Fetal interventions in critical left heart lesions

Rationale, risks and benefits

G. Tulzer
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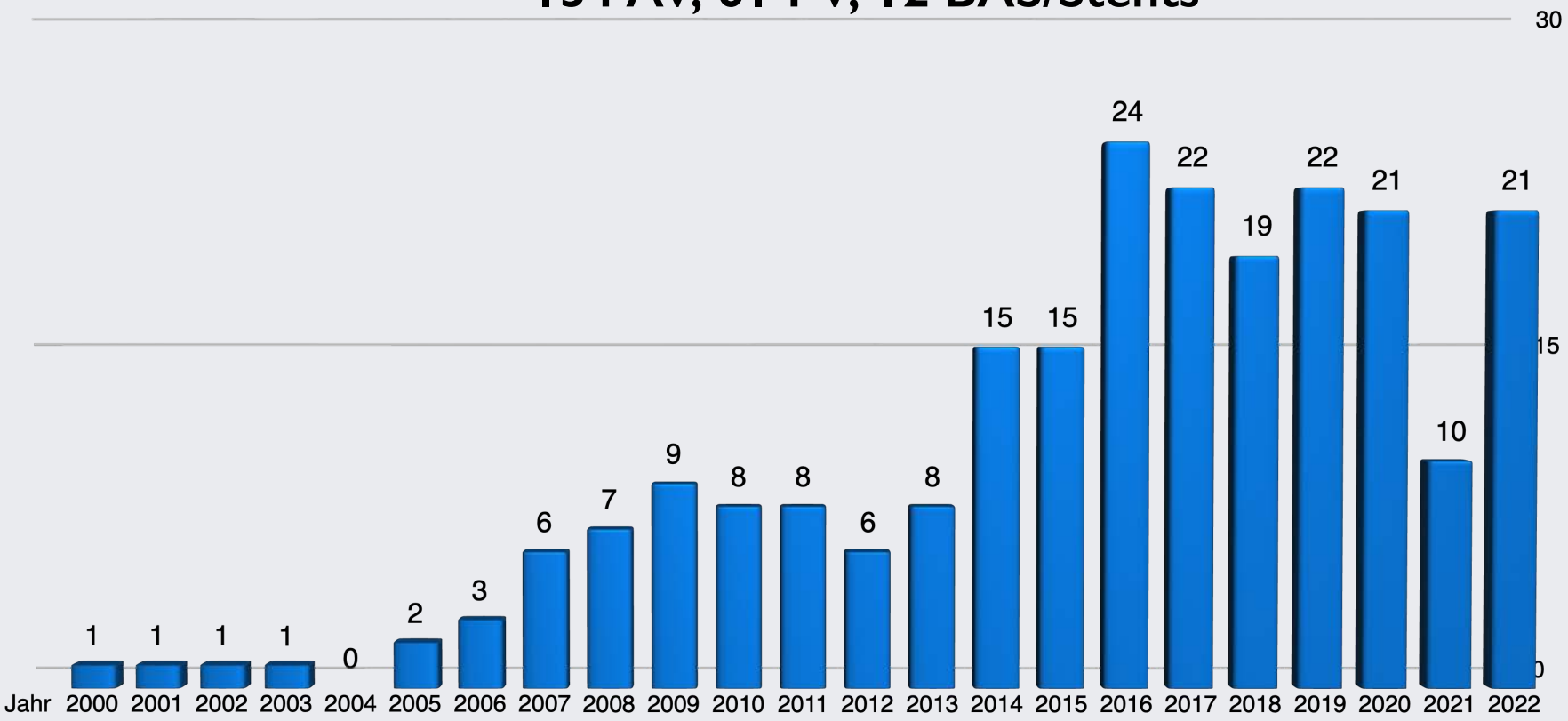
Kinder-Herz Zentrum Linz

Prenatal Cardiac Interventions
CHC LINZ-AUSTRIA

(n=227, until 2023)

154 AV, 61 PV, 12 BAS/Stents



CRITICAL LEFT HEART LESIONS

- Critical valvar aortic stenosis

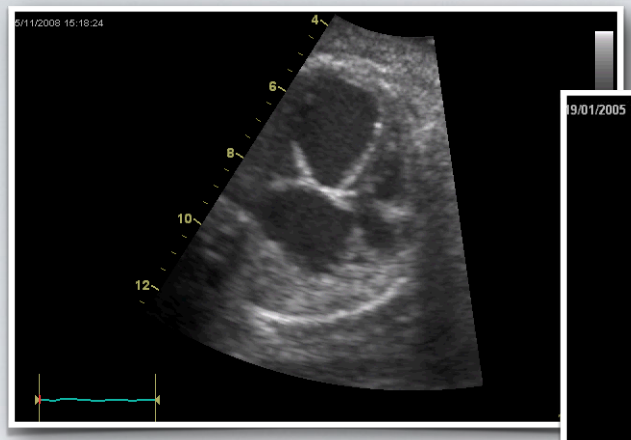
- Closed or severely restrictive foramen ovale in HLHS or critical left ventricular outflow obstructions

CRITICAL AORTIC STENOSIS
RATIONALE

- Ensure survival
- To change a UV to a BV outcome
- To improve QoL and long term survival

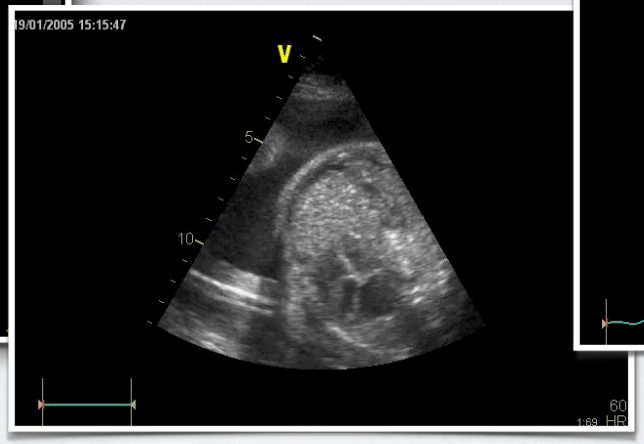
Case Selection

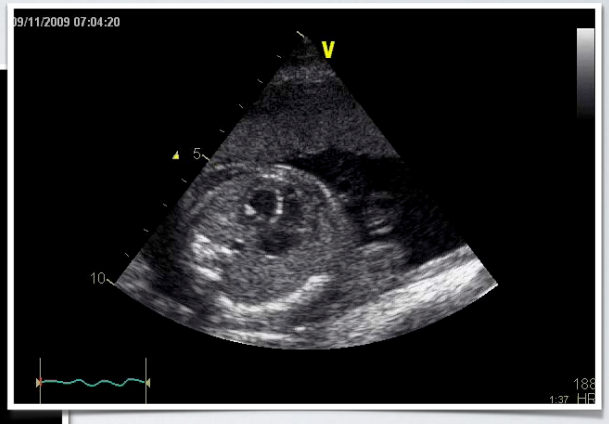
CRITICAL AORTIC STENOSIS



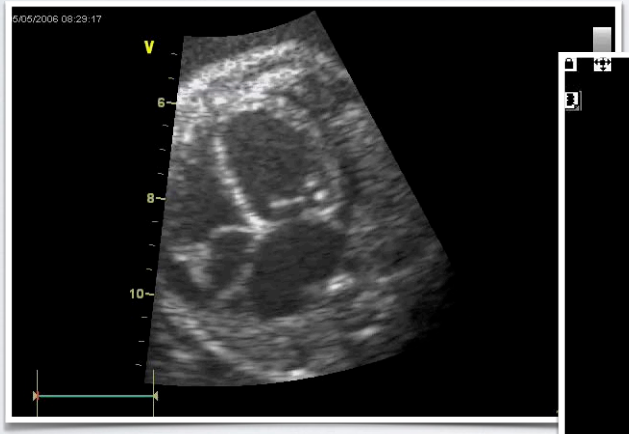
EFE

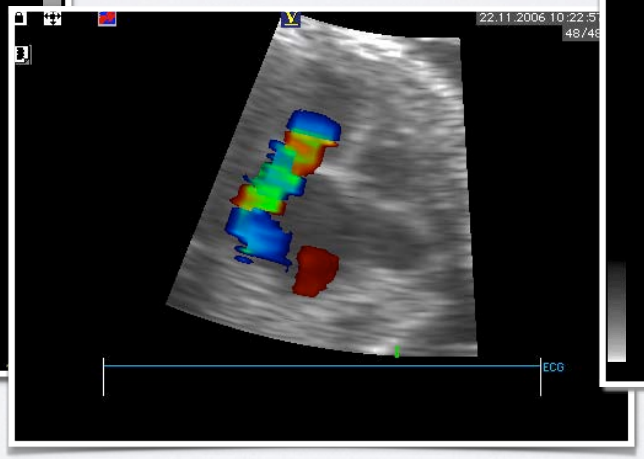
Hydrops



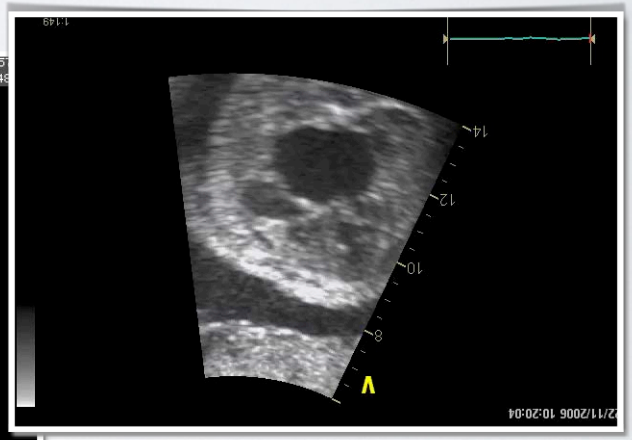


MR





Giant LA



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AORTIC STENOSIS

Results / outcome depend on:

- Patient selection
- Technique (experienced team)
- Postnatal management

AORTIC STENOSIS
RESULTS / OUTCOME

- Survived?
- BV instead of UV
  - Natural history?
  - BV if not Norwood…
  - BV at hospital discharge or
  - BV at 1 year without PHT

Indication: survival

CRITICAL AS + HYDROPS

- IUD and neonatal mortality: close to 100%

  Vogel M et al: J Am Coll Cardiol. 2011 Jan 18;57(3):348–55
  Mallmann MR et al: Fetal Diagn Ther. 2019 Oct 8;1–8

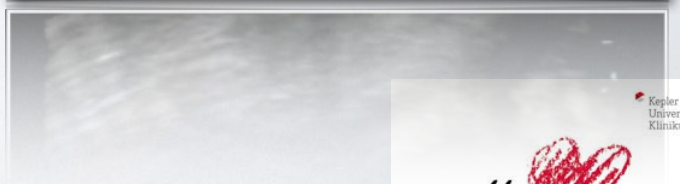
- <u>Fetal intervention in CAS with hydrops: Linz</u>

Ultrasound Obstet Gynecol 2021; 57: 119–125
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.22138

Fetal aortic valvuloplasty may rescue fetuses with critical aortic stenosis and hydrops

A. TULZER[1], W. ARZT[2] and G. TULZER[1]

  - N=14
  - Hydrops resolved in 9 (IUD:3, NND:2)
  - **Alive and biventricular: 6 (42%)**



