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Original Article

Neonatal management and outcomes of prenatally diagnosed CHDs

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Abstract *Objectives:* The aim of this study was to determine the probability of intervention at birth after prenatal diagnosis of CHD. *Methods:* A 10-year retrospective study including all foetuses with a prenatally diagnosed CHD and those delivered in a tertiary-care cardiac centre between January, 2002 and December, 2011 was carried out. Patients were classified into eight groups according to the anticipated risk of neonatal intervention. *Results:* The need for urgent intervention and/or PGE1 infusion within the first 48 hours of life was 47% (n = 507/1080): 72% (n = 248) for CHD at risk for a Rashkind procedure, 77% (n = 72) for CHD with ductal-dependent pulmonary flow, 13% (n = 22) for CHD with potentially ductal-dependent pulmonary flow, 94% (n = 62) for CHD with ductal-dependent systemic flow, 29% (n = 88) for CHD with potentially ductal-dependant systemic flow, 50% (n = 4) for total anomalous pulmonary venous connection, and 17% (n = 1) for CHD with atrio-ventricular block. In all, 34% of the patients received PGE1 infusion and 21.4% underwent urgent catheter-based or surgical interventions; 10% of patients without anticipated risk (n = 10) underwent an early intervention; 6.7% (n = 73) of the patients died; and 55% (n = 589) had an intervention before discharge from hospital. *Conclusion:* Half of the neonates with foetal CHD benefited from an urgent intervention or PGE1 infusion at birth. We recommend scheduled delivery and in utero transfer for transposition of the great arteries, double-outlet right ventricle with sub-pulmonary ventricular septal defect, total anomalous pulmonary venous connection, CHD with atrio-ventricular block with heart rate <50, all ductal-dependant lesions, and CHD with potentially ductal-dependant systemic flow.

Keywords: CHD; outcome; in utero transfer

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Several studies have shown that prenatal diagnosis of CHD at risk of neonatal distress improves their morbidity and mortality.[1–5] Ductal-dependent CHDs for pulmonary or systemic circulation require an infusion of prostaglandin at birth and subsequent surgery or catheterisation within the first few days of life.[6] Transposition of the great arteries and hypoplastic left heart syndrome may be at risk of immediate neonatal distress due to the restriction of the foramen ovale, and are therefore generally delivered at centres able to perform a Rashkind procedure immediately after birth.[7,8] Finally, some types of CHD may require urgent neonatal surgery, such as total anomalous pulmonary

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venous connection, even if they are rarely diagnosed before birth.[9] These foetuses are generally scheduled to be born in specialised centres that are able to perform urgent cardiac surgical or interventional procedures at birth.[10] Our healthcare system has developed a systematic foetal screening for CHD in all pregnancies that allows a high detection rate of CHD.[11] Owing to the specific organisation of prenatal diagnosis in Paris area, a large number of foetal CHD cases are delivered in our tertiary referral centre. We are aware that this model is specific to our healthcare system, and that it does not apply to other economic, geographical, and demographic contexts. Nevertheless, it allows the analysis of immediate postnatal management of neonates who were prenatally diagnosed with a CHD.

For these reasons, we sought to determine for each CHD the probability of immediate intervention at birth as well as the need for interventions performed before hospital discharge in a large series of foetuses with CHD who were delivered on site.

Population and methods

We included all foetuses with a prenatally diagnosed CHD at our institution from January, 2002 to December, 2011 and who were delivered at our maternity unit. We excluded foetuses whose diagnosis had been made at our centre but were born elsewhere. We also excluded patients who had non-structural heart defects such as tumours, antenatal cardiomyopathies, isolated foetal arrhythmias, and isolated conduction disorders. We excluded from the analysis newborns for whom compassionate care had been planned with the family, and therefore did not undergo any cardiac intervention after birth.

We reviewed the history of pregnancy: the reason for referral for foetal echocardiography, the gestational age at diagnosis of CHD, and the final foetal diagnosis of CHD. Neonatal data collected were as follows: postnatal diagnosis of CHD, neonatal early and urgent interventions performed during the first 48 hours of life, surgery, and interventional catheterisation; need for PGE1 infusion; and the non-urgent curative or palliative interventions – surgical or interventional catheterisation – performed before discharge.

We classified our patients into eight groups on the basis of the prenatal diagnosis of CHD and the anticipated neonatal risk according to the anticipated neonatal physiology of the CHD:

- CHD at risk for a Rashkind procedure at birth: transposition of the great arteries with and without ventricular septal defect, transposition of the great arteries with ventricular septal defect and pulmonary stenosis, double-outlet right ventricle with sub-pulmonary ventricular septal defect, and atrio-ventricular discordance with ventriculo-arterial concordance.
- CHD ductal-dependent for pulmonary flow – atresia or obstruction with abnormal ductal flow such as aorta-to-pulmonary or bidirectional – pulmonary atresia with intact ventricular septum, severe pulmonary valve stenosis, pulmonary atresia with ventricular septal defect, Ebstein's anomaly or tricuspid valve dysplasia with organic or functional pulmonary atresia, and other functionally univentricular heart defects with pulmonary atresia.
- CHD potentially ductal-dependent for pulmonary flow: Ebstein's anomalies and tricuspid valve dysplasia without pulmonary atresia, pulmonary valve stenosis, tetralogy of Fallot and variants, and other functionally univentricular heart defects with pulmonary stenosis, with normal ductal flow such as pulmonary-to-aorta.
- CHD ductal-dependent for systemic flow – atresia or obstruction with retrograde flow in the aortic arch – hypoplastic left heart syndrome, aortic valve atresia or severe stenosis, and interruption of the aortic arch.
- CHD potentially ductal-dependent for systemic flow: coarctation of the aorta with or without ventricular septal defect, aortic valve stenosis, and univentricular heart defects with risk of coarctation.
- Total anomalous pulmonary venous returns: isolated or associated with another CHD.
- Atrio-ventricular block associated with a CHD.
- CHD with a priori no risk of early intervention at birth.

Review of medical records was approved by the hospital's local committee on clinical investigation.

Results

Description of the foetal cohort

Between January, 2002 and December, 2011, 2464 foetal heart defects were referred to us for expertise. Finally, there were 1592 live births, 799 terminations of pregnancy, and 73 in utero foetal deaths. Of the 1592 live births, we excluded 334 patients born outside our centre and 120 patients who had non-structural heart defects. In total, 58 newborns received compassionate care at birth, and were therefore not included in the analysis of cardiac interventions after birth. Finally, 1080 newborns delivered alive at our centre were included.

The reason for referral for foetal echocardiography was confirmation of a suspected CHD at the mid-trimester ultrasound screening in 83.8% of cases and systematic screening for conditions at risk of

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CHD – foetal, maternal, or familial – in 15.6% of cases. Gestational age at diagnosis ranged from 10 to 40 weeks, with a mean of 24 weeks.

Neonatal interventions

The need for intervention or PGE1 infusion during the first 48 hours of life was noted for the eight anticipated groups of CHD (see Table 1). The type of intervention could be a Rashkind procedure, an urgent interventional catheterisation, or an urgent cardiac surgery. Each patient could have several interventions – for example, a newborn with transposition of the great arteries could have a Rashkind procedure and prostaglandin infusion.

Table 2 describes the non-urgent interventions performed before discharge. These interventions could be curative or palliative, surgery, or interventional catheterisation. In total, 589 patients (55%) of the cohort needed an intervention before discharge.

In all, 31 patients had curative catheterisation, including 30 perforation and/or dilatation of the pulmonary valve atresia or stenosis and one dilatation of an aortic stenosis in a non-rescue situation. The 12 palliative catheterisations were for patients with pulmonary atresia not suitable for biventricular repair (n = 5) or tetralogy of Fallot (n = 7) who underwent arterial duct stenting or dilatation of the ventricular pulmonary outflow tract. In total, 394 patients received complete surgical repair: 292 transposition

Table 1. Neonatal interventions within the first 48 hours after birth.

