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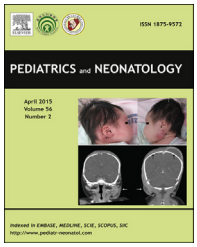

REVIEW ARTICLE

Fetal Cardiac Interventions

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Abstract The present article aims to highlight fetal cardiac interventions (FCIs) in terms of indications, strategies, and fetal prognoses. FCIs of the early years were predominantly pharmacological therapies for fetal arrhythmia or heart block. A transplacental transmission of therapeutic agents has now become the main route of pharmacological FCIs. There have been various FCI strategies, which can be categorized into three types: pharmacological, open FCIs, and closed FCIs. Rather than as a routine management for materno-fetal cardiac disorders, however, FCIs are only applied in those fetal cardiac disorders that are at an increased risk of mortality and morbidity and warrant an interventional therapy. Pharmacological FCIs have been well applied in fetal arrhythmias but require further investigations for novel therapeutic agents. The development of open FCI in humans is an issue for the long run. Closed FCIs may largely rely on advanced imaging techniques. Hybrid FCIs might be the future goal in the treatment of fetal heart diseases.

1. Introduction

With the steady development of medical imaging techniques, fetal cardiac interventions (FCIs) have drawn considerable attention due to the potential merits of prenatal diagnosis and successful management of fetal cardiovascular anomalies, arrhythmias, and heart failure.[1] FCIs are carried out to improve fetal cardiac function, promote fetal intrauterine development and survival, and enhance postnatal survival.[2] Rather than being a routine management for materno-fetal cardiac disorders, however, FCIs are only applied in those fetal cardiac disorders that have an increased risk of mortality and morbidity and warrant an interventional therapy.[3] There are now various FCI strategies, which can be categorized into three types: pharmacological, open FCIs, and closed FCIs. Of these, closed FCIs can be further subtyped into indirect and direct closed FCIs. The present article aims to highlight FCIs in terms of indications, strategies, and fetal prognoses.

2. Principles of FCIs

The theoretical principles for FCIs have been described in guidelines that not only conform to ethics but also take into account the fetal prognoses and maternal safety (Table 1).

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Table 1	Principles for fetal cardiac interventions.
Fetus	✧ The congenital heart defect may have poor postnatal therapeutic effect without prenatal intervention ✧ The intervention may prevent or reduce the development of the cardiac defect and improve postnatal prognosis
Mother	✧ Maternal safety must be guaranteed ✧ Maternal fertility must not be affected
Technique	✧ The *in-utero* intervention is technically feasible ✧ A multidisciplinary team serves to support the technical application

Prenatal intervention is suitable only for a small subset of fetal conditions, including severe aortic stenosis, pulmonary atresia, and intact atrial septum; therefore intervention should only be offered to candidates fulfilling strict selection criteria.[4] Intrauterine valvuloplasty of a severely stenotic pulmonary valve or a pulmonary atresia with intact ventricular septum aims to prevent hypoplasia of the right ventricle and to enable postnatal biventricular repair.[2] The aim of aortic balloon valvuloplasty for critical aortic stenosis with a small left ventricle or a normal sized left ventricle but poor function is to increase the chances of biventricular repair, and to alter the natural history of mid gestation fetal aortic stenosis toward evolving hypoplastic left heart syndrome (HLHS).[3,5] HLHS often presents in late gestation, and therefore it cannot be caught in time for fetal intervention as there would be insufficient time for fetus *in-utero* development after intervention.[6] Successful fetal aortic valvuloplasty may result in improvement of *in-utero* aortic and mitral valve growth, left ventricular ejection fraction, bidirectional flow across the foramen, and antegrade flow in the transverse arch.[7] Aortic stenosis with a high velocity, good ventricular function, and forward flow in the arch are important preconditions for fetuses to transit to postnatal treatment. A small ventricle may suggest non-eligibility for a prenatal procedure.[4] The most important selection criterion for fetuses is critical aortic valve stenosis evolving HLHS. Other selection criteria include a left ventricular long-axis Z-score of >-3, retrograde flow in the aortic arch, and left-to-right shunt across the foramen ovale.[8] Under these principles, the inclusion criteria (i.e., indications) for the treatment of fetal cardiac disorders are primarily arterial level and atrial level abnormalities, whereas the exclusion criteria are predominantly from maternal aspects (Table 2).

3. Pharmacological FCIs

FCIs of the early years are predominantly pharmacological therapies for fetal arrhythmia or heart block[3] to preserve the intrauterine growth environment with the precondition of maternal safety, in order to achieve a favorable delivery in due course after a general evaluation of fetal growth and development that would thereby facilitate postnatal treatment.[9] At present, transplacental transmission of therapeutic agents is the main route of pharmacological FCIs. Alternative approaches include umbilical vein transmission, fetal intramuscular injection, and fetal intravascular passages. The use of invasive approaches is very limited in clinical practice, and they were only recommended in those with a very low transplacental passage rate due to severe hydrops.[9] Fetal arrhythmias can be divided into three types: fetal tachycardia (heart rate >180 beats/minute), bradyarrhythmias (heart rate <110 beats/minute), and fetal ectopy (irregular rhythm).[9]

Fetal supraventricular tachycardia is characterized by a 1:1 atrioventricular conduction, usually with a heart rate of 200–300 beats/minute, either paroxysmal or incessant, and it is associated with fetal hydrops in 36–64%.[10] Supraventricular tachycardia is regarded as a cause of nonimmune hydrops fetalis with an increased risk of perinatal mortality.[10] Sustained supraventricular tachycardia (>12 hours) and lower gestation showed direct correlations with hydrops.[11] Clinical observations revealed that the gestational age at delivery was significantly greater in those with intrauterine management than those without.[11] In 1975, Eibschitz et al[12] reported successful intrapartum treatment by intravenous propranolol for fetal ventricular tachycardia. Atasaral et al[10] reported that a fetus developed tachycardia at a heart rate of 240 beats/minute in the 34th week of gestation, which was managed with maternal administration of sotalol 120 mg twice/day on Day 1 of treatment, then tapered to 80 mg twice/day. The fetal heart rate dropped to 140 beats/minute and the fetus was stable until normal vaginal delivery.

The prognosis for fetal atrioventricular heart block related to congenital heart defects can be extremely poor, with a combined fetal and neonatal mortality of >80%. Scheduled early delivery, pacing at a reduced ventricular rate, and dual-chamber pacing have proved to be

Table 2	Inclusion and exclusion criteria of cardiac disorders for fetal cardiac interventions.
	Congenital heart defect
Inclusion	
Left heart system	✧ Critical aortic valve stenosis evolving hypoplastic left heart syndrome ✧ Restrictive atrial level communication evolving hypoplastic left heart syndrome ✧ Severely stenotic mitral valve
Right heart system	✧ Pulmonary atresia with intact septal septum ✧ Pulmonary atresia with ventricular septal defect with hypoplasia of the pulmonary artery ✧ Tetralogy of Fallot with hypoplasia of the pulmonary artery
Others	✧ Severe type of double outlet right ventricle ✧ Complete transpositions of great vessels with restrictive atrial level communication
Exclusion	
Fetus	✧ Associated with severe malformations of other organs ✧ Multiple gestations
Mother	✧ Cervical incompetence ✧ Contraindications for the use of narcotics or uterine contraction inhibitor