

# Journal für **Kardiologie**

Austrian Journal of Cardiology

Österreichische Zeitschrift für Herz-Kreislauserkrankungen

**The Fetal Heart Program: A  
Multidisciplinary Model and  
Approach to Contemporary  
Comprehensive Care for  
Cardiovascular Conditions Before  
Birth // The Fetal Heart Program  
des Children's Hospital in  
Philadelphia, USA**

Falkensammer CB, Rychik J  
*Journal für Kardiologie - Austrian  
Journal of Cardiology* 2016; 23  
(5-6), 118-126

Homepage:

**[www.kup.at/kardiologie](http://www.kup.at/kardiologie)**

Online-Datenbank  
mit Autoren-  
und Stichwortsuche



Offizielles  
Partnerjournal der ÖKG



Member of the ESC-Editor's Club



Offizielles Organ des  
Österreichischen Herzfonds



**ACVC**  
Association for  
Acute CardioVascular Care

In Kooperation  
mit der ACVC

Indexed in ESCI  
part of Web of Science

Indexed in EMBASE

Krause & Pachernegg GmbH • Verlag für Medizin und Wirtschaft • A-3003 Gablitz

P.b.b. 02Z031105M,

Verlagsort: 3003 Gablitz, Linzerstraße 177A/21

Preis: EUR 10,-

# Veranstaltungskalender

## Hybrid-Veranstaltungen der Herausgeber des **Journals für Kardiologie**

Finden Sie alle laufend aktualisierten Termine  
auf einem Blick unter

[www.kup.at/images/ads/kongress.pdf](http://www.kup.at/images/ads/kongress.pdf)

# The Fetal Heart Program: A Multidisciplinary Model and Approach to Contemporary Comprehensive Care for Cardiovascular Conditions Before Birth

C. B. Falkensammer, J. Rychik

**Kurzfassung:** In der vorliegenden Übersichtsarbeit wird das multidisziplinäre Modell zur Erkennung und Behandlung von fetalen kardiovaskulären Erkrankungen des „Fetal Heart Program of the The Cardiac Center at The Children’s Hospital of Philadelphia, CHOP, Philadelphia, USA“ vorgestellt und berichtet einige anschauliche Fallbeispiele.

**Schlüsselwörter:** fetale kardiovaskuläre Erkrankungen, Früherkennung durch fetale Echokardiographie

**Abstract:** This review describes the multidisciplinary model for early diagnosis and therapy of

fetal cardiovascular diseases at the “Fetal Heart Program of The Cardiac Center at The Children’s Hospital of Philadelphia, CHOP, Philadelphia, USA” and reports some typical cases. **J Kardiol 2016; 23 (5–6): 118–26.**

**Key words:** fetal cardiovascular disease, early diagnosis by use of fetal echocardiography

## ■ Introduction

Heart conditions in the young are often related to primary cardiac malformations or secondary cardiovascular manifestations due to other developmental abnormalities. In the past, congenital heart disease would typically come to identification with the presentation of symptoms in infancy or childhood. Circulatory collapse in the newborn, or a murmur, respiratory symptoms or poor growth in a child would signal the possibility of a cardiac condition. In the current era, most forms of cardiac malformation are identified through ultrasound detection while still in the womb. With fetal circulation providing bypass and while receiving maternal support, human beings with even the most severe forms of cardiac disease may thrive and do well, without manifestation of significant symptoms, up until separation from mother at the time of birth. The ability to detect cardiac malformations with exquisite detail through ultrasound techniques while *in utero* has truly revolutionized our approach to managing congenital heart disease. In fact, “birth defects” of the heart is an obsolete term, as these anomalies are no longer detected at birth, but rather at an extended period prior to birth. As such, care and management of these conditions must also start way before birth, at the time of first detection *in utero*.

Advances in fetal echocardiography achieved over the past 30 years provide for an incredibly clear window into the anatomy and physiological consequences of fetal cardiovascular disease [1]. We can now assess with great detail very tiny structures as early as 13–14 weeks gestation. We can characterize blood flow patterns and observe for changes in states of health and disease as the fetus progresses forward through pregnancy. These tools allow us the opportunity to offer optimal care and management services beyond just anatomical diagnosis. One can comprehend complex physiologies and stratify complex conditions, thereby offering counseling, guidance and ed-

ucation to expectant parents. One can utilize this rich collection of pre-birth data to best plan for individual postnatal care. One can make recommendations for site of delivery and immediately offer treatment at birth, thereby creating a smooth and seamless transition from the safety of the womb to the outside environment. Such steps can decrease the degree of instability at birth present for complex conditions thereby making these infants better candidates for the coming interventional treatment, be it surgery or catheter-based. Optimizing the state of the first few moments of life can reduce the risks of early end-organ insult. In particular it can contribute to a reduction in brain injury, thereby optimizing the potential for best neurocognitive outcomes, with the brain now recognized to be so vulnerable and at risk in our children with congenital heart disease [2, 3].

Currently, we have a unique opportunity to develop a specialized program of care for the fetus with cardiovascular disease. Not only can we detect and diagnose, but we can create innovative ways to test fetal physiology to provide new information, potentially offer treatment before birth, and provide counseling and support for the family as they deal with the challenges of carrying a fetus with heart disease. In this review, we will discuss some of these new aspects of care and provide some case examples of how a multidisciplinary Fetal Heart Program can offer these unique services.

## ■ Understanding Complex Physiology: The Valuable Tools of Fetal Echocardiography

Congenital heart disease manifests in a very wide manner. There are dozens of different conditions ranging from simple septal defects, to obstruction of the outflow tracts, to transposition of great vessels, and to univentricular conditions just to name a few. Often these conditions occur in combination. Each has its own unique physiology and in the fetus, each may have unique manifestations and findings based on the gestational age of assessment. For example, aortic stenosis presenting at 18 weeks gestation may continue to remain as simple aortic valve disease at birth, or based on specific findings, it may progress in severity to critical narrowing requiring early intervention at birth. Some fetuses with aortic stenosis and

Received and accepted: April 15, 2016.

From the Fetal Heart Program, The Cardiac Center at The Children’s Hospital of Philadelphia, Philadelphia, USA

**Correspondence:** Christine B. Falkensammer, MD, The Cardiac Center at The Children’s Hospital of Philadelphia, 34th Street and Civic Center Boulevard, Philadelphia, PA 19104, USA; e-mail: falkensammerc@email.chop.edu

poor left ventricular function manifest arrest of left ventricular development and progress towards inadequacy of the left side and hypoplastic left heart syndrome (HLHS) [4]. Genetic signaling as of yet still undetermined, may play a role in programming which path such a fetus may take. Flow characteristics may contribute as well, which is the primary argument for altering blood flow patterns *in utero* through interventions with the hope of stimulating growth of structures.

Doppler echocardiography in the fetus provides for a tremendous amount of information concerning fetal circulatory physiology. Assessment can be made across intracardiac structures such as atrioventricular or semilunar valves. Flow across the ductus arteriosus can help predict whether a fetus with pulmonary obstruction will require support with prostaglandin infusion after birth. For example, in tetralogy of Fallot measurement of a pulmonary annulus that is less than 50% that of the aorta and reversal of flow in the ductus arteriosus are features which predict the need for early neonatal surgery and can help guide delivery plans and counseling [5].

Venous flow patterns assessed by Doppler echocardiography in particular can be quite informative. A hypertrophic, poorly compliant right ventricle can be carefully characterized by looking at the inflow pattern across the tricuspid valve (normal double-peak, or abnormal single-peak) as well as by looking at flow across the ductus venosus and umbilical vein, structures proximal to and upstream of the heart which carry placental venous return to the fetal circulation. Ductus venosus flow should normally be phasic and all antegrade, while umbilical venous flow is always normally continuous, non-phasic and antegrade. Significant reversal of flow with atrial contraction in the ductus venosus or pulsations in the umbilical vein indicate abnormal downstream right ventricular compliance. Such findings are characteristics of cardiomyopathy such as seen in the heart of a recipient partner in the twin-twin transfusion syndrome [6].

Assessment of pulmonary arterial and venous flow has been informative in the fetus. Pulmonary vascular resistance is normally high in fetal life, which drops dramatically with placental separation and the first breaths taken. Therefore, very specific patterns of flow have been identified [7]. For the pulmonary veins, flow is phasic with timing of the cardiac cycle, but normally always antegrade. In the hypoplastic left heart syndrome, there is an inadequate left ventricle and often mitral stenosis or atresia. Thus, pulmonary venous return must make its way into the left atrium and across the foramen ovale left to right to the right atrium. Restriction at the level of the foramen ovale, which is severe in approximately 5% of fetuses with HLHS, will impede pulmonary venous egress, raising left atrial pressure. This can result in severe changes in the pulmonary vasculature, leading to injury and a pulmonary vasculopathy that can manifest as respiratory insufficiency at birth. Such neonates then have not only the congenital heart disease of HLHS, but also have damaged lungs, leading to very poor outcome [8]. Evaluation of this phenomenon can be undertaken by Doppler interrogation of the pulmonary veins. Marked reversal of flow with atrial contraction indicates the presence of impediment to left atrial egress and left atrial hypertension [9].

As a means of provoking an informative response, we investigated the technique of offering maternal hyperoxygenation in order to test the reactivity of the pulmonary vasculature in our fetuses with HLHS [10]. Maternal hyperoxygenation leads to an increase in fetal oxygenation, and in healthy lungs at the proper gestational age, will lead to pulmonary vasodilation, which can be characterized using fetal echocardiography. Approximately 20 minutes of maternal hyperoxygenation when a fetus is beyond 34 weeks gestation will lead to pulmonary arterial changes with a decrease in resistance from baseline as measured through the Doppler-derived pulsatility index. Absence of this response in fetuses with suspected abnormal pulmonary vasculature such as those with HLHS and highly restrictive atrial septum, in combination with information gathered concerning pulmonary vein flow may lead to consideration of fetal intervention to open the atrial septum through catheter techniques or prompt a plan for immediate intervention at birth to open the atrial septum.

Investigational interests of late have focused on using Doppler echocardiography to measure vascular resistance within the placental circulation and compare to the cerebral circulation in normal and congenital heart disease. Vascular resistance can be measured utilizing Doppler waveform signals and is calculated as the peak systolic velocity minus the end-diastolic velocity divided by the mean velocity for one cardiac cycle. In the normal healthy state, placental resistance as measured by Doppler interrogation of the umbilical artery, should always be low and cerebral resistance as measured by Doppler interrogation of the fetal middle cerebral artery should always be high. These are the natural autoregulatory control mechanisms for directing flow distribution selectively towards the placenta. However in conditions of fetal circulatory distress (eg, growth restriction, placental insufficiency, fetal cardiomyopathy or myocarditis etc.) autoregulatory mechanisms lead to a natural attempt to preserve cerebral blood flow, resulting in a drop in middle cerebral artery resistance, often to a level that is even lower than the umbilical artery. When that occurs, in essence the brain is stealing flow from the placenta and is referred to as “cephalization,” indicating a maldistribution of blood flow. Such alterations in the expected ratio of middle cerebral to umbilical artery resistance ratios have now been well described in various forms of congenital heart disease [11]. For example, fetuses with HLHS and small aorta have decreased middle cerebral artery resistance compared to normal. This may be due to the cerebral microcirculatory vasodilation in response to an anatomical impediment to aortic flow. Conversely, fetuses with pulmonary stenosis or atresia have increased aortic flow and often exhibit elevated middle cerebral artery resistance, perhaps reflecting compensatory vasoconstriction in the face of abundant flow [12]. Such changes in distribution of flow may influence brain development and may be associated with neurocognitive deficits seen in some survivors of congenital heart surgery later in life [13].

## ■ Heart Care Before Birth: Treating the Fetus with Cardiovascular Disease

Not only can we characterize complex flow patterns within the fetal circulation, but in addition we can now commence treatment strategies *in utero*. The most common and well-accept-

one form of fetal treatment is anti-arrhythmic medication given to mothers for fetal arrhythmia [1]. Strategies and protocols to treat supraventricular tachycardia and atrial flutter are available by administering agents that readily cross the placenta into the fetal circulation such as digoxin, sotalol or flecainide. Fetal bradycardia due to acquired heart block secondary to maternal autoimmune disease can be managed with steroid treatment to prevent decline in heart rate and heart function, and with beta agonists to stimulate heart rate. Pacing of the fetal heart is theoretically conceivable [14], however logistical limitations such as lead and generator size and placement have been challenges which limit this potential strategy to date.

Fetal intervention through catheter-based techniques is increasing in frequency and is still evolving in application. Access to the fetal heart through percutaneous needle puncture of the maternal abdomen, uterus, and fetal chest is possible using ultrasound guidance and is very much dependent upon operator skill [15]. Fetal aortic valvuloplasty for aortic stenosis is possible with data suggesting that in some fetuses, left ventricular recruitment and growth can take place preventing the development of HLHS [16]. Opening of the atrial septum *in utero* in HLHS with intact or restrictive atrial septum is possible; however technique, efficacy and proper timing of such an intervention remain of question [17]. Fetal surgery for congenital heart disease is still not available as utilization of cardiopulmonary bypass techniques, mandatory for most forms of intra-cardiac surgery, leads to placental injury and dysfunction. However, the principles of fetal surgery for a variety of non-cardiac conditions have been well established and are currently applied to anomalies such as spina bifida and chest masses with good success [18]. Safe access to the fetal chest allows for fetal surgery for cardiovascular conditions that may not require cardiopulmonary bypass such as pericardial teratoma.

Much thought is currently being given to the use of pharmacological strategies to improve the fetal circulatory state and perhaps influence organ development. While we have demonstrated the utility of maternal hyperoxygenation as a short-term diagnostic tool in HLHS, we have also demonstrated that this maneuver can induce pulmonary vasodilation, increase pulmonary venous return, and improve filling of the left atrium and left ventricle in the fetus at the tail end of the 3<sup>rd</sup> trimester of pregnancy. Fetuses with the unusual finding of an aneurysm of the atrial septum bowing right to left can have severe limitation to filling of the left ventricle with evidence for retrograde flow in the transverse aorta. By offering a short period of maternal hyperoxygenation, we have demonstrated improved filling of the left ventricle with conversion of retrograde into antegrade flow across the arch [19]. An important question to answer is whether or not sustained maternal hyperoxygenation with increased left sided return can lead to growth of borderline small left sided structures, if administered in a therapeutic manner for days or weeks at a time [20]. Clinical trials of such a strategy are being currently considered.