	Patients at risk	PGE1	Neonatal intervention in the first 48 hours	Rashkind procedure	Interventional catheterisation	Surgery	PGE1 and/or Neonatal intervention
All Patients							
All patients	1080	369	231	217	12	5	507
		34%	21.4%	20%	1%	0.5%	47%
All patients excluding CHD with a priori no risk of neonatal intervention	982	362	229	215	11	4	497
		37%	23.3	22%	1%	0.5%	51%
CHD at risk for a Rashkind procedure (Group1)							
TGA	207	88	151	151	0	0	170
		43%	73%	73%	0%	0%	82%
TGA with VSD	108	32	46	46	0	0	63
		30%	43%	43%	0%	0%	58%
DORV with sub-pulmonary VSD	13	2	1	1	0	0	3
		15%	8%	8%	0%	0%	23%
TGA with VSD and pulmonary stenosis	15	2	10	10	0	0	11
		13%	67%	67%	0%	0%	73%
Atrio-ventricular discordance	1	0	1	1	0	0	1
		0%	100%	100%	0%	0%	100%
All	345	124	209	209	0	0	248
%		36	61	61	0	0	72
CHD with ductal-dependent pulmonary flow (Group 2)							
Pulmonary atresia, critical pulmonary valve stenosis	37	37	0	0	0	0	37
		100%	0%	0%	0%	0%	100%
Pulmonary atresia with VSD	35	17	0	0	0	0	17
		49%	0%	0%	0%	0%	49%
Ebstein, tricuspid dysplasia with pulmonary atresia	5	2	0	0	0	0	2
		40%	0%	0%	0%	0%	40%
Other CHD with pulmonary atresia	17	16	0	0	0	0	16
		94%	0%	0%	0%	0%	94%
All	94	72	0	0	0	0	72
%		77	0	0	0	0	77
CHD with potentially ductal-dependent pulmonary flow (Group 3)							
Pulmonary valve stenosis	20	11	0	0	0	0	11
		55%	0%	0%	0%	0%	55%
Ebstein, tricuspid dysplasia with pulmonary valve stenosis	15	1	0	0	0	0	1
		7%	0%	0%	0%	0%	7%
Tetralogy of Fallot and variants	113	6	1	1	0	0	7
		5%	1%	1%	0%	0%	6%
Other CHD with pulmonary stenosis	15	2	1	1	0	0	3
		13%	7%	7%	0%	0%	20%
All	163	20	2	2	0	0	22
%		12	1	1	0	0	13
CHD with ductal-dependent systemic flow (Group 4)							
HLHS	45	44	2	2	0	0	44
		98%	4%	4%	0%	0%	98%
Aortic valve atresia	3	2	0	0	0	0	2
		67%	0%	0%	0%	0%	67%
Interruption of the aortic arch	18	16	1	1	0	0	16
		89%	6%	6%	0%	0%	89%
All	66	62	3	3	0	0	62
%		94	5	5	0	0	94

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Table 1. *Continued*

	Patients at risk	PGE1	Neonatal intervention in the first 48 hours	Rashkind procedure	Interventional catheterisation	Surgery	PGE1 and/or Neonatal intervention
CHD with potentially ductal-dependent systemic flow (Group 5)							
Coarctation of the aorta with and without VSD	236	66	3	0	3	0	67
		28%	1%	0%	1%	0%	28%
Aortic valve stenosis	22	9	7	0	7	0	12
		41%	32%	0%	32%	0%	55%
Other CHD with risk of coarctation of the aorta	42	9	1	1	0	0	9
		21%	2%	2%	0%	0%	21%
All	300	84	11	1	10	0	88
%		28	4	0	3	0	29
Total anomalous pulmonary venous returns (Group 6)							
Total anomalous pulmonary venous return	7	0	4	0	0	4	4
		0%	57%	0%	0%	57%	57%
CHD with total anomalous pulmonary venous return	1	0	0	0	0	0	0
		0%	0%	0%	0%	0%	0%
All	8	0	4	0	0	4	4
%		0	50	0	0	50	50
CHD with Atrio-ventricular block (Group 7)							
CHD with Atrio-ventricular block	6	0	1	0	1	0	1
%		0	17	0	17	0	17
CHD with a priori no risk of neonatal intervention							
Common arterial trunk	18	2	0	0	0	0	2
		11%	0%	0%	0%	0%	11%
Univentricular hearts	16	2	0	0	0	0	2
		13%	0%	0%	0%	0%	13%
Absent pulmonary valve with intact septum	2	0	0	0	0	0	0
		0%	0%	0%	0%	0%	0%
Atrio-ventricular septal defect	13	0	0	0	0	0	0
		0%	0%	0%	0%	0%	0%
VSD, DORV with sub-aortic VSD	20	2	1	1	0	0	2
		10%	5%	5%	0%	0%	10%
Congenitally corrected TGA	15	0	1	1	0	0	1
		0%	7%	7%	0%	0%	7%
Heterotaxy syndromes	3	0	0	0	0	0	0
		0%	0%	0%	0%	0%	0%
Others	11	1	0	0	1	1	3
		9%	0%	0%	9%	9%	27%
All	98	7	2	2	1	1	10
%		7	2	2	1	1	10

