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Fetal interventions in congenital heart disease

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Fetal Interventions – Aims & Indications

- Aortic stenosis with evolving HLHS
  - Maintain a biventricular circulation
- HLHS with intact or restrictive atrial septum
  - Improve postnatal survival
- Pulmonary atresia with intact ventricular septum
  - Biventricular circulation

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Background

- Fetuses with critical aortic stenosis may progress to HLHS
- High pressure LV may impair RV filling and promote hydrops
- Predicting which fetuses with AS will develop HLHS is essential to optimize patient selection for fetal intervention

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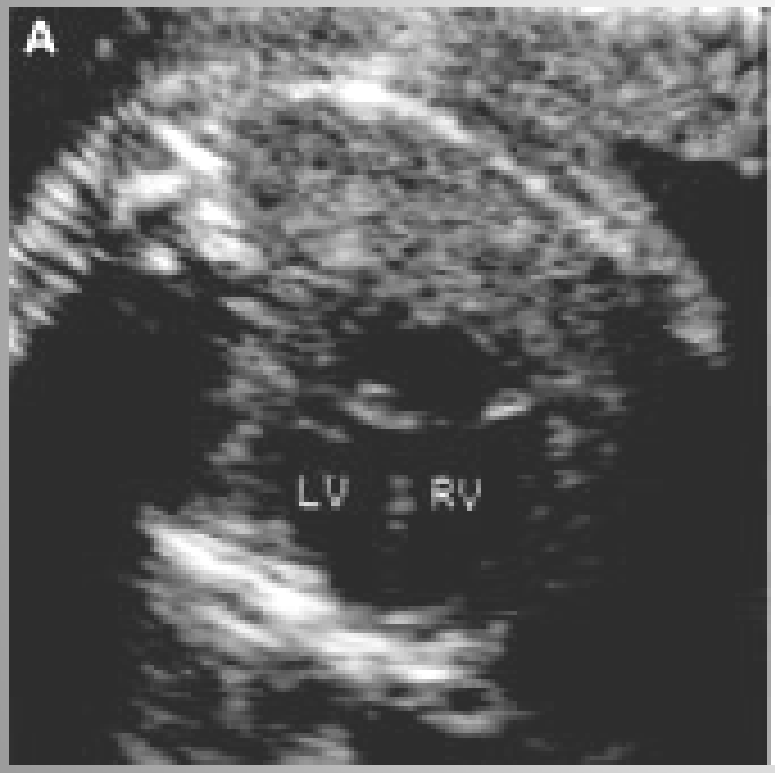
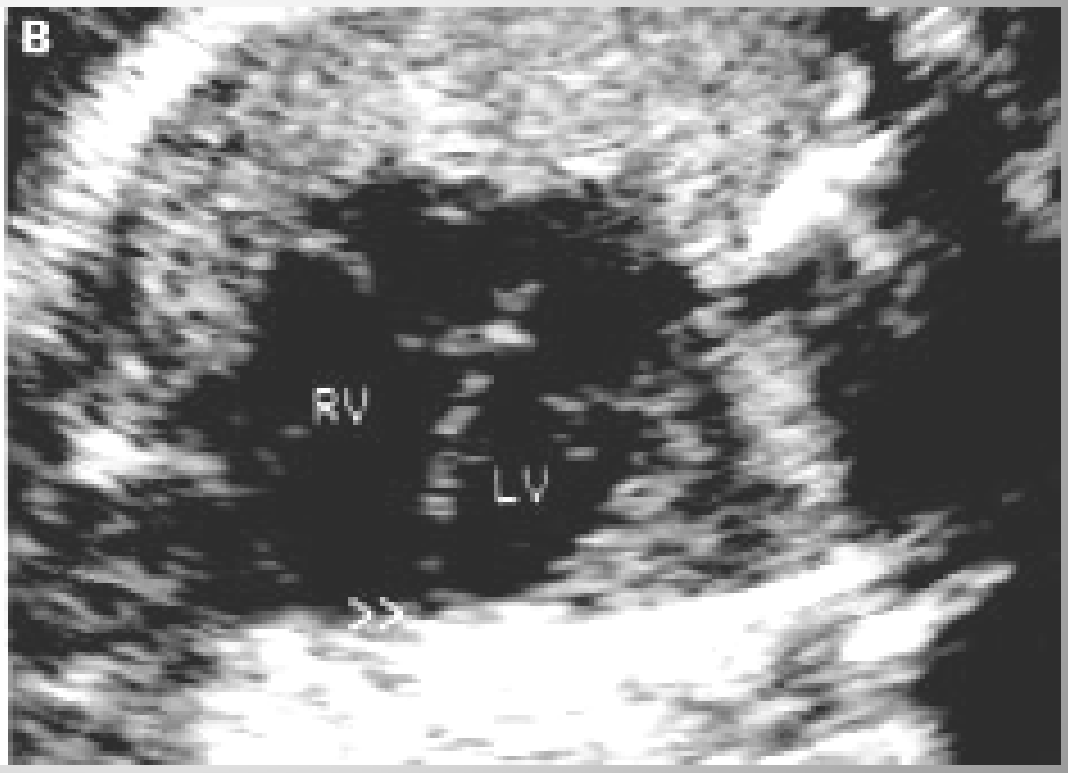
Progression of aortic stenosis to HLH