Furthermore, thought has been given to the notion of possibly promoting neurodevelopment in our fetuses with congenital heart disease in whom neurocognitive impairment is common. Fetal MRI studies of the brain in congenital heart disease dem-

onstrate delayed maturation in brain development [21], altered cerebral metabolism [22] and reduced levels of cerebral oxygenation [23]. Fetal life however is a known period of plasticity, with the potential for modification of neuronal state. Perhaps increasing oxygen delivery to the brain through maternal hyperoxygenation may mitigate some of the deficits seen. Agents such as progesterone or caffeine are known promoters of neural growth and development and may find a place in our armamentarium of fetal treatment in the near future.

## ■ The Multidisciplinary Model: Caring for Fetus and Mother Before Birth

Optimal care for the fetus with a cardiovascular condition involves a team of specialists with a variety of skills. Fetal imaging through echocardiography is essential, but not sufficient. In addition to fetal diagnosis, care for the mother/family both physical and emotional are emerging as important aspects of comprehensive care. The conventional departmental barriers of “obstetrics” versus “pediatrics” are not ideal when dealing with a fetal cardiovascular condition. The best care is offered when there are teams of specialists interested in a mutual positive outcome for both fetus and mother. Such teams should include: fetal (pediatric) cardiologists, maternal fetal medicine specialists, obstetricians, nurse coordinators, genetic counselors, psychologist/social workers as well as specialists on the receiving end after birth specifically neonatologists, cardiac intensivists and cardiac surgeons. Multidisciplinary review of cases allows for the voicing of opinions and perspectives that can be shared amongst healthcare providers, creating an individualized plan of care for each unique patient set.

In order to optimize communication amongst a variety of clinical services, stratification of types of congenital heart disease and determination of resource utilization for different levels of disease is important. We designed and developed a fetal congenital heart disease classification system that is extremely valuable in characterizing the delivery needs of the fetus with heart disease (Tab. 1). This classification scheme relates to delivery needs and resource utilization and does not necessarily indicate the overall severity of the condition or the prognosis. Simple forms of heart disease not requiring any specialized delivery care are labeled class I. Conditions which require initiation of prostaglandin infusion such as pulmonary atresia or critical coarctation of the aorta but who are predicted to be stable at birth are class II. Fetuses with transposition of the great arteries, or total anomalous pulmonary venous return may be unstable at birth and may require urgent cardiac care and are thus labeled as class III. Finally, there are some conditions that are known to potentially manifest severe instability at birth such as HLHS with intact atrial septum or congenital complete heart block with fetal heart rate less than 50 bpm. For these fetuses, performance of an IMPACT procedure (immediate postpartum access to cardiac therapy) is indicated. In this category, the fetus is delivered via a Caesarian section in our cardiac operating room and the newborn is immediately taken to an adjacent operating room or catheterization laboratory. A rapid evaluation is undertaken and immediate intervention can then be offered, minimizing the amount of time between the safety of in-utero placental support and ex-utero life without intervention. Such fetuses are labeled class IV and re-

**Table 1.** The Children's Hospital of Philadelphia's Fetal Heart Program. Delivery Classification Scale for Fetal Cardiovascular Disease. © Fetal Heart Program, Children's Hospital of Philadelphia. Reprint with kind permission.

|                                                                    | Definition                                                                      | Examples                                                                                                                                | Action                                                                                                                                                                                                                                       | Personnel                                                                                         |
|--------------------------------------------------------------------|---------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| Class I                                                            | No hemodynamic instability anticipated                                          | VSD, "pink" TOF, AV canal, truncus arteriosus, left ventricle-right ventricle size disproportion with suspicion of possible coarctation | <ul style="list-style-type: none"> <li>– Evaluation and monitoring</li> <li>– Either no vascular access, or at discretion of neonatologist a peripheral IV may be placed</li> <li>– No PGE infusion</li> </ul>                               | Neonatology                                                                                       |
| Class II                                                           | Ductal dependent lesions, stable hemodynamics anticipated                       | Pulmonary atresia, critical coarctation, critical aortic stenosis, HLHS                                                                 | <ul style="list-style-type: none"> <li>– Vascular access via umbilical vein</li> <li>– PGE infusion</li> <li>– Most commonly no UA line; however, UA may be placed at discretion of neonatologist or by request of CICU attending</li> </ul> | Neonatology                                                                                       |
| Class III                                                          | Possibility or likelihood of hemodynamic instability                            | TGA, TAPVR                                                                                                                              | <ul style="list-style-type: none"> <li>– Vascular access via umbilical vein</li> <li>– PGE infusion</li> <li>– Umbilical arterial line</li> </ul>                                                                                            | Neonatology and cardiology                                                                        |
| IMPACT Procedure (Immediate post-partum access to cardiac therapy) | Hemodynamic instability is anticipated at separation from placental circulation | HLHS + IAS, Ebstein's anomaly, CHB, hydropic fetus                                                                                      | <ul style="list-style-type: none"> <li>– C-section in cardiac facility (operating room, cath lab, hybrid room) with neonatal resuscitation in adjacent cardiac facility</li> </ul>                                                           | Cardiac intensive care, cath lab, cardiac anesthesia, cardiac surgery, echo imaging, as necessary |

AV = atrioventricular canal defect; cath = catheterization; CHB = complete heart block; HLHS = hypoplastic left heart syndrome; IAS = intact atrial septum; PGE = prostaglandin E1 infusion; TAPVR = total anomalous pulmonary venous return; TGA = transposition of the great arteries; TOF = tetralogy of Fallot; UA = umbilical artery; VSD = ventricular septal defect

quire the harnessing of substantial medical personnel and resources for an orchestrated, planned delivery.

An additional important aspect of a comprehensive Fetal Heart Program is the identification of the essential nature of counseling and family support. The importance of this aspect of care cannot be overstated. How information is conveyed and the educational process that families undergo is critical to the well being of the emerging family unit. Fetal counseling must achieve the goals of explaining the findings, often complex in nature, as well as explaining the potential plan going forward, treatment strategies, as well as outcomes both short and long term. Families often need to make critical decisions related to termination of the pregnancy or perhaps palliative care and non-intervention at birth. It remains a challenging endeavor for healthcare providers to excel at this task, however an organized approach with repeated patient encounters can help. At our Fetal Heart Program, counseling is offered through direct engagement with physicians as well as highly trained dedicated nurse coordinators, skilled in understanding all aspects of fetal care. A social worker and psychologist are available to assist families in need of these services.

Congenital heart disease manifests in a wide variety of conditions. In order to create a more common language amongst a variety of healthcare providers, we thought it would be helpful to generate a commonly accepted scale of disease severity and thus designed a unique grade of fetal cardiovascular disease severity [24]. The severity of the heart disease is judged based on factors such as complexity of care, prognosis following surgery, as well as short and long-term outcomes. In order to validate the scale we tested it both internally at The Children's Hospital of Philadelphia as well as with a number

of other major national centers in the United States. Our "Fetal Cardiovascular Disease Severity Scale" can function as a common means to communicate disease severity to patients and can be helpful in designing clinical research studies to look at variables such as maternal stress and overall quality outcomes, based on disease specifics (Tab. 2).

