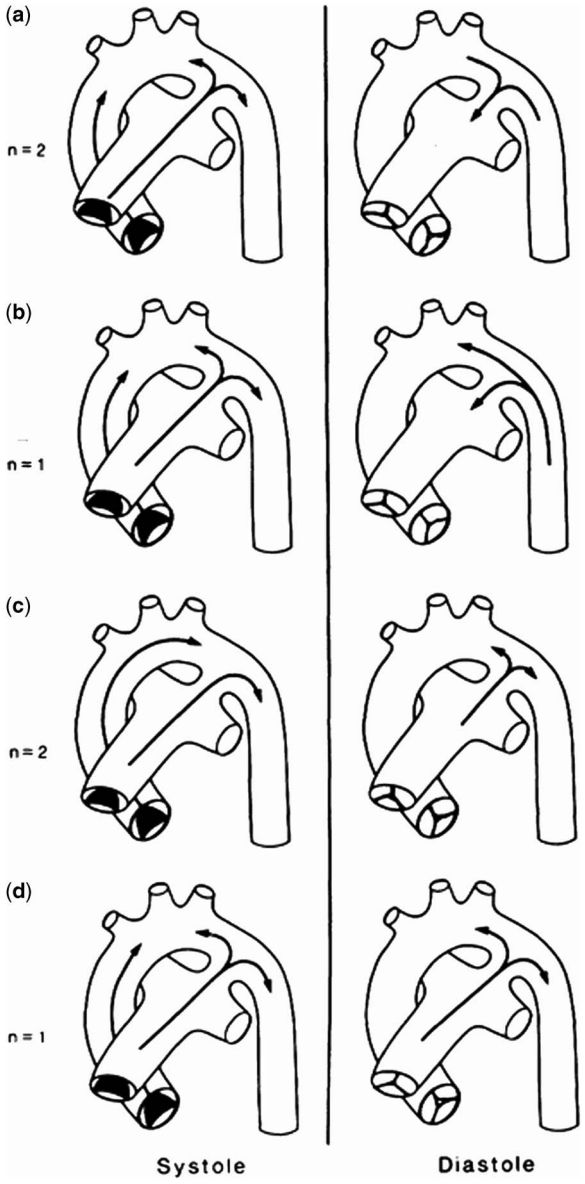

Figure 3.
Arterial duct flow in the presence of aortic stenosis. Arterial duct flow in six neonates with aortic stenosis and congestive heart failure is illustrated. In all six, right-to-left flow across the arterial duct occurred during systole. In diastole, three demonstrated left-to-right flow, whereas the other three had right-to-left flow. Those with left-to-right arterial duct flow during diastole had modest inter-atrial communications. Retrograde aortic arch flow generally occurred in those patients with associated coarctation of the aorta. Antegrade aorta flow was present in all six patients (reprinted with permission from Bass et al[11]).

study comparing low-dose epinephrine to low- and moderate-dose dopamine infusions, both infusions increased mean arterial blood pressure similarly.[12] Although epinephrine was associated with more tachycardia in the first 24 hours in comparison with dopamine, this observation did not persist. After 24 hours of treatment, patients treated with epinephrine tended to have lower heart rates than those treated with dopamine. There were no significant long-term adverse effects between the two infusions in this study. Comparison between epinephrine and dopamine infusions in a neonatal piglet model suggests that both infusions are effective in increasing cardiac index.[13] In this model, epinephrine was associated with slightly less myocardial oxygen consumption than dopamine.

Vasoconstrictors may be required to augment organ perfusion pressure and coronary artery perfusion pressure. However, the utility of vasoconstrictors should be weighed with detrimental effects increased systemic vascular resistance may have on left ventricular dysfunction.

Several adult studies have investigated the use of dobutamine challenge to determine hemodynamic alterations in the presence of aortic stenosis.[14] Patients with mild or moderate aortic stenosis tend to display increased cardiac output in response to dobutamine. In contrast, patients with severe aortic stenosis demonstrate lower mean arterial blood pressure and lower or equivalent measures of cardiac output. Thus, the use of dobutamine in critical aortic stenosis may not be beneficial.

Neonates with critical aortic stenosis may exhibit ventricular dysfunction with an elevation in systemic vascular resistance. For this reason, agents that vasodilate peripheral vascular beds, such as sodium nitroprusside, or improve myocardial contractility while providing peripheral vasodilation, such as milrinone, may be attractive adjuncts to therapy. Because peripheral vasodilation may impair the coronary artery perfusion pressure necessary with elevated left ventricular end-diastolic pressure in critical aortic stenosis, these therapies should be avoided.

