

When coronary arteries need systolic pressure: surgical considerations

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Abstract

OBJECTIVES: Patients with pulmonary atresia and intact ventricular septum (PA-IVS) may have coronary sinusoids connected to a hypertensive right ventricle. Coronary perfusion may then completely depend on the right ventricular systolic pressure wave; decompression of the right ventricle can be deleterious in these patients. This study was set to investigate the treatment strategies and outcomes of patients with coronary sinusoids.

METHODS: National multicentre retrospective analysis over 15 years (1985–2010) in a population of ~10.2 million people. All patients with PA-IVS and coronary sinusoids were identified from local databases. All angiograms, echocardiograms, surgical reports and outcome data were reviewed.

RESULTS: Thirty patients were identified. Right ventricular-dependent coronary circulation was present in nine patients (30%). A systemic-to-pulmonary artery shunt was created in 23 patients (77%) at a median age of 13.0 days (range: 1–479). A bidirectional Glenn was performed in 20 children at a median age of 7.8 months (range: 2.1–112.9) and 11 children proceeded to a Fontan repair at a median age of 3.6 years (range: 2.1–19.6). Pulmonary valve perforation and angioplasty were performed in six children and in three a simultaneous decompression procedure was also done. Ten patients died (33%). Four died at the time of systemic-to-pulmonary artery shunt and three during the bidirectional Glenn shunt. In all these patients myocardial ischaemia was reported.

CONCLUSIONS: Mortality in PA-IVS with sinusoids is high. Right ventricular coronary dependence may lead to early death if the right ventricular systolic pressure wave is interrupted. Adequate understanding of the underlying pathology and pathophysiology is essential before attempting any procedure in this subgroup of children.

Keywords: Sinusoids • Congenital heart • Right ventricular dependence • Shunt • Coronary abnormality

INTRODUCTION

Pulmonary atresia with intact ventricular septum (PA-IVS) represents a heterogeneous group of abnormalities. The overall 5-year survival of patients with PA-IVS varies from 60 up to 91%, with most deaths occurring in the early years [1–8]. Multiple surgical and interventional treatment options are available for these patients: some are based on right ventricular (RV) morphology, some on the size of the tricuspid valve and others on the size of the infundibulum or the presence of sinusoids [9–13]. The high mortality reflects that management strategies are still inadequately tailored to patient needs.

The assessment of the coronary blood supply is important when deciding on a treatment strategy [9]. Coronary artery fistulae connected to a hypertensive right ventricle are seen in ~30–60% of patients with PA-IVS [9, 14, 15]. Myocardial perfusion in these can either be normal from the aorta, complex or dual with

competitive flow to the coronary arteries from the right ventricle through sinusoids or even solely dependent on the right ventricle—so-called right ventricle-dependent coronary circulation (RVDCC) [1, 3, 4, 16].

Stenosis and even atresia can occur at multiple levels of the coronary system. The purpose of this study was to investigate the treatment strategies, coronary morphology and outcomes of patients with PA-IVS with coronary sinusoids.

PATIENTS AND METHODS

This multicentre study was conducted at the four national centres for congenital and paediatric cardiology in Belgium, a country with a population of 10.8 million people. All records of 120 patients with the diagnosis of PA-IVS who presented in the period 1985–2010 were retrospectively reviewed to

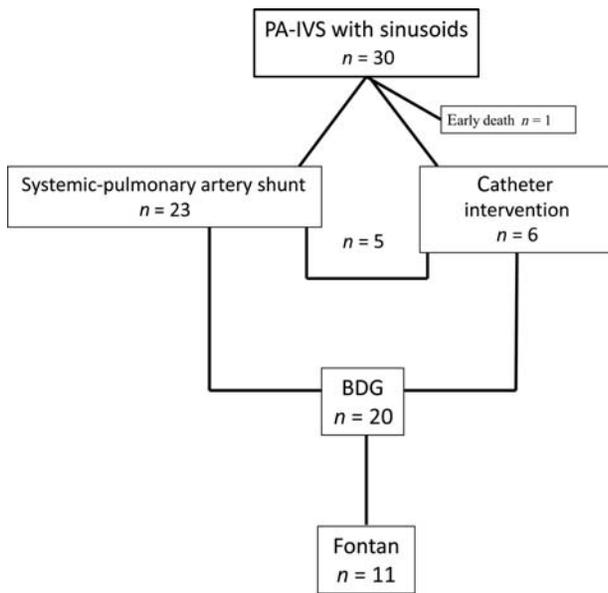


Figure 1: Patient management. BDG: bidirectional Glenn shunt.

identify patients with coronary sinusoids connected to the right ventricle.