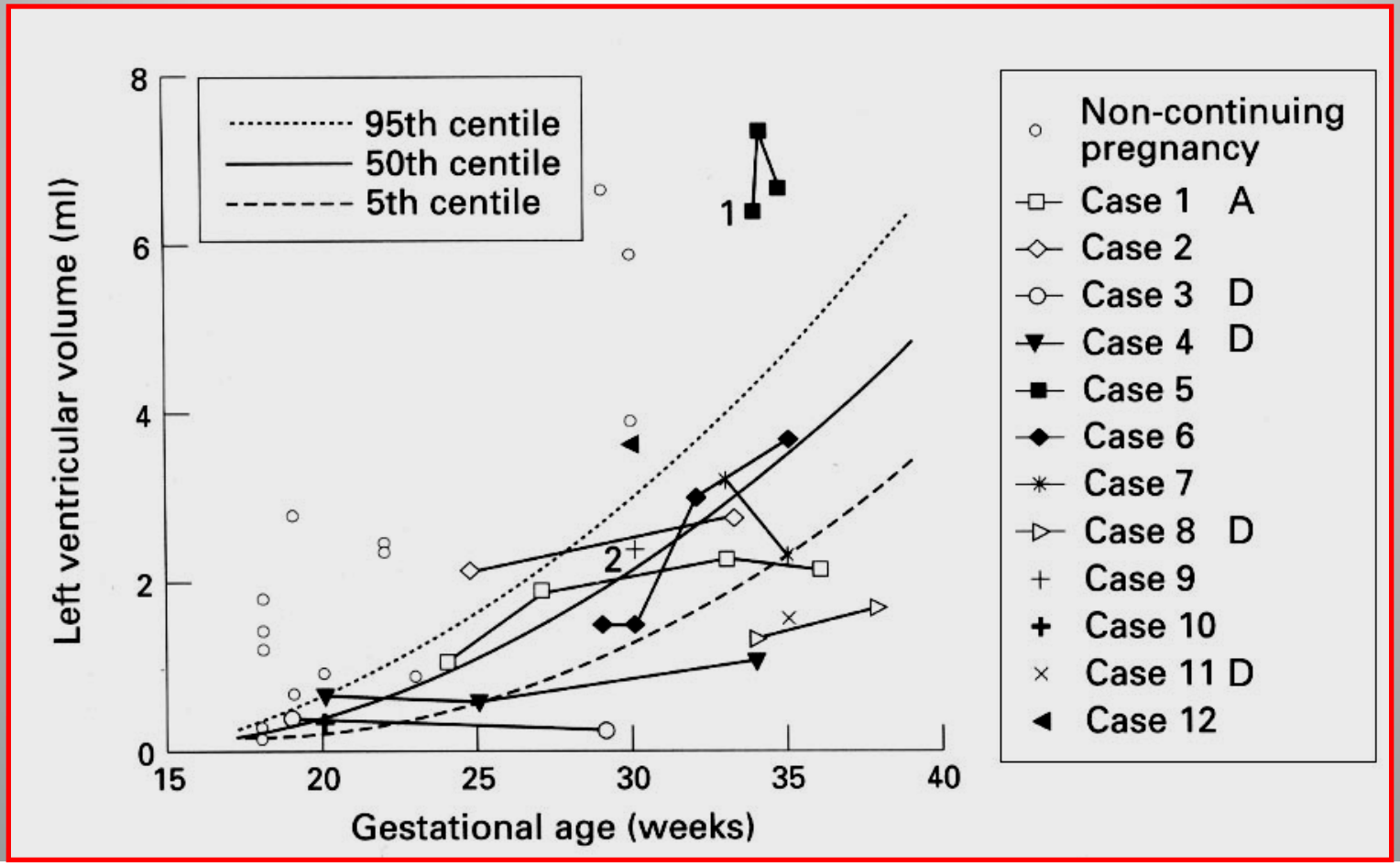


24 weeks

33 weeks

Natural history and outcome of aortic stenosis diagnosed prenatally

John M Simpson, Gurleen K Sharland



Aortic stenosis progressing to HLHS

- LV may be normal sized or dilated
- Severe aortic stenosis
- Severe LV dysfunction
- Reversal of normal fetal flow patterns across the PFO and aortic arch
- Increased endo-myocardial echogenicity
- LV growth stops on serial echocardiograms

Development of HLHS

- Only a small subset of HLHS patients, those with patency (ie, not atresia) of the mitral and aortic valves and with only mild hypoplasia of the left ventricle, may be amenable to a 2-ventricle repair
- In some cases, HLHS may be the consequence of abnormal myocyte proliferation, despite normal antegrade flow to the left ventricle

Progression of fetal aortic stenosis

- Fetuses with AS and evolving HLHS
  - invariably demonstrate reversed blood flow in the TAA
  - left-to-right flow across the foramen ovale
  - monophasic MV inflow
  - moderate-to-severe LV dysfunction in midgestation
- These findings may:
  - aid in parental counselling about postnatal outcome
  - be useful for identification of appropriate candidates for fetal aortic valvuloplasty to prevent progression of AS to HLHS

Characteristics of evolution to HLHS

Demographic, Anatomic, and Physiological Data at Diagnosis and Late Gestation in Fetuses With AS That Evolved to HLHS and Those Maintaining a Biventricular Circulation at Birth

	HLHS (n=17)		Biventricular Circulation (n=6)	
Variable	Diagnosis	Late Gestation	Diagnosis	Late Gestation
Gestational age, wk	22.4±4.1	32.4±2.8	23.2±3.8	34.7±2.2
LV length Z-score	1.1±1.9	−3.4±2.1‡	0.7±1.0	−0.2±0.9§
MV diameter Z-score	−1.0±0.9	−4.3±1.3‡	−0.8±1.2	−1.9±1.2§‖
AoV diameter Z-score	−2.4±1.0	−4.6±0.9‡	−2.0±2.5	−3.2±0.8§‖
AAo diameter Z-score	−0.4±1.9	−2.1±2.9‡	−0.4±2.1	1.7±3.9§
RV length Z-score	0.9±1.0	0.7±1.3	−0.1±1.3	−0.3±0.9
TV diameter Z-score	1.5±1.5	1.9±0.8	0.5±1.8	1.6±1.6
PV diameter Z-score	1.0±1.1	2.0±1.6	0.3±1.3	1.7±2.0
Retrograde TAA flow	17/17 (100)*	14/14 (100)*	0/6 (0)†‡	0/6 (0)†§
Left-to-right FO flow	15/17 (88)*	14/14 (100)*	1/6 (17)†‡	1/5 (20)†§
Monophasic MV inflow	10/11 (91)*	8/8 (100)*	0/4 (0)†‡	0/2 (0)†§
Moderate to severe LV dysfunction	16/17 (94)*	14/14 (100)*	0/6 (0)†‡	1/6 (17)†§

Tworetzky et al, 2006

Aims of fetal cardiac interventions

1) Promote ventricular growth and function
   - Univentricular ➔ Biventricular circulation
   - Aortic stenosis with evolving HLHS
   - Pulmonary stenosis or atresia and evolving HRHS

2) Improve survival
   - HLHS with intact atrial septum
   - Salvage procedures (e.g. hydrops)

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Allan, Sharland, Tynan, 1989

The natural history of the hypoplastic left heart syndrome.

