Pulmonary Atresia With Intact Ventricular Septum With Borderline Tricuspid Valve: How Small Is Too Small

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PA/IVS is a rare, heterogenous congenital heart defect anatomically defined by complete obstruction to the right ventricular outflow tract with varying degrees of hypoplasia of the right ventricle and tricuspid valve. This lesion can have associated coronary artery anomalies and, in some cases, right ventricular-dependent coronary circulation. Due to the wide spectrum of presenting anatomic and clinical features, the treatment options are often dictated by the degree of development of the tricuspid valve and right ventricle. The purpose of this review is to discuss the spectrum of pulmonary atresia with intact ventricular septum morphologies and to evaluate the surgical decision-making process and approaches to surgical repair with respect to the impact of hypoplastic right-sided cardiac features.

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Central Message

This review discusses the spectrum of PA/IVS morphologies and evaluates the surgical decision-making process and approaches to surgical repair with respect to anatomic features.

INTRODUCTION

Pulmonary atresia with intact ventricular septum (PA/IVS) is a rare congenital cardiac defect, occurring in approximately 4–8 per 100,000 live births and accounts for 1–3% of all congenital cardiac defects in children [1–6]. PA/IVS is anatomically defined by complete obstruction to the right ventricular outflow tract (RVOT) with varying degrees of hypoplasia of the right ventricle (RV) and tricuspid valve (TV). These characteristics have important hemodynamic and physiologic consequences in the newborn period due to compromised antegrade pulmonary blood flow through the RVOT. As a result, an alternative source of pulmonary blood flow is required for survival, often presenting as a ductal-dependent lesion in the neonatal period. PA/IVS is uniformly fatal if untreated. Moreover, as in many other forms of congenital heart disease, a wide spectrum of anatomic features exists for PA/IVS, and surgical treatment approaches and patient outcomes are most often dictated by the degree of hypoplasia of the tricuspid valve and right ventricle as well as coronary anatomy. The purpose of this review is to evaluate the surgical decision-making process and approaches to surgical repair with respect to the impact of hypoplastic right-sided cardiac features.

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CLINICAL AND ANATOMIC DEFINITION

PA/IVS is characterized by (1) atresia of the pulmonary valve that results in the absence of a functional connection between the RVOT and pulmonary arterial bed and (2) the presence of an intact ventricular septum that allows no connection between the right and left ventricles. These features distinguish PA/IVS from other seemingly related congenital defects including pulmonary atresia with a ventricular septal defect (PA/VSD) as well as from severe forms of Ebstein's anomaly of the tricuspid valve, which can also present with RVOT obstruction (RVOTO).

Anatomically and developmentally, PA/IVS represents a wide spectrum of related defects and abnormalities of the RV and TV, resulting in "upstream" antegrade RVOTO reduced or absent pulmonary blood flow. As a result, varying degrees of "downstream" right ventricle and pulmonary artery hypoplasia exist with associated coronary artery anomalies. Most commonly, the pulmonary arteries are hypoplastic with normal arterial wall architecture and branching. The following is an anatomic summary of the spectrum of right-sided cardiac lesions-associated PA/IVS anomalies:

- **Tricuspid valve**: TV size can vary significantly with PA/IVS. Most commonly, the valve is hypoplastic and dysplastic manifesting with stenosis and/or regurgitation. The size of the tricuspid valve annulus has been correlated with RV size and morphology as well as with the presence of coronary anomalies. TV annulus *Z*-scores of ≤4 correlate with a unipartite ventricle, while TV *Z*-scores ranging from −2 to 0 are usually associated with a tripartite ventricle. TV *Z*-scores ranging from −4 to −2 are thus associated with variable degrees of RV hypoplasia. In 5−10% of PA/IVS patients, the TV annulus may be inferiorly displaced similar to that seen in Ebstein's anomaly of the TV [1−3].
- **Right ventricle**: The size and morphology of the right ventricle similarly varies in PA/IVS. The RV may be severely hypoplastic with a small cavity and marked muscular hypertrophy or it may be large, dilated, and thin-walled. The observed variation is often a result of the degree of intracavitary muscular overgrowth. The normal morphologic RV is characterized by 3 components (ie, tripartite): an inlet, a trabecular body, and the infundibular outlet. The majority of PA/IVS (60−80%) patients present with well-formed, tripartite right ventricles. For those with bipartite RVs (15−30%), apical trabecular overgrowth results in a loss of functional chamber size with an RV composed of just an inlet and body and no identifiable outlet. Rarely (2−10%), patients will present with a unipartite RV resulting from significant infundibular and apical trabecular overgrowth with a severely hypoplastic ventricle that is composed of only an inlet portion [2,3].
- **Coronary arteries**: PA/IVS is commonly associated with coronary anomalies. In approximately 50−70% of patients, coronary sinusoids that have persisted since fetal life directly communicate through fistulae from a hypoplastic RV to the coronary arterial bed [2,6−8]. The persistence of these fistulae is believed to be a direct result from the presence of a hypertensive RV in PA/IVS. Thus, patients with severely hypoplastic and hypertensive RVs are more likely to have RV-coronary artery fistulae. The presence of RV-coronary fistulae predisposes to the development of more proximal coronary artery stenoses or, in the most extreme cases, aortocoronary atresia (ie, coronary ostial atresia). As a result, in approximately 25% of cases, right ventricular-dependent coronary circulation (RVDCC) exists, which is defined as coronary blood flow that is either partially or completely dependent upon retrograde blood flow from the RV [3]. RVDCC is clinically important as RV decompression (relief of RVOT obstruction or initiation of cardiopulmonary bypass or extracorporeal membranous oxygenation support) may lead to complications of coronary artery steal and ischemia, including sudden death. Furthermore, in the presence of RVDCC, the myocardium is receiving a higher proportion of deoxygenated blood compared to that derived from antegrade aortic blood flow, which may predispose to development of ventricular dysfunction over time.
- **Pulmonary valve atresia**: In PA/IVS, the spectrum of pulmonary atresia varies from anatomic valvar (membranous) atresia to complete muscular atresia. Valvar (or membranous) pulmonary atresia is a milder form of RVOTO in which the pulmonary valve is atretic with a small valve annulus; however, structurally identifiable valve leaflets may be present. The leaflets may be fused and/or dysplastic with a thin membrane contributing to RVOTO. The RV and infundibulum are usually structurally developed. Muscular pulmonary atresia, occurring in approximately 25% of cases, represents a more severe form of RVOTO characterized by complete obliteration of the muscular infundibulum. This is more commonly associated with severe RV hypoplasia as well the presence of coronary artery anomalies, including RVDCC.
- **Supravalvular pulmonary circulation:** Most commonly, the supravalvular pulmonary circulation is supported by a left-sided patent ductus arteriosus associated with confluent pulmonary arteries. The pulmonary artery architecture is that of a normal branching pattern arising from a main pulmonary trunk. The main pulmonary trunk may be hypoplastic depending upon the degree of pulmonary atresia and antegrade pulmonary blood flow. The branch PAs are usually fairly well developed. The presence of major aortopulmonary collateral arteries is rare in PA/IVS and much more common in PA/VSD.

PATHOPHYSIOLOGY AND CLINICAL PRESENTATION

The hallmark pathophysiologic feature in PA/IVS is RVOTO. This feature results in obstruction to both pulmonary and systemic circulations. Neonates often present with ductal-dependent circulation that is further impacted by the presence of a small ductus arteriosus. A patent ductus arteriosus is the sole source of pulmonary blood flow. Further, in the presence of an intact ventricular septum, egress of RV blood flow is dependent upon the presence of concomitant tricuspid regurgitation and right-to-left shunting through an atrial level shunt (ie, patent foramen ovale or atrial septal defect) or through the persistence developed coronary sinusoids or fistulae to the coronary circulation. Both of these processes, therefore, affect and/or are dependent upon the RV pressure. In the presence of significant (moderate to severe) tricuspid regurgitation, RV pressures may more closely approximate normal values with less association of developed coronary fistulae. To the contrary in the presence of a competent tricuspid valve with little to no regurgitation, RV pressures may be significantly increased (ie, suprasystemic) with developed coronary fistulae or RVDCC. Importantly, the reliance upon coronary artery fistulae to decompress the RV results in the delivery of deoxygenated systemic venous blood to the myocardium, which may predispose to reduced right- and left-sided ventricular function.