All medical records, surgical reports, echocardiograms and catheterization data from the participating centres were reviewed by a single cardiologist. Standard descriptive and demographical data were also obtained from patient records. A total of 30 patients were included for analysis (Fig. 1).

It is important to realize that the diagnosis changed considerably as catheterization procedures have changed over the years. We excluded some patients ($n=5$) who were diagnosed as PA-IVS, but a RV angiogram before intended fulguration showed critical pulmonary stenosis on review.

Description of coronary anatomy was based on angiographic data. Supra-aortic, selective coronary artery and RV injections were evaluated to provide a detailed account of the coronary arteries and sinusoids. The presence of sinusoids, description of coronary ostia, presence and site(s) of stenosis were evaluated. RVDCC was defined as the presence of either (i) one or two major coronary arteries with severe stenosis or complete obstruction (ii) the presence of coronary atresia or (iii) a large part of the left ventricle solely perfused by the right ventricle through the sinusoids. Follow-up angiographies, when present, were used to determine the progression of the sinusoids and coronary perfusion (Fig. 2).

RV morphology, tricuspid valve measurements and z-score were calculated using echocardiographic and catheterization data. The right ventricle was classified according to whether inlet, outlet and apical portions were present as suggested by Anderson *et al.* [17].

Patient condition at last follow-up was noted. If a patient died and a post-mortem examination had been performed, the reports were appraised. Histological examinations were also recorded if available.

ETHICS AND STATISTICS

Approvals by the local medical ethics committees were obtained at all participating centres. Data were analysed using SPSS for

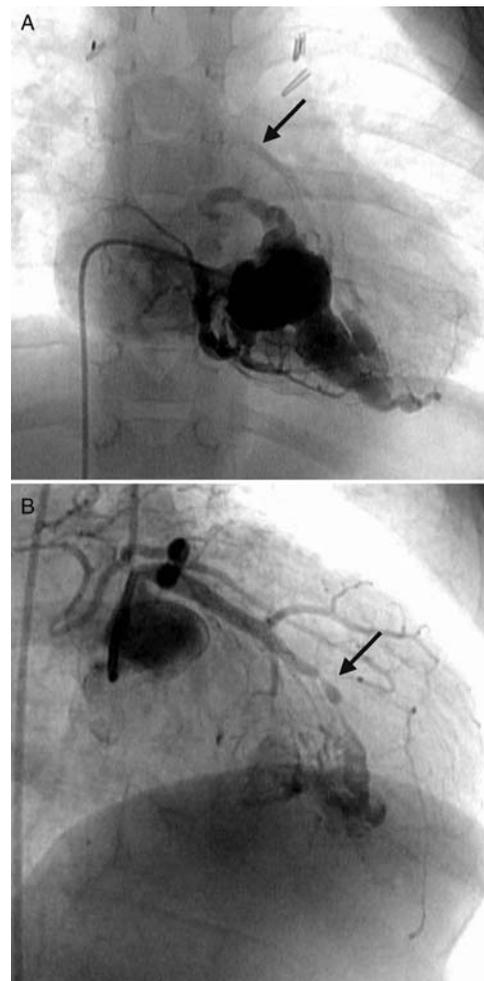


Figure 2: Right ventricular-dependent coronary circulation. Typical example of RVDCC. (A) RV angiogram shows sinusoids. Note retrograde filling of the left coronary artery (arrow). (B) Aortogram shows connection of left anterior descending to right ventricle. Note multiple stenosis (arrow).

windows® (Chicago, IL, USA, version 18). Data are presented as medians with minimum and maximum values and 95% confidence intervals where appropriate. The Kaplan–Meier survival analysis was used to compare freedom of death in different groups.

