Published in final edited form as:

Pediatrics. 2009 September ; 124(3): e510–e518. doi:10.1542/peds.2008-2014.

In Utero Valvuloplasty for Pulmonary Atresia With Hypoplastic Right Ventricle: Techniques and Outcomes

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Abstract

BACKGROUND—Prenatal intervention for fetuses with pulmonary atresia with an intact ventricular septum (PA/IVS) has the potential to alter right heart physiologic features in utero, facilitating right heart growth and improving the prospect of a biventricular outcome after birth.

METHODS—Since 2002, we have considered prenatal intervention for fetal PA/IVS in patients with (1) membranous pulmonary atresia, with identifiable pulmonary valve (PV) leaflets or membrane; (2) an intact or highly restrictive ventricular septum; and (3) right heart hypoplasia, with a tricuspid valve annulus z score of -2 or below and an identifiable but small right ventricle. Intervention was performed through direct cardiac puncture under ultrasound guidance, with percutaneous access or access through a limited laparotomy.

RESULTS—Ten fetuses underwent attempted balloon dilation of the PV in utero. The first 4 procedures were technically unsuccessful, and the most-recent 6 were technically successful. Compared with control fetuses with PA/IVS who did not undergo prenatal intervention and had univentricular outcomes after birth, the tricuspid valve annulus, right ventricle length, and PV annulus grew significantly more from midgestation to late gestation in the 6 fetuses who underwent successful interventions.

Financial Disclosure: The authors have indicated they have no financial relationships relevant to this article to disclose.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

CONCLUSIONS—In utero perforation and dilation of the PV in midgestation fetuses with PA/IVS is technically feasible and may be associated with improved right heart growth and postnatal outcomes for fetuses with moderate right heart hypoplasia in midgestation. There is an important learning curve for this procedure, and much remains to be learned about the selection of appropriate fetuses for prenatal intervention.

Keywords

congenital heart disease; fetal ultrasonography; heart and blood vessels; prenatal diagnosis

Pulmonary atresia with an intact ventricular septum (PA/IVS) is associated with variable hypoplasia of the right ventricle (RV), tricuspid valve (TV), and RV outflow tract. At the most-severe end of the spectrum, there is fibromuscular atresia of the RV outflow tract, severe RV and TV hypoplasia, and major abnormalities of the coronary arteries. At the more-favorable end of the spectrum, there is membranous atresia of the pulmonary valve (PV), a relatively normal-sized RV and TV, and no gross abnormalities of the coronary arterial system. Postnatal series have demonstrated that coronary anatomic features and RV and TV sizes are the most important determinants of univentricular versus biventricular outcomes.^{1–8}

In 2000, we initiated a program for prenatal cardiac intervention in fetuses with aortic stenosis with evolving hypoplastic left heart syndrome, established hypoplastic left heart syndrome with an intact or highly restrictive atrial septum, or PA/IVS.^{9–13} We hypothesized that in utero perforation and dilation of the PV in fetuses with PA/IVS would allow antegrade blood flow through the RV, potentially stimulating right heart growth and function and improving the chances of postnatal survival with a biventricular circulation. Previous case reports demonstrated the feasibility of fetal intervention for 3 fetuses with valvar pulmonary stenosis or PA/IVS.^{14–16} The aim of this study was to describe our experience with fetal intervention for PA/IVS, with a focus on technical aspects of fetal PV perforation and balloon dilation, growth of right heart structures, and postnatal outcomes.

METHODS

Patients

This study included all fetuses who underwent attempted in utero balloon dilation of the PV at our center. Patients were considered for intervention after prenatal diagnosis of PA/IVS at our program or referral from another center. Patients were offered intervention only if the following were present: (1) membranous pulmonary atresia, with identifiable PV leaflets or membrane, no systolic opening, and no color Doppler ultrasound flow across the PV; (2) an intact or highly restrictive ventricular septum; and (3) right heart hypoplasia, with a TV annulus z score below -2 and an identifiable but qualitatively small RV.