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Guidelines for fetal valvuloplasty

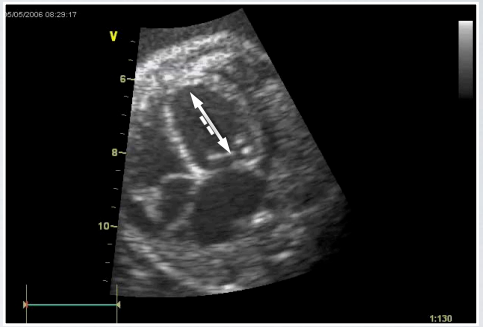
Mäkikallio et al 2006	McElhinney et al 2009 Threshold Score ≥ 4
Critical aortic stenosis or atresia With reversal of flow in aortic arch No obvious LVOT Obstruction	Aortic valve Z score > -3.5 AoV Vmax > 20 mmHg *Not* aortic atresia
LV length Z score > -2 MV Z score > -3	LV long axis Z score > 0 LV short axis Z score > 0 Mitral valve Z score >
Monophasic Left to ri Bidire ary venous waveforms	
LV function capable of generating 10 mmHg AoV 15 mm Hg MR	nt > 20 mm Hg

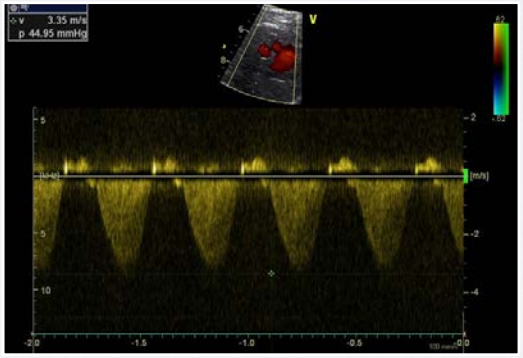
Predictors of HLHS

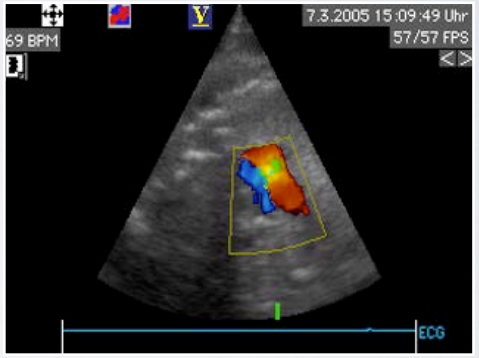
Predictors of BV outcome

EVOLVING - HLHS

- dilated poorly contracting LV with EFE
- reverse aortic arch flow
- left to right shunt at FO





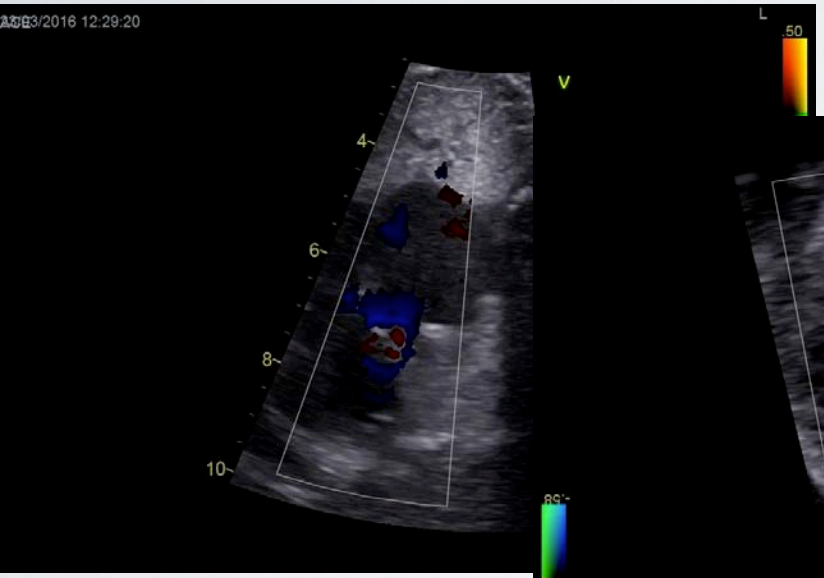


salvagable?