RESULTS

Patient characteristics are summarized in Table 1. There was a slight male preponderance (60%), and the median birth weight was 3.2 kg (2.4–4.5). The management of the whole group is depicted in Fig. 1. Systemic-to-pulmonary artery shunts were performed in 23 patients (77%) at an early age (median age: 13 days). Bidirectional Glenn (BDG) was performed in 20 children (67%) at a median age of 7.8 months (range: 2.1–112.9) and 11 children proceeded to a Fontan circulation at a median age of 3.6 years (range: 2.1–19.6). Pulmonary valve perforation and valvoplasty were performed in six children, of whom three also had a decompression procedure (RV outflow patch and overhaul).

Morphology

The tricuspid valves were very small at diagnosis, with a median z-score of -6.8 (Table 1). The right ventricle was classified as

Table 1: Patient characteristics

Description	Number (n)
Patients	30
Male	18
Female	12
Birthweight (kg)	
Median	3.2
Range	2.4–4.5
Age at S-P shunt (day)	
Median	13
Range	1–479
Tricuspid valve z-score	
Median	-6.8
Range	-0.9 to -12.0
Age follow-up (year)	
Median	8.4
Range	0.1–25.4

S-P shunt: systemic-to-pulmonary artery shunt.

unipartite in 2 (6%), bipartite in 14 (47%) and tripartite in 14 (47%). Single coronary ostia were observed in seven patients, two with absent left and five with an absent right coronary artery ostium. Coronary abnormalities are depicted in Table 2. There were seven (23%) mon coronary systems that were dominantly right coronary (70%). In general, the sinusoids had multiple connections to the coronary arteries. Fourteen sinusoids were associated with coronary artery stenosis of which 6 (20%) were multiple (Table 2). RVDCC was present in nine infants (30%).

When last seen, 18/20 were in NYHA functional class I or II during a median follow-up of 8.4 years. During the follow-up period, only three sinusoids showed regression.

Mortality

The total mortality for patients with sinusoids was 10/30 (33%) (Table 2). Deaths are summarized:

- One neonatal death at 9 days of age shortly after a balloon atrioseptostomy and before a shunt could be performed. This was unexpected and no complication related to the septostomy was noticed on echocardiography.
- Four patients died around the time of first surgery. One child died at induction for anaesthesia and could not be resuscitated.

Table 2: Coronary morphology and mortality

Patient no	Sinusoid connections	Stenosis	RVDCC	Age of death	Time of death	
1	RCA, LAD	Single				
2	RCA					
3	RCA, LAD, Cx	Multiple, no ostium RCA	Yes	1.1 year	BDG	CPR, LVAD
4	RCA	Multiple, no ostium LCA		34 days	Shunt	Intramural coronary artery
5	RCA, Cx	Single				
6	LAD, Cx					
7	RCA, LCA					
8	RCA, LAD, Cx, PD	Multiple, no ostium RCA				
9	RCA, LCA, PD	Multiple		14 days	Shunt	Bradycardia induction
10	RCA, LAD, Cx, PD	Multiple	Yes			
11	RCA, LAD	Single		11 days	Shunt	Not weaned off CPB
12	RCA, LAD					
13	RCA, LAD, Cx	Single				
14	RCA, LAD, Cx					
15	RCA	No ostium LCA	Yes	9 days	Neonatal	BAS
16	RCA, LAD, Cx					
17	RCA, LAD, Cx	Single	Yes	8 months	BDG	CPB, Stent, ECMO
18	RCA, LAD, Cx	No ostium RCA	Yes			
19	RCA, LAD					
20	RCA, LAD, Cx, PD	Single	Yes	3.6 month	Hospital	Unexpected
21	RCA, LAD			1.4 year	Home	Unexpected
22	RCA, LAD, Cx			41 days	Shunt	Ischaemic myocardium
23	RCA, LAD, Cx					
24	RCA, LAD, Cx, PD	Multiple, no ostium RCA	Yes			
25	RCA, LAD					
26	RCA, LAD					
27	RCA, LAD	Multiple	Yes			
28	RCA, LAD	Single				
29	LAD	Single				
30	LCA	No ostium RCA	Yes		BDG	Ischaemic myocardium

RCA: right coronary artery; LAD: left anterior descending; Cx: circumflex; PD: posterior descending; BDG: bidirectional Glen shunt; CPR: cardiopulmonary resuscitation; LVAD: left ventricular assist device; CPB: cardiopulmonary bypass; BAS: balloon atrioseptostomy; ECMO: extracorporeal membrane oxygenator.