The clinical presentation of PA/IVS in the neonatal period is usually one of cyanosis. The cyanosis is due to the absence of antegrade pulmonary blood flow through the RVOT and to the presence of an obligate right-to-left atrial level shunt. The cyanosis is usually accompanied by mild tachypnea. Severe respiratory distress is uncommon, which helps to differentiate the cyanosis from that due to a primary pulmonary etiology such as neonatal respiratory distress syndrome. In the presence of an unrestricted atrial level right-to-left shunt and maintenance of a patent ductus arteriosus, normal neonatal hemodynamics may be achieved until surgical repair can be achieved.

SURGICAL MANAGEMENT OF PA/IVS

Due to the heterogenous combination of anatomic features that may exist among PA/IVS patients, the medical and surgical management may be complex. The spectrum of TV and RV abnormalities as well as the presence of coronary anomalies must, therefore, be carefully evaluated to determine the optimal approach to either surgical palliation or complete biventricular correction.

Initial Medical Management and Stabilization

Following birth, initial medical management and stabilization is focused upon ensuring adequate pulmonary circulation and systemic oxygenation. Initial medical therapy in the neonatal period is critical to optimize the patient's metabolic profile and end-organ function prior to further palliation or surgical repair. Use of respiratory support ranging from the delivery of supplemental oxygen to initiation of mechanical ventilation, and the use of inotropic therapy may be required to correct metabolic derangements and systemic acidosis. Importantly, initiation of prostaglandin E1 infusion is necessary to maintain patency of the ductus arteriosus to provide a stable source of pulmonary blood flow and intercirculatory mixing. In addition, ensuring the presence of an unrestricted atrial level right-to-left shunt is required. If necessary, catheter-based balloon atrial septostomy may be performed.

Neonatal Palliation or Surgical Repair Options and Treatment Algorithms

Depending upon the anatomic features and physiologic consequences of PA/IVS, various palliation and surgical repair options exist for this neonatal population. The surgical repair and palliative options for PA/IVS include:

- Complete, biventricular repair with completely separate pulmonary and systemic circulations and 2 ventricles.
- Hybrid (1.5 ventricle) repair that partially separates the pulmonary and systemic circulations; however, it preserves 2 functioning ventricles. This is performed for cases with RVs incapable of completely supporting the entire systemic venous return. A superior cavopulmonary shunt (ie, bidirectional Glenn) is performed to provide a direct source of pulmonary blood flow, while the systemic venous return from the IVC returns to the right side of the heart as usual and is directed to the pulmonary circulation through a surgically reconstructed RVOT.
- Single ventricle (univentricular) palliation completely separates the pulmonary and systemic circulations with only a single ventricle responsible for systemic cardiac output.
- Primary cardiac transplantation is rarely performed for cases of PA/IVS with aortocoronary atresia that have mortality rates approaching 100% despite surgical or nonsurgical palliation [9,10].

Treatment algorithms and surgical/palliative management decisions are determined by the likelihood for complete, biventricular repair. These determinations are primarily dependent upon the constellation of the aforementioned morphologic and functional features of the tricuspid valve and right ventricle. Fundamental to these decisions are the following:

1. Determination of whether the RV can either support (or can be rehabilitated to support) a full pulmonary circulation and systemic venous return.
2. RV morphology (unipartite, bipartite, or tripartite) and degree of membranous vs muscular pulmonary atresia.
3. TV size, morphology, and function.
4. Presence of and extent of coronary sinusoids or fistula, presence of RVDCC, coronary artery stenosis, or presence of aortocoronary atresia.

While several previously published series have sought to evaluate various management algorithms for the treatment of PA/IVS, continued debate exists due a wide variety of opinions related to the best anatomic and preoperative metrics to assess likelihood for surgical or palliative success. In fact, several studies have reviewed surgical outcomes and associations between various measurable factors and success of surgical repair. These series suggest that the likelihood for biventricular repair is increased in the presence of the following factors: TV *Z*-score ≥ -2, presence of a tripartite (or near normal size) RV, the absence of RVDCC, and degree of tricuspid regurgitation [1,3,6,11–16]. However, several limitations seem to exist with these metrics and that should be the focus of continued investigation. Regarding the use of TV *Z*-score, an inherent limitation is that this measurement is only focuses upon 1 aspect (ie, TV annular size) of a multidimensional issue and does not represent the impact of leaflet morphology or status of the subvalvular apparatus. Other echocardiographic measurement or metrics to consider include the ratio of TV diameters, RV volume measurements, as well as tricuspid:mitral valve ratio.