DORV = double-outlet right ventricle; HLHS = hypoplastic left heart syndrome; IUFD = intra-uterine foetal deaths; PGE1 = prostaglandin E1; TGA = transposition of the great arteries; TOP = termination of pregnancy; VSD = ventricular septal defect

The first column gives the overall rate of intervention for each group of CHD (without double counting) and the following columns detail the proportion of the different interventions

of the great arteries or double-outlet right ventricles, 98 left-sided obstruction, and four right-sided obstructions; 156 patients received surgical palliation, 80 for left-sided lesions and 65 for right-sided lesions. For 44% of patients who received surgical palliation (n = 69), palliative surgery was the first stage of a curative programme. In addition, four non-emergency interventions (0.7%) were performed during the second day of life, 301 between the second day and the end of the first week (51%), and 279 (47.4%) after the first week of life.

Of the 369 patients who received PGE1 infusion after birth, 361 (98%) underwent surgical or catheter-based interventions before discharge. The eight remaining patients died before intervention – five hypoplastic left heart syndrome, one Ebstein anomaly with pulmonary atresia, one single ventricle with pulmonary atresia, and one common arterial trunk with interrupted aortic arch.

Accuracy of prenatal diagnoses

In some cases, the postnatal diagnosis differed from the prenatal diagnosis. This could result in an urgent neonatal intervention that was not planned before birth. Indeed, we can notice in Table 1 that six patients needed a Rashkind procedure, although this had not been planned prenatally. In our centre, of the 1258 live births delivered locally, we found 133 (10.6%) discordances between prenatal and postnatal diagnoses with potential impact on neonatal or long-term care strategies. Table 3 describes all the cases where the modification of the diagnosis led to an unplanned urgent intervention/PGE1 infusion after birth or an intervention before discharge. Conversely, some errors in the postnatal diagnosis resulted in the cancellation of a planned intervention. In the majority of cases of this latter situation, this cancelled intervention was mostly a prostaglandin infusion – for

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Table 2. Interventions before hospital discharge (after the first 48 hours).

	Patients	Intervention before discharge	Curative catheterisation	Palliative catheterisation	Complete repair	Palliative surgery
CHD at risk for a Rashkind procedure	345	298	0	0	292	6
		86%	0%	0%	85%	2%
CHD with ductal-dependent pulmonary flow	94	70	15	8	0	51
		74%	16%	9%	0%	54%
CHD with potentially ductal-dependent pulmonary flow	163	37	15	4	4	14
		23%	10%	3%	2%	9%
CHD with ductal-dependent systemic flow	66	59	0	0	16	43
		89%	0%	0%	24%	65%
CHD with potentially ductal-dependent systemic flow	300	116	1	0	78	37
		39%	0%	0%	26%	12%
Total anomalous pulmonary venous returns	8	0	0	0	0	0
		0%	0%	0%	0%	0%
Conduction disorders	6	2	0	0	1	1
		33%	0%	0%	17%	17%
CHD with a priori no risk of early intervention	98	7	0	0	3	4
		7%	0%	0%	3%	4%
All	1080	589	31	12	394	156
%		55	3	1	36.5	14

The first column gives the overall rate of intervention for each group of CHD (without double counting) and the following columns detail the proportion of the different interventions.

example, a pulmonary atresia that turned to be a pulmonary stenosis after birth with no need to maintain ductal patency.