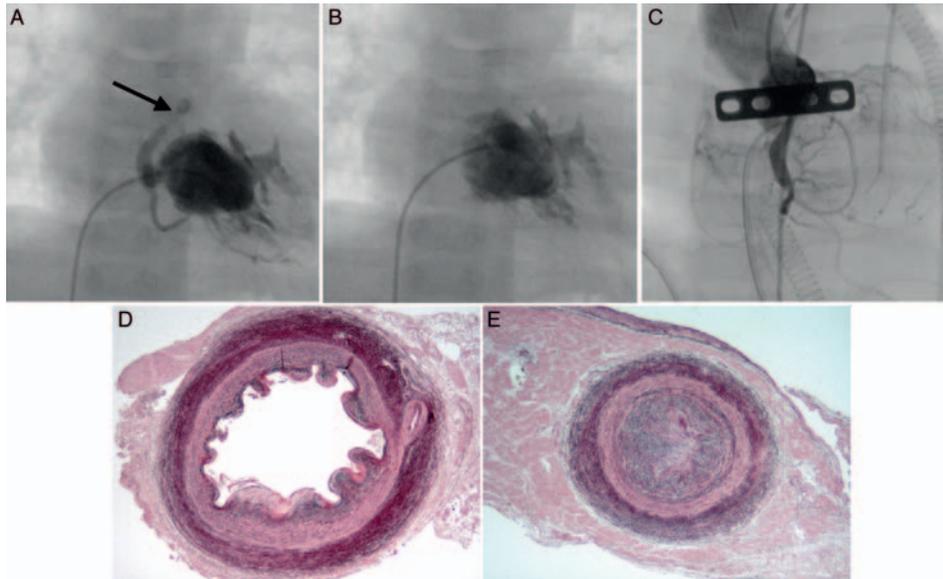


Figure 3: Filling and pathology right coronary artery pre and postoperative. (A) RV angiogram systole: contraction of RV creates a large pulse wave through the fistula into the RCA; note proximal stenosis on RCA (arrow); (B) diastolic frame: subtotal collapse of RCA in diastole; (C) supravulvar aortic injection on ECMO: the stented proximal RCA is patent, aortic pressure is not able to perfuse the distal RCA with no distal flow. Sternal fixation and ECMO cannulas. (D) Elastica-Von Gieson stain: original magnification $\times 25$ of proximal RCA after removal of stent: note significant hyperplasia of the intima. (E) Distal part of the RCA with extensive hypertensive arteriopathy: fibrosis of the intimal layer subtotal occlusion.

One death occurred during placement of systemic-to-pulmonary artery shunts and another two within 4 and 8 days following shunt placement.

- Another three children died within 24 h after BDG operation. One suffered a circulatory arrest and was taken back to theatre where a left ventricular assist device was installed. The surgeon reported that the myocardium looked infarcted. The second patient with dual perfusion could not be weaned from bypass. The right coronary artery showed preoperatively a significant stenosis close to the origin, with distally a marked systolic pulse wave due to sinusoidal flow; the sinusoid was tied off and the coronary artery was stented in theatre. The patient could not be weaned off bypass and extracorporeal membrane oxygenator was instituted; the myocardium did not recover despite a patent proximal right coronary artery but no distal coronary flow; angiography and histology are shown in Fig. 3. The third patient was reported as developing myocardial ischaemia and died within hours after surgery.
- In two patients, the cause of death was not clear.

RVDCC was present in five (50%) of those who died (Table 2).