Interventions were performed under innovative therapy approval by the institutional review boards of Children's Hospital Boston and the Brigham and Women's Hospital. The parents were informed about the known maternal and fetal risks and potential benefits, on the basis

of our experience with other fetal interventions, and provided written informed consent.^{9,11,13}

Cardiac Measurements

Cardiac measurements were recorded from complete fetal echocardiograms obtained the day before fetal intervention and in late gestation. The TV annulus was measured at the hinge points in diastole, at the time of maximal opening. The PV annulus was measured at the hinge points in systole. RV length was measured at end-diastole from the TV annulus to the RV apex. Measurements were expressed as absolute dimensions and *z* scores, according to gestational age, that were based on unpublished normative data obtained at our institution from ~200 fetuses (the number varied, depending on the structure) without congenital heart disease. The *z* score equations used for this study were based in part on recently acquired normative data and differed from those used in a previous report from our center.¹⁷

Technique for PV Perforation and Dilation

Intervention was performed under maternal general anesthesia with inhalational agents, to promote uterine relaxation and to enable fetal manipulation for positioning. The fetus was premedicated with intramuscularly administered fentanyl, atropine, and pancuronium. With ultrasound visualization, manual version was performed to optimize the fetal position. If the optimal position could not be achieved or imaging was inadequate, then a limited maternal laparotomy without uterine exteriorization or incision was performed. The RV outflow tract was accessed through direct puncture, by using a 19-gauge ultra-thin-walled cannula (Fig 1). The trajectory of access was through a subcostal approach on the fetal chest or through an intercostal space adjacent to the sternum. With the cannula tip in the RV outflow tract, the atretic PV was perforated with the stylet of a 19-gauge cannula or with an ultrasharp, 22-gauge, Chiba needle introduced through the cannula. A 0.014-inch, floppy-tipped guidewire was positioned in a branch pulmonary artery or the ductus arteriosus, and a coronary angioplasty balloon was inflated across the valve. After the final balloon deflation, the wire, balloon, and cannula were removed.

Data Analyses

Outcomes included procedural success (inflation of a balloon across the PV with unequivocal antegrade flow, as detected with color Doppler ultrasonography), pregnancy outcome, growth of right heart structures, and postnatal outcome. A biventricular circulation was defined as a circulation in which the RV was the only source of blood flow to the pulmonary circulation, with systemic arterial oxygen saturation of >90% with room air, with or without interatrial communication.

Because of the small number of fetuses who underwent interventions, results are presented in descriptive form. For comparison, measurements of right heart structures from 15 control fetuses with PA/IVS who did not undergo prenatal intervention and had either a biventricular or functionally univentricular outcome are presented. The *z* scores of these right heart structures and changes from midgestation to late gestation were compared between control fetuses who had univentricular circulations after birth, fetuses who had

biventricular circulations after birth, and fetuses who underwent successful interventions, with 1-way analysis of variance and posthoc testing with the Bonferroni method.

RESULTS

Patients

From July 2002 (first procedure) through February 2008, pulmonary valvuloplasty was scheduled and maternal anesthesia was administered for 11 fetuses with PA/IVS. In 1 of these cases, the procedure was not attempted because of maternal considerations (see below); therefore, valvuloplasty was attempted for 10 fetuses, at a median gestational age of 24 weeks (range: 21–28 weeks). Five fetuses were male. Three fetuses received initial diagnoses at our center or within our usual geographic referral base, whereas 8 were referred from other centers.

Procedural Outcomes

Overall Results—As detailed in Table 1, the first 4 attempted pulmonary valvuloplasty procedures were technically unsuccessful, and the subsequent 6 were successful. In another case, the mother was anesthetized and attempts to position the fetuses with manual version were performed. At that point, maternal arrhythmia was suspected and the procedure was cancelled pending evaluation, which yielded normal results. The procedure was rescheduled for the following day, but the mother experienced premature rupture of membranes. Unless otherwise specified, presented data refer to the 10 fetuses for whom cardiac puncture and PV dilation were attempted.

Fetuses who underwent successful interventions were older (range: 23–28 weeks; median: 26 weeks) than were those who did not (range: 21–24 weeks; median: 23 weeks), but this difference was not statistically significant. A limited laparotomy was performed in 6 procedures, 3 of which were unsuccessful and 3 successful. Fetal hemodynamic instability (bradycardia and left ventricular dysfunction) complicated 6 cases (4 unsuccessful and 2 successful) but resolved with treatment in all cases.¹³

Technically Unsuccessful Procedures—In the first 2 procedures, the 19-gauge cannula was introduced into the RV outflow tract but the guidewire could not be advanced across the PV and valve perforation was not attempted. Both procedures were discontinued after treatment of fetal hemodynamic instability. In the third procedure, the cannula could not be positioned in the RV outflow tract because of the fetal position; because the mother declined laparotomy, the intervention was abandoned. In the fourth procedure, a Chiba needle was used to perforate the atretic PV and a wire was advanced into the pulmonary artery. During exchange of the needle for the balloon catheter, fetal instability developed and the procedure was discontinued. Although there was a small color Doppler ultrasound jet across the PV after the procedure, the procedure was considered a technical failure.