Allan LD, Sharland G, Tynan MJ.

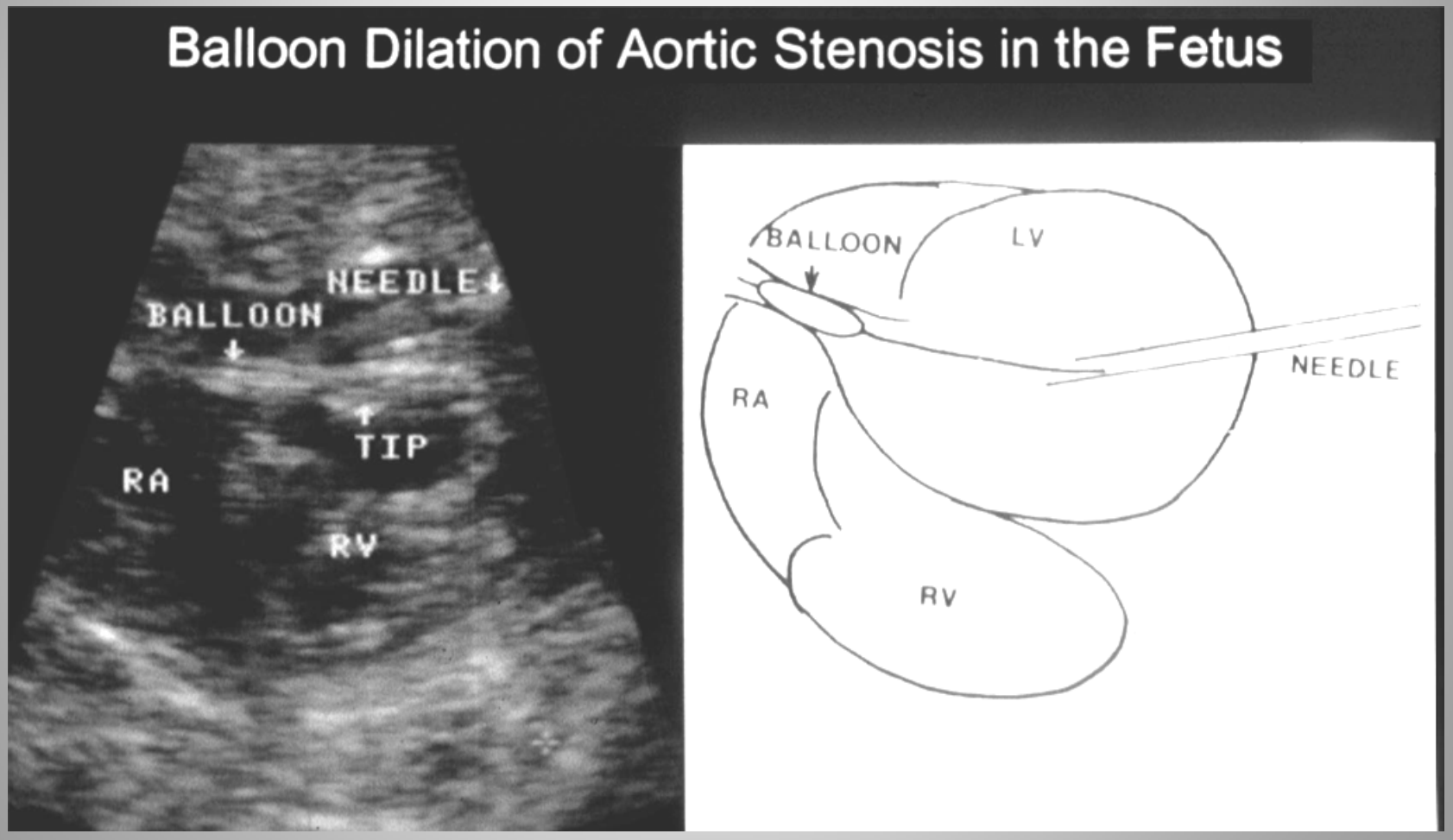
Department of Perinatal, Guy's Hospital, London, U.K.

In a fetus, examined initially at 22 weeks gestation, we identified the echocardiographic features of a dilated, hypertrophied and poorly contracting left ventricle. The presumptive diagnosis was critical aortic stenosis. Subsequent scans at 32 weeks and at term showed that the left ventricle had not grown since the first study such that the left ventricle had developed the appearance of a hypoplastic and densely echogenic chamber. Thus, in some forms of the hypoplastic left heart syndrome, the left ventricle can be of normal size or even dilated in early pregnancy. This may mean that the more subtle sign of poor left ventricular contraction could be overlooked in a routine four-chamber view obstetric scan.

Balloon dilatation of the aortic valve in the fetus: a report of two cases.

Maxwell D, Allan, LD, Tynan M, Br Heart J. 1991 May;65(5):256-8.

Fetal Intervention - 1990s



Tynan, Guy's Hospital

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Fetal Intervention - 1990s

- 4 patients
- 5 attempts
- 2 balloon dilation successfully performed
- 1 intrauterine death
- 2 neonatal deaths
- 1 long term survivor
- Technical complication balloon fragments sheared off in the LV wall in 2.

Tynan, Guy's Hospital

Outcome of Fetal Interventions World-wide

Kohl et al

- 14 fetuses
- 8 had aortic stenosis
- 2 had aortic atresia
- 2 had pulmonary atresia & intact ventricular septum
- 2 had aortic stenosis & pulmonary atresia

There was only 1 long term survivor

Fetal Intervention - 1990s

Problems

- Poor outcome
- Ultrasound imaging of limited quality
- Fetal position critical
- Limitations of the available equipment

