

## Original Article

# Fetal cardiac intervention and fetal cardiac surgery: where are we in 21st century?

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**Abstract:** Fetal cardiac intervention is an in-utero cardiac procedure done in fetuses with heart diseases like severe aortic stenosis with evolving hypoplastic left heart syndrome, hypoplastic left heart syndrome with an intact or restricted atrial septum, pulmonary atresia with an intact ventricular septum, fetal heart block obstructed total anomalous pulmonary venous return, pericardial collection. The successful biventricular repair can be done in post-natal life after aortic or pulmonary valvuloplasty. Fetal bypass is very challenging because of different physiology. Low prime volume with the high flow can be used to prevent an inflammatory response.

**Keywords:** Fetal cardiac intervention, fetal cardiac surgery, fetal bypass, fetal aortic valvuloplasty

## Introduction

Fetal cardiac intervention and cardiac surgery is an emerging branch. Cardiac development is completed by eight weeks of gestation. With developed fetal imaging like fetal echocardiography and fetal MRI (Magnetic resonance imaging), most congenital heart disease can be detected by the 12th week. Primary morphological changes in the heart during the fetal period like valvular lesions can cause secondary changes in the heart like ventricular hypoplasia. Therefore early intervention during a fetal period can prevent secondary changes. Fetal cardiac intervention commonly used in fetal aortic stenosis, hypoplastic left heart syndrome, pulmonary atresia with an intact ventricular septum, fetal tachycardia, bradycardia, heart failure. For fetal cardiac surgery, appropriate extracorporeal support is needed as fetal physiology is different from neonatal physiology. Unfortunately, no study on human fetal bypass published to date. But there are few studies on the animal model which showed post bypass placental dysfunction is very much common due to fetal stress, prime volume and extracorporeal surface [1].

## Fetal cardiac intervention

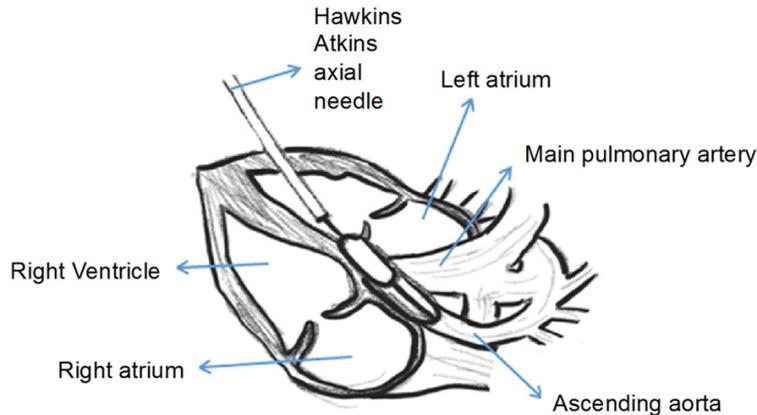
First-time fetal cardiac intervention was done in 1975 for fetal ventricular tachycardia [2]. In 1987, first fetal cardiac pacing was done due to complete heart block-induced fetal hydrops fetalis. The first fetal balloon aortic dilatation was done 25 years ago [3].

Fetal cardiac intervention is indicated in many cardiac lesions like restricted or intact atrial septum and severe aortic stenosis (AS) with evolving hypoplastic left heart syndrome, severe mitral stenosis, and pulmonary atresia with the intact ventricular septum (PA-IVS), pulmonary atresia with ventricular septal defect with small pulmonary artery, complete transposition of great vessel with restricted atrial communication or intact atrial septum. Contraindications are multiple gestations, major anomalies, contraindication to anesthetic drugs. Fetal cardiac intervention is mainly subdivided into pharmacological intervention and closed intervention [4].

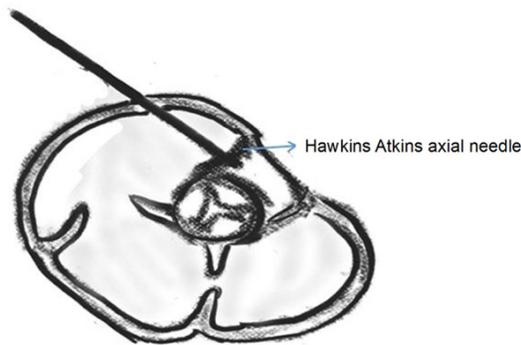
### *Pharmacological intervention*

Apart from transplacental injection other routes of medications are umbilical vein injection, fetal

## In-utero fetal cardiac procedure



**Figure 1.** Fetal aortic valvuloplasty is performed using 18 G/19 G Hawkins Atkins needle, 0.014 inch coronary guide wire and Maverick coronary balloon.