Technically Successful Procedures—In all 6 subsequent procedures, the PV was dilated successfully. In 5 of those procedures, the PV was perforated with a Chiba needle. In the other procedure, the sharp-tipped stylet of a 19-gauge cannula was introduced across the

valve directly. Balloons (nominal diameter: 2.5–2.75 mm) were inflated to pressures yielding balloon: annulus diameter ratio of 1.2:1 to 1.3:1.

Pregnancy Outcomes

Nine fetuses progressed to term delivery (>36 weeks). One pregnancy was terminated after an unsuccessful intervention (patient 3). For the patient who did not undergo intervention because of suspected maternal arrhythmia, amniotic fluid volume stabilized and the pregnancy progressed to term with no further complications or attempts at fetal intervention.

Growth of Right Heart Structures

Echocardiographic Findings—Baseline and follow-up echocardiographic data are presented in Table 2 and depicted in Fig 2. Absolute dimensions of the TV, RV, and PV differed ~10% between fetuses who underwent technically successful versus unsuccessful interventions.

Technically Unsuccessful Procedures—Follow-up prenatal echocardiographic data were available for 3 of the 4 fetuses who underwent unsuccessful valvuloplasty; in the fourth case, the parents chose to terminate the pregnancy. For those fetuses, TV, RV, and PV *z* scores generally decreased (Fig 2). In 2 cases, the follow-up study was performed only 2 to 3 weeks after intervention; later follow-up echocardiographic studies were performed but could not be obtained.

Technically Successful Procedures—Follow-up fetal echocardiograms were reviewed for all 6 of the fetuses who underwent successful interventions. For all or nearly all of those fetuses, TV, RV, and PV *z* scores increased from before the intervention to the latest prenatal echocardiogram (Table 2 and Fig 2). For 5 fetuses, antegrade pulmonary outflow was maintained throughout the remainder of pregnancy; for the other fetus, no antegrade flow was seen in late-gestation studies.

Postnatal Outcomes

Overall Results—All 9 live-born patients underwent neonatal interventions, including balloon pulmonary valvuloplasty in 6 cases and surgical procedures in 8 cases, and were alive at follow-up times ranging from 0.5 to 5.8 years of age.

Technically Unsuccessful Procedures—For the first 2 live-born patients, PV atresia was confirmed at birth. Both patients underwent neonatal intervention with RV outflow tract augmentation and a systemic-to-pulmonary artery shunt, followed by bidirectional Glenn and Fontan procedures, and are alive at 3.3 and 5.8 years of age. The third live-born fetus, for whom the valve was crossed with a needle but not dilated with a balloon, the PV was atretic at birth. The patient underwent neonatal balloon pulmonary valvuloplasty, followed by a RV outflow tract patch, a systemic-to-pulmonary artery shunt, and then a bidirectional Glenn procedure. The patient for whom the procedure was abandoned before intervention is alive after neonatal, transcatheter, PV perforation and dilation, with an intermediate circulation.

Technically Successful Procedures—For 5 of the 6 patients who were born after successful prenatal interventions, there was antegrade pulmonary outflow on the first neonatal echocardiogram. At the time of this writing, the first 4 of those patients are alive at 2.2 to 3.0 years of age, with biventricular circulation, after neonatal RV outflow tract augmentation and/or systemic-to-pulmonary artery shunting, followed by closure of the atrial septal defect and the systemic-to-pulmonary artery shunt if present. The fifth patient who underwent a successful procedure had severe RV hypoplasia and a RV-dependent coronary circulation and underwent only a systemic-to-pulmonary artery shunt to provide pulmonary blood flow. That patient had the smallest TV z score in midgestation and had only modest flow across the valve after prenatal intervention; at 1.5 years of age, the patient has a bidirectional Glenn circulation, with a plan to continue univentricular management. The patient who most recently underwent a successful procedure is alive at 6 months of age after undergoing RV outflow tract augmentation and a systemic-to-pulmonary artery shunt as a newborn. The RV size is almost normal, and right heart anatomic features and function are favorable for biventricular repair, which is planned within the next few months.