Our Fetal Heart Program at The Children's Hospital of Philadelphia has developed an interest in maternal psychological stress following fetal diagnosis of congenital heart disease. We found that a significant percentage of mothers exhibit substantial clinically important psychological distress [25]. Nearly 40% exhibited traumatic stress, 31% significant anxiety, and over 20% clinical depression in a series of 59 mothers. No doubt this influences maternal health, which in turn may negatively influence the developing fetus. In order to further study this phenomenon, we recently analyzed maternal salivary cortisol levels in pregnant women carrying a fetus with heart disease. Not surprisingly, cortisol levels were markedly elevated in comparison to controls. The exact influence of elevated maternal cortisol on fetal well-being and the neonatal post-natal state are worthy of further exploration. Importantly as well, is answering the question of whether specific stress-reduction techniques may reduce maternal cortisol and thereby offer a physiological benefit to the fetus.

## ■ Summary

Ideal care for the fetus with cardiovascular disease today is best offered within the context of a team approach such as in a Fetal Heart Program. Not only are diagnostics important, but the capacity to acquire detailed understanding of complex physiologies, offer innovative fetal care, and provide multidis-

**Table 2.** Fetal Cardiovascular Disease Severity Scale. © Fetal Heart Program, Children's Hospital of Philadelphia. Reprint with kind permission.

| Status  | Definition                                                                                                    | Treatment                                                                                                                                                                                                                                | Prognosis/ Anticipated Outcome                                                                                                      | Brief Summary Description                                                                                                                              | 2V* | 1V* |
|---------|---------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----|
| Level 1 | Cardiovascular finding with minimal, if any, negative impact on well-being.                                   | None.                                                                                                                                                                                                                                    | Excellent/Normal Quality of Life                                                                                                    | No significant disease.                                                                                                                                | •   |     |
| Level 2 | Cardiovascular abnormality where treatment may be necessary. Postnatal follow-up is necessary.                | Medical management may be required in utero or after birth. Surgery or catheter therapy is possible but will need to await postnatal assessment to be certain.                                                                           | Excellent/Normal Quality of Life                                                                                                    | Mild disease, need for intervention (surg/cath) possible.                                                                                              | •   |     |
| Level 3 | Cardiovascular abnormality/ simple form of congenital heart disease (two-ventricle).                          | Surgery or catheter therapy will, with certainty, be required.                                                                                                                                                                           | Excellent/Normal Quality of Life                                                                                                    | One intervention (surg/cath) necessary with excellent outcome.                                                                                         | •   |     |
| Level 4 | Cardiovascular abnormality/ complex form of congenital heart disease (two-ventricle).                         | Surgery will, with certainty, be required. Further additional interventions or surgery may be necessary at some point in life.                                                                                                           | Good/Close to Normal Quality of Life                                                                                                | One intervention necessary, multiple interventions (surg/cath) are possible over lifetime; good outcome.                                               | •   |     |
| Level 5 | Cardiovascular abnormality/ complex form of congenital heart disease, single ventricle or two-ventricle type. | Fontan surgical palliation strategy required for single ventricle patients; or, surgery for two-ventricle repair will, with certainty, be required and further intervention or surgery will, with certainty, be necessary in the future. | Prognosis is fair-to-good; infant is likely to survive surgery. Quality of life may be impaired or duration of life may be limited. | Single ventricle strategy, low risk; two-ventricle strategy, with definite need for additional procedures over lifetime; fair-to-good overall outcome. | •   | •   |
| Level 6 | Cardiovascular abnormality/ complex form of congenital heart disease, single ventricle or two-ventricle type. | Fontan surgical palliation strategy required, but is at high risk; or, two-ventricle repair but at high risk.                                                                                                                            | Prognosis is poor-to-fair. Risk of death is possible; long-term complications are highly likely. Survival beyond childhood is poor. | Single ventricle strategy, high risk; two-ventricle strategy with variable outcome and limited life expectancy.                                        | •   | •   |
| Level 7 | Cardiovascular abnormality/ complex form of congenital heart disease with very poor prognosis.                | Intervention may be offered, but expected outcome is poor.                                                                                                                                                                               | Fetal or perinatal demise likely, despite intervention.                                                                             | Poor outcome. Survival beyond early period of life not expected.                                                                                       | •   | •   |

\* 2V: two ventricle; 1V: single ventricle.

ciplinary services to fetus and family are essential. The following are some unique examples of challenging cases we have experienced which highlight the benefits of such a multidisciplinary approach.