**Figure 2.** Pulmonary valve perforation with catheter inserted to right ventricular outflow tract with 10-15 degree angulations.

intramuscular injection, fetal intravascular injection and fetal intracardiac injection. Fetal medical therapy with digoxin is used in fetal heart failure due to poor placental transfer of digoxin due to hydrops [5].

### *Closed intervention*

5% prenatally diagnosed congenital heart diseases (CHD) including Severe AS (1.6%), PA-IVS (1.9%), and severe pulmonary stenosis (1.5%) can be critical and therefore require intrauterine intervention. Early diagnosis and treatment of treatable CHD improves ventricular growth and angiogenesis [6].

### **Aortic valvuloplasty in evolving hypoplastic left heart syndrome**

Fetuses with severe aortic stenosis evolve into hypoplastic left heart syndrome if not treated in

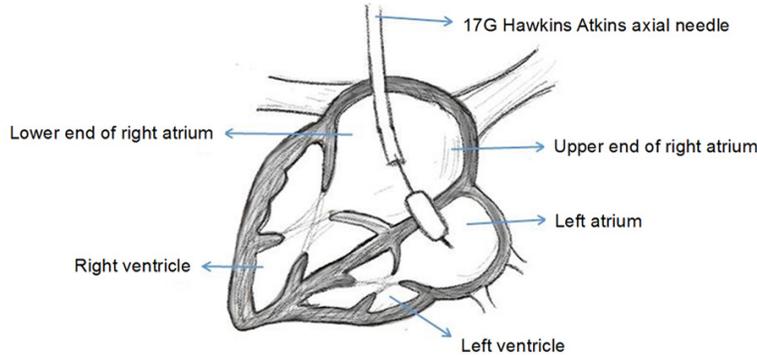
the fetal period. Severe aortic stenosis causes systolic and diastolic dysfunction of the left ventricle and increased left atrial and left ventricle filling pressure which causes left ventricular underdevelopment due to redistribution of flow from the left atrium to the right atrium [7]. Following are the echocardiography criteria suggestive of progression to hypoplastic left heart syndrome-narrow aortic jet more than 2 m/s, dilated dysfunctional left ventricle, neo development of mitral regurgitation, monophasic mitral inflow

Doppler, left to right shunt across foramen ovale, reversal of flow in the aortic arch, abnormal pulmonary vein flow, endocardial fibroelastosis [8]. Predicting criteria for biventricular repair was described like; left ventricle long axis z score >0, left ventricle short-axis z score >0, aortic annulus z score >-3.5, mitral valve annulus z score >-2, mitral regurgitation or aortic stenosis maximum gradient more than 20 mm of hg and left ventricular pressure more than 47 mm of hg and ascending aortic z score >0.57) [9, 10]. Fetal aortic valvuloplasty is commonly performed between 21-32 weeks (**Figure 1**). 18 G/19 G Hawkins Atkins needle/Chiba needle/M3 coaxial needle, 0.014-inch coronary guidewire, Maverick/Hiyuru/Relysis coronary balloon are used. Apical left ventricular puncture is done well-aligned to left ventricular outflow tract and prepared guidewire balloon assembly is advanced through the needle. The balloon to annulus ratio of 1-1.2 provides the best result. Fetal aortic regurgitation is the most common complication which resolves within few weeks [11]. According to the study by Freud et al 43% of patients following aortic valvuloplasty underwent biventricular repair [12]. As per the International fetal cardiac intervention registry, in 2015 80% of patients in the fetal aortic valvuloplasty group lived and 40% underwent biventricular repair [13].

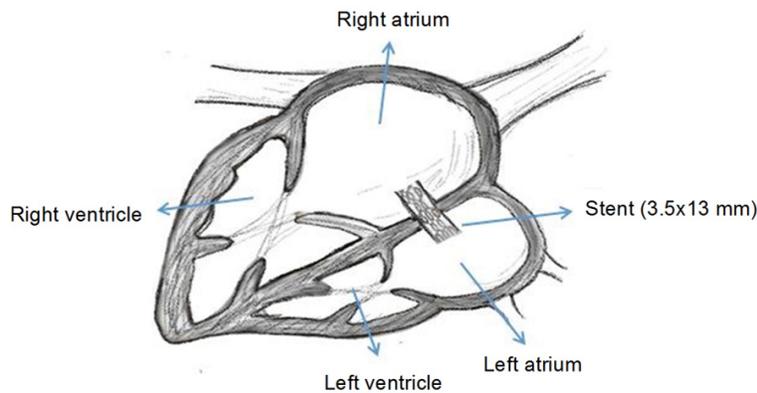
### **Pulmonary valve perforation in pulmonary atresia with intact ventricular septum**

Fetuses with PA-IVS developed hypertrophy and hyperplasia of the right ventricular muscle