Comparison With Control Fetuses

Right heart anatomic dimensions for 15 control fetuses with PA/IVS who did not undergo prenatal intervention are depicted in Fig 2, along with those for fetuses who underwent attempted pulmonary valvuloplasty. In the comparison group, 6 fetuses had biventricular postnatal outcomes and 9 had functionally univentricular outcomes. For control fetuses who proceeded to univentricular outcomes, TV, RV, and PV z scores were lower in the initial echocardiograms, compared with fetuses with biventricular outcomes, and generally there were minimal increases in absolute TV, RV, and PV dimensions during gestation, with concomitant decreases in z scores. In contrast, for control fetuses with biventricular outcomes, absolute dimensions tended to increase and z scores remained essentially the same.

Midgestation z scores tended to be lower for fetuses who underwent successful prenatal interventions than for control fetuses with biventricular outcomes, but the growth trajectories over the course of gestation were similar, with minimal changes or slight increases in z scores. Midgestation z scores for TV diameter, RV length, and PV diameter did not differ between control fetuses with univentricular postnatal outcomes and fetuses who underwent successful prenatal interventions. However, there were significant differences between control fetuses with univentricular outcomes and fetuses who underwent technically successful interventions with respect to late-gestation z scores and changes in z scores from midgestation (before intervention) to late gestation (after intervention) (Table 3).

DISCUSSION

Feasibility and Outcomes

We have shown that prenatal PV perforation and dilation can be performed successfully in fetuses in midgestation, with maintenance of valvar patency throughout gestation and continued growth of right heart structures. Because of the small numbers and limited follow-

up data on fetuses who underwent unsuccessful procedures, the growth trajectory of the TV, RV, and PV could not be compared for fetuses who underwent successful versus unsuccessful interventions. However, when fetuses who underwent successful interventions were compared with untreated control fetuses with PA/IVS who proceeded to univentricular postnatal outcomes, right heart structures grew significantly more from midgestation to late gestation in fetuses who underwent intervention. Although this is a small series from which conclusions cannot be drawn, fetal pulmonary valvuloplasty seems to alter the in utero natural history of PA/IVS. Additional experience will be necessary to substantiate these preliminary findings.

Of 6 fetuses who underwent successful prenatal interventions, the first 4 are alive with biventricular circulations, whereas the fifth has a very small RV with a RV-dependent coronary circulation and the sixth has an intermediate palliative circulation with favorable RV size and function for biventricular repair. In contrast, of the 3 patients who underwent technically unsuccessful interventions and progressed to term delivery, 2 have functionally univentricular circulations and 1 has an intermediate circulation. Although these findings are encouraging, there are too few patients for determination of whether prenatal pulmonary valvuloplasty increases the likelihood of a biventricular circulation after birth or whether a certain age or right heart size range is most likely to benefit.

Technical Considerations

The geometry of the RV outflow tract in a hypoplastic RV, with a narrow, short, curved segment below the valve, makes prenatal pulmonary valvuloplasty a technically challenging procedure. It is necessary first to enter the RV outflow tract with the right trajectory and then to perforate the atretic valve. As reported previously, the high incidence of fetal hemodynamic instability during attempted ventricular access increases the complexity. The fact that our first 4 attempts failed and our subsequent 6 procedures succeeded indicates a steep learning curve for the procedure. Although every case is different, we suspect that placement of a 19-gauge cannula in the RV outflow tract, followed by perforation of the valve with a 22-gauge Chiba needle, is the most-reliable technique for opening the valve. It may be important that the first 4 procedures were in fetuses at 24 weeks of gestation, whereas 4 of the 6 successful procedures were in older fetuses, but the absolute sizes of right heart structures were similar in the 2 groups.

Patient Selection

The underlying objectives of prenatal intervention for PA/IVS are to promote right heart growth and functional development and to increase the chances of postnatal survival with a biventricular circulation. To this end, identification of potential candidates should be based on a combination of factors, including (1) the likelihood of progression to a univentricular circulation after birth without fetal intervention, (2) the possibility of altering that trajectory through promotion of prenatal right heart growth, and (3) the likelihood of technical success. From the perspective of patient selection for prenatal intervention, there are 3 basic categories into which fetuses with PA/IVS fall. Fetuses with fibromuscular atresia of the outflow tract are not good candidates, because they seldom have an identifiable PV to perforate and they are more likely to have coronary anomalies and severe RV hypoplasia

and thus to be born with a functionally univentricular circulation regardless of intervention. At the other end of the spectrum are fetuses with a normal-sized RV, for whom there is a high likelihood of achieving a biventricular circulation with 1 postnatal procedure, without fetal intervention. For this group, there is little foreseeable benefit to prenatal pulmonary valvuloplasty. Between these extremes are fetuses with an identifiable but atretic PV, a patent subvalvar RV outflow tract, and variable right heart hypoplasia. Some of those fetuses might achieve a biventricular circulation with multiple postnatal procedures, whereas others might undergo multiple procedures and still have a univentricular circulation. It is this group that includes the most-reasonable candidates for prenatal intervention, that is, fetuses for whom improved right heart growth may make the difference between a univentricular circulation and a biventricular circulation.