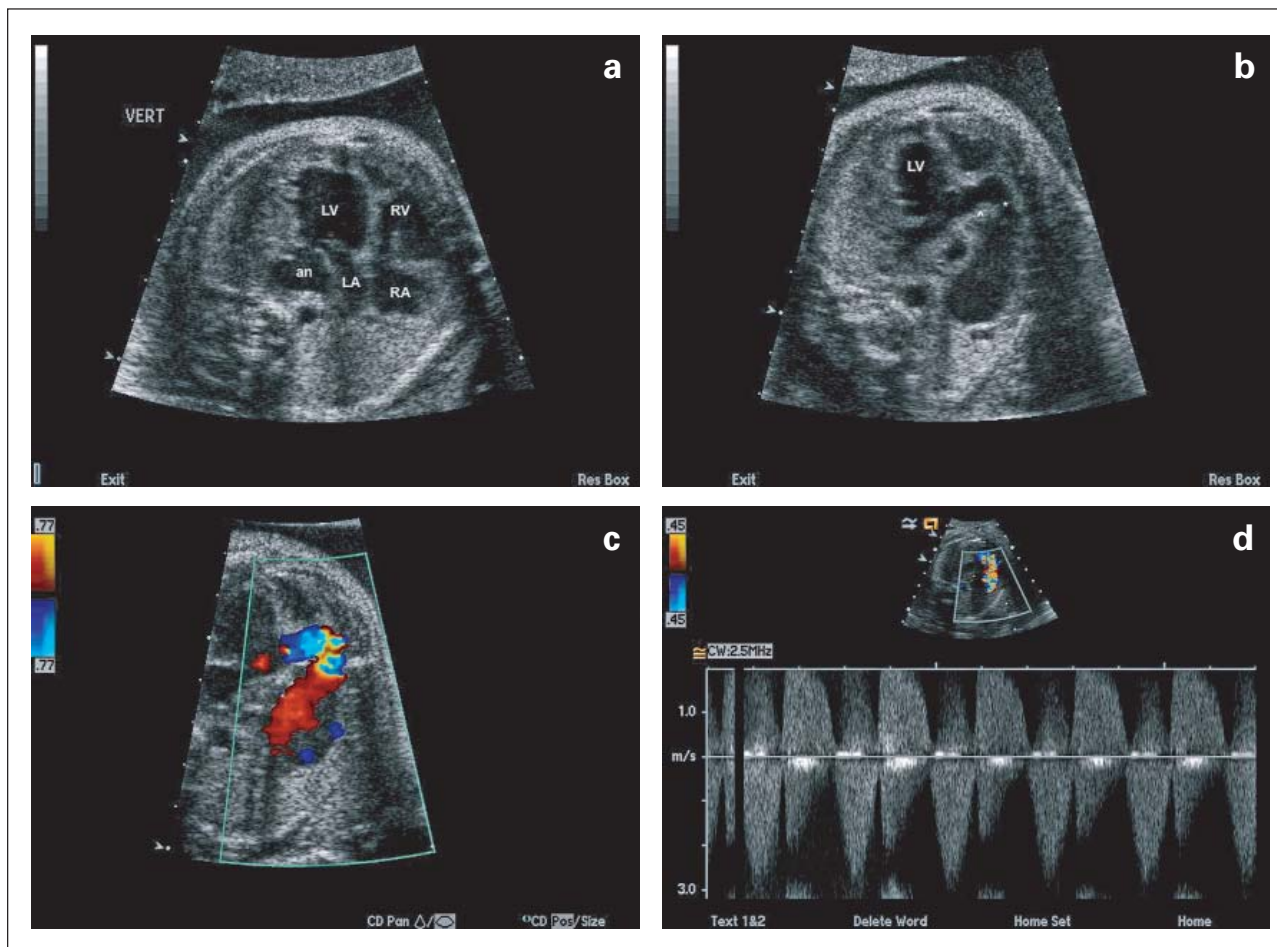
## ■ Case Examples

### Aortico-Left Ventricular Tunnel

A fetal echocardiogram was performed at 21 weeks of gestation for concerns of fetal hypoplastic left heart syndrome on level 2 ultrasound. The study demonstrated thickened aortic leaflets with aortic stenosis and apparent backward flow across the aortic valve, raising suspicion for aortic valve dysplasia. The 'aortic insufficiency' was severe, based on the holo-diastolic retrograde flow across the arch. There was severe left ventricular dilation and systolic dysfunction. In addition, there was a large aneurysm of the left ventricle, arising below the mitral valve and extending posteriorly. The mitral annulus measured low normal. Shunting across the foramen ovale was bi-directional. The right ventricular systolic function was diminished and there was mild-moderate tricuspid regurgitation. There were absent end-diastolic flow in the umbilical artery, umbilical ve-

nous pulsations and low diastolic flow in the middle cerebral artery. No hydrops and no extracardiac anomalies were identified. Cardiac findings and risk for fetal demise was discussed with the parents. The parents opted to proceed with the pregnancy and the pregnancy was followed closely. On serial follow up, there was resolution of the tricuspid valve regurgitation, and normalization of the umbilical arterial and umbilical venous flow pattern. Serial assessment demonstrated diminished interval growth of the mitral valve with subsequent development of mitral hypoplasia. A follow-up echocardiogram at 29 weeks gestation suggested presence of an aortico-LV tunnel (Fig. 1a–d). It became apparent, that the regurgitant jet was not generated through the aortic valve but rather through a tunnel surrounding the aortic annulus. There was no development of congestive heart failure or fetal growth restriction.

A female infant was delivered at 39 weeks gestation via repeat Cesarean section, via a class III delivery. The birth weight was 3890 g. APGAR scores were 6 at one minute and 8 at five minutes. The infant cried and was vigorous at delivery but did have increased respiratory effort and grunting and therefore CPAP was started. Umbilical lines were placed and PGE-1 was ini-



**Figure 1.** (a). Apical 4 chamber view with a dilated left ventricle and a left ventricular aneurysm arising below the mitral valve and extending posteriorly aneurysm (an); (b). distorted left ventricular outflow tract with thickened aortic valve (A) and aorto-LV tunnel (\*); (c). color imaging demonstrating retrograde flow across the aorto-LV tunnel; (d). Doppler imaging at the level of the aorto-LV tunnel with to and fro flow across. © Fetal Heart Program, Children's Hospital of Philadelphia. Reprint with kind permission.

tiated. The newborn was promptly admitted to CICU for further assessment and treatment. A postnatal echocardiogram confirmed the prenatal diagnosis. The infant was intubated for progressive respiratory acidosis. The infant developed systemic hypotension requiring fluid boluses and dopamine. She developed coronary ischemic episodes with ST segment depression. An abdominal ultrasound was suspicious for pneumatosis. As surgical palliation was felt to carry exceptionally high risk the family was consulted regarding the distinct possibility of post-cardiotomy ECMO support. Evaluation for heart transplantation was performed prior to surgery on account of the poor prognosis. On DOL 3 she underwent over-sewing of the aorto-LV tunnel, oversewing of the mitral valve, atrial septectomy, ligation of the patent ductus arteriosus, 4 mm Blalock-Taussig shunt and Damus-Kaye-Stansel anastomosis. Due to inability to wean off bypass the infant was initiated on ECMO and listed for heart transplant. On DOL 7 an organ heart became available and she underwent cardiac transplantation. Recovery from heart transplantation was complicated by ectopic atrial tachycardia. She was discharged home at 7 weeks of life and has continued to do well over a year post transplant.

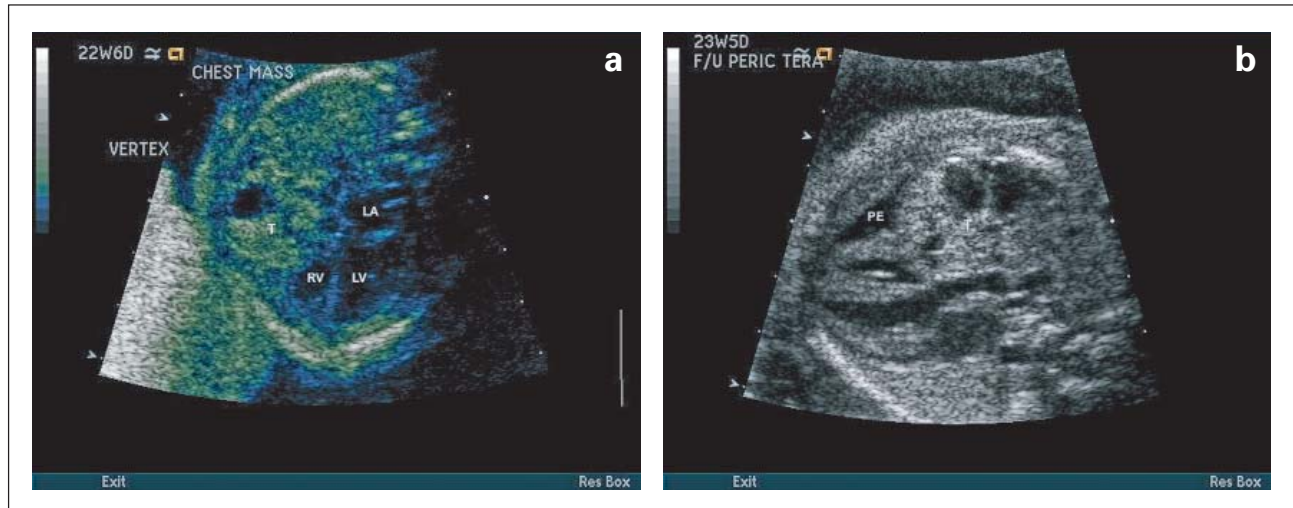
#### Discussion

Aortic insufficiency is an exceptionally rare finding in fetuses and infants. When noted, presence of an aorto-LV tunnel should also be considered. The severe runoff from the 'aortic

insufficiency' via the aorto-LV tunnel makes these patients vulnerable to ischemic injury in the mesenteric and coronary circulations. Our patient had also developed a large aneurysm of the left ventricle due to the eccentric jet of this chronic and severe 'aortic insufficiency' being directed towards the left ventricular free wall. In addition, mitral hypoplasia had developed, presumably from distortion due to the aneurysm and altered loading conditions. Surgical palliation to a Norwood procedure with ligation of the aortic LV tunnel and closure of the mitral valve in an attempt to decompress the LV as a bridge to transplant was deemed to likely be the only feasible strategy for salvaging this infant.

