Absent pulmonary valve syndrome. Surgical and clinical outcome with long-term follow-up

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Abstract

Objective: To identify a large group of patients operated for absent pulmonary valve syndrome (APVS), and describe the outcomes of various subgroups and surgical strategies.

Methods: Thirty-six consecutive patients operated during 1979—2004 were included. Thirty-one percent furthermore had other vascular abnormalities. Eighty-three percent had airway obstruction symptoms before surgery. Twenty-eight percent were ventilator dependent, while 72% underwent repair electively. The median age and weight at repair were 0.8 years (4 days—24 years) and 6.7 kg (1.8—56 kg). The surgical approach was modified several times, including the following: homograft conduit (14%), monocusp valve (39%), and no pulmonary valve (47%). All patients underwent ventricular septal defect (VSD) patching. Seventy-four percent underwent right ventricular outflow tract resection and 91% underwent transannular patching. Pulmonary artery reduction plasty was performed in 86%.

Results: The follow-up was 94% complete. Nineteen percent had died. The median follow-up time was 9.2 years (1 day—20.5 years). Survival after repair was 82% at 1 year and 79% at 5, 10, and 15 years. Postoperative survival was strongly associated to preoperative ventilator dependency \( (p = 0.002) \). The current New York Heart Association (NYHA) classification was established in 93% of survivors. Eighty-nine percent were in NYHA 1 or 2, 11% were in NYHA 3. No patient was in NYHA 4. Freedom from reoperation 1, 5, and 10 years after repair was 78, 65, and 55%, respectively.

Conclusions: The surgical outcome of APVS was closely related to preoperative ventilator dependency. Efforts to improve the surgical outcome should be focused on identifying and correcting this.

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1. Introduction

Absent pulmonary valve syndrome (APVS) is a rare congenital cardiac malformation including dysplasia or absence of leaflet tissue and severe incompetence of the pulmonary valve, pulmonary annular stenosis, and dilatation of the pulmonary artery system, often leading to a varying degree of airway compression at the tracheal and major bronchial arborization level [1,2]. APVS is most commonly found as a variant of tetralogy of Fallot with a reported incidence of 5% in these patients [3], but case reports have described APVS associated with other congenital cardiac syndromes including type B interrupted aortic arch [4], transposition of the great arteries [5], pulmonary branching abnormalities [6—8], atrioventricular septal defect (ASD) [9], and persistent ductus arteriosus [10—12] as well as agenesis of ductus arteriosus [13]. APVS has also been described in DiGeorge syndrome [14].

The aim of the present study was to identify a large group of patients operated for APVS in order to describe the surgical and clinical outcome of various subgroups of patients, as well as analyze the effect of different surgical strategies.

2. Materials and methods

Forty patients undergoing surgery for APVS at The Royal Children’s Hospital between August 1975 and July 2004 were identified.

Since 1979, when our department database was initiated, 36 consecutive patients have been recorded when undergoing APVS repair.
Another four patients appeared in the database but did not belong to the consecutive series. These included one patient that received the repair at Guys Hospital, London, UK, and underwent further surgery at our institution after migrating to Australia, and three patients operated during 1975–1977 who first appeared in the database when they returned for conduit replacement. These patients were not included in the study.

All patient histories including operation reports were retrieved, and data were extracted from these.

We attempted to contact all families of survivors for a short interview in order to classify them according to the New York Heart Association (NYHA) classification for congestive heart failure, and to retrieve information on subsequent operations performed on patients who have left the care of our institution.

2.1. Patient material (consecutive patients)

Thirty-six patients (23 females, 13 males) were treated at our institution.

Thirty-five patients (97%) had APVS as a variant of tetralogy of Fallot anatomy, while one had APVS with double outlet right ventricle, double committed ventricular septal defect (VSD), and the aorta anterior to the main pulmonary artery.

Eleven patients (31%) with tetralogy of Fallot type anatomy had associated vascular abnormalities (Table 1). Two patients (5%) had DiGeorge syndrome.

In the early era of the experience, the diagnosis was made by angiography and/or intraoperatively. More recently, with the improvement of ultrasonic resolution, the diagnosis has been initially made on echocardiography, and angiography has been used regularly in many patients to assess the branch pulmonary arteries. CT scan and MRI are also increasingly used to assess the pulmonary anatomy.

Thirty patients (83%) had symptoms of airway obstruction of variable severity before surgery. Ten patients (28%) were ventilator dependent up to surgery (median age at repair: 97 days (4–215 days)). The other 26 patients (72%) underwent the repair as an elective procedure (median age at repair: 409 days (75 days–24 years)).

The preferred method during the period of the study to investigate the degree of airway compression has been a bronchogram, since the airway compression tends to involve not only the central main airways but also involves more peripheral airways. More recently, the role of high-resolution CT scanning has been explored. However, the assessment of the severity of airway compromise is ultimately a clinical one based on the difficulty with ventilation and the ability to wean from the ventilator.

Over all, the median age at repair was 0.8 years (4 days–24 years), while the median weight was 6.7 kg (1.8–56 kg).

2.2. Surgical procedures

Six patients (15%) had received a surgical procedure prior to the repair (right modified Blalock-Taussig shunt (n = 1), PDA ligation (n = 1), pulmonary balloon valvulotomy (n = 1), right upper lobectomy (n = 1), and bowel surgery (n = 2)). Thirty-five patients (97%) had the repair performed as a one-stage procedure.

One patient had the repair performed as a two-stage procedure, starting with main, left, and right pulmonary artery plication and interruption of the systemic collateral arteries to the right lower lobe at 4 months of age, followed by ASD and VSD closure at 3 years of age.

During the study period (1979–2004), the surgical strategy changed several times.

2.3. Myocardial protection/perfusion strategy

Seven out of the eleven patients operated between 1979 and 1987 received a period of deep hypothermic circulatory arrest (median duration: 45 min, range: 25–68 min). All other operations were performed using continuous cardiopulmonary bypass and aortic cross-clamping with cardiopect
domia.

2.4. Pulmonary valve management

During the period 1979–1994, 6 out of 22 patients had a pulmonary monocusp constructed, while 16 had no pulmonary valve installed. During 1994–1995, five consecutive patients had homograft valves installed (three trileaflet aortic, two pulmonary valves which were reduced to bileaflet valves). Since 1997, 9 out of 10 patients have had monocusp pulmonary valves constructed.

A total of 14 patients (39%) received a pulmonary monocusp valve made from a variety of materials: untreated autologous pericardium (n = 6), glutaraldehyde-treated homograft pericardium (n = 1), tailored aortic homograft (n = 2), tailored pulmonary homograft (n = 2), pulmonary artery trunk wall (n = 2), or 0.1 mm Gore-Tex membrane (n = 1).

A total of 19 patients (53%) had some form of pulmonary valve inserted at the time of the repair. Seventeen patients (47%) had no monocusp or homograft inserted and were left with free pulmonary regurgitation.

All 35 patients with tetralogy of Fallot received patch closure of a malalignment VSD. Twenty-six (74%) of these underwent RVOT resection and 32 (91%) underwent transan
turnal patching of the right ventricular outflow tract/pulmonary orifice.

The patient with APVS with double outlet right ventricle with double committed VSD and the aorta anterior to the

Table 1

<table>
<thead>
<tr>
<th>Associated vascular abnormalities</th>
<th>Number</th>
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</thead>
<tbody>
<tr>
<td>Great arteries</td>
<td></td>
</tr>
<tr>
<td>LPA from ascending aorta</td>
<td>2</td>
</tr>
<tr>
<td>LPA from PDA/descending aorta</td>
<td>1</td>
</tr>
<tr>
<td>LPA from left subclavian artery</td>
<td>1</td>
</tr>
<tr>
<td>Right aortic arch</td>
<td>3</td>
</tr>
<tr>
<td>Double aortic arch</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
<tr>
<td>TAPVD (supracardiac)</td>
<td>1</td>
</tr>
<tr>
<td>MAPCAs to the right lower lobe</td>
<td>1</td>
</tr>
<tr>
<td>LAD from the RCA</td>
<td>1</td>
</tr>
</tbody>
</table>