There is limited information about prenatal predictors of postnatal outcomes in fetuses with PA/IVS.¹⁷ Both anatomic and physiologic characteristics are likely to be important, but many patients are in the middle of the severity spectrum, and postnatal management choices almost certainly play an important role regarding outcomes for some patients. In studies of newborns with PA/IVS, TV *z* scores below -3 at birth were predictive of failure to achieve a biventricular circulation. Similarly, we found previously that fetal TV *z* scores below -3 in midgestation were associated with univentricular outcomes.¹⁷ Much remains to be learned regarding the appropriate selection of fetuses with PA/IVS for prenatal intervention.

Limitations

This study is limited by its small size and nonrandomized design. In addition, because many of our patients were referred from other centers, follow-up data were sometimes limited, and decisions about postnatal management likely varied according to institutional practice.

CONCLUSIONS

Our initial results are promising, but fetal intervention for PA/IVS remains an experimental therapy. As we gain experience, it will be necessary to compare the outcomes of this approach with those of postnatal transcatheter and surgical interventions that are currently the standard of care. The risk to the fetus is not small, and the risk/benefit balance must be clear before prenatal intervention becomes accepted therapy.

Acknowledgments

This work was supported by the National Institutes of Health under award number: T32HL007572.

This study was supported by contributions from the Kenrose Kitchen Table Foundation.

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FIGURE 1.

Echocardiographic images obtained during the intervention for patient 7. A, This 4-chamber view demonstrates a hypoplastic RV (arrow). B, In this oblique projection, the 19-gauge cannula can be seen passing through the uterus, amniotic cavity, and chest wall of the fetus and approaching the RV outflow tract (arrow). C, This short-axis image demonstrates the tip of the Chiba needle in the pulmonary artery (arrow). D, After successful valvuloplasty, color Doppler ultrasound flow imaging demonstrates an antegrade jet of flow across the patent PV (arrow).

FIGURE 2.

Graphs depicting TV annulus diameter (A), RV length (B), and PV annulus diameter (C) at the time of intervention and at the last follow-up fetal echocardiogram. Data from fetuses who underwent technically successful prenatal interventions are indicated by the red squares and lines, whereas data from those who underwent unsuccessful interventions are indicated by the orange squares and lines. Fetuses who did not undergo prenatal intervention are depicted for comparison; the green circles and lines indicate data from fetuses who had functionally univentricular outcomes after birth ($n = 9$), and the blue circles and lines indicate data from fetuses who had biventricular outcomes ($n = 6$). The black lines indicate z scores, as specified.

TABLE 1

Details of Prenatal Pulmonary Valvuloplasty

<u>Patient No.</u>	<u>EGA, wk</u>	<u>Laparotomy Performed</u>	<u>Successful Introduction of Cannula Into RVOT</u>	<u>Successful Perforation of PV</u>	<u>Successful Balloon Dilation of PV</u>	<u>Antegrade Flow Present After Procedure</u>	<u>Treated for Hemodynamic Instability</u>
1	24	Yes	Yes	No	No	No	Yes
2	22	Yes	Yes	No	No	No	Yes
3	21	No	No	No	No	No	Yes
4	24	Yes	Yes	Yes	No	Yes (+)	Yes
5	23	No	Yes	No	Yes	Yes (+++)	Yes
6	27	Yes	Yes	Yes	Yes	Yes (+++)	Yes
7	28	No	Yes	Yes	Yes	Yes (++)	No
8	24	Yes	Yes	Yes	Yes	Yes (+++)	No
9	26	Yes	Yes	Yes	Yes	Yes (++)	No
10	26	No	Yes	Yes	Yes	Yes (++)	No

EGA indicates estimated gestational age; RVOT, right ventricular outflow tract.