Survival

Of the 1080 newborns, 73 (6.7%) died before discharge, including one patient (0.1%) on the first day of life, 28 (2.6%) within the first week of life, and 44 (4%) after the first week of life.

Table 4 describes the survival rates of each group of anticipated risk before discharge from hospital.

Discussion

This cohort is a highly selected series of foetal CHD delivered at our institution. Indeed, the proportion of complex CHD is high and different from the usual distribution of foetal CHD diagnosed in our geographic area.[12] Therefore, our results with regard to the need for urgent intervention cannot be extrapolated to the general population of foetal CHD. Our study was designed to describe the actual need for neonatal interventions or PGE1 infusion after prenatal diagnosis of CHD in a large series of foetuses for which a neonatal programme had been anticipated.

Overall, an early intervention/PGE1 infusion within the first 48 hours was needed in 47% of the cases, with 21.4% of the patients needing surgical or catheter-based interventions. This high proportion of early intervention is due to the referral of all foetuses with CHD at high risk to our institution for perinatal management.[13] In addition, a number of CHD cases without anticipated risk of neonatal intervention (9%) were also delivered in our centre. After exclusion of these CHD cases with a priori no risk for early neonatal intervention, the proportion of early intervention was 51%. Approximately half of the foetuses with CHD who were delivered at our institution did not require urgent intervention, whereas the need for intervention was presented to the parents before birth and this motivated delivery at our site. This first result clearly confirms the fact that prenatal diagnosis may not be sufficiently precise to predict immediate postnatal physiology.

In the group of CHD for which a Rashkind procedure was considered prenatally, the proportion of Rashkind was high in patients with simple transposition of the great arteries (73%), but much lower in patients with transposition of the great arteries and ventricular septal defect (43%) and was only 8% in patients with double-outlet right ventricles with sub-pulmonary ventricular septal defect, who are supposed to have a physiology similar to that of patients with transposition of the great arteries with ventricular septal defect. These results are in line with the proportion of early Rashkind in this defect (9%) reported by Al Soufi and colleagues.[14] These differences between CHD that may have a physiology of transposition of the great arteries after birth raise the

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Table 3. Discordant postnatal diagnoses leading to unexpected interventions before discharge.

Prenatal diagnosis	Expected physiology	Postnatal diagnosis	Unexpected neonatal intervention before discharge
Tricuspid atresia with mild pulmonary stenosis	Potentially ductal-dependent pulmonary flow	Discordant atrioventricular connection with hypoplastic right ventricle and normal ventriculo-arterial connexion	Rashkind procedure
Malalignment with ventricular septal defect	A priori no risk of neonatal intervention	Double-outlet left ventricle with pulmonary stenosis	PGE1, Rashkind procedure and complete surgical repair
Congenitally corrected transposition of the great arteries with hypoplastic right ventricle with risk of coarctation	Potentially ductal-dependent systemic flow	L-looped transposition of the great arteries	Rashkind procedure and complete surgical repair
Interruption of the aortic arch	Ductal-dependent systemic flow	Double-outlet right ventricle with sub-pulmonary ventricular septal defect and pulmonary stenosis	Rashkind procedure
Double-outlet right ventricle "Tetralogy of Fallot type"	Potentially ductal-dependent pulmonary flow	Double-outlet right ventricle with sub-pulmonary ventricular septal defect and pulmonary stenosis	Rashkind procedure
Common arterial trunk	A priori no risk of neonatal intervention	Pulmonary atresia with ventricular septal defect	PGE1, temporary palliative surgery (temporary Blalock–Taussig shunt)
Isolated permimembranous ventricular septal defect	A priori no risk of neonatal intervention	Coarctation with ventricular septal defect	PGE1, temporary palliative surgery (aortic arch repair and pulmonary banding)
Congenitally corrected transposition of the great arteries with ventricular septal defect	A priori no risk of neonatal intervention	Transposition of the great arteries with ventricular septal defect	Rashkind procedure, complete repair
Common arterial trunk	A priori no risk of neonatal intervention	Common arterial trunk with interrupted aortic arch	PGE1, death before surgery
Single ventricle with mitral atresia, no risk of coarctation	A priori no risk of neonatal intervention	Single ventricle with mitral atresia and coarctation	PGE1, palliative surgery (aortic arch repair and pulmonary banding)
Tricuspid atresia, no risk of coarctation	A priori no risk of neonatal intervention	Tricuspid atresia, ventriculo-arterial discordance, coarctation	PGE1, palliative surgery (aortic arch repair and pulmonary banding)
Aortopulmonary window	A priori no risk of neonatal intervention	Aortopulmonary window, VSD, coarctation	PGE1, complete repair