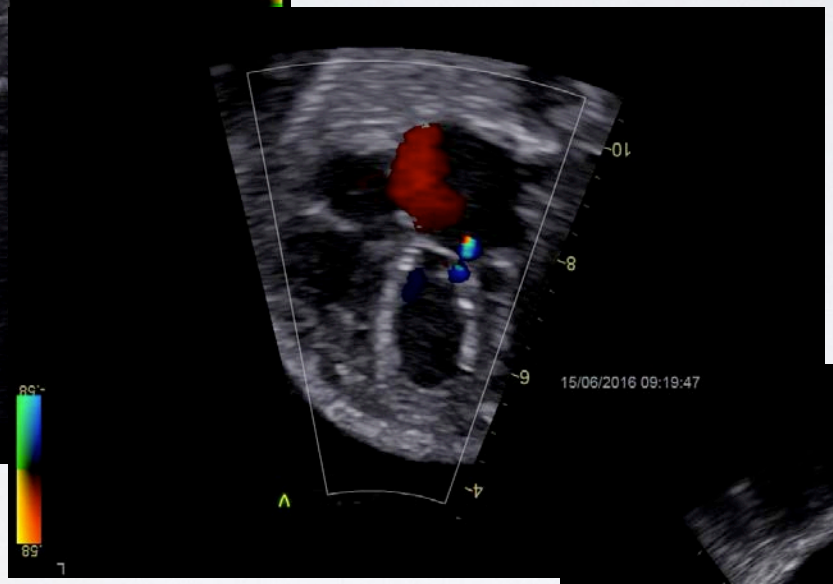
- LV long-axis
- LV pressure

CRIT.AS - SEVERE MR +/- HYDROPS

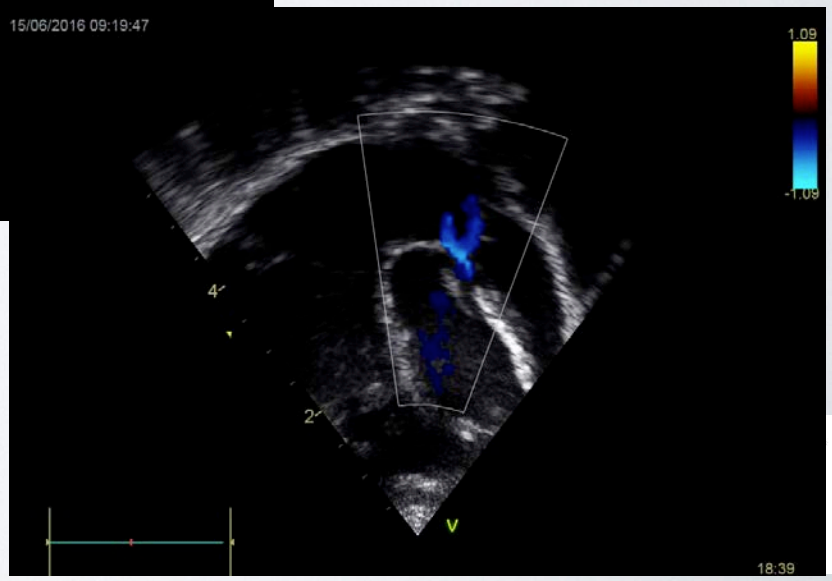
28 weeks



1 week after Intervention



Neonate



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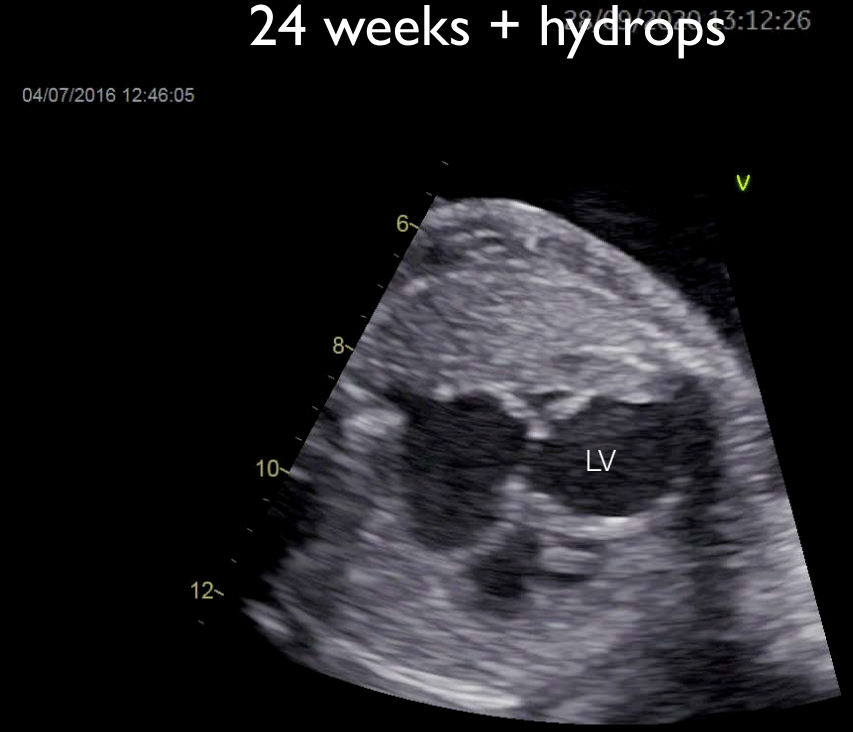
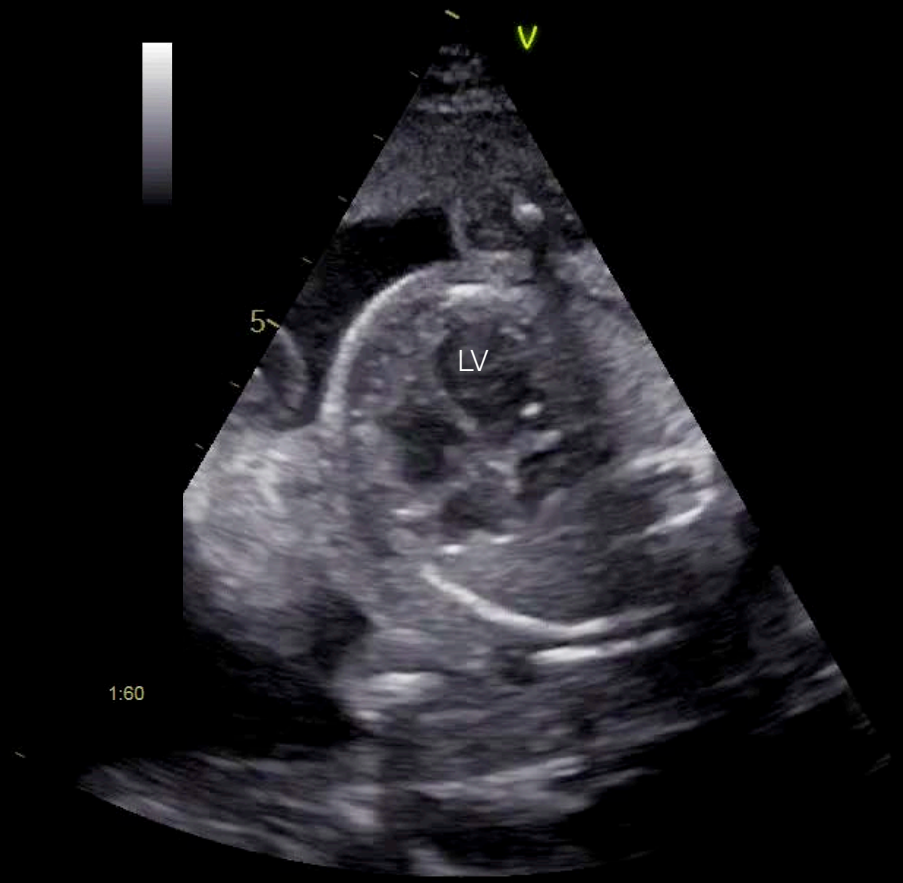
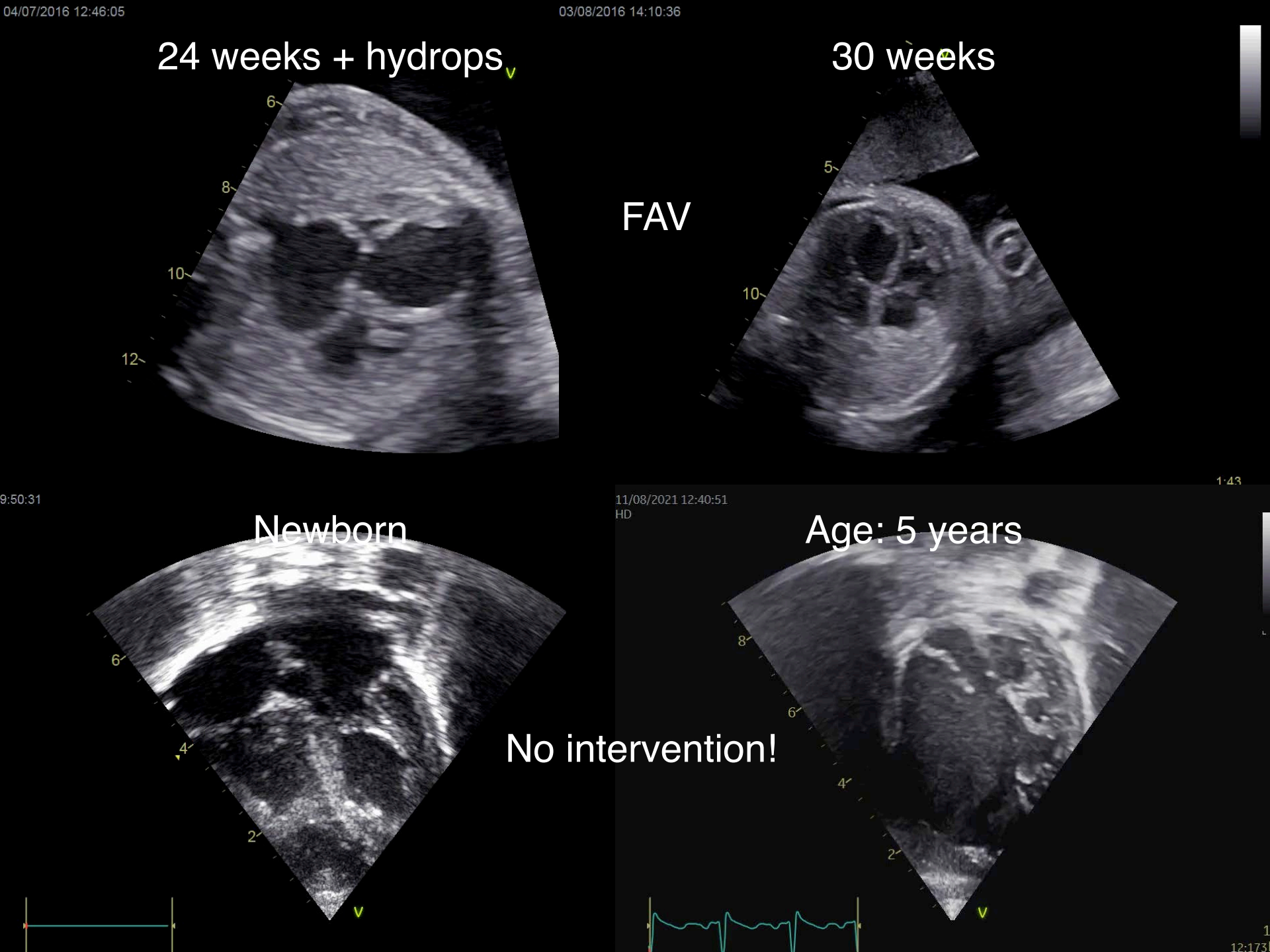
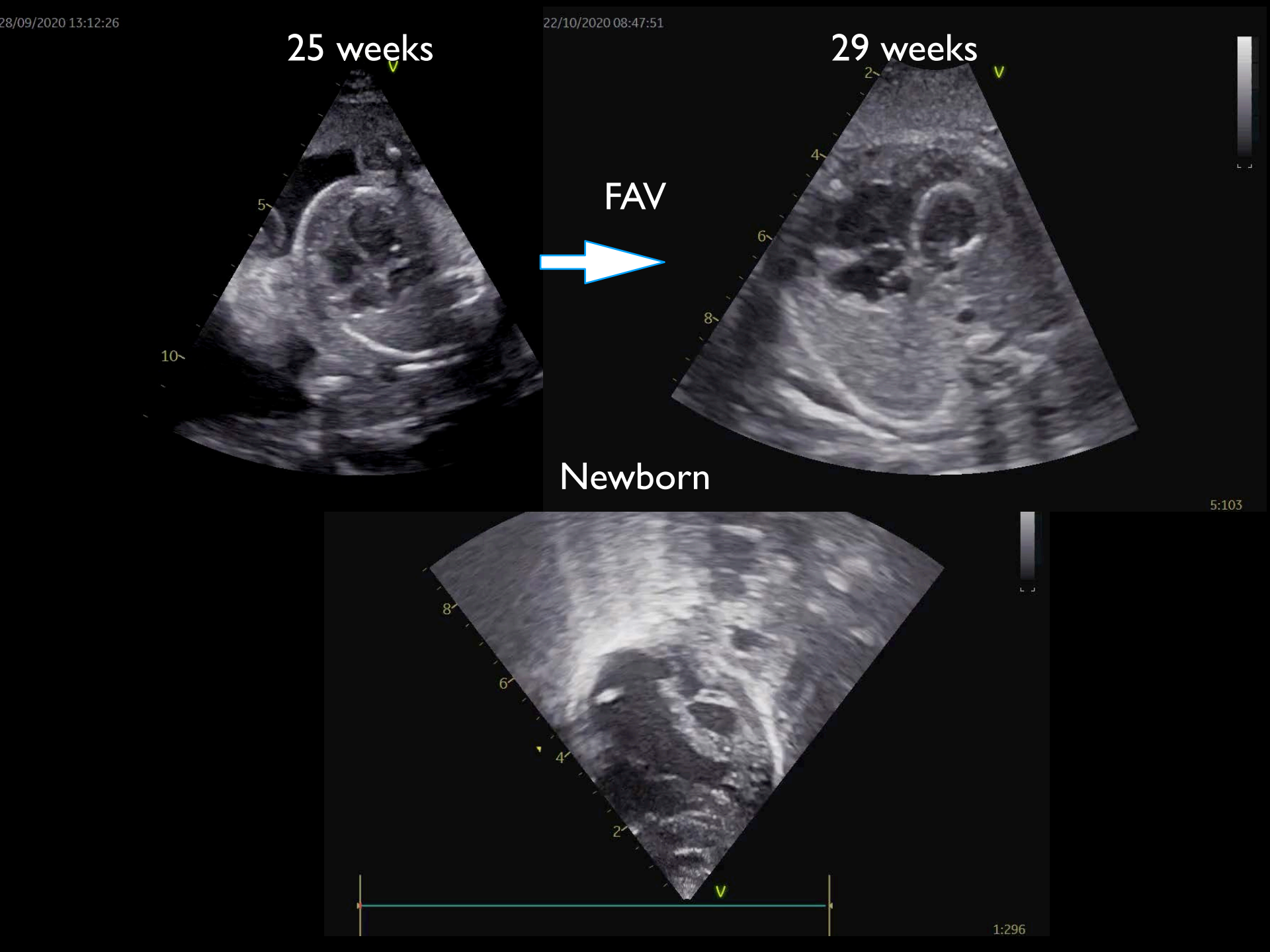
24 weeks + hydrops



25 weeks

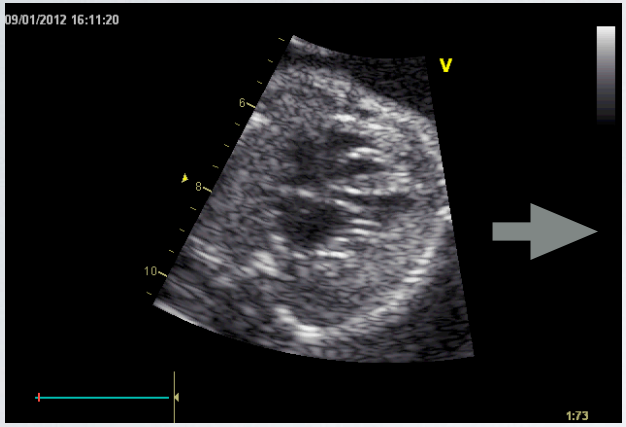



04/07/2016 12:46:05
24 weeks + hydrops
03/08/2016 14:10:36
30 weeks
FAV
9:50:31
Newborn
11/08/2021 12:40:51
HD
Age: 5 years
No intervention!