#### Pericardial Teratoma

A fetal echocardiogram was performed at 23 weeks of gestation for concerns of a fetal chest mass on level 2 ultrasound. It demonstrated a structurally normal heart with a large, heterogeneous tumor arising from the right atrial aortic pericardial fold (Fig. 2a). The tumor measured about  $2 \times 3$  cm in size and was about 1.5 times the size of the heart. The tumor itself compressed the right atrium and impaired filling into the right ventricle. There was no tricuspid and no mitral valve regurgitation. The bi-ventricular systolic function appeared normal. There was a small pericardial effusion. The combined cardiac output was 347 ml/kg/min. The left cardiac output was higher than the right cardiac output with the left measuring 180 ml/kg/min and



**Figure 2.** (a). Large, heterogeneous intrapericardial mass arising from the right atrial aortic pericardial fold, compressing the right atrium. T: pericardial teratoma; (b). significant interval growth of the intrapericardial mass and pericardial effusion. PE: pericardial effusion. © Fetal Heart Program, Children's Hospital of Philadelphia. Reprint with kind permission.

the right measuring 167 ml/kg/min, consistent with moderate impediment to flow into the right side of the heart with overall moderately diminished cardiac output (lower limit of normal is 400 cc/kg/min). Doppler flow patterns in the ductus venosus, umbilical artery, umbilical vein, and middle cerebral artery were all within normal limits for gestational age. No hydrops and no extracardiac anomaly were identified.

We discussed the cardiac findings and overall poor prognosis because of tendency for rapid tumor growth with the parents. A follow up echocardiogram was performed 6 days later to assess the tumor growth rate (Fig. 2b). There was an approximately 25% increase of tumor size with moderate right ventricular compression. The bi-ventricular systolic shortening remained normal. There was moderate pericardial effusion. The combined cardiac output was significantly diminished at 283 cc/kg/min. Doppler flow patterns in the ductus venosus, umbilical artery, umbilical vein, and middle cerebral artery continued to be within normal limits for gestational age and there was no fetal hydrops.

A multidisciplinary meeting was held, including cardiology, maternal fetal medicine, cardiac surgery and fetal surgery. Disease progression and potential options were discussed with the family such as nonintervention, termination of pregnancy and fetal surgical intervention with resection of the tumor. The following day, at 24 weeks 0 days gestation, the patient underwent *in utero* surgery for resection of the fetal intrapericardial tumor. A laparotomy and hysterotomy was performed exposing the fetus's chest. A median sternotomy was performed. The pericardium was opened and a very large cystic tumor was seen, attached along the aorta and RV free wall near the AV groove. Under ultrasound guidance, the tumor was mobilized and resected. Hemostasis was assured. The wound was irrigated and a drain was positioned in the mediastinum. The chest was closed and the fetus returned to the uterus. Amniotic fluid volume was restored and the uterus was closed. The uterus was returned to the abdominal cavity and the midline incision was closed. Continuous fetal echocardiographic monitoring was performed throughout. There was an isolated epi-

sode of fetal bradycardia to 70 bpm not requiring code medications and fetal cardiac function remained vigorous for the entire procedure. The patient was admitted to the special delivery unit for further monitoring. She was discharged home on postop day 5 and remained on bedrest.

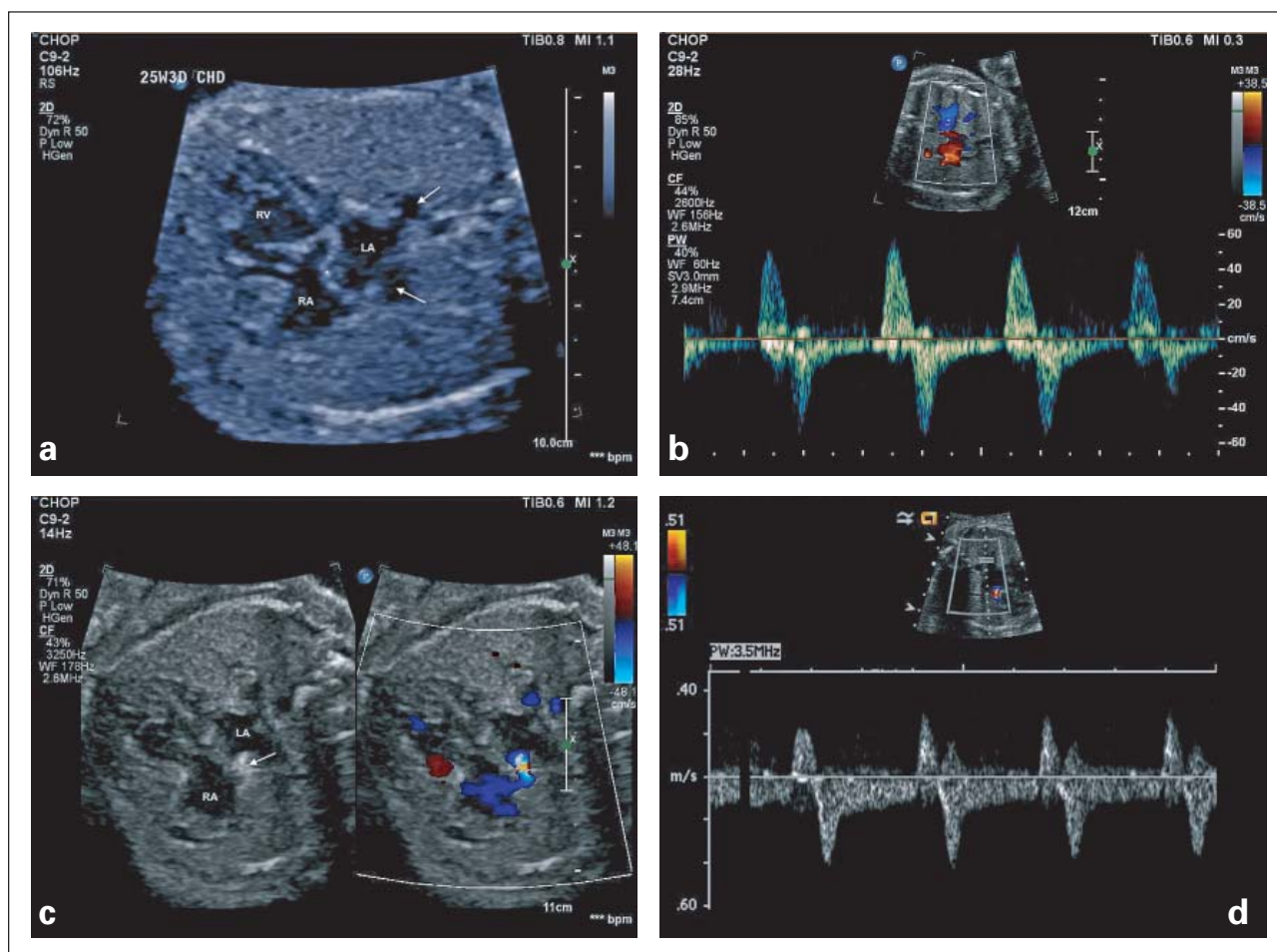
The pregnancy was followed closely. On follow-up ultrasound examinations, there was no sign of recurrent tumor growth or pericardial effusion. A male infant was delivered at 37 weeks gestation via low transverse Cesarean section, via a class III delivery. APGAR scores were 8 and 9. The birth weight was 3480 g. The infant was intubated for respiratory distress. A small round skin defect and dehiscence of the lower part of the sternotomy site was noted. The defect was covered and the newborn was admitted to NICU for further management. An echocardiogram demonstrated no residual or recurrent tumor, normal cardiac anatomy and normal cardiac function. On DOL 1 the infant was taken to the operating room for re-approximation of the sternum and closure of the skin defect. He was extubated on DOL 2. Mediastinal fluid cultures were positive for *Staphylococcus warneri* and he completed a 7 day course of antibiotics. He was discharged home on DOL 12 and has remained symptom- and recurrence-free as a toddler.

### Discussion

Fetal pericardial teratomas are rare but potential fatal. Typical diagnostic findings are its heterogeneous and multicystic nature, location at the base of the heart and associated pericardial effusion. Because of its location, compression of the cardiac structures and great vessels can occur. Cardiac compromise can occur from both, direct compression of cardiac structures by the tumor and/or the associated pericardial effusion. With development of cardiac compromise, there is high risk for fetal death. Possible management strategies include early delivery to postnatal care, *in utero* pericardiocentesis or fetal tumor resection.

### HLHS with Highly Restrictive Atrial Septum

A fetal echocardiogram was performed at 25 weeks of gestation for concerns of congenital heart disease on level 2 ultra-



**Figure 3.** (a). HLHS with highly restrictive intraatrial septum. The atrial septum (+) is bowing left to right, the pulmonary veins are dilated (arrows); (b). Doppler pattern in the left pulmonary vein with forward (below baseline) : reverse (above baseline) VTI ratio of 1.5:1, indicating a significantly restrictive left atrial egress; (c). after fetal intervention the stent (arrow) is noted across the intraatrial septum. Left to right flow across the stent by color imaging. The left atrium is decompressed and the pulmonary veins are less dilated; (d). Doppler pattern in the left pulmonary vein after intervention with forward (below baseline) : reverse (above baseline) VTI ratio of 4.5:1. © Fetal Heart Program, Children's Hospital of Philadelphia. Reprint with kind permission.

sound, which demonstrated hypoplastic left heart syndrome (HLHS) with severely restrictive atrial septum (Fig. 3a, b). There was aortic and mitral stenosis and severe left ventricular hypoplasia. The aortic arch was severely hypoplastic and with retrograde perfusion. The left atrial egress was severely restrictive with left to right shunting across a tiny intra-atrial communication. The pulmonary veins were prominently dilated with bi-directional flow within. The forward : reverse VTI ratio was 1.5 : 1, suggestive of significant atrial septal restriction. There was trivial tricuspid regurgitation. The right ventricular systolic function was normal. The Doppler flow pattern in the umbilical artery, umbilical vein, ductus arteriosus, ductus venosus and middle cerebral artery were all within normal limits. No hydrops and no extracardiac anomalies were identified.

The diagnosis and poor prognosis of this critical heart defect was discussed with the family. Options presented to the family at that gestational age were cardiac non-intervention with comfort care of the newborn, opening up of the atrial septum immediately postnatally at which time severe pulmonary effects of left atrial hypertension may have already developed, and fetal cardiac intervention with atriotomy. Given the poor postnatal prognosis with this cardiac defect, the family opted

to proceed with fetal cardiac intervention. A multiservice consultation was held with the family, including fetal cardiology, interventional cardiology and the Center for Fetal Diagnosis and Treatment (CFTD) outlining risks and benefits of fetal cardiac intervention procedure.

At 27 weeks 4 days gestation, the patient underwent fetal cardiac intervention with percutaneous placement of a stent in the fetal atrial septum under ultrasound guidance. After acceptable fetal positioning was confirmed by ultrasound, maternal general anesthesia was induced and fetal anesthesia and paralysis was provided. Under ultrasound guidance, an 18-gauge Sharc cannula was advanced through the maternal abdomen and uterus into the fetal chest cavity. The fetal right atrium was entered. A 22-gauge Chiba needle was advanced through the Sharc cannula, and across the atrial septum into the cavity of the left atrium. A 0.014 inch guidewire was inserted and its tip entered the pulmonary vein. A 2.5 × 8 mm mini vision coronary stent catheter was advanced over the guidewire and the stent was deployed across the atrial septum. At conclusion of the procedure, there was evidence of fetal hemopericardium and fetal bradycardia. Fetal resuscitation was required including drainage of the hemopericardium via a second needle and fetal administration epinephrine which resulted in normaliza-

tion of the fetal heart rate. The stent was noted in good position within the septum but angled somewhat acutely within the plane of the septum. There was good decompression of the left atrium and improvement of the pulmonary venous flow pattern with forward : reverse VTI ratios being greater than 3 : 1 (Fig. 3c, d). The patient remained hospitalized for 72 hours after the procedure.

The pregnancy was followed closely. On follow up ultrasound examinations, there continued to be good left atrial decompression, normal right ventricular and tricuspid valve function, trivial pericardial effusion, and there was no sign of congestive heart failure or growth restriction. Maternal hyperoxygenation testing was performed at 36 weeks of gestation and demonstrated only mildly increased diastolic forward flow after maternal administration of oxygen. A fetal MRI was performed at 36 weeks gestation to assess the lung parenchyma and demonstrated no evidence of pulmonary lymphangioectasia or 'nutmeg appearance'.

A male infant was delivered at 39 weeks gestation via cesarean section and the utilization of an IMPACT procedure, anticipating that additional opening of the atrial septum may be necessary with increased pulmonary venous return after delivery. Birth weight was 3425 g and APGARs were 8 and 9 at one and five minutes respectively. The infant was moved to the hybrid room. Umbilical lines were placed and PGE was initiated. Despite reassuring APGARs and minimal respiratory distress the infant had persistent respiratory acidosis and required intubation. An echocardiogram was performed and demonstrated a modestly increased transatrial gradient across the stent, thickened atrial septum and cardiac anatomy as described in the fetus. Radiofrequency ablation of the atrial septum and placement of an additional atrial stent to allow nonrestrictive pulmonary venous return was attempted but complicated by atrial perforation and hemopericardium. The infant underwent pericardiocentesis, followed by urgent sternotomy for pericardial evacuation, primary repair of the left atrial perforation, atrial septectomy and fetal stent removal. The postoperative period was complicated by atrial arrhythmias, systemic hypotension, and lactic acidosis. A cardiac catheterization was performed on DOL 3 and demonstrated pulmonary overcirculation with Qp:Qs of 4:1, and a low PVR (1.3–1.6 WU). The infant underwent temporizing bilateral branch pulmonary artery band placement the same day. Following this procedure, his hypotension and lactic acidosis markedly improved. Ultimately, the infant underwent Norwood procedure on DOL 14 with placement of a 4 mm right modified Blalock Taussig shunt, PDA ligation and removal of the bilateral branch PA bands. He was discharged home at 7 weeks of life. Pre-Glenn catheterization demonstrated an acceptable PVR of 2.5 WU with a transpulmonary gradient of 10–12 mmHg. At four months of age, the patient underwent BT shunt takedown and bidirectional Glenn procedure. He continues to do well from a cardiopulmonary standpoint in late infancy.

### Discussion

Hypoplastic left heart syndrome with intact and highly restrictive intra-atrial communication is associated with high mortality. Left-atrial hypertension results in elevated pulmonary venous pressure, pulmonary venous arterialization, lymphan-

giectasia and elevated pulmonary vascular resistance. *In utero* decompression of the left atrium may decrease the injury to the lungs and improve survival. With increased pulmonary venous return after delivery, additional postnatal enlargement of the intra-atrial communication is often necessary. In our case, atrial septectomy needed to be performed which subsequently led to significant pulmonary overcirculation. After temporary placement of bilateral pulmonary artery bands, stage 1 and 2 surgeries could be performed successfully.

### Conflict of Interest

None

### References:

- Donofrio MT, Moon-Grady AJ, Hornberger LK, et al. Diagnosis and treatment of fetal cardiac disease: a scientific statement from the American Heart Association. *Circulation* 2014; 129: 2183–242.
- Paladini D, Alfieri Z, Carvalho JS, et al. Prenatal counselling for neurodevelopmental delay in congenital heart disease. The results of a worldwide survey of experts' attitudes advise caution. *Ultrasound Obstet Gynecol* 2016; [Epub ahead of print].
- Marino BS, Lipkin PH, Newburger JW, et al. Neurodevelopmental outcomes in children with congenital heart disease: evaluation and management: a scientific statement from the American Heart Association. *Circulation* 2012; 126: 1143–72.
- Allan LD, Sharland G, Tynan MJ. The natural history of the hypoplastic left heart syndrome. *Int J Cardiol* 1989; 25: 341–3.
- Quartermain MD, Glatz AC, Goldberg DJ, et al. Pulmonary outflow tract obstruction in fetuses with complex congenital heart disease: predicting the need for neonatal intervention. *Ultrasound Obstet Gynecol* 2013; 41: 47–53.
- Rychik J, Tian Z, Bebbington M, et al. The twin-twin transfusion syndrome: spectrum of cardiovascular abnormality and development of a cardiovascular score to assess severity of disease. *Am J Obstet Gynecol* 2007; 197: 392 e1–8.
- Rasanen J, Huhta JC, Weiner S, Wood DC, Ludomirski A. Fetal branch pulmonary arterial vascular impedance during the second half of pregnancy. *Am J Obstet Gynecol* 1996; 174: 1441–9.
- Rychik J, Rome JJ, Collins MH, DeCampi WM, Spray TL. The hypoplastic left heart syndrome with intact atrial septum: atrial morphology, pulmonary vascular histopathology and outcome. *J Am Coll Cardiol* 1999; 34: 554–60.
- Chintala K, Tian Z, Du W, Donaghue D, Rychik J. Fetal pulmonary venous Doppler patterns in hypoplastic left heart syndrome: relationship to atrial septal restriction. *Heart* 2008; 94: 1446–9.
- Szwast A, Tian Z, McCann M, Donaghue D, Rychik J. Vasoreactive response to maternal hyperoxygenation in the fetus with hypoplastic left heart syndrome. *Circ Cardiovasc Imaging* 2010; 3: 172–8.
- Kaltman JR, Di H, Tian Z, Rychik J. Impact of congenital heart disease on cerebrovascular blood flow dynamics in the fetus. *Ultrasound Obstet Gynecol* 2005; 25: 32–6.
- Szwast A, Tian Z, McCann M, Soffer D, Rychik J. Comparative analysis of cerebrovascular resistance in fetuses with single-ventricle congenital heart disease. *Ultrasound Obstet Gynecol* 2012; 40: 62–7.
- Williams IA, Fifer C, Jaeggi E, Levine JC, Michelfelder EC, Szwast AL. The association of fetal cerebrovascular resistance with early neurodevelopment in single ventricle congenital heart disease. *Am Heart J* 2013; 165: 544–550 e1.
- Boudjemline Y, Rosenblatt J, de La Vil- leon G, Benifla JL, Bonnet D, Jouannic JM. Development of a new lead for in utero fetal pacing. *Prenat Diagn* 2010; 30: 122–6.
- Tulzer G, Arzt W. Fetal cardiac interventions: rationale, risk and benefit. *Semin Fetal Neonatal Med* 2013; 18: 298–301.
- Freud LR, McElhinney DB, Marshall AC et al. Fetal aortic valvuloplasty for evolving hypoplastic left heart syndrome: postnatal outcomes of the first 100 patients. *Circulation* 2014; 130: 638–45.
- Kalish BT, Tworetzky W, Benson CB et al. Technical challenges of atrial septal stent placement in fetuses with hypoplastic left heart syndrome and intact atrial septum. *Catheter Cardiovasc Interv* 2014; 84: 77–85.
- Adzick NS, Thom EA, Spong CY, et al. A randomized trial of prenatal versus postnatal repair of myelomeningocele. *N Engl J Med* 2011; 364: 993–1004.
- Channing A, Szwast A, Natarajan S, Degenhardt K, Tian Z, Rychik J. Maternal hyperoxygenation improves left heart filling in fetuses with atrial septal aneurysm causing impediment to left ventricular inflow. *Ultrasound Obstet Gynecol* 2015; 45: 664–9.
- Kohl T. Chronic intermittent maternal-fetal hyperoxygenation in late gestation may improve on hypoplastic cardiovascular structures associated with cardiac malformations in human fetuses. *Pediatr Cardiol* 2010; 31: 250–63.
- Licht DJ, Shera DM, Clancy RR, et al. Brain maturation is delayed in infants with complex congenital heart defects. *J Thorac Cardiovasc Surg* 2009; 137: 529–36.
- Miller SP, McQuillen PS, Hamrick S, et al. Abnormal brain development in newborns with congenital heart disease. *N Engl J Med* 2007; 357: 1928–38.
- Sun L, Macgowan CK, Sled JG, et al. Reduced fetal cerebral oxygen consumption is associated with smaller brain size in fetuses with congenital heart disease. *Circulation* 2015; 131: 1313–23.
- Davey BT, Donofrio MT, Moon-Grady AJ, et al. Development and validation of a fetal cardiovascular disease severity scale. *Pediatr Cardiol* 2014; 35: 1174–80.
- Rychik J, Donaghue DD, Levy S, et al. Maternal psychological stress after prenatal diagnosis of congenital heart disease. *J Pediatr* 2013; 162: 302–7.

# Mitteilungen aus der Redaktion

Besuchen Sie unsere Rubrik

## ☒ Medizintechnik-Produkte



Neues CRT-D Implantat  
Intica 7 HF-T QP von Biotronik



Artis pheno  
Siemens Healthcare Diagnostics GmbH



Philips Azurion:  
Innovative Bildgebungslösung

Aspirator 3  
Labotect GmbH



InControl 1050  
Labotect GmbH

## e-Journal-Abo

Beziehen Sie die elektronischen Ausgaben dieser Zeitschrift hier.

Die Lieferung umfasst 4–5 Ausgaben pro Jahr zzgl. allfälliger Sonderhefte.

Unsere e-Journale stehen als PDF-Datei zur Verfügung und sind auf den meisten der marktüblichen e-Book-Readern, Tablets sowie auf iPad funktionsfähig.

## ☒ Bestellung e-Journal-Abo

### Haftungsausschluss

Die in unseren Webseiten publizierten Informationen richten sich **ausschließlich an geprüfte und autorisierte medizinische Berufsgruppen** und entbinden nicht von der ärztlichen Sorgfaltspflicht sowie von einer ausführlichen Patientenaufklärung über therapeutische Optionen und deren Wirkungen bzw. Nebenwirkungen. Die entsprechenden Angaben werden von den Autoren mit der größten Sorgfalt recherchiert und zusammengestellt. Die angegebenen Dosierungen sind im Einzelfall anhand der Fachinformationen zu überprüfen. Weder die Autoren, noch die tragenden Gesellschaften noch der Verlag übernehmen irgendwelche Haftungsansprüche.

Bitte beachten Sie auch diese Seiten:

**Impressum**

**Disclaimers & Copyright**

**Datenschutzerklärung**