PGE1 = prostaglandin E1; VSD = ventricular septal defect

Table 4. Survival before hospital discharge.

	Death before hospital discharge [n (%)]
CHD at risk for a Rashkind procedure	8 (2.3)
CHD with ductal-dependent pulmonary flow	13 (12.1)
CHD with potentially ductal-dependent pulmonary flow	3 (2.1)
CHD with ductal-dependent systemic flow	25 (39.6)
CHD with potentially ductal-dependent systemic flow	16 (5.2)
Total anomalous pulmonary venous returns	1 (12.5)
Atrio-ventricular block associated with CHD	0 (0)
CHD with a priori no risk of early intervention	7 (6.5)
All	73 (6.7)

question of the need to deliver all these foetuses in tertiary-care centres.

The risk of neonatal rescue surgery for total anomalous pulmonary venous connection is high (50%). It remains very difficult to detect this CHD prenatally and even more difficult to predict venous blockage. Seal et al described 424 cases of total anomalous pulmonary venous connection,[9] and only eight had a prenatal diagnosis. In our local series, only 10 out of 95 patients were diagnosed before birth.[15] Echocardiographic signs leading to referral are limited, and diagnosis is challenging even for expert sonographers.[16] Indeed, all foetuses with a prenatal diagnosis of abnormal pulmonary venous return should be delivered in a centre with cardiac surgery facilities.

The urgent intervention rate for CHD with conduction disorders is low in the first 48 hours of life (17%). Only patients with atrio-ventricular blocks that were poorly tolerated haemodynamically or with a heart rate <50/minute before birth were implanted on an urgent basis. The other patients were implanted before discharge. Jaeggi et al reported poorer outcomes – more foetal death, more foetal hydrops, and more neonatal death – for CHD patients with atrioventricular blocks compared with isolated atrioventricular blocks.[17] Even if the underlying CHD is not at risk of neonatal distress, this group of patients should be closely monitored and a planned delivery at a surgical cardiac centre should be organised.

For CHD ductal-dependent for pulmonary or systemic flow, patients did not require urgent procedures except prostaglandin infusion. Very few patients with hypoplastic left heart syndrome benefited from a Rashkind procedure (4%). Urgent interventions were rarely indicated in this group in our series. In other studies, authors report a higher rate of Rashkind procedures in patients with hypoplastic left heart syndrome[18,19] (between 10 and 15% of patients). This difference is easily explained by the highest trend to choose compassionate care for hypoplastic left heart syndrome patients in our centre. Indeed, restriction of the foramen ovale is considered an important risk factor for mortality after first-stage palliation in neonates.[18] This might have influenced the decision to choose compassionate care for neonates who had this characteristic.

CHD potentially ductal-dependent for systemic flow needed prostaglandin more often (29%) than CHD potentially ductal dependent for pulmonary flow (14%). The need for ductal patency after birth remains very difficult to predict for coarctation of the aorta, as confirmed by the numerous reports on this topic.[20–23] Our sensitivity to predict this risk is close to that of other reports in the literature. As previously reported, left–right asymmetry diagnosed during mid-trimester is more predictive of coarctation than left–right asymmetry diagnosed during the third trimester. A recent study[24] found 45% sensitivity for the prenatal diagnosis of coarctation. The rate increased up to 75% when the diagnosis was made before 28 weeks of gestation. In our practice, we accept a high rate of false-positive cases to avoid misdiagnosed coarctation and the risk of severe neonatal left ventricular dysfunction if the coarctation occurs without close surveillance. This policy also helps us in detecting left heart-associated cardiac anomalies, hard to detect before birth, such as bicuspid aortic valve or mitral anomalies.

In contrast, several recently published studies found antenatal arguments for predicting the need for prostaglandin in CHD with right outflow tract obstruction.[25–27] Quatermain et al, showed that using the direction of the ductal flow is both highly sensitive and highly specific, whereas using pulmonary valve diameter Z-score and pulmonary valve-to-aortic valve diameter ratio is sensitive but poorly specific. Theses markers may help the foetal cardiologist to predict the need for neonatal intervention; however, the availability of a paediatric cardiologist after birth to confirm the diagnosis and to indicate urgent treatment at birth remains necessary.

Although there is no doubt on the need for neonatal life-saving treatments in some CHD, scheduled delivery and in utero transfer in a cardiac centre remain highly controversial. Some teams have

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reported that newborns who are delivered in a local centre have identical outcomes to those who are delivered in a tertiary-care centre.[28] Similarly, other reports have shown that neonates can be delivered safely outside a specialised centre with a low mortality rate.[29] When organising delivery of a foetal CHD case, the potential need for intervention and the type of intervention that might be necessary are crucial, but the site in which delivery should be planned should be chosen according to a variety of factors such as the availability of a paediatric cardiologist on site to confirm the diagnosis, the possibility to perform interventions on site, and the geographical proximity of surgical centres.

It is of note that the cardiac indication to scheduled delivery in a cardiac centre remains a challenging issue. Indeed, delivery in a tertiary-care centre remains indisputable for simple transposition of the great arteries but is questionable for transposition of the great arteries with large ventricular septal defects and double-outlet right ventricles with subpulmonary ventricular septal defect. In utero transfer probably limits morbidity for hypoplastic left heart syndrome with prenatal restrictive foramen ovale, total anomalous pulmonary venous connection, and CHD with atrio-ventricular block if the heart rate is less than 50/min before birth or if the foetus shows signs of poor tolerance (hydrops).[10,30] Conversely, for at least half of the CHD patients in our series, the only intervention performed within the first 48 hours was prostaglandin infusion, which can be performed in every neonatal intensive care unit.

Nevertheless, errors in prenatal diagnosis are an important limitation to indicate a safe delivery outside a specialised centre. Indeed, we have shown that, in rare cases, the postnatal diagnosis may be different from the foetal diagnosis. This may result in an urgent unplanned intervention. In five cases, the modification of the diagnosis led to an urgent atrioseptostomy. Delivery in a cardiac centre allows avoiding haemodynamic compromise by reducing the delay between the diagnosis and the intervention. It is still essential that these newborns be delivered in a centre where a paediatric cardiologist is available at any time to confirm/inform the foetal diagnosis. The rate of concordance between prenatal and postnatal diagnosis is high in our group, but still it can be argued that delivery in a dedicated centre may reduce the risk by allowing unplanned interventions more rapidly.

In addition, more than half of the infants (55%) included in this study underwent a planned intervention before leaving the hospital. For a number of CHD cases, this planned intervention was not needed before the first 48 hours of life, but would have required secondary transfer of the neonate to our centre if the child was born elsewhere. The improvement in perinatal management of complex CHD also has consequences on neurodevelopmental outcomes of newborns with CHD by reducing the time between birth and surgery and avoiding prolonged cyanosis and acidosis.[31,32] Delivery in a cardiac centre may help reduce this delay. It has also been suggested that the transport time between hospitals of newborns with CHD had significant risks of morbidity and additional costs.[33,34] In addition, preservation of the mother and child proximity after birth may have beneficial psychological consequences for both. Finally, eight patients had an unplanned surgical intervention – temporary palliative intervention or complete repair – after correction of the cardiac diagnosis, although not planned prenatally. Early confirmation of the diagnosis is necessary to better plan neonatal non-urgent interventions that have to be performed before discharge.

