Pulmonary Atresia with Intact Ventricular Septum (PA-IVS)

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& DGPK guideline committee

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Guideline PA-IVS
Definition

- malformation of right-sided cardiac structures with heterogeneous morphological appearance

- 75-80% isolated membraneous atresia of the pulmonary valve;
  combined with infundibular atresia in 18-25%
- intact ventricular septum
- hypoplasia of tricuspid valve, right ventricle, and pulmonary artery (PA) trunk
- significant hypertrophy of the right ventricle
- usually normal sized branch PAs
- right atrial enlargement
- atrial septal defect
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anatomic variations

RV size and morphology

Piers E.F Daubeney et al. Pulmonary atresia with intact ventricular septum: Range of morphology in a population-based study
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anatomic variations

Tricuspid valve malformation
• concomitant Ebstein's malformation in 8-9 %

• in rare cases (~ 5 %) with severe tricuspid regurgitation, RV and tricuspid valve annulus are dilated, with poor systolic RV function

• prevalence PA-IVS: 0.3 – 0.45 / 10,000 live births
  PAN: 0.3 % of all congenital heart defects
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Definition – Basic information

• considerably variable **anomalies of the coronary arteries**: => stenoses / sinusoids / fistulas

- clear correlation to the grade of RV hypoplasia
- myocardial sinusoids or small fistula between RV cavity and coronary arteries are frequent: 40-50%

RV-angiogram (lateral view) displaying multiple small connections to both coronary arteries
RV-dependent coronary circulation (RVDCC) (7-9%)

- coronary ectasia or very large fistulas
- coronary fistulas without aorto-coronary connection
- stenosis or discontinuations of large coronary artery branches
- coronary perfusion of relevant portions of the LV being supplied by the RV
RV-dependent coronary circulation

- coronary perfusion of relevant portions of the LV being supplied by the RV

must be excluded before valvotomy of the pulmonary atresia is considered

RV angiogramm (RAO) with atretic RVOT and filling of major part of LCX and LAD
Hemodynamics

- duct-dependent pulmonary blood flow
- inadvertent interatrial communication with right-to-left shunt
- suprasystemic RV pressure
- tricuspid regurgitation (variable)
clinical presentation:
- neonates/infants:
  - mild cyanosis due to right-to-left shunt at atrial level
  - duct closure causes acute severe cyanosis
  - severe cyanosis combined with congestive heart failure in the rare case of restrictive PFO
  - in the rare case of severe enlargement of RA due to severe TR respiratory distress due to bronchial compression
- older children: duct dependent / shunt dependent cyanotic heart disease

• differential diagnoses:
  - tricuspid atresia, critical pulmonary stenosis, Ebