Antenatal diagnosis of total anomalous pulmonary venous connection in functional single ventricle hearts: Outcomes over 13-year period

Precyilia Fernandes¹, Lito Mantagou¹, Ram Ramaraj¹,
Umbur Agarwal² and Joyce Su Ling Lim¹

Ultrasound
2018, Vol. 26(1) 42–48
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DOI: 10.1177/1742271X17751256
journals.sagepub.com/home/ult

Abstract

Introduction: A functionally single cardiac ventricle seen on foetal ultrasound scan carries a guarded prognosis. The antenatal diagnosis of anomalous pulmonary venous connection (APVC) remains challenging, if there is no associated structural cardiac abnormality. Antenatally, a combination of complex cardiac anomaly with suspected isomerism should raise the possibility of associated total anomalous pulmonary venous connection (TAPVC). There needs to be a high index of suspicion for TAPVC, in functional single ventricle and suspected isomerism, as this carries a very grim outcome postnatally. We illustrate foetal echocardiographic findings of suspected TAPVC and review outcomes of antenatal versus postnatal diagnosis of TAPVC with functional single ventricle.

Methods: We retrospectively reviewed our database over 13 years, focusing on foetal cardiac diagnosis, pregnancy outcomes, management and outcomes of livebirths with diagnosis of TAPVC with functional single ventricle.

Results: Thirteen patients were included in the review. For the nine antenatal patients, three pregnancies were terminated and six babies were born alive (four babies had compassionate care, two babies had cardiac surgery). One baby is alive at 8.5 years, after Fontan surgery. For the four postnatal patients, three babies had compassionate care (one alive at age 8.1 years) and one baby had cardiac surgery (died age nine weeks). Ten of the 13 patients have right atrial isomerism. Of these 10 patients, only two are alive. For the three non-isomeric babies, only one baby is still alive. There is heterogeneity of the type of TAPVC diagnosed with no particular group that offered better survival.

Conclusion: Antenatal diagnosis of TAPVC, even in the context of functional single ventricle remains challenging. If isomerism is suspected, targeted evaluation of pulmonary venous connection should be done. This combination of cardiac lesion carries a very grim outcome. The ability to make this diagnosis antenatally will add to the information and counselling given to these parents.

Keywords

Foetal anomaly, antenatal, total anomalous pulmonary venous connection, functional single ventricle, isomerism, outcome

Date received: 9 September 2017; accepted: 3 December 2017

Introduction

A functionally single cardiac ventricle seen on foetal ultrasound scan carries a guarded prognosis. Postnatal outcome for functionally single ventricle

¹Alder Hey Children's NHS Foundation Trust, Liverpool, UK

²Liverpool Women's NHS Foundation Trust, Liverpool, UK

Corresponding author:

Joyce Su Ling Lim, Alder Hey Children's NHS Foundation Trust, Liverpool L12 2AP, UK.
Email: joyce.lim@alderhey.nhs.uk

hearts following staged palliative (non-corrective) cardiac surgery has reasonable prognosis with some patients now surviving into their 30s and 40s. The diagnosis of anomalous pulmonary venous connection (APVC) remains a challenge in foetal life, especially in the absence of associated congenital heart disease.^{1,2} A high index of suspicion in the light of an underlying complex cardiac anatomy, as well as suspicion of isomerism should increase the chances of the diagnosis of APVC. The combination of a functionally single ventricle heart associated with total anomalous pulmonary venous connection (TAPVC) carries a very grim prognosis,³⁻⁸ as compared to a functionally single ventricle with no anomalous pulmonary veins.

The first part of this paper briefly reviews the usual foetal echocardiography findings of suspected TAPVC.

The second part of this paper aims to review the cases from a single tertiary cardiac unit over a 13-year period, to assess the outcomes of this cohort of patients with functionally single ventricle with TAPVC.

Towards the end of this article, we have also included Appendix 1 comprising a brief overview of definition of functionally single ventricle and the usual management plan, the description of APVC and isomerism.

Foetal echocardiography findings of suspected TAPVC and type of TAPVC

The common echocardiographic features for antenatal suspicion or diagnosis of TAPVC include the increased distance of descending aorta from left atrium and the presence of pulmonary venous confluence in the 4 chamber view, the vertical vein, pulmonary vein colour and pulsed Doppler and signs of suspected obstruction.^{9,10} Colour flow Doppler is helpful to determine whether the pulmonary veins are connected to the left atrium or to the pulmonary venous confluence. Colour Doppler interrogation also helps to differentiate other vascular and non-vascular structures (e.g. dilated oesophagus may mimic a vertical vein or pulmonary venous confluence). Figure 1 shows the image of a normal foetal heart.

Depending on the type of TAPVC, there will be variation to the site of the connection of the vertical vein to the systemic vein. Obstruction within the vertical vein or anywhere along the course of the APVC can be suspected if there is increased in Doppler flow pattern.

In supracardiac TAPVC, the ascending vertical vein is seen as an 'extra' vessel usually parallel to the superior vena cava (SVC) or thoracic descending aorta, in the sagittal view. This vessel is seen usually either connected to the innominate vein or the SVC. The Doppler colour flow is in the cranial direction for ascending

Figure 1. Normal relation of descending aorta (Desc Ao) with left atrium (LA) with close proximity of both structures, in the 4-chamber view.

Figure 2. Patient A: suspected TAPVC in 4-chamber view with increased distance of left atrium (LA) to descending aorta (Desc Ao).

vertical vein. Figures 2 to 4 show images of foetal echocardiography with suspected supracardiac TAPVC. Figure 5 shows confirmed supracardiac TAPVC postnatally, using cardiac computerised tomography angiogram or cardiac CT angiogram.

In infracardiac TAPVC, the descending vertical vein is seen as an 'extra' vessel coursing parallel to the descending aorta and inferior vena cava (if one is present), and caudally below the diaphragm. This usually connects to the hepatic vein or ductus venosus. The Doppler colour flow is in the caudal direction for the descending vertical vein.

In mixed TAPVC, where there is a mixture of supracardiac and infracardiac connection, there may be ascending as well as descending vertical veins.

Figure 3. Patient A: pulmonary venous confluence (PulmVC) behind left atrium (LA) with colour flow Doppler confirming no connection of confluence to LA in 4-chamber view.

Figure 4. Patient A: ascending vein (Asc Vv) behind and parallel to descending aorta (Desc Ao) in sagittal view with colour flow Doppler in cranial direction.

Figure 5. Patient A: postnatal cardiac CT confirmation of supracardiac TAPVC with pulmonary venous confluence (PulmVC) and ascending vein (Asc Vv) to right superior vena cava (view from the back of patient).

Not infrequently, there may be no pulmonary venous confluence, but rather individual pulmonary veins which drain independently to the various systemic venous connections. In such cases, the outcome is uniformly fatal, as postnatally the ability to reconnect multiple anomalous pulmonary veins together is very challenging, with extremely high risk of recurrence of pulmonary vein stenosis.

Review of cases

Method and material

Using our tertiary foetal and paediatric cardiac database, we identified 30 cases which were diagnosed either antenatally or postnatally with TAPVC associated with complex congenital cardiac lesions. These cases were identified during a 13-year period from October 2003 to October 2016. We excluded 11 cases which were not associated with functional single ventricle. We also

excluded a further six antenatal cases which were diagnosed at another foetal unit which also referred patients to our cardiac surgical centre, as we had incomplete antenatal data. We reviewed case notes for the remainder of 13 patients who had diagnosis of TAPVC with functional single ventricle. We divided the patients into antenatal and postnatal group. We also looked at the outcomes of these patients in relation to the isomeric status and type of TAPVC.

Results

Thirteen patients had a diagnosis of TAPVC associated with functional single ventricle over a 13-year period at our tertiary cardiac centre.

Antenatal VS postnatal group

Of the 13 patients with TAPVC and functional single ventricle, nine were diagnosed antenatally and four were diagnosed postnatally. Figure 6 shows antenatal and postnatal diagnosis and outcomes.

In the antenatal group, the nine babies were diagnosed between 20 weeks and 30 weeks 4 days (median 20 weeks 5 days). Three pregnancies were terminated before 21 weeks of gestation. Of the six babies who were born alive, compassionate care was decided for four babies. Three of these four babies died at four, six and eight days of age, respectively. One baby survived till 260 days. Two babies underwent palliative cardiac surgery (TAPVC repair and staged univentricular palliative cardiac surgery). One died at seven days of life after surgery. The other baby is still alive at the age of 8.5 years, having undergone Fontan completion (third stage of the staged univentricular palliative surgery), but has

continuing pulmonary venous issues and remains very cyanosed.

The detailed antenatal cardiac diagnosis and postnatal cardiac diagnosis for the antenatal group are shown in Figure 7. There was one major discrepancy between the antenatal and postnatal cardiac diagnosis, which occurred in a lady with high body mass index.

In the postnatal group, all four babies were diagnosed within the first three days of life. Of these four babies, three had compassionate care and one had surgery. In the compassionate care group, two babies have since died (at two and five days of age), whilst one is still alive at 8.1 years. The only baby who had surgery, died at nine weeks of age from multi-organ failure and pulmonary vein stenosis.

The detailed cardiac diagnosis for the postnatal group is shown in Figure 8.

For the whole cohort of antenatally diagnosed group (nine babies), only one in nine (11%) survived. Survival amongst the six live-born babies of the antenatal group was one in six (16%). Survival in the postnatal group was one in four (25%). Overall survival for the whole group for live-born was 2 in 10 (20%). Survival in those who had surgery was one in three (33%).

Isomeric status

Amongst the antenatal group of nine babies, six babies had suspected isomerism antenatally, including the three pregnancies which were terminated and three other babies who had confirmation of right atrial isomerism postnatally. The remainder of the three babies did not have suspicion of isomerism antenatally. Of these three babies, two were confirmed to have right atrial isomerism postnatally, whilst one other baby was confirmed to be non-isomeric. Amongst the antenatal

Figure 6. Antenatal (AN) and postnatal (PN) diagnosis and outcomes.

TOP: termination of pregnancy; TAPVC: total anomalous pulmonary venous connection.

Patient	Antenatal cardiac diagnosis	Postnatal cardiac diagnosis	Outcome
1	Unbalanced CAVSD, pulmonary atresia, suspected APVC, ? isomeric	N/A	TOP
2	Dextrocardia, unbalanced CAVSD, DORV, TGA, hypoplastic pulmonary arteries, suspected APVC, ? isomeric	N/A	TOP
3	Unbalanced CAVSD, interrupted IVC, mixed TAPVC (to innominate and below diaphragm), DORV, Aortic atresia, ? isomeric	N/A	TOP
4	Unbalanced CAVSD, DORV, hypoplastic pulmonary arteries, TAPVC, ? isomeric	Unbalanced CAVSD, DORV, hypoplastic pulmonary arteries, mixed TAPVC, right atrial isomerism	Compassionate care, died at 260 days of age
5	Large VSD, over-riding aorta, small pulmonary artery. Suspected TAPVC (high BMI). Also multicystic kidneys. Isomerism not suspected antenatally	Unbalanced CAVSD, DORV, Pulmonary stenosis, infracardiac TAPVC to splenic vein, right atrial isomerism. Additional multicystic horseshoe kidneys, imperforate anus, abnormal bronchus, partial choanal atresia	Compassionate care, died at 8 days of age
6	DILV, hypoplastic right ventricle, TGA, suspected APVC, ? isomeric	DILV, DORV, hypoplastic right ventricle, subpulmonary stenosis, large VSD, obstructed infra-diaphragmatic TAPVC, right atrial isomerism	Compassionate care, died at 6 days of age
7	small LV, VSD, suspected APVC. Isomerism not suspected antenatally	small LV, VSD, supracardiac TAPVC. Isomeric status unknown	Compassionate care, died at 4 days of age
8	CAVSD with single large atrium, common ventricle, TGA, subpulmonary stenosis, APVC likely infracardiac, ? isomeric	CAVSD, common atrium, no ventricular septum, TGA, subpulmonary stenosis, infracardiac TAPVC, right atrial isomerism	Surgery, Died at 7 days of age
9	CAVSD, pulmonary atresia. Isomerism not suspected antenatally	Unbalanced CAVSD, pulmonary atresia, infracardiac TAPVC, right atrial isomerism	Surgery, has had completion of Fontan, remains cyanosed, alive at 8.5 years of age

Figure 7. Cardiac diagnosis of antenatally diagnosed patients and outcomes.

CAVSD: complete atrioventricular septal defect; DORV: double outlet ventricle; TGA: transposition of great arteries; APVC: anomalous pulmonary venous connection; IVC: inferior vena cava; DILV: double inlet left ventricle; VSD: ventricular septal defect; TOP: termination of pregnancy; N/A: not applicable.

group of babies who are born alive (six babies), five babies had right atrial isomerism and one was non-isomeric.

In the antenatal group of five babies with right atrial isomerism, three had compassionate care and two underwent palliative surgery. The three babies who had compassionate care died at 6 days, 8 days and 260 days of age, respectively. Of the two babies who had surgery, one died at seven days of age, whilst another is still alive at 8.5 years of age after having undergone Fontan completion, but had continuing pulmonary venous issues and remains very cyanosed.

The only non-isomeric baby had compassionate care and died at age four days.

For the postnatal group (four babies), only two babies had confirmed right atrial isomerism. Both of these babies had compassionate care with one dying at five days of age, and another still alive at 8.1 years of age. One baby, who was not isomeric with hypoplastic left heart syndrome, had compassionate care and passed away at two days of age. Another patient's isomeric status was not evaluated before death. This baby had cardiac surgery but died at nine weeks of age with pulmonary vein stenosis and multi-organ failure.

Type of TAPVC

In the antenatal group, TAPVC was suspected in eight of the nine babies antenatally, whilst one baby with

complete atrioventricular septal defect, and pulmonary atresia was not suspected to have TAPVC until after birth.

In the three women who underwent termination of pregnancy, one foetus was suspected to have mixed TAPVC, whilst the other two had TAPVC of unknown type. Unfortunately, post-mortem was not performed for these terminated foetuses.

For the antenatal group who continued to birth (six babies), only two babies had the type of TAPVC correctly diagnosed antenatally, three babies did not have the type of TAPVC confirmed till postnatally, whilst one baby was not suspected to have TAPVC until postnatally. There was a mix of type of TAPVC in this group – one baby with supracardiac TAPVC, four babies with infracardiac TAPVC and one baby with mixed TAPVC. Irrespective of the type of TAPVC, all babies have since died except for one baby with infracardiac TAPVC with functionally single ventricle who is currently alive at the age of 8.5 years, who has had Fontan completion but has continuing pulmonary venous issues and remains cyanosed.

In the postnatal group (four babies), one baby had supracardiac TAPVC, two babies had infracardiac TAPVC and one baby had mixed TAPVC. There is only one baby who is currently alive at age 8.1 years with infracardiac TAPVC and functionally single ventricle, whose parents had elected for compassionate care.

Patient	Antenatal cardiac diagnosis	Postnatal cardiac diagnosis	Outcome
10	N/A	Unbalanced CAVSD, aorta from right ventricle, pulmonary atresia, supracardiac TAPVC to SVC, right atrial isomerism	Compassionate care, died at 5 days of age
11	N/A	Unbalanced CAVSD, DORV, infracardiac TAPVC, TGA, sub pulmonary stenosis, right atrial isomerism	Compassionate care, still alive at 8.1 years of age
12	N/A	Hypoplastic left heart syndrome, infracardiac TAPVC. Non isomeric	Compassionate care, died at 2 days of age
13	N/A	Mitral atresia, small left ventricle, DORV, multiple VSD, mixed TAPVC with multiple confluence. Isomeric status unknown	Surgery, died at 9 weeks of age with obstructed pulmonary veins and multiorgan failure

Figure 8. Cardiac diagnosis of postnatally diagnosed patients and outcomes.

CAVSD: complete atrioventricular septal defect; DORV: double outlet ventricle; TAPVC: total anomalous pulmonary venous connection; TGA: transposition of great arteries.