Our local protocol is to indicate in utero transfer for all CHD except for some very low risk conditions (ventricular septal defect, atrioventricular septal defect). We are aware that this practice is not affordable in all centres in all countries according to economic, geographic, and logistical issues. In the light of these results, we created four levels of risk based on the prenatal physiology and provide recommendations for delivery planning (Table 5). In utero transfer is mandatory for foetuses with transposition of the great arteries, hypoplastic left heart syndrome with restrictive foramen ovale, total anomalous pulmonary venous connection, and CHD with atrioventricular block with heart rate <50 bpm because of high risk of neonatal urgent intervention in this group. We highly recommend transfer of pulmonary and systemic ductal-dependant lesions because of the frequent need for intervention before discharge (74 and 89%) and to avoid risk and costs of postnatal transfer. We highly recommend transfer for

Table 5. Recommendations for delivery planning in a cardiac centre.

Group A: In utero transfer is mandatory
TGA
Atrio-ventricular discordance with ventriculo-arterial concordance
HLHS with restrictive FO
Total anomalous pulmonary venous connection (group 6)
CHD with atrioventricular block with heart rate <50 bpm or hydrops
Group B: In utero transfer is highly recommended
TGA with VSD
DORV with sub-pulmonary VSD
CHD with atrioventricular block with heart rate >50 bpm, no hydrops
All ductal-dependant lesion for systemic or pulmonary flow (group 2 and 4)
Potentially ductal-dependant lesion for systemic flow (group 3)
Group C: In utero transfer is recommended
Potentially ductal-dependant lesion for pulmonary flow (group 5)
Group D: In utero transfer is not recommended
CHD with a priori no risk (group 8)

DORV = double-outlet right ventricle; FO = foramen ovale; TGA = transposition of the great arteries; VSD = ventricular septal defect

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the potentially dependant systemic flow group as rates of neonatal intervention and PGE1 infusion were higher than the group with potentially ductal-dependant pulmonary flow. Furthermore, we think that close echocardiographic monitoring of these patients is required after birth to avoid haemodynamic compromise. We recommend transfer for patients with potentially ductal-dependent pulmonary flow: 12% of these patients needed PGE1 infusion, 23% of them required intervention before discharge, and 2% died before discharge. In addition, a non-negligible part of patients in Table 3 had discordance involving the right ventricular outflow tract. This attitude can potentially be discussed by the local prenatal team according to prenatal markers of risk, known local accuracy rates of foetal cardiac echocardiography, and availability of a paediatric cardiologist in the local centre. Transfer is not recommended for patients with a priori no risk for neonatal intervention; however, we recommend that a paediatric cardiologist should be available for postnatal early echocardiography in the local centre at any time to confirm the diagnosis and anticipate unplanned intervention in case of discordance.

Clearly, patients with potential ductal-dependant flow are more challenging. As we discussed, various recent retrospective articles are available to help the foetal cardiologist to better predict postnatal need for PGE1 infusion.[20–27] Particular attention should be given to evaluating the accuracy of theses markers. With the aim of improving prenatal prediction of neonatal intervention before discharge, further prospective studies should be conducted. In addition, new imaging tools, such as three dimensional ultrasound and foetal cardiac MRI 35–38 can be used to add value in the diagnosis of complex outflow tract anatomy.

Conclusion

In this audit of a large cohort of newborns in a reference cardiac centre, the proportion of patients who benefited from an intervention in the first 48 hours of life was 47%, and the proportion of patients who underwent interventions before discharge was 55%. We confirmed that scheduled delivery and in utero transfer should not be extended generally to all CHD patients, but should remain mandatory for transposition of the great arteries, hypoplastic left heart syndrome with restrictive foramen ovale, total anomalous pulmonary venous connection, and CHD with atrioventricular block with heart rate <50 bpm and highly recommended for CHD with ductal-dependant systemic and pulmonary flow and potentially ductal-dependant systemic flow. Errors in prenatal diagnosis can lead to unplanned interventions. To reduce this risk, improving diagnosis concordance by training foetal echocardiographers and developing new imaging tools should be a priority.

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Conflicts of Interest

None.

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