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Fetal Intervention

Collaboration

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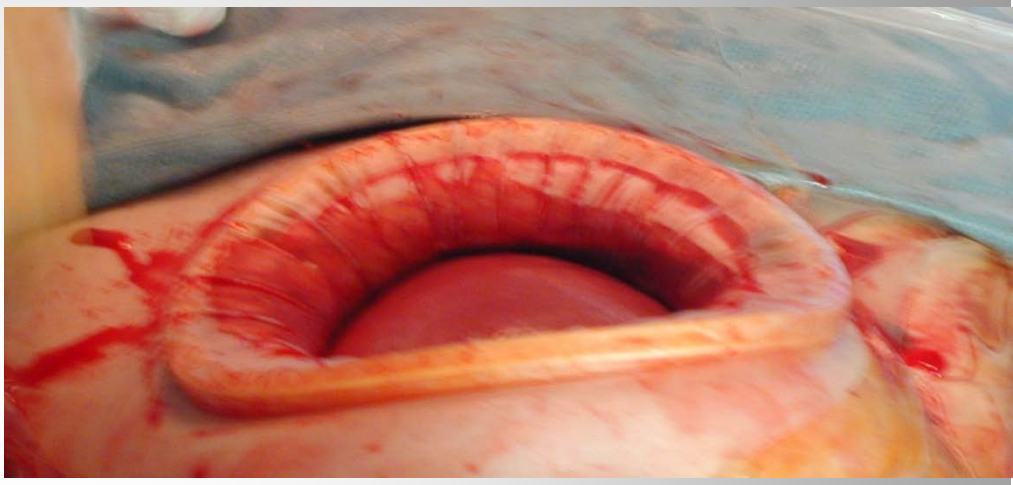
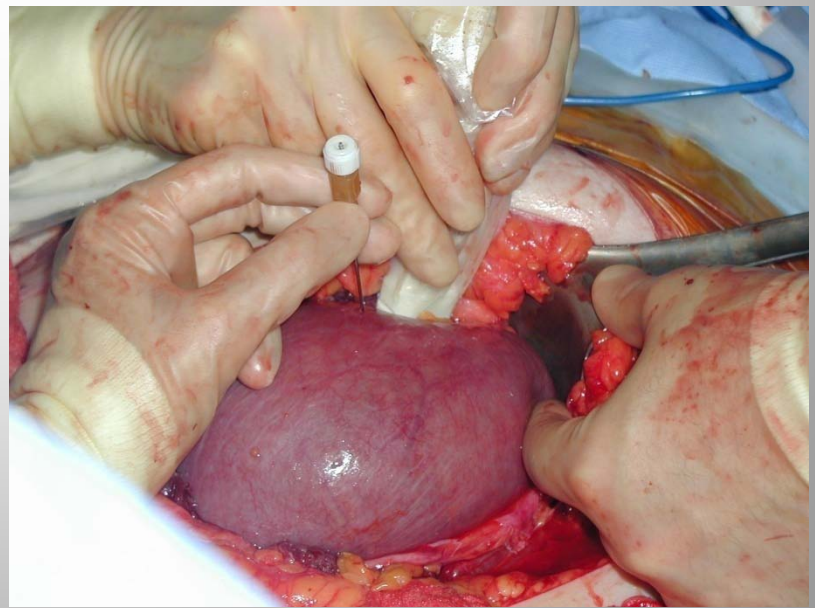
Transuterine Technique – Fetal Aortic Valvuloplasty





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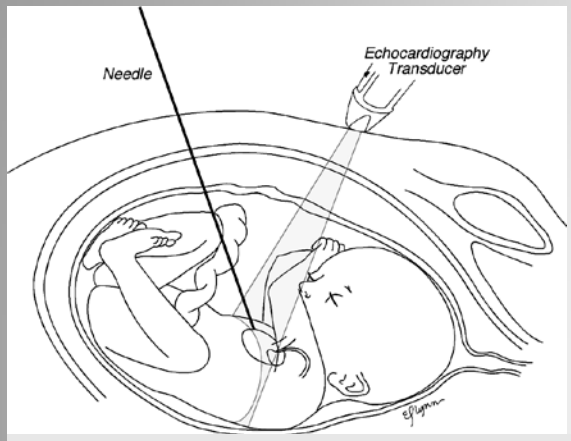
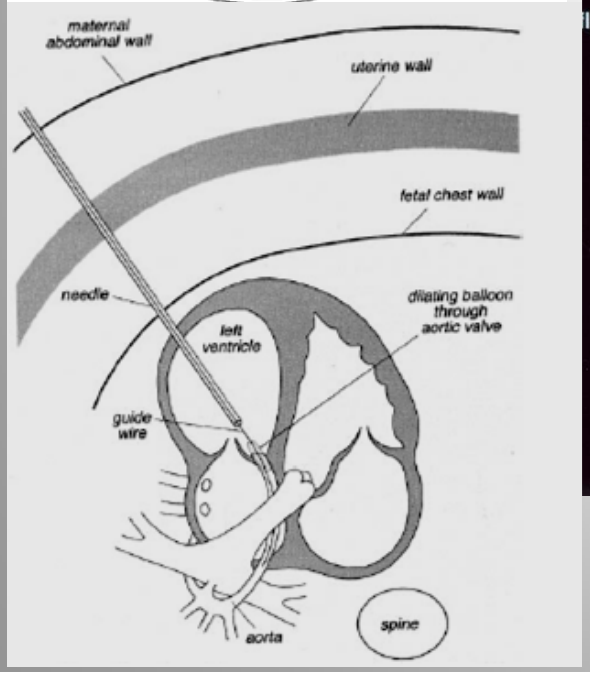
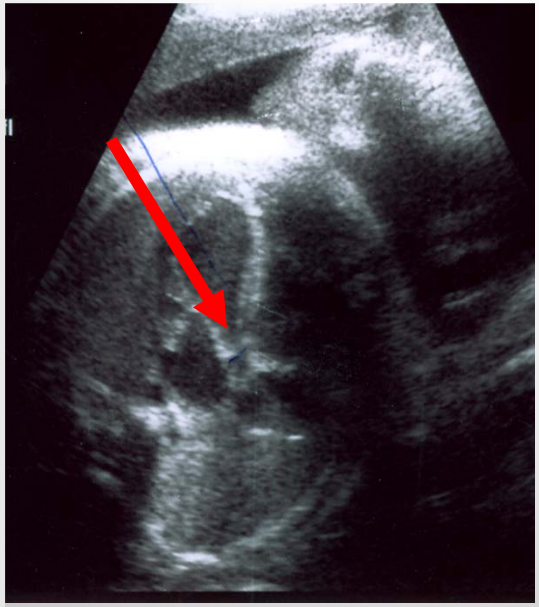
Fetal aortic valvoplasty
Percutaneous technique







- Ultrasound guided
- Percutaneous/Transuterine
- Maternal anaesthesia
- Uterine relaxation
- Fetal positioning
- Fetal anesthesia
- 19G needle
- 0.014" wire
- Coronary balloon

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Balloon dilation of aortic valve in fetus

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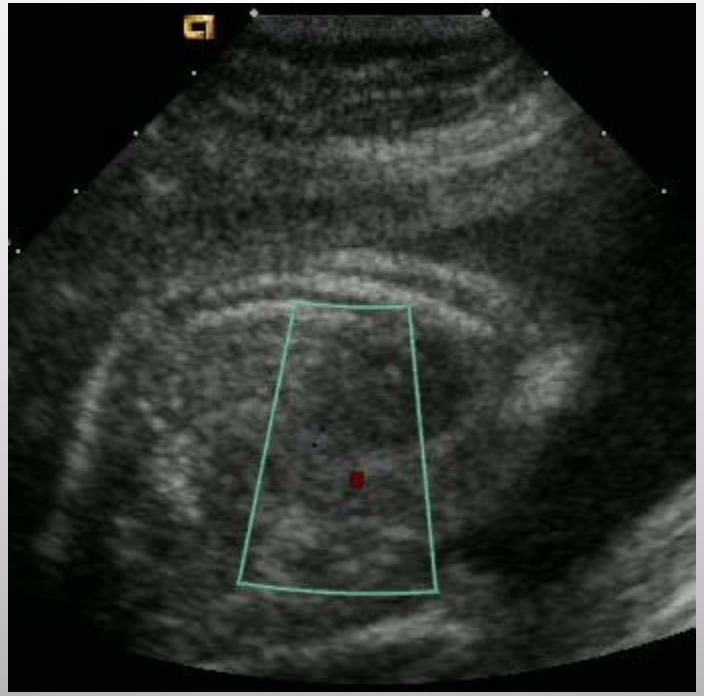
Fetal Aortic Regurgitation

Antegrade flow



Aortic regurgitation

Fetal Aortic Regurgitation?

- Intentionally over-sizing balloon
- Resolves within weeks
- Well Tolerated
  - Low systemic resistance – placenta
  - High LV EDP
- Could there be beneficial effects?
  - Volume loading LV

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Attempted fetal aortic valvoplasty
n=84

Still In Utero
n=3

Technically Unsuccessful
N=15 (17%)
9/37 (24) vs. 6/47 (12)

Technically Successful
n=69

Fetal Demise
n=9 (1/9 TOP)
Fetal Loss due to procedure
8/84 (~10%)

Live Born
n=72

Tworetzky 2010

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Attempted fetal aortic valvoplasty
n=84

Live born
n=72

Comfort care, n=1
Died from sepsis, n=1
Died post-transplant, n=1

Rx HLHS from birth
n=48

Biventricular from birth
n=21

Converted to 2V after BDG
N=4

n=4

ACHIEVED BIVENTRICULAR CIRCULATION
n=25

Median age 2.3 yrs
(all after BDG)

Median age at follow-up:
2.8 yrs (0.5, 8.3)

Tworetzky 2010

Complications of fetal aortic ballooning

- Bradycardia requiring Rx (40%) - treatable
- Moderate-severe AR (40%) - resolves
- Hemopericardium requiring drainage n=3
- Balloon rupture n=2
- Peri-procedural fetal demise (10%)

Courtesy: Wayne Tworetzky

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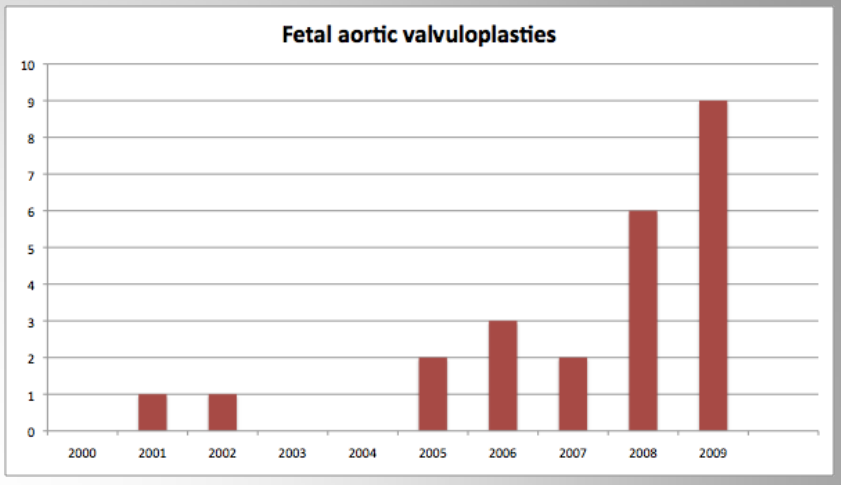
Gerald Tulzer
Linz, Austria



- December 2001- January 2010
- 24 attempted fetal aortic valvoplasties in 23 fetuses
- Median GA: 26+4 weeks (21+4 to 32+1 weeks)
- 4 fetuses had advanced end-stage heart failure with hydrops.

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Results

- Successful: 15/23 fetuses (70%)
- Technical failure: 8/23 (33%)

  5 HLHS, 2 IUD,
  1 repeated successfully
- Overall mortality: 3/23 (13%)
- Biventricular circulation 10/15 successful procedures (67%) 1 IUD
- F/U: median 27 months (4 - 63 months):

  Aortic balloon alone (no surgery): 3

  Ross-Konno operation: 6 (+MVR: 1)

  Coarct. repair: 1 severe AR, PHT - died @ 3 months

Results

Functional outcome

- Ross Konno 6
- F/U 5 years 2
  - Normal LV function and PAP 1
  - Mitral valve replacement 1
- Elevated PAP 3
  - Pacemaker for CHB 1

Death at 6 weeks post op (NEC) 1

Technical success (15/23)
Non -biventricular outcome (5/15)

- Born with HLHS 5
  - Hybrid 2
  - Norwood 3

Technical Failure

- 8/23 pts
  - IUD 2
  - HLHS 6 (all alive)

Gerald Tulzer, Austria

Complications

pericardial effusion >3mm	3/24	no drainage
bradycardia	9/24	intracardiac therapy
thrombosis LV	5/24	stop, repeat procedure
balloon tear off	2/24	wait
Aortic regurgitation	11/24	resolved
IUD	3/24	

Hypoplastic Left Heart Syndrome With Intact or Highly Restrictive Atrial Septum

Outcome After Neonatal Transcatheter Atrial Septostomy

Antonios P. Vlahos, MD; James E. Lock, MD; Doff B. McElhinney, MD; Mary E. van der Velde, MD

1990 – 2002 Children's Hospital Boston

n=33 (10% of all HLHS)

Died Prior to Stage I
n = 7 (21%)

Stage I
n = 26

Died < 30 days
10/26 (38%)

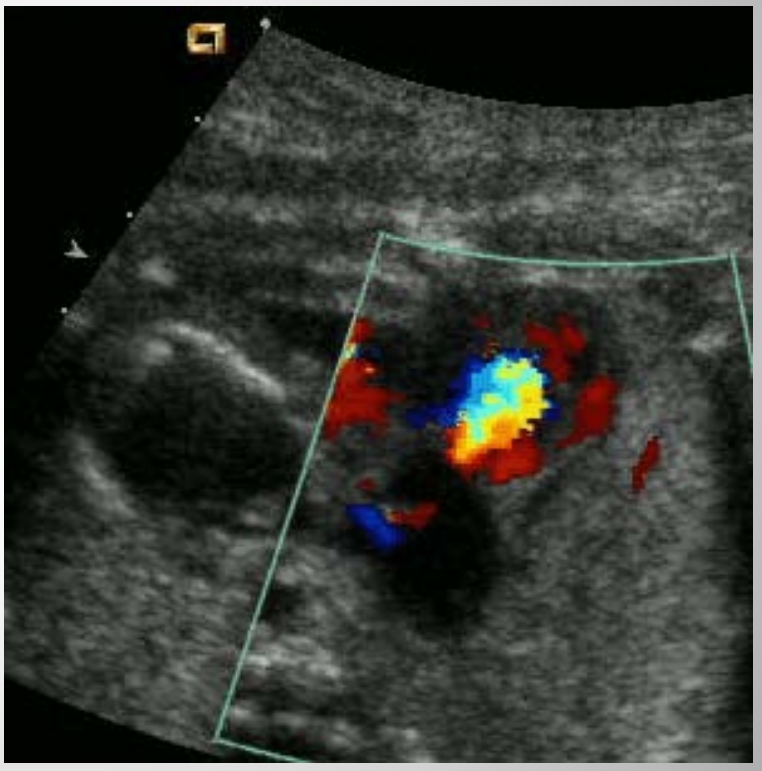
Overall survival was 48% at 30 days

(Vlahos et. al. Circulation

HLHS with Restrictive or Intact Atrial Septum

- 10-12% of HLHS patients have a restrictive ASD
- Increased peri-operative mortality
- Left atrial hypertension
  - pulmonary parenchymal changes
  - pulmonary artery+venous remodeling and hypertension
- HLHS with RAS can be detected prenatally
- Planned delivery – cath lab or operating room for urgent left atrial decompression

HLHS with restrictive or intact atrial septum



Marshall , Boston

Problems with HLHS with IAS

- Thick septum
- Prone to re-stenosis
- Cannot perform a "septostomy"
- 19G cannula and a 3 mm balloon

Stent placement

- Larger cannula 18G
- Larger balloon 4 mm
- Access via left atrium

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HLHS with IAS BAS

Procedures n=24

Tech. Unsuccess. N=3
Stage1 Surv =1
Stage1 Died =1
Stage1 Died =1
(stent no flow)

Tech Success n=21
(stent x 2)

In Utero n=0

Fetal Demise n=2

Liveborn n=19
After tech success
No Cath 9/19

Liveborn

Stage1 n=19

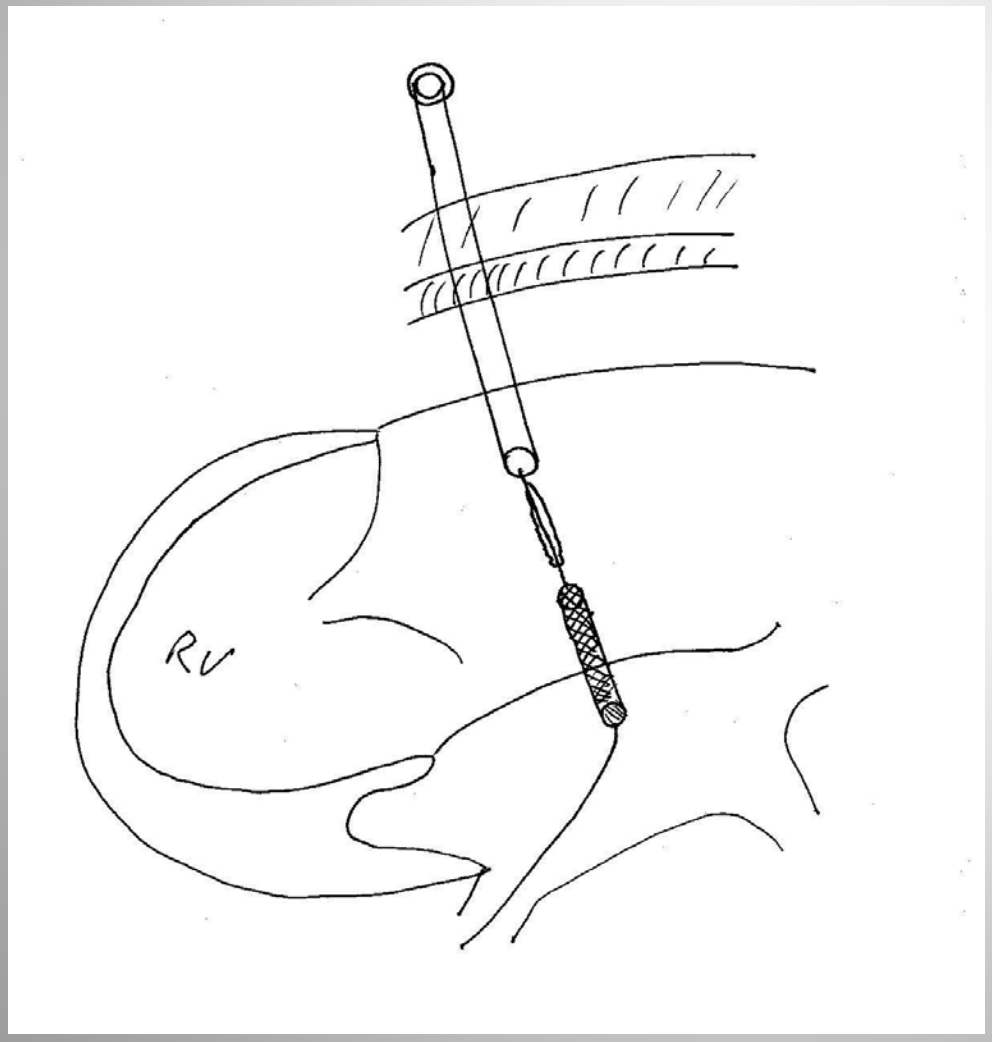
Stage1 Survival to d/c = 14/19

Late deaths n=3

Current survival 11/19 >50%

Tworetzky, 2010

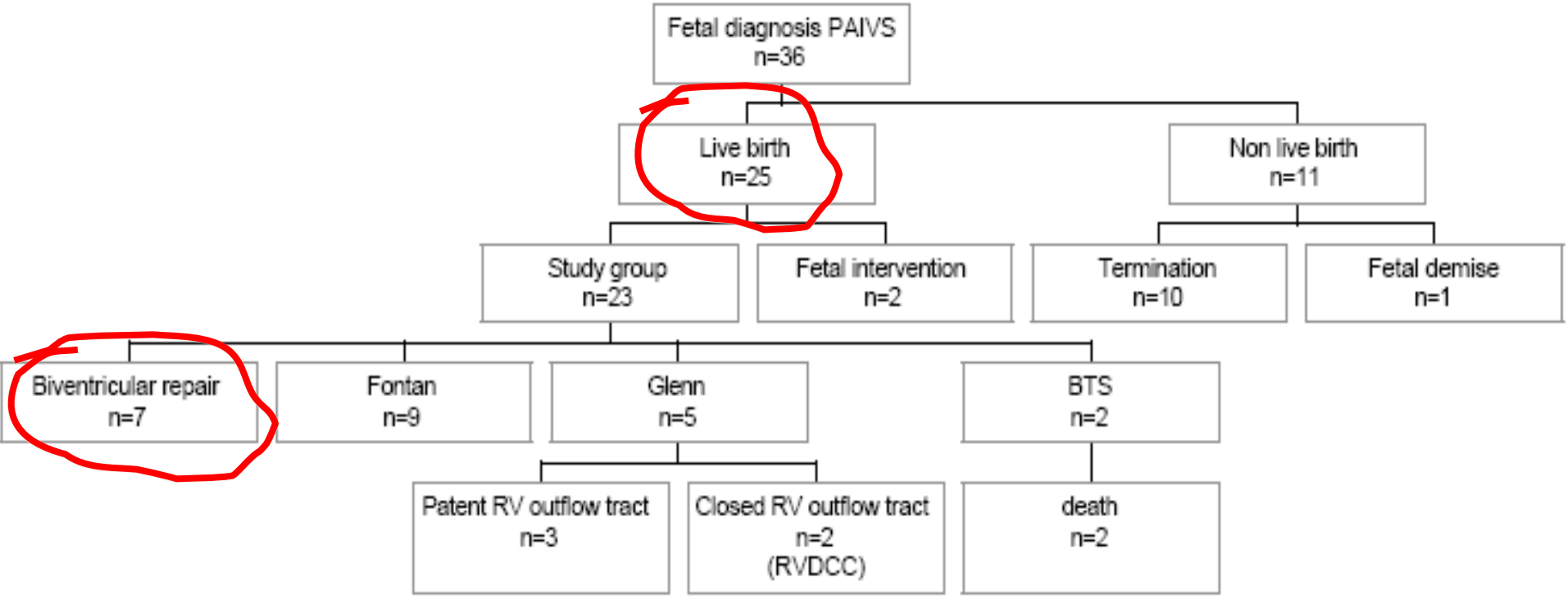
HLHS Intact Atrial Septum
Fetal Stent Placement