LPA, left pulmonary artery; PDA, patent ductus arteriosus; MAPCA, major aorto-pulmonary collateral artery; TAPVD, total anomalous pulmonary venous drainage; LAD, left anterior descending artery; RCA, right coronary artery.
main pulmonary artery had a REV (reparation à l'étage ventriculaire) procedure performed.

2.5. Pulmonary artery management

Thirty-one patients (86%) had reduction arterioplasty of the pulmonary artery system performed. In the remaining five patients (14%), the pulmonary arteries were judged not to cause airway compression, and were not reduced.

The decision to perform pulmonary arterioplasty and the method chosen for this was left to the surgeons’ judgment, although often dictated by the symptoms as well as the presenting anatomy.

Twenty-three patients (64%) had aneurysmal dilatation of the pulmonary artery trunk and all had this surgically corrected (pulmonary artery trunk resected and replaced by homograft conduit ($n=5$) or pulmonary artery trunk arterioplasty performed ($n=18$)).

Aneurysmal dilatation of the branch pulmonary arteries was found in 34 right pulmonary arteries and 29 left pulmonary arteries. In 30 and 25, respectively, reduction arterioplasty was performed by plication or wall excision.

3. Ethics

Approval to perform the follow-up, including contacting patients, was obtained from the Ethics in Human Research Committee of our hospital.

4. Statistics

Data were analyzed using Statistica 6.0® (StatSoft® Inc., Tulsa, OK, USA).

Follow-up data were analyzed using Kaplan—Meier statistics and differences between groups survival was analyzed using logrank test. All Kaplan—Meier statistics and comparisons between curves were based on the 36 consecutive patients operated at The Royal Children’s Hospital.

Since the data was skewed with 31 patients under the age of 2 years and 5 patients above 1.6—24 years, continuous data were reported as median and range, and nonparametric statistics were applied.

A limited risk factor analysis based on survival after repair was performed using logistic regression and Cox proportional hazards analysis. Further risk factor analysis was performed between matched groups with more than five in each group using chi-square test.

5. Results

Concurrent follow-up was 94% complete (34 of 36 patients).

For the last two patients, the latest follow-up was conducted more than 9 years ago.

Follow-up data regarding current NYHA classification and further cardiac operations performed could be obtained in 27 out of 29 patients last known to be alive (Table 2).

### 5.1. Survival/mortality

Seven patients (19%) had died after the repair. Five of these were less than 10 months old, and died during the postoperative course, without leaving hospital. Two of these (5%) died within 30 days after repair. The cause of death was withdrawal of treatment in patients unweanable after prolonged ventilation ($n=4$) and unexplained cardiac arrest on the first night after REV procedure ($n=1$).

In the remaining two patients who died after discharge following the initial repair (1.1 and 1.3 years old), the cause of death was sudden death 24 h after hospitalization for pneumococcal sepsis ($n=1$) and inability to wean from extracorporeal circulation at reoperation for repair of a residual VSD ($n=1$).

The median follow-up time was 9.2 years (1 day—20.5 years).

The survival after repair was 82% (CI: 65—92%) at one year and 79% (CI: 61—90%) at 5, 10, and 15 years.

The survival after repair is shown in Fig. 1.

### 5.2. Respiratory function

Five out of ten patients with ventilator dependency preoperatively (50%) died after repair. The median age of the ventilator-dependent patients at the time of repair was 97 days (4—215 days). For the ventilator-dependent patients there was no difference in the age at repair between the survivors (median: 88 days, range: 13—143 days) and the deceased (median: 106 days, range: 4—215 days) (Mann—Whitney $U$-test: $p=0.84$).