Histology

Post-mortem examinations were performed in four patients. A single coronary artery with an intramural pathway was observed in Patient no 4. It was described as having an 'acute angle take-off', which led to compression between the pulmonary arterial trunk and a dilated aortic root with massive myocardial ischaemia. Angiographic review reported this as absent left coronary ostium with multiple stenoses. This was the patient who died during induction of anaesthesia. Pathological specimens of three patients, two died around the time of shunt placement and one during Glenn operation, showed critical stenosis

of at least one major coronary artery. Large parts of the lumens were obliterated. Histology showed marked hypertensive vasculopathy with fibromuscular dysplasia and myxoid appearance of the vessel walls.

Statistics

A Kaplan–Meier survival analysis was performed (Fig. 4). There was no significant difference in dying due to stenosis on the sinusoids vs no stenosis and so for having RVDCC ($P = 0.62$).

DISCUSSION

Our results show that the presence of fistulous connections to the coronary arteries is associated with a clinically important mortality (10/30), with half of these occurring in what was considered an RVDCC. Similar mortality rates were found in one of the largest series of this rare disorder ($n = 87$) by Calder *et al.* [18]. In other, smaller series, mortality also varied between 20 and 30% [3, 9, 14]. Interestingly, in all studies including ours, there is a significant early mortality at the first procedure, whether it be percutaneous intervention or surgical shunt placement. Even though frequently reported, these early deaths require more analysis to develop new and more adequate management strategies.

Sinusoids are primitive embryological remnants that initially supply the cardiac muscle. They have connections with both the cardiac veins and arteries before involution [19]. If these sinusoids persist, single or multiple stenoses are common and were present in 47% of the cases in our cohort.

Most of these children die due to myocardial ischaemia or dysrhythmias. In a patient with RVDCC, some specific pathophysiological surgical aspects need to be considered. A number

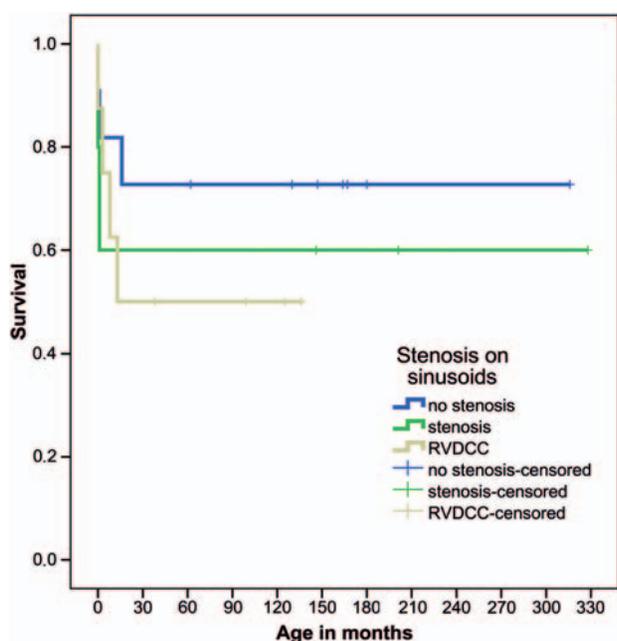


Figure 4: Kaplan–Meier analysis in patients with and without stenosis on the sinusoids and RVDCC.

of risk factors emerge when such a patient is sent to the theatre. Firstly, for the reason that they have to be nil per mouth beforehand, preload and thus right heart pressure, may drop if not properly hydrated: this may impair systolic flow to the area supplied by the right ventricle-dependent perfusion. At the time of induction of anaesthesia patients may become hypotensive with ventricular hypocontractility, which may result in myocardial ischaemia in RVDCC—as demonstrated by the patient with an abnormal coronary artery during anaesthesia. Furthermore, during cardiopulmonary bypass (CPB) and following cross-clamping of the aorta, cardioplegia is instituted. In most cases, standard techniques are employed presuming that the coronaries are normal and perfuse the heart at low pressure. Cardioplegic solution may not reach the RV-dependent segments, which may lead to ‘warm ischaemia’ and necrosis. Similarly, at the end of surgery, normal coronary washout procedures may not reperfuse the RVDCC. It can thus be inferred that cardiac arrest should be avoided in these patients, since their physiology sets them up for early mortality. This combination of events was most likely the cause of the perioperative deaths reported in this study. Diastolic run-off resulting from either a surgical shunt or a stented ductus may further aggravate the situation because of coronary steal. Obviously, these patients are also at high risk for sudden unexpected deaths.