Mechanical ventilation

Neonates with critical aortic stenosis often exhibit respiratory insufficiency related to cardiogenic shock. Mechanical ventilation assists with enhancing oxygen delivery and decreasing metabolic stress by decreasing work of breathing. Positive pressure ventilation may impair systemic venous return, and therefore minimising mean airway pressure is recommended. This can be achieved by utilising lower-positive end-expiratory pressures (4–6 mmHg), while preventing atelectasis with peak inspiratory pressure sufficient to maintain the functional residual capacity of the lungs. Adequate gas exchange should be the goal. Hypocarbia may impair cerebral blood flow in an already poorly perfused infant, and it may enhance right-to-left shunting through a patent ductus arteriosus by decreasing pulmonary vascular resistance, which alters systemic circulation as described previously. Maintenance of oxygen concentrations

exceedingly above normal levels can have detrimental effects for similar reasons.

Haemoglobin

Titration of haemoglobin concentration in an effort to improve oxygen delivery should be considered, although the potential adverse effects of volume overload, infection exposure, and donor exposure should be weighed.

Central nervous system regulation

Decreasing the metabolic requirements for the systemic circulation, especially the central nervous system, may be necessary to regulate the balance of oxygen delivery and metabolic consumption. Narcotic and benzodiazepine boluses or infusions are useful adjuncts in this. Dexmedetomidine may be considered; however, administration can decrease the heart rate, which may be important in maintaining cardiac output in the neonatal myocardium. Deep sedation with neuromuscular blockade and relative hypothermia will also decrease systemic metabolic consumption.

If neuromuscular blockade is necessary, it may be advisable to consider electroencephalographic monitoring to assess the level of sedation and assess for seizure activity, which can both increase cerebral metabolism and affect long-term neurologic prognosis.

Others

Such unstable neonates should impart a low threshold to consider sepsis as a contributing factor to shock upon presentation or while waiting for a definitive intervention, whether from maternal factors, intestinal ischaemia, or nosocomial sources. Stress corticosteroid administration should be considered in neonates poorly responsive to inotropic support. Finally, glucose administration, in addition to parenteral nutritional support, is important to initiate early, given the highly catabolic state upon presentation.

Intervention discussion

Critical care management should be carried out while simultaneously involving multi-specialty providers including paediatric cardiologists and paediatric cardiothoracic surgeons. Institutional variability will obviously dictate primary intervention for treatment of critical aortic valve stenosis, whether surgical or cardiac catheterisation based. Rapid communication with either should occur, mindful that urgent relief of obstruction is paramount to improving systemic circulation. Mechanical circulatory support should be available as many neonates will present to intervention unstable.

Overall assessment of other structures in the left heart should be considered as well, as long-term survival appears to be closely related to the initial decision regarding suitability of the neonate for two-ventricle versus single-ventricle repair.[15] In a retrospective review of 65 neonates with critical aortic stenosis, 43 patients believed to have adequate left ventricular size for two-ventricle repair were evaluated. In comparison with the neonates who survived aortic valvotomy,
the 14 patients who died had significantly smaller aortic valve annulus diameter, aortic root and arch diameter, left ventricle size, and mitral valve diameter. Importantly, seven patients initially treated in the two-ventricle pathway underwent subsequent Norwood operations, of which six died.

Similarly, in a more recent multi-institutional study, long-term survival based on the decision for a single-ventricle instead of a two-ventricle pathway was related to smaller aortic valve annulus, left ventricle size, mitral valve diameter, and the severity of endocardial fibroelastosis.[6] In this model of single versus biventricular repair, it was predicted that 52% of patients who underwent biventricular repair would have had an improved 5-year survival had a Norwood operation been performed initially.

In addition to involving imaging and interventional specialists, it may be important to consider early involvement of cardiac transplantation services. In this sense, transplant evaluations can occur expeditiously in addition to discussions on the risk to benefit ratio regarding exposure to donor products.

Conclusion

Critical aortic stenosis is a rare but highly morbid form of neonatal CHD, presenting in many cases with cardiogenic shock and multi-organ dysfunction. Regardless of institutional preferences for surgical or catheterisation-based interventions in relieving left ventricular outflow obstruction, optimal pre-intervention critical care management is important. Few studies have detailed specific recommendations for this specific shock pathophysiology, but optimising oxygen delivery while minimising oxygen consumption may stabilise neonates until a definitive intervention. The pre-intervention approach and long-term pathway of such patients should include a multi-disciplinary medical team including cardiologists, cardiothoracic surgeons, and cardiac transplantation specialists.

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Conflicts of Interest

None.

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