SUMMARY OF OUR INSTITUTIONAL APPROACH TO SURGICAL MANAGEMENT

Our multidisciplinary, institutional approach to the surgical management and treatment algorithms applied for PA/IVS favor an aggressive pursuit of a complete, biventricular repair

when feasible. Both fetal and neonatal echocardiographies are utilized to characterize the various anatomic features and obtain accurate measurements of the size, morphology, and function of both the TV and RV, nature of pulmonary atresia, status of the ductus arteriosus, and atrial level shunt. In the presence and/or suspicion of coronary artery fistulae or RVDCC, cardiac catheterization is performed to evaluate the extent of fistula burden and status of the coronary circulation.

A summary of our approach to surgical management includes the following fundamental principles:

- Exclude RVDCC by cardiac catheterization.
- Consider primary cardiac transplantation in the presence of coronary ostial (ie, aortocoronary) atresia.
- Exclude hybrid (1.5 ventricle) or biventricular repairs with TV *Z*-score of <3.
- Evaluate TV and RV morphology and function with TV *Z*-scores >3.
- Aggressive approach to RV decompression (RVOT reconstruction with transannular patch, pulmonary valvotomy, or catheter-based radiofrequency ablation of membranous pulmonary atresia), assurance of adequate pulmonary blood flow (modified Blalock-Taussig systemic to pulmonary artery shunt or bidirectional Glenn), improving TV inflow, and increasing RV size (ie, RV overhaul procedure) during primary surgical repair when possible. An initial BT shunt that is needed during the neonatal period may not be needed anymore later on and may get coiled in the catheterization lab.

We believe that achieving a final complete, biventricular repair when possible should be the goal for all PA/IVS patients. Early RV decompression should promote both TV and RV growth through improved antegrade pulmonary blood flow so that the rehabilitated right heart should be able to support a full systemic venous return and cardiac output. Importantly during this process, the presence of a small atrial level shunt (ie, patent foramen ovale or restrictive atrial septal defect) may be necessary to ensure an adequate systemic cardiac output and support the developing right heart.

SURGICAL OUTCOMES

While surgical management for PA/IVS remains challenging, surgical outcomes have improved in recent decades as the implications of the wide spectrum of anatomic features for this condition have been elucidated. Several multicenter series published in the early 1990s through the mid-2000s reported ~80% overall discharge survival and ~60% 10−15-year survival following surgical repair [1,2,6]. A more recent 2014 report by Schneider et al reported an 87% survival rate at 10 years follow-up in a series of 60 patients [17]. Moreover, in their 2016 single-center study of 33 PA/IVS patients, Zheng et al reported survival rates of 97%, 94%, and 88% at 1, 5, and 15 years of follow-up for patients undergoing single-stage repairs, and 90%, 88%, and 69% survival rates at 1, 5, and 15 years for patients undergoing staged repair [18]. In these series, lower tricuspid valve *Z*-score and smaller RV size were associated with reduced survival. Similarly, the presence of RVDCC has been associated with increased mortality risk. In a recent 2018 report, Elias et al demonstrated significantly reduced 10-year survival in Fontan palliated PA/IVS patients in the presence (77%) vs absence (96%) of RVDCC [19].

SUMMARY AND CONCLUSIONS

PA/IVS represents a complex and heterogenous congenital cardiac defect with a tremendous spectrum of anatomic right-sided heart lesions and physiologic consequences. As a result, the perinatal management and surgical decision-making process for these patients in the neonatal period remains a challenge. A multidisciplinary team approach to accurately assess and the physiologic needs and anatomic characteristics of each patient are required to achieve optimal treatment success. Critical to the surgical decision-making algorithm is assessment of tricuspid valve and right ventricle size and morphology. A clinically useful cutoff for single ventricle and hybrid (1.5 ventricle) vs biventricular repair appears to be a tricuspid valve *Z*-score of −2 to −3. For patients in the moderately hypoplastic range (TV *Z*-scores >−2), aggressive surgical techniques to improve TV inflow, enlarge the RV through a RV apex overhaul, and decompress the RVOT may aid in rehabilitating the RV so as to achieve a biventricular circulation through either a staged or single-stage repair.

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