Histological evidence supports our postulation of myocardial infarction being an important cause of death. The vessels were also described as demonstrating obstructive hypertensive vasculopathy with fibrotic changes. The vessel lumens were indeed obliterated over a long distance in these cases. A previous necropsy series also reported severe narrowing and obliteration of the coronary lumen in up to 50% of cases [20]. This would indicate that in some of these patients, obstructions require extremely high perfusion pressures to provide adequate myocardial oxygenation; normal aortic diastolic pressure will not

provide adequate myocardial perfusion through such coronary arteries. Moreover, such high pressures are known to further induce progressive obliterative vasculopathy. In this small subgroup, there is a very high risk of death as they are essentially ‘pre-programmed’ to die early. Little can be done at present, except a neonatal cardiac transplant to avoid inevitable demise. Giglia *et al.* [9] also reported progression of a stenosis and total occlusion of the left coronary artery. These findings emphasize the unpredictability of stenosis in patients with sinusoids and explain the variety of clinical evolution in the various reports [3, 14, 21].

Coronary artery abnormalities associated with sinusoids are common but highly variable in these patients. A single coronary ostium was observed in seven patients, remarkably similar to the findings of Calder *et al.*, also with absent right coronary aortic connection being more frequent than left [18]. Three of these monocoronary arteries were considered RVDCC. Comparable with previous reports, the presence of sinusoids and RVDCC was not associated with a higher risk of death related to this subgroup only [5].

Seventy-seven percent (23/30) of patients had a systemic-to-pulmonary artery shunt. This is not unusual since many physicians would regard a shunt as the best treatment for this select group of patients. One patient was quite old (479 days) at the first shunt procedure in 1986 when shunts were often delayed as long as possible. Most of the group was managed adopting a univentricular strategy due to a small tricuspid valve and hypoplastic right ventricle. Three of our patients had pulmonary valve perforation and RV decompression performed, all of whom survived, but none had an RVDCC. The Boston group previously reported that RV decompression was safe in patients with fistulas only, but found that two of six died where singular stenoses were present and that 3/3 with multiple stenoses and/or occlusion of one coronary artery died. This highlights the fact that coronary artery anatomy should be carefully investigated in patients with sinusoids and that decompression of the right ventricle should not be attempted in the latter group. We speculate that if a stenosis is present, but supplies mostly a hypoplastic right ventricle and provided that the left myocardium will not be compromised by ischaemia, decompression could be cautiously considered. Involution of the right ventricle would have no effect in this situation, since the only option is a univentricular route. However, coronary perfusion must be very carefully studied beforehand.

What can we offer these patients? Hypotension and hypocontractile conditions should be avoided at all costs both during surgery and percutaneous interventions. It is also imperative to establish the precise coronary anatomy. Angiography is essential in these patients. Not only is an RV angiogram required, but also proper aortography to demonstrate proximal coronary anatomy or competitive flow from an RVDCC. Alternative surgical strategies should be considered, especially techniques where right heart pressures are maintained, e.g. veno-venous bypass on a beating heart or off-pump surgery [22, 23]. Cardiac transplant has been successful in infants with atresia of both coronary arteries [24]. The question still remains when to list these very special high-risk patients for transplant. In the current studied subjects HTX was not seen as a valuable option by the parents or the physician. Most importantly, one should maintain a high index of suspicion and awareness in a child with PA-IVS and coronary sinusoids, especially during procedures.

Limitations

The study is limited by its retrospective nature. In order to reduce observer bias and variability, all echocardiograms and angiograms were independently re-examined by a single cardiologist. The numbers are small, but the study analysed a highly select subgroup of patients and represents a sizeable cohort of this condition.

CONCLUSIONS

Mortality in PA-IVS with sinusoids is high and heterogeneous coronary abnormalities are frequently encountered in this group. RV coronary dependence may lead to early death if the RV systolic pressure wave is interrupted. Adequate understanding of the underlying pathology and pathophysiology is essential before attempting any procedure in this subgroup of children. Management should be tailored to coronary anatomy. Some patients have progressive fixed coronary obstruction and limited treatment options.

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