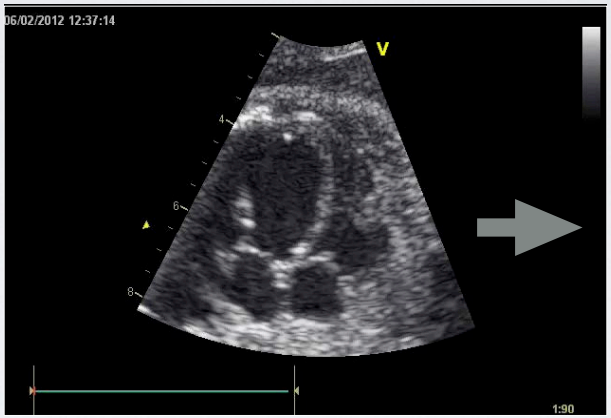

28/09/2020 13:12:26
25 weeks
22/10/2020 08:47:51
29 weeks
FAV
Newborn
5:103
1:296

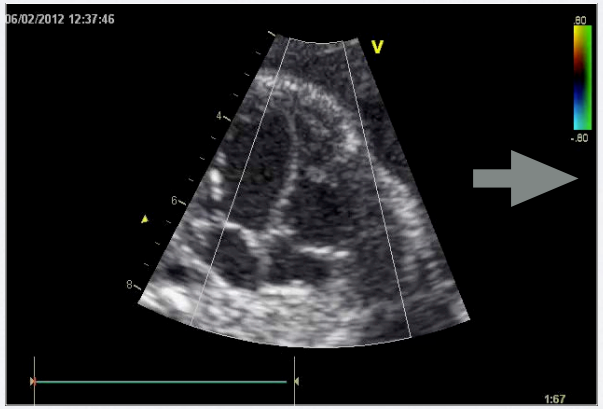
CRITICAL AORTIC STENOSIS - LV RECOVERY

22+4

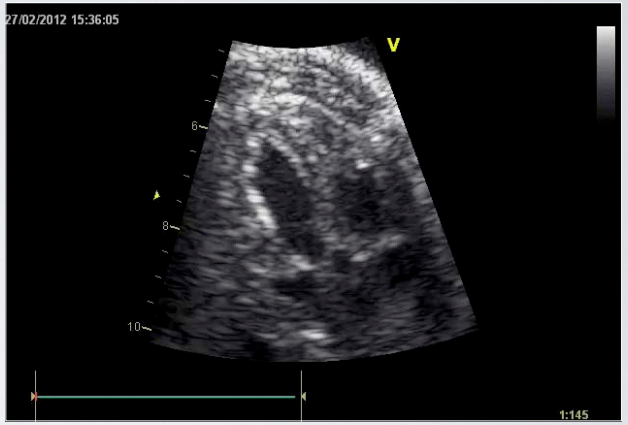


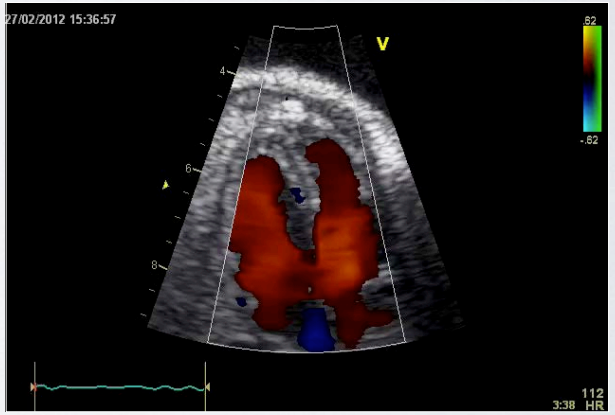
27+1





30+0





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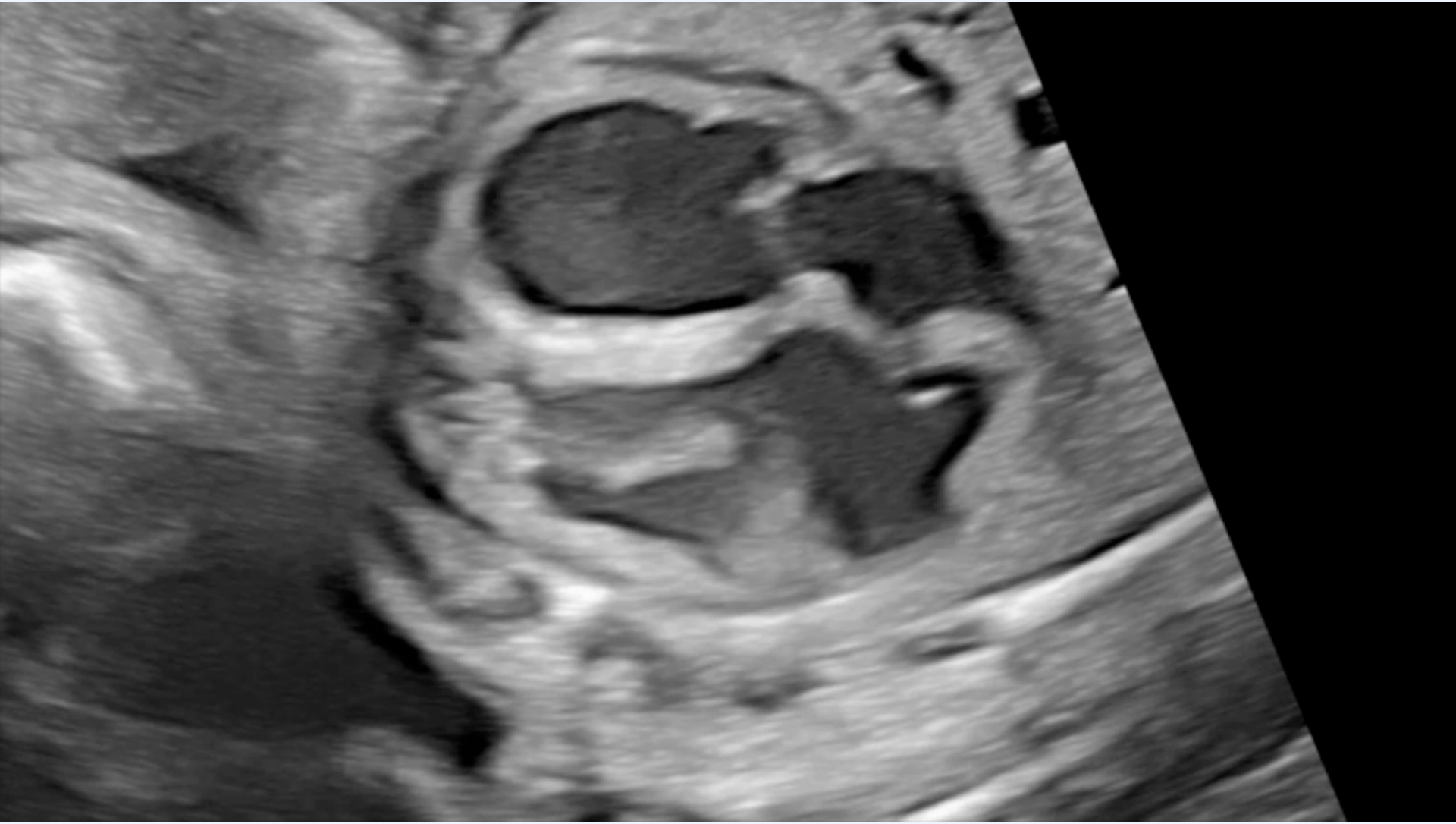
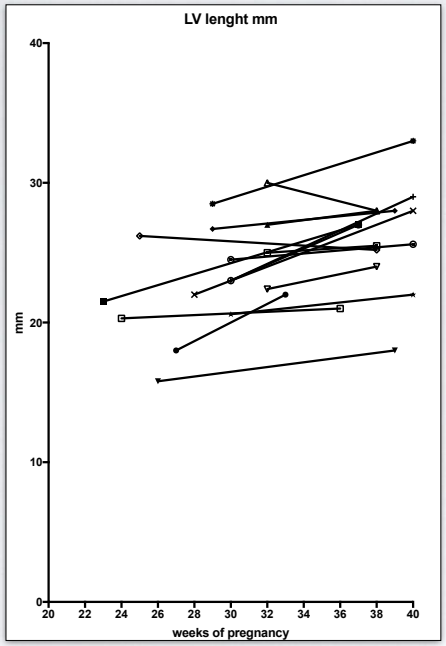
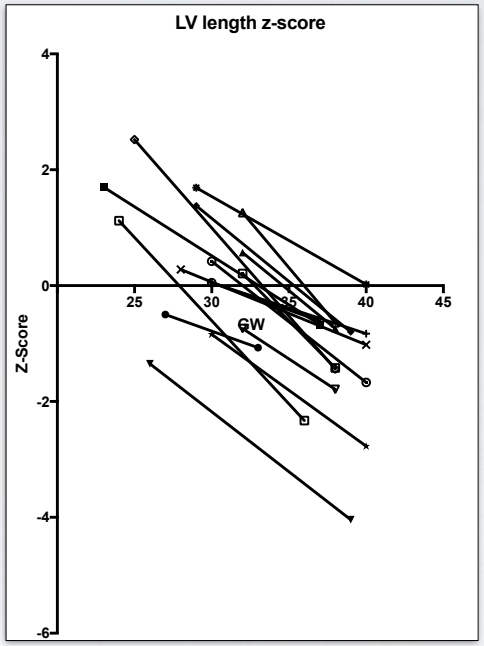


LV GROWTH AFTER INTERVENTION





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FAV - Complications?
N= 144 procedures

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- Procedure related mortality:
  - 8% overall
    - 14 % early (8/57)
    - **3.4% recent (3/87) p<0.027**
  - Bradycardia: 33% (unchanged)
  - Pericardial effusions: 14%
  - LV thrombus: 14%

Tulzer A et al: Complications associated with fetal cardiac interventions – prevalence and management: experience from 213 procedures Fetal Diagnosis & Therapy (in press)

Comparison of complications associated with FAV in the early and recent period

Complication	Early (N=57)	Recent (N=85)	p-value
IUD pr	8 (14%)	3 (4%)	**0.03**
Bradycardia	17 (30%)	30 (35%)	0.59
Pericardial Effusion	6 (11%)	8 (9%)	1.00
Thrombus-formation	10 (18%)	10 (12%)	0.34

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Tulzer A et al: Complications associated with fetal cardiac interventions – prevalence and management: experience from 213 procedures Fetal Diagnosis & Therapy (in press)

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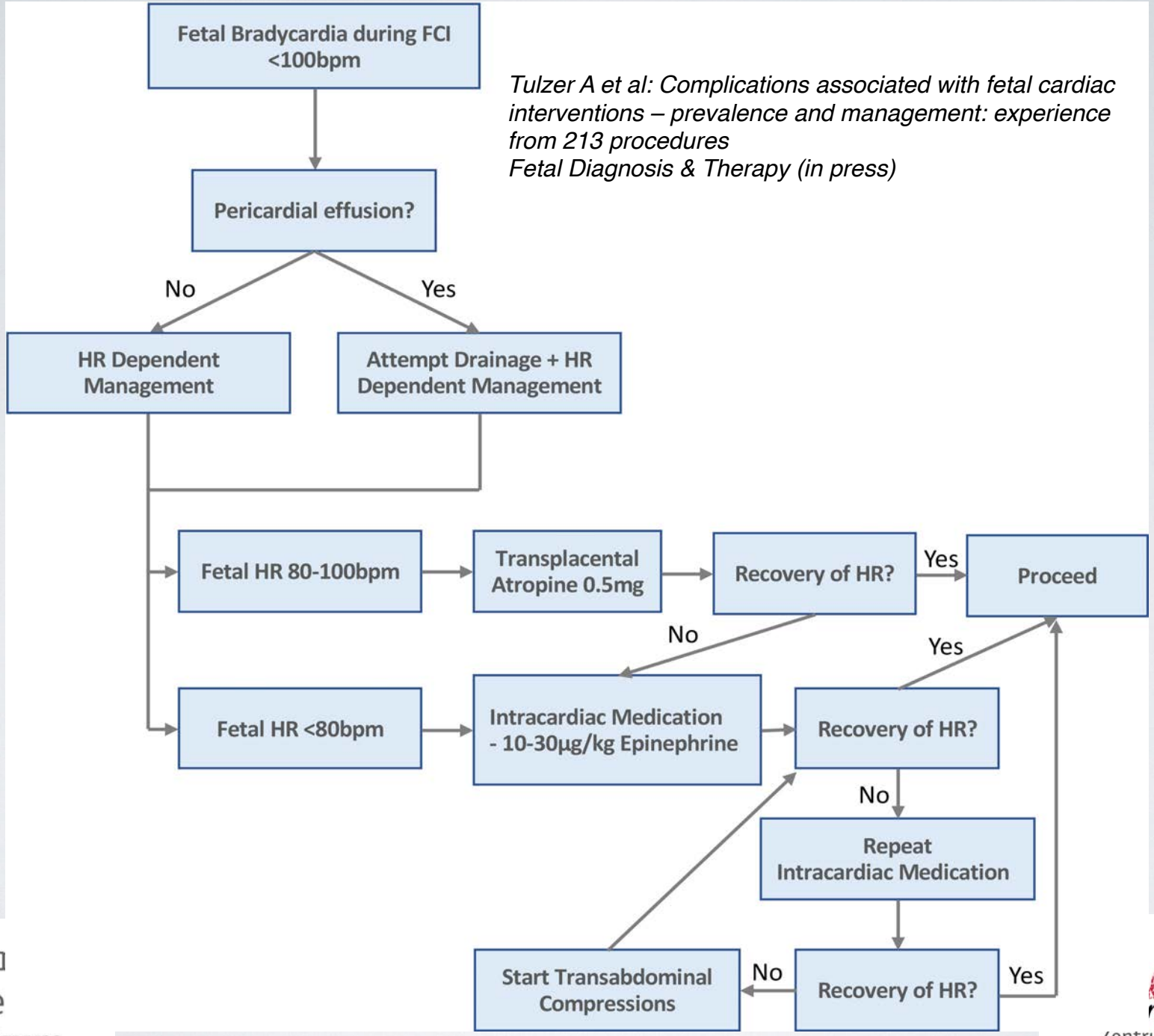