Conclusion and discussion

On reviewing our data, we have found that the outcome for TAPVC with functional single ventricle is poor. The percentage survival for the antenatally diagnosed group was 16%. Overall survival for live-born for the whole group (antenatal and postnatal) is 20%. Even those who had cardiac surgery have had limited survival. There is no difference in postnatal outcomes in either antenatal or postnatal diagnosis group. Because of small numbers, the actual percentages become less relevant. The outcome of our group of babies is similar to other published data.^{3–8}

Most of our babies (8 of 13 patients) with functional single ventricle and TAPVC had associated right atrial isomerism.

There was heterogeneity in the types of TAPVC seen. Due to our small patient numbers, it was not possible to ascertain differential outcomes based on type of TAPVC. Although a high proportion (eight of nine babies) of antenatally diagnosed group had suspected TAPVC, only two babies had the type of TAPVC correctly diagnosed antenatally. This further emphasizes the point that if there is a high index of suspicion and targeted review of the pulmonary venous confluence, especially in the context of functional single ventricle and isomerism, TAPVC can be diagnosed. However, it remains challenging to be able to diagnose the type of TAPVC antenatally.

We acknowledge that our patient numbers were small, as this combination of cardiac anomaly is not common, but is more frequently seen in isomerism.

As the postnatal survival is poor for this cohort of babies, it is useful to be able to diagnose this combination of cardiac anomaly antenatally.⁷ Provided there is high index of suspicion of this combination of cardiac issues, a more detailed antenatal review of pulmonary veins to actively look for TAPVC will be useful to help add to the information provided and counselling given to these parents.

Acknowledgments

Pediatric cardiology and cardiac surgical colleagues who were involved in the care of these patients.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethical approval

Permission for audit and retrospective review of this cohort has been sought and approved by the Audit Department of Alder Hey Hospital.

Guarantor

Dr Joyce Lim.

Contributors

PF and AL collected and reviewed the data. UA and RR were involved in the patient care, reviewed the data and proof read the manuscript. JL was involved in the patient care, reviewed the data and prepared the manuscript.

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Appendix 1

Brief description of functionally single ventricle and usual management plan, anomalous pulmonary venous connection and isomerism

Functionally single ventricle and usual management plan

A functionally single ventricle is defined as any heart where there is only one good size ventricle that is used to support both the systemic and pulmonary circulation. There is usually a larger good size ventricle and another smaller size ventricle. The larger ventricle can either be the left ventricle or the right ventricle.

Irrespective of the morphology of the larger ventricle, the cardiac surgery that is performed is only ever able to compensate for the deficient smaller ventricle, but never totally able to correct the smaller ventricle. As such, cardiac surgery is offered as a palliative (non-corrective) procedure that involves three stages in the first 4–6 years of

the baby's life. The aim is for the baby to finally have the completion of Fontan (third stage) procedure between 4–6 years of age. Fontan procedure is where the pulmonary circulation is totally separated from the systemic circulation.

Anomalous Pulmonary Venous Connection and types

Anomalous pulmonary venous connection can be divided into partial (PAPVC) or total (TAPVC). PAPVC occurs when some of the pulmonary veins do not connect to the left atrium. TAPVC occurs when all pulmonary veins do not drain to the left atrium. There is usually a pulmonary venous confluence which drains superiorly, inferiorly or to the heart. These can be divided into supracardiac (where the pulmonary veins drain to the innominate vein or SVC), cardiac (where the pulmonary veins drain to the coronary sinus), infracardiac (where the pulmonary veins drain inferiorly to the ductus venosus, hepatic veins or inferior vena cava) or mixed TAPVC (where there is combination of supracardiac, infracardiac or cardiac). Not infrequently there can be more than one pulmonary venous confluence, which are usually smaller and will then increase the risk of pulmonary venous stenosis after surgery.

Isomerism

Atrial isomerism or heterotaxy syndromes is diagnosed when there is a combination of bilateral right or left sided atrial appendages, bilateral right or left sided bronchial pattern, absent or multiple spleen which may have variable function, intestinal malrotation and hepatic issues. Atrial isomerism is frequently also associated complex congenital cardiac anomalies, as well as heart rhythm issues. Right atrial isomerism is usually associated with more complex cardiac lesions and carries a very grim outcome. Left atrial isomerism is usually associated with less complex cardiac lesions and more likely to be associated with heart block, and carries a better long term outcome.