TABLE 2
Echocardiographic Data Before and After Attempted Prenatal Pulmonary Valvuloplasty

Patient No.	EGA, wk	TV Annulus Diameter, cm	TV Annulus z Score	RV Length, cm	RV Length z Score	PV Annulus Diameter, cm	PV Annulus z Score
<u>Technically unsuccessful</u>							
1	Baseline	23.7	0.46	0.93	-3.3	0.27	-4.0
	Follow-up	26	0.45	1.2	-2.7	0.3	-4.1
2	Baseline	22.3	0.35	0.96	-2.6	0.24	-4.0
	Follow-up	36	0.46	1.07	-5.5	0.3	-6.0
3	Baseline	21.1	0.36	1.57	1.4	0.37	-0.8
	Follow-up	NA					
4	Baseline	23.4	0.43	1.07	-2.4	0.3	-3.3
	Follow-up	27.2	0.49	1.2	-3.1	0.3	-4.4
<u>Technically successful</u>							
5	Baseline	23	0.45	1.2	-1.6	0.41	-1.1
	Follow-up	34.9	0.8	1.87	-2.6	0.64	-2.1
6	Baseline	27.4	0.59	1.2	-3.2	0.36	-3.6
	Follow-up	35.5	0.95	1.8	-3.0	0.6	-2.7
7	Baseline	28.3	0.55	1.17	-3.5	0.32	-4.4
	Follow-up	35	0.82	2.12	-1.8	0.47	-4.0
8	Baseline	23.9	0.37	0.82	-3.9	0.2	-5.3
	Follow-up	35.1	0.81	2.03	-2.1	0.41	-4.7
9	Baseline	25.9	0.37	0.96	-3.8	0.22	-5.4
	Follow-up	37	0.6	1.56	-4.1	0.53	-3.8

<u>Patient No.</u>	<u>EGA, wk</u>	<u>TV Annulus Diameter, cm</u>	<u>TV Annulus z Score</u>	<u>RV Length, cm</u>	<u>RV Length z Score</u>	<u>PV Annulus Diameter, cm</u>	<u>PV Annulus z Score</u>
10	Baseline	26.1	0.4	1.22	-2.7	0.3	-4.2
	Follow-up	35.7	0.97	2.2	-1.7	0.6	-2.8

EGA indicates estimated gestational age; N/A, not applicable

TABLE 3
Right Heart z Scores for Fetuses Who Underwent Successful Prenatal Interventions and Control Fetuses

Variable	Technically Successful Intervention (N = 6)	No Prenatal Intervention, Biventricular Outcome (N = 6)	No Prenatal Intervention, Univentricular Outcome (N = 9)
Gestational age, mean ± SD, wk			
Before intervention (midgestation)	25.7 ± 2.0 ^a	23.1 ± 1.6	21.2 ± 3.2
After intervention (late gestation)	35.5 ± 0.8 ^a	33.2 ± 2.2	31.3 ± 3.0
Time between studies, mean ± SD, wk	9.8 ± 2.0	10.7 ± 1.1	9.7 ± 3.0
TV diameter z score, mean ± SD			
Before intervention (midgestation)	-3.1 ± 0.8	-1.4 ± 1.5 ^b	-3.5 ± 1.0
After intervention (late gestation)	-2.2 ± 1.0 ^a	-2.0 ± 2.0 ^a	-4.8 ± 0.4
Change from midgestation to late gestation	+0.8 ± 0.9 ^a	-0.6 ± 1.9	-1.3 ± 1.0
RV length z score, mean ± SD			
Before intervention (midgestation)	-3.1 ± 0.9	-1.9 ± 1.0 ^c	-3.1 ± 1.2
After intervention (late gestation)	-2.5 ± 0.9 ^b	-3.5 ± 0.8	-4.2 ± 1.2
Change from midgestation to late gestation	+0.6 ± 1.1 ^{b,d}	-1.8 ± 1.0	-1.2 ± 1.0
PV diameter z score, mean ± SD			
Before intervention (midgestation)	-4.0 ± 1.6	-2.0 ± 1.5 ^c	-4.4 ± 1.6
After intervention (late gestation)	-3.3 ± 1.1 ^b	-3.4 ± 1.6 ^b	-5.1 ± 0.7
Change from midgestation to late gestation	+0.7 ± 1.0 ^c	-1.4 ± 2.2	-1.2 ± 1.3

^aP .01, compared with no prenatal intervention, univentricular outcome.

^bP .05, compared with no prenatal intervention, univentricular outcome.

^cP .1, compared with no prenatal intervention, univentricular outcome.

^dP .01, compared with no prenatal intervention, biventricular outcome.