Tulzer A et al: Complications associated with fetal cardiac interventions – prevalence and management: experience from 213 procedures
Fetal Diagnosis & Therapy (in press)

Ultrasound Obstet Gynecol 2016; **48**: 373–381
Published online 4 August 2016 in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.15876

Natural history of 107 cases of fetal aortic stenosis from a European multicenter retrospective study

H. M. GARDINER*, A. KOVACEVIC†, G. TULZER‡, T. SARKOLA§, U. HERBERG¶, J. DANGEL**, A. ÖHMAN††, J. BARTRONS‡‡, J. S. CARVALHO§§, H. JICINSKA¶¶, V. FESSLOVA***, I. AVERISS*, M. MELLANDER†† and the Fetal Working Group of the AEPC

- 38 fullfilled the criteria for eHLHS
- BV without intervention: **23.7%!**

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RESULTS -BOSTON

Ultrasound Obstet Gynecol. 2018 Aug;52(2):212-220. doi: 10.1002/uog.17530. Epub 2018 Jul 4.

Improved technical success, postnatal outcome and refined predictors of outcome for fetal aortic valvuloplasty.

Friedman KG[1,2], Sleeper LA[1,2], Freud LR[1,2], Marshall AC[1,2], Godfrey ME[1,2], Drogosz M[1], Lafranchi T[1], Benson CB[3,4], Wilkins-Haug LE[3,4], Tworetzky W[1,2].

- McElhinney 2009:
  - 54 techn. successful procedures, 45 newborns
  - 29% of successful procedures had BV outcome
  - if Score >= 4: 50% had BV outcome

- Friedmann 2018:
  - 101 techn.successful procedures, 93 newborns
  - 59% BV outcome in more recent era (hospital discharge)
  - LV pressure > 47 mmHg, large ascending aorta diameter

Kovacevic A, Öhman A, Tulzer G, Herberg U, Dangel J, Carvalho JS, et al.

Fetal hemodynamic response to aortic valvuloplasty and postnatal outcome: a European multicenter study.

Ultrasound Obstet Gynecol. (2018) 52:221–9.

- 7 European centers
- 59 fetuses after successful FAV
- Matched cohorts
- similar BV and UV outcomes

- Improvements of fetal hemodynamics
- Preservation of left heart growth
- Improved survival in FAV survivors

International Fetal Cardiac Intervention Registry

J Am Coll Cardiol 2015;66:388–99

245 intracardiac Interventions
18 institutions (North- Southamerica)

186 Aortic valves, 16 Pulmonary valves
43 Others

AS: Discharge with biventricular circulation:

with Intervention: 31,3% vs 18,5% without Intervention

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Vorisek CN et al:

Postnatal circulation in patients with aortic stenosis undergoing fetal aortic valvuloplasty: systematic review and meta-analysis.

Ultrasound Obstet Gynecol. (2022) 59:576–584.

- 7 Studies
- 266 fetuses after FAV
- F/U 12 months - 13 years
- 51,9% BV if FAV was successful vs 38,9%

- No prospective randomized trials
- No control groups

Fetal aortic valvuloplasty may lead to a survival benefit in patients with critical aortic stenosis and evolving hypoplastic left heart syndrome, if procedure related mortality does not exceed 12%

Pickard SS, Wong JB, Bucholz EM, Newburger JW, Tworetzky W, Lafranchi T, et al. Fetal aortic valvuloplasty for evolving hypoplastic left heart syndrome: a decision analysis. Circ Cardiovasc Qual Outcomes. (2020)

Ultrasound Obstet Gynecol 2022
Published online in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.24792.

Valvuloplasty in 103 fetuses with critical aortic stenosis: outcome and new predictors for postnatal circulation

A. TULZER[1], W. ARZT[2], R. GITTER[1], E. SAMES-DOLZER[3], M. KREUZER[3], R. MAIR[3] and G. TULZER[1]

[1]*Children's Heart Center Linz, Department of Pediatric Cardiology, Kepler University Hospital, Medical Faculty of the Johannes Kepler University, Linz, Austria;* [2]*Institute of Prenatal Medicine, Kepler University Hospital, Medical Faculty of the Johannes Kepler University, Linz, Austria;* [3]*Children's Heart Center Linz, Department of Pediatric Cardiac Surgery, Kepler University Hospital, Medical Faculty of the Johannes Kepler University, Linz, Austria*

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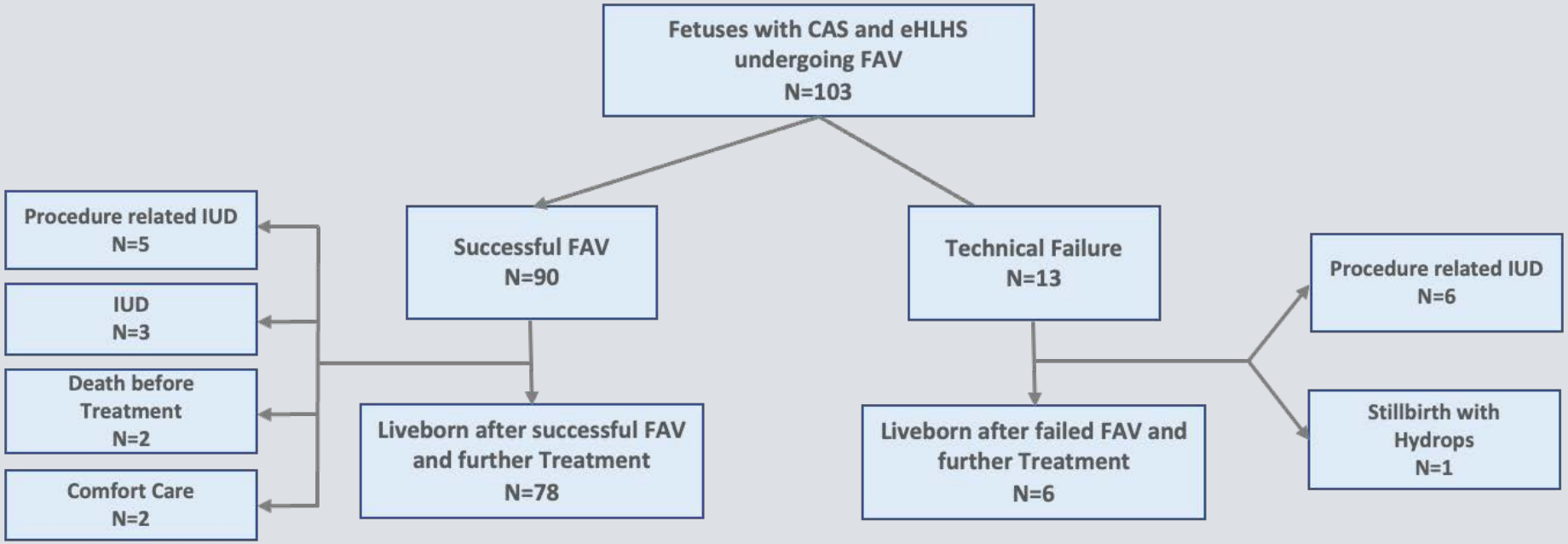
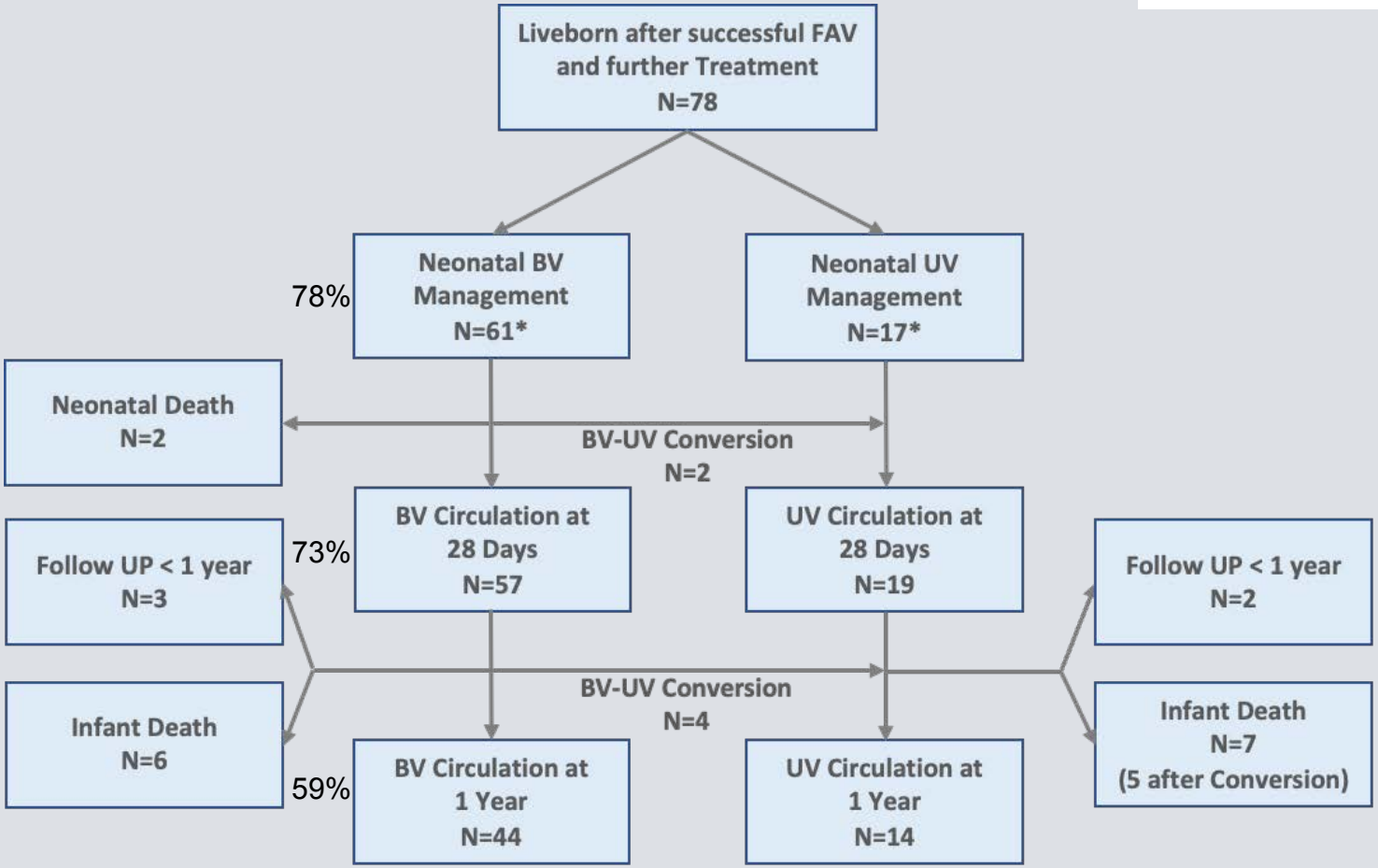
FAV - Linz 2001-2020