## In-utero fetal cardiac procedure



**Figure 3.** Perforation of the inter-atrial septum after piercing the right atrium with 18 G/17 G needle.



**Figure 4.** Stenting of the inter-atrial septum defect with short length stent (3.5×13 mm).

with low right ventricular volume. Pulmonary valvuloplasty is done in the fetus of 21-32 week with membranous pulmonary atresia with tricuspid valve z score <-2. The right ventricular outflow tract is approached through via subcostal approach or intercostals space next to the sternum. Cannula tip is directed towards pulmonary valve and inserted to right ventricular outflow tract with 10-15 degree angulation (**Figure 2**). Balloon-annulus ratio is 1.2-1.3 and balloon length should be 8-10 mm to prevent right ventricular free wall dilatation [14]. Some of the predictors of single ventricular outcome are tricuspid valve: mitral valve ratio  $\leq 0.83$ , right ventricle: left ventricle length ratio  $\leq 0.64$ , pulmonary valve: aortic valve ratio  $\leq 0.75$ , tricuspid inflow duration/cardiac cycle length  $\leq 36.5\%$  [15]. Biventricular repair has been achieved in some center yielding good results where fetal pulmonary valvuloplasty has been performed in utero in pulmonary atresia with an intact ventricular septum [16].

### Atrial septoplasty or atrial stenting in hypoplastic left heart syndrome with intact atrial septum or restricted atrial septum

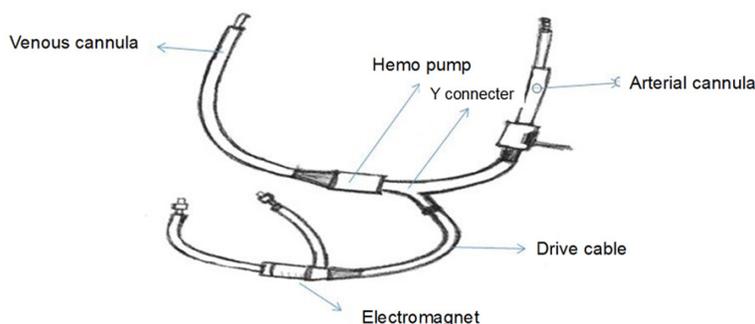
Hypoplastic left heart syndrome with intact or restricted atrial septum causes an increase in left atrial pressure followed by increase pulmonary vascular pressure which increases mortality and morbidity after stage 1 palliation. Indications of intervention are pulmonary venous doppler forward: retrograde velocity-time integral ratio less than 3, maternal hyper-oxygenation (post 28 weeks) less than 10% reactivity [17]. Right atrium is punctured perpendicular to inter atrial septum with an 18 G/17 G needle which can be advanced to perforate the septum. Then either balloon is inserted (**Figure 3**) or short length stent (3.5×13 mm) (**Figure 4**) is inserted. As per international fetal cardiac intervention registry data 65% of patients underwent successful intervention but there was no difference in discharge survival [13].

According to the largest single-center experience creation of atrial communication of more than 3 mm was associated with higher postnatal oxygen saturation and better outcome after stage 1 palliation [18].

### Fetal cardiac surgery

Fetal cardiac surgery is the most challenging part of cardiac surgery as fetal physiology and fetal response to extracorporeal circulation is different from the neonate. To date no original article, a case report was published but few articles were published regarding the effect of extracorporeal circulation on the animal fetus. Non-physiological flow causes placental vasoconstriction followed by placental dysfunction due to reduced placental blood flow. Hypothermia increases sympathetic response which escalates blood viscosity and finally reduces

## In-utero fetal cardiac procedure



**Figure 5.** Inline axial flow pump.

placental blood flow. From a maternal point of view hypothermia also increases uterine contraction especially during the rewarming phase. So, hypothermia is not favorable like neonate [19]. Pulsatile blood flow with high blood flow is needed for adequate fetoplacental perfusion and to reduce placental dysfunction. It reduces vascular resistance through preserving fetomaternal nitric oxide biosynthesis and prevents fetal renin-angiotensin-aldosterone pathway [20]. No or ultralow prime volume is needed to reduce the endothelial reaction. More amount of primed maternal blood dilutes fetal hemoglobin [21]. There are two types of fetal bypass circuits with or without placenta. In case of prolonging bypass without placenta is preferred because of chances of hypoxemia [22]. Continuous hemodiafiltration combined with steroid can reduce inflammatory response [23]. Experimental animal research works without the use of prime volume with the inline axial flow, the pump has also yielded promising outcomes (Figure 5) [24].

### Conclusion

Successful planning and implementation of fetal cardiac intervention can increase biventricular repair in postnatal life in patients with severe aortic stenosis with evolving hypoplastic left heart syndrome and pulmonary atresia with an intact ventricular septum. Minimal prime volume with high flow normothermic bypass can be used with good outcomes.

### Disclosure of conflict of interest

None.

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