Tworetzky, 2010

Pulmonary Atresia with IVS
Outcomes After Fetal Diagnosis

Table 1: Fetal PA/IVS: Demographics and Post-Natal Outcomes, 1990-2004



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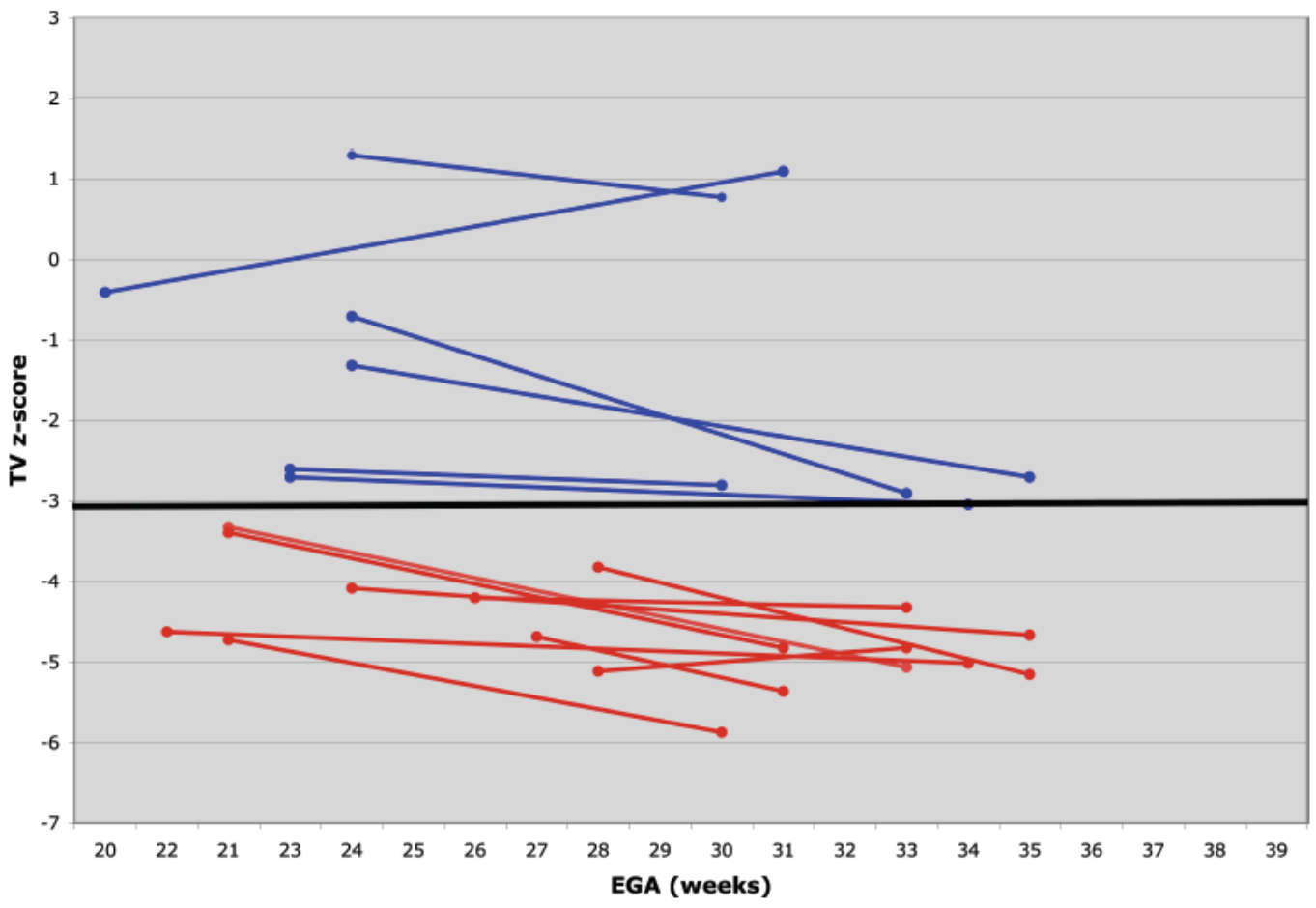
PAIVS
Fetal Predictors of Postnatal 2V Repair

Figure 1: TV-z score at early and late fetal echo as indicator of biventricular repair



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Fetus with Pulmonary Atresia with IVS "Hypoplastic Right Heart Syndrome"

Determinants of Outcome in Fetal Pulmonary Valve Stenosis or Atresia with Intact Ventricular Septum

Kevin, Fouron, Masaki, Smallhorn, Chaturvedi, Jaeggi - Toronto / Montreal

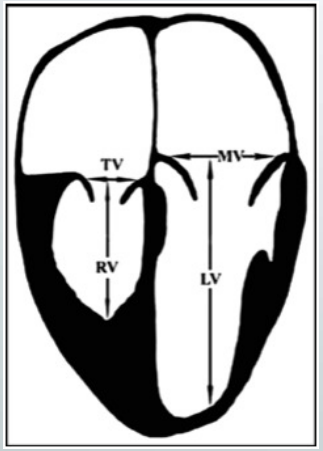
Am J Cardiol 2007;99:699-703

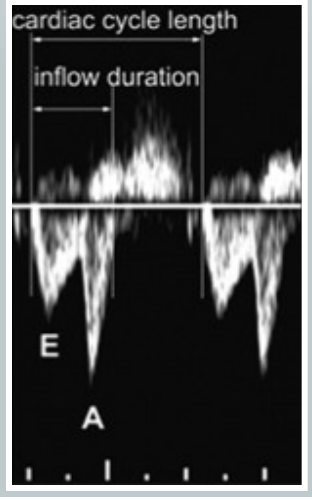
Prediction of a non - biventricular outcome:

- TV / MV ratio < 0.7
- RV / LV length ratio < 0.6
- TV inflow duration < 31.5%
- Presence of sinusoids

If 3/4 were present: Sensitivity: 100%

Specificity: 75%





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Fetal balloon pulmonary valvotomy

Sharland 2006

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Pulmonary Atresia with Intact Ventricular Septum n=12

Pt#	GA	Result	Outcome		Current
1	26	-	liveborn	1V	s/p BDG
2	26	-	liveborn	1V	s/p BDG
3	23	-	TOP		
4	23	+	alive		s/p BDG
5	22	+++	liveborn	balloon only	biventricular
6	24	++	liveborn	balloon+shunt	biventricular
7	27	+++	liveborn	RVOT+shunt	biventricular
8	24	+++	liveborn	balloon+RVOT	biventricular
9	26	++	liveborn	BTS coronary anomalies	
10	26	++	liveborn	RVOT + BTS	biventricular
11	28	++	liveborn	RVOT+BTS	biventricular?
12	26	++	liveborn	RVOT+BTS	?

Tworetzky Dec 2010

London / Linz experience

Pulmonary atresia with intact septum / critical PS

Proc	GA	Result	Outcome	
1	26	+++	Liveborn, **biventricular**, balloon+shunt	Linz
2	26	-	Liveborn 32w, Charge Syndr., died after shunt	Linz
3	29	+++	Liveborn 36w, cath+shunt, **biventricular**	London
4+5	24	+++	Re-atresia, 2nd proc 31w +++, 1.5 ventricle	London
6	29	-	Placental bleeding, delivery – IVH – died	London
7+8	31	+	No succ, 2nd proc 32w, 1.5 ventricle	Linz
9	28	+++	Liveborn, balloon+shunt, **expected biventricular**	Linz
10	29	+++	In utero	Linz

Balloon dilation of pulmonary valve in fetus

- It is feasible
- RV can be decompressed
- TR may improve and there may be growth of TV, RV and pulmonary valve
- However valve may restenose or become atretic
- Complications eg placental bleeding, pericardial effusion, bradycardia may occur
- Technically challenging
- Still need to learn a lot more patient selection

Summary

- Technical success is dependent on
  - patient selection
  - fetal position
  - dedicated experienced team
- Complications are frequent, but can be managed in the majority of cases

Fetal interventions – influence on outcome

- Interventions on the fetal aortic valve, atrial septum and pulmonary valve can be performed
- Procedure is successful
- Are the fetuses surviving because of the procedure??
- These techniques likely to continue although currently they may have questionable benefit
- Improved technology may allow much earlier interventions and so may influence the outcome

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Future Directions

- Natural History Studies
- Animal Models
- Equipment
- Imaging