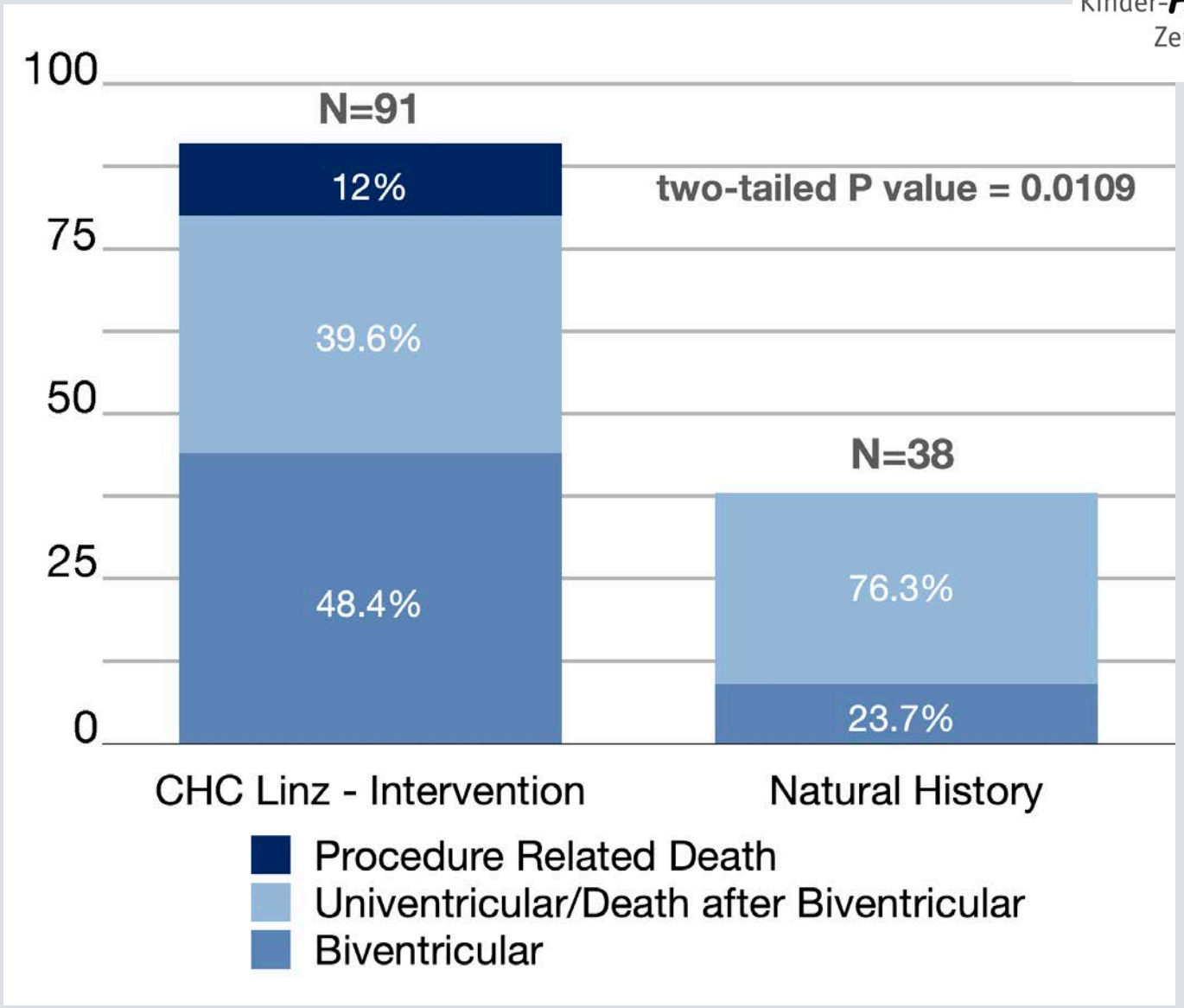


Postnatal Outcome



*including one patient after hybrid management

Results CHC Linz vs. „Natural-History“



Gardiner et al. Natural history of 107 cases of fetal aortic stenosis from a European multicenter retrospective study. Ultrasound Obstet Gynecol. 2016 Sep;48(3):373-81.

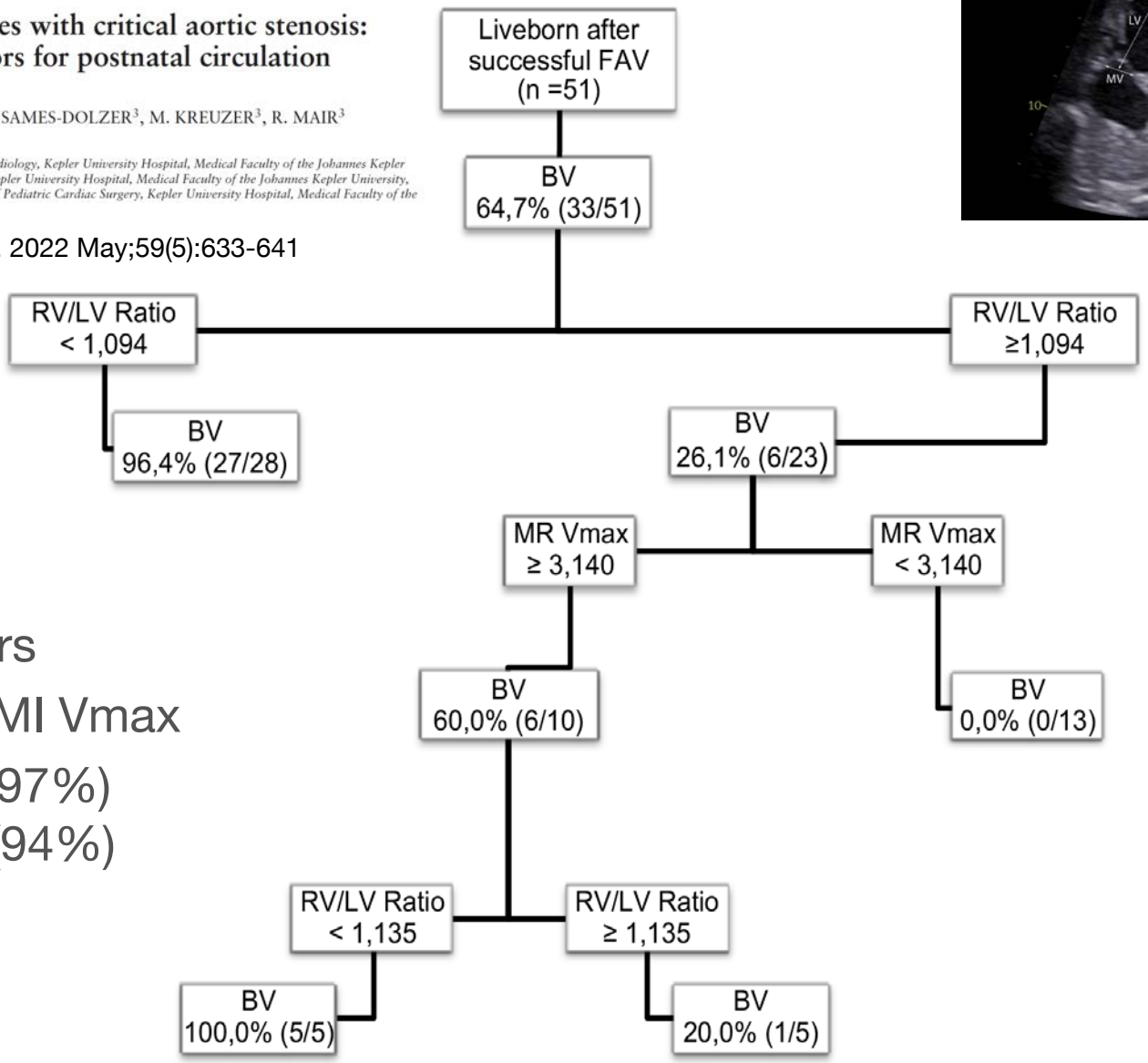
Predictors of postal BV circulation

Valvuloplasty in 103 fetuses with critical aortic stenosis: outcome and new predictors for postnatal circulation