The survival of patients undergoing elective surgery not requiring preoperative ventilator support versus patients with ventilator dependency prior to surgery is shown in Fig. 2.

![Fig. 1. Survival after APVS repair (Kaplan—Meier).](https://academic.oup.com/ejcts/article-abstract/29/5/682/360388)
There was a significant difference in the immediate postoperative survival between these groups (logrank test: \(p = 0.002\)).

5.3. Pulmonary valve management

None of the 17 patients that were left without a pulmonary valve at the repair, later had a pulmonary valve inserted (median follow-up 13.7 years, range 0.2—20.5 years). One patient that primarily had an autologous monocusp inserted, later had a pulmonary homograft inserted.

The NYHA classification of patients at follow-up according to the type of pulmonary valve used is shown in Table 2. There was no significant difference in NYHA classification (NYHA class 1 vs NYHA classes 2, 3, or 4) between patients with a monocusp and patients with no pulmonary valve (chi-square test: \(p = 0.78\)).

The survival according to type of pulmonary valve is shown in Fig. 3.

Two out of five patients having homografts installed had died. Two were ventilator dependent before APVS repair, and one died, while the other was lost to follow-up after leaving the hospital. Analysis of survival after the three different valve managements revealed a trend (‘homograft’ vs ‘no valve’, logrank test: \(p = 0.051\)). However, the numbers, particularly for the homograft group, remain small and statistical significance was not reached and the homograft patients may have been a higher risk group.

5.4. Perfusion strategy

The survival of patients operated using either circulatory arrest or continuous perfusion with aortic cross-clamping and cardioplegic arrest is shown in Fig. 4.

The perfusion strategy did not appear to affect survival (logrank test: \(p = 0.11\)), but this may be a reflection of the small sample size.

5.5. Reoperations

Five patients (14%) were reoperated within the first 30 days after the repair (left main bronchopexy \((n = 1)\), pericardial drainage \((n = 2)\), and permanent pacemaker insertion \((n = 2)\)).

Seven patients (19%) have had further surgery performed more than 30 days after the initial repair (homograft conduit insertion and pulmonary artery plasty \((n = 2)\), RVOT resection and pulmonary artery plasty \((n = 2)\), pulmonary artery plasty \((n = 1)\), RVOT resection \((n = 1)\), and residual VSD closure \((n = 1, died)\)).

The freedom from reoperation is shown in Fig. 5.

5.6. Risk factor analysis

A further limited analysis with logistic regression and Cox proportional hazards method was performed, using survival as a categorical outcome for the former and using survival time for the latter analysis.
Seven potential risk factors were included: age at operation, preoperative ventilator dependency, perfusion strategy, era of surgery (before 1985, 1985–1995, and after 1995), pulmonary valve management, pulmonary artery management, and reoperation. On univariate analysis, age and ventilator dependency were identified as strongly correlated with survival (age: \( p = 0.02 \) and ventilator dependency: \( p = 0.005 \)). The other factors were not significant, and in particular there was no apparent effect of surgical era on the results (\( p = 0.63 \)).

Multivariate analysis is not appropriate or possible for two reasons—firstly, the small sample size, and secondly because several risk factors are closely correlated with one another, and hence confound one another.

We considered that ventilator dependency due to airway disease was the major risk factor, and that age was likely to be a confounding factor. All ventilator-dependent patients were under 8 months old. To try and further dissect the interrelationship, we compared the ventilator-dependent patients (\( n = 10 \), median age at repair 97 days, range: 4–215 days) to an age-matched group (\( n = 6 \), median age at repair 139 days, range: 6–188 days). Five of the ventilator-dependent patients (50%) died after repair, before leaving hospital, while all in the age-matched group were discharged alive (chi-square test: \( p = 0.037 \)). Within the limitations of the small numbers in each group, it appears that ventilator dependency rather than age is the major predisposing factor to a fatal outcome.

6. Discussion

This study reports a 25-year consecutive series of patients undergoing repair of APVS with a 79% five-year survival. It revealed that preoperative ventilator dependency was the major independent risk factor for mortality after APVS repair.

With APVS being such a rare cardiac malformation, our present series, like previously published series, represent relatively small numbers of patients operated over several years (Karl et al. [15]: 19 patients in 8 years, Snir et al. [16]: 22 patients in 8 years, Godart et al. [17]: 37 patients in 18 years, Chowdhury et al. [18]: 46 patients in 8.5 years, and Hew et al. [19]: 54 patients in 38 years). All the series are therefore likely to reflect a development of different surgical approaches, perfusion strategies, and changes in postoperative intensive care. This poses a problem when analyzing data to assess the outcome of different approaches. The outcome may reflect the era rather than separate techniques. However, while being aware of this limitation, we still found it relevant to analyze our material.

The survival in our consecutive series was 82% after 1 year and 79% from 2 years and beyond. This is similar to previously published series from other institutions (Snir et al. [16] had 13.6% mortality within 3 months of repair, using homograft insertions in 22 patients; Hew et al. [19] had 80% 1-year and 78% 10-year survival, using various procedures, and Chowdhury et al. [18] had 91% 8.5-year survival, using various procedures).

Other groups [15,16,19,20] have previously suggested that pulmonary valve competence is important to achieve early survival. Our patients receiving homograft insertions during 1994–1995 reflected a change in policy driven by the results from Great Ormond Street Hospital, London [15,16]. The previously described improvement in early survival with homograft use was not confirmed by our data. We found no significant survival differences between the groups having no pulmonary valve, monocusp valves and homograft conduits, but our homograft series remain small.

There was no significant difference in NYHA class related to whether the patients had no pulmonary valve or a monocusp valve. However, our study lacks an adequate group with valved conduits to be able to assess eventual right ventricular failure occurring later in life, in comparison to patients with free pulmonary regurgitation.

Airway morbidity differentiates APVS from other variations of the Fallot anatomy spectrum. As previously mentioned, 10 of our consecutive patients (28%) were ventilator dependent up to surgery, and half of these died before leaving hospital, while mortality was 2 out of 26 patients not ventilated before the repair (\( p = 0.002 \)). The over all survival was closely related to airway pathology being the cause of death in five of seven patients, while the last two died immediately after a surgical procedure. Beyond this there was no further mortality. As in previous series, mortality occurred in the younger patients, since the primary risk factor, preoperative ventilator dependency, was only present in this age group.

We found that half the reoperations in our consecutive patients were related to unsatisfactory airway relief. The other half was related to technical problems with the cardiac repair.

Today The Royal Children’s Hospital’s policy for handling these patients includes the following: in patients without airway compromise, conventional tetralogy of Fallot repair is performed. This includes transatrial VSD closure, infundibular resection as necessary, and pulmonary annular patch enlargement as necessary. A monocusp of pericardium or goretex may be constructed according to the individual surgeon’s preference.

If there is no airway compromise, reduction of relatively enlarged pulmonary arteries is not regularly performed. Only in ventilator-dependent newborn infants with severe airway compromise, reduction of both pulmonary arteries will be
performed. If the infant continued to remain ventilator dependent, then pulmonary valve homograft replacement will be performed. We have not used the Lecompte manoeuvre as described by Hraska [21].

We believe that investigations of airway anatomy should be performed in patients with preoperative ventilator dependency, since the surgical outcome of this group may warrant further aggressive surgical reconstruction of the airways.

7. Conclusions

The outcome of APVS repair was closely related to ventilator dependency before surgery. Efforts to improve the surgical outcome should be focused on identifying airway pathology and if possible correcting this. We could not identify associations between survival and age at operation, perfusion strategy, era of surgery, pulmonary valve management, pulmonary artery management, or reoperation.

References