A. TULZER[1], W. ARZT[2], R. GITTER[1], E. SAMES-DOLZER[3], M. KREUZER[3], R. MAIR[3] and G. TULZER[1]

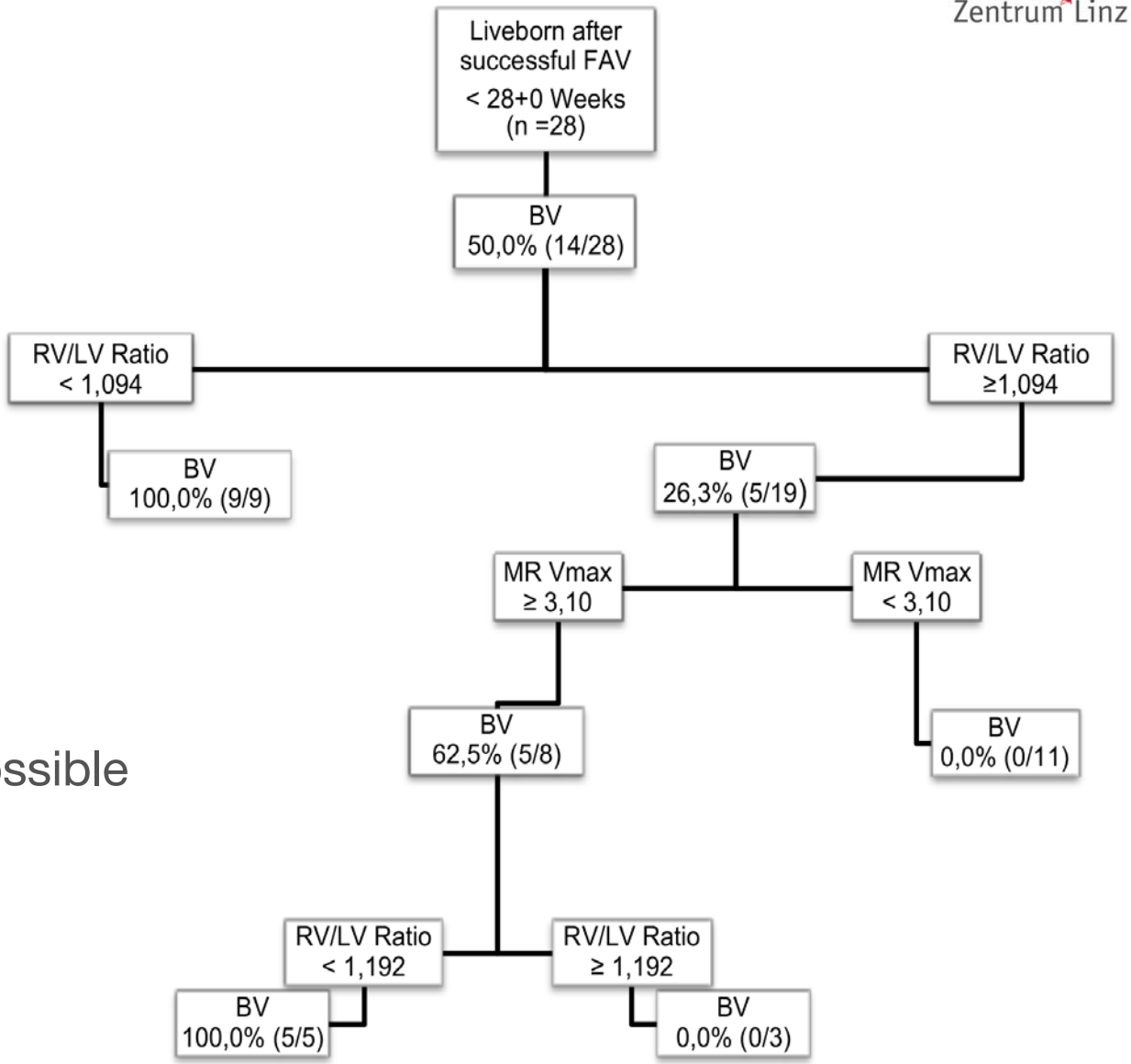
[1]*Children's Heart Center Linz, Department of Pediatric Cardiology, Kepler University Hospital, Medical Faculty of the Johannes Kepler University, Linz, Austria;* [2]*Institute of Prenatal Medicine, Kepler University Hospital, Medical Faculty of the Johannes Kepler University, Linz, Austria;* [3]*Children's Heart Center Linz, Department of Pediatric Cardiac Surgery, Kepler University Hospital, Medical Faculty of the Johannes Kepler University, Linz, Austria*

Ultrasound Obstet Gynecol. 2022 May;59(5):633-641



- 3 parameters
  - RV, LV, MI Vmax
- Sensitivity (97%)
  Specificity (94%)

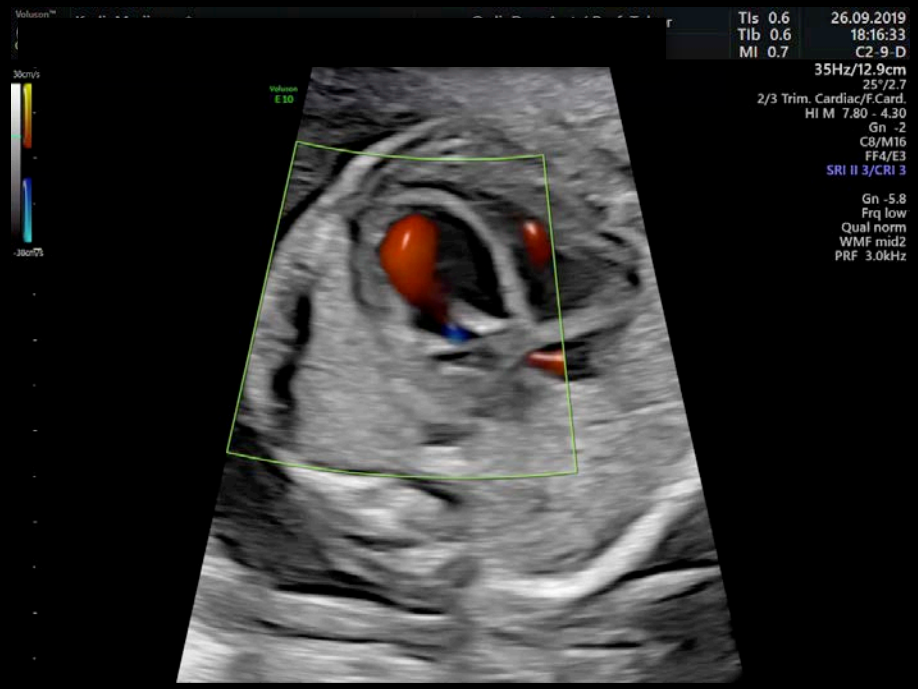
Predictors for GA < 28 weeks

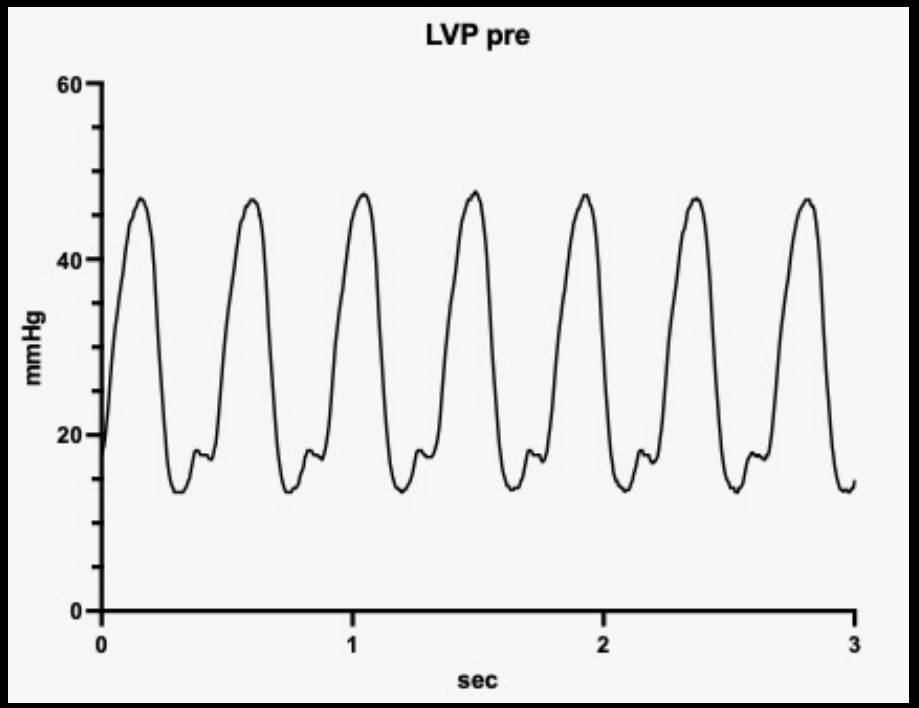


- BV Outcome possible for smaller LVs

Tulzer A et al. Valvuloplasty in 103 fetuses with critical aortic stenosis: outcome and new predictors for postnatal circulation. Ultrasound Obstet Gynecol. 2021 in press

FETAL INTRACARDIAC PRESSURE





Annals of Biomedical Engineering, Vol. 49, No. 5, May 2021 (© 2020) pp. 1364–1379
https://doi.org/10.1007/s10439-020-02683-x

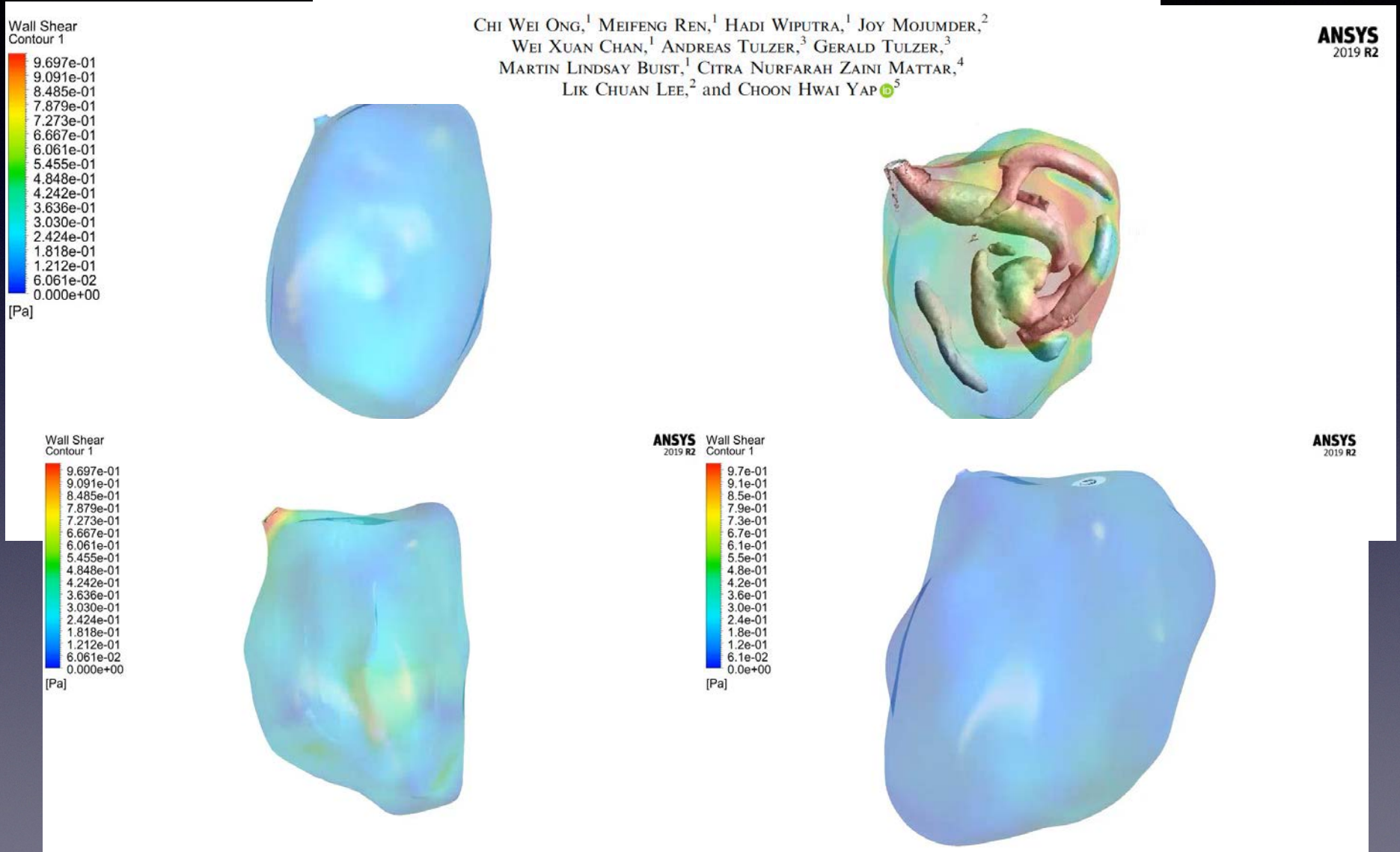
BMES BIOMEDICAL ENGINEERING SOCIETY

Check for updates

Original Article

Biomechanics of Human Fetal Hearts with Critical Aortic Stenosis

CHI WEI ONG,[1] MEIFENG REN,[1] HADI WIPUTRA,[1] JOY MOJUMDER,[2] WEI XUAN CHAN,[1] ANDREAS TULZER,[3] GERALD TULZER,[3] MARTIN LINDSAY BUIST,[1] CITRA NURFARAH ZAINI MATTAR,[4] LIK CHUAN LEE,[2] and CHOON HWAI YAP[5]



FAV Summary

- FAV in selected fetuses mit CAS and eHLHS
  - Can be performed with high success-rate and acceptable mortality
  - Leads to immediate morphological and functional improvements
  - Our data support the concept that FCI may improve postnatal BV-outcome rates
  - Still significant morbidity and mortality in the first years of life
  - RV/LV ratios combined with MR velocity are easy to measure and helpful tools to select potential candidates

Postnatal BV Strategies

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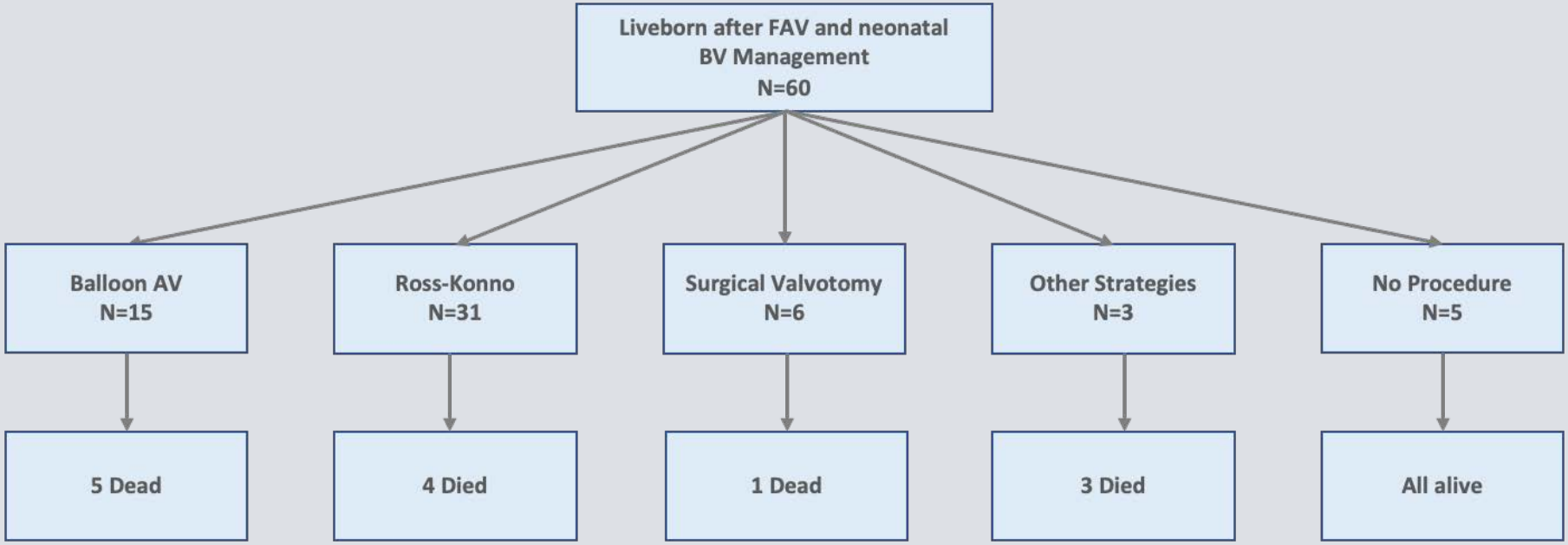

FETAL HLHS WITH INTAKT ATRIAL SEPTUM

- 6% of fetuses with HLHS, restrictive F.O.: 22%
- 1-year survival < 30%
- Secondary pulmonary damage - lymphagiectasia
- Emergency neonatal procedures
- Remaining high Mortality and Morbidity

A.P. Vlahos, J.E. Lock, D.B. McElhinney, M.E. van der Velde
Hypoplastic left heart syndrome with intact or highly restrictive atrial septum: outcome after neonatal transcatheter atrial septostomy
Circulation, 109 (2004), pp. 2326-2330

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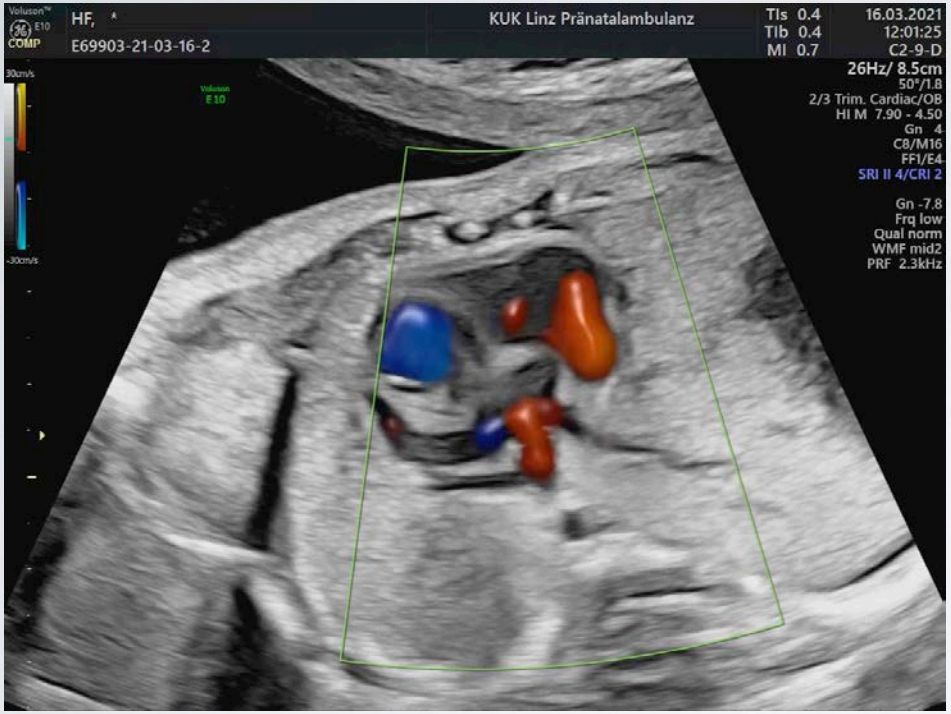

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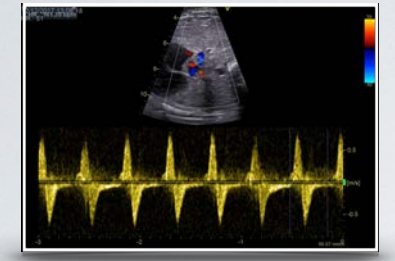
RESTRICTIVE OR CLOSED FORAMEN OVALE IN HLHS



CHANCES

- Better pulmonary development
- Avoid neonatal emergency procedures

RISKS

- Procedure related death
- Bradycardia / bleeding
- PRM, prem. labour, infection

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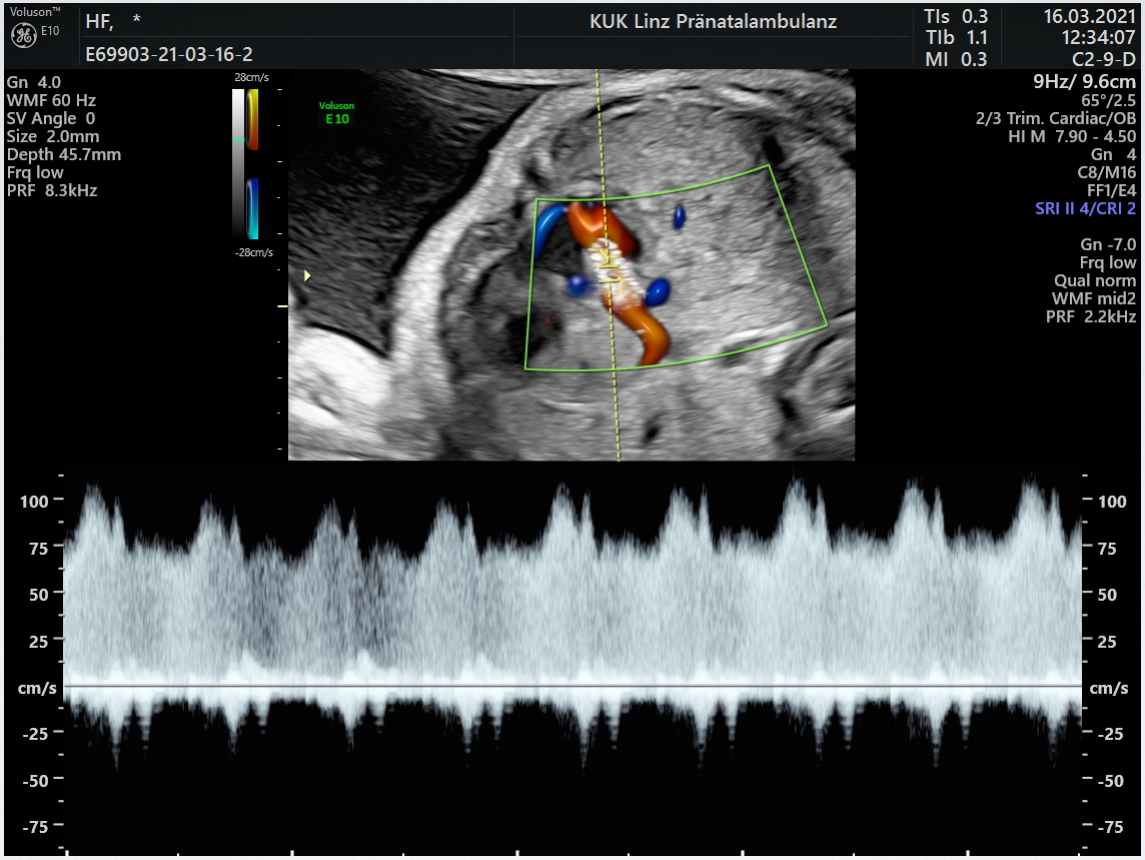

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FETAL HLHS WITH INTAKT ATRIAL SEPTUM

EXPERIENCE WITH STENTING

- 2013 Toronto: 4 fetal stents - 2 alive
- 2014 Boston: 10 stents: only 4 correct - 2 alive
- 2014 Bonn: 2 stents: 1 IUD, 1 neonatal death

FETAL HLHS WITH RESTRICTIVE OR INTAKT ATRIAL SEPTUM

LINZ EXPERIENCE

- 12 Cases
  - Dilation alone: 5 cases
  - Stents: 7 cases:
    - 1 CAS: stent embolized to LV - liveborn: removed at Ross-Konno surgery
    - 3 late stents (37 and 38 weeks): 2 deaths after Norwood, 1 alive after Fontan
    - 3 stents at 28 weeks: 1 IUD unexpected, 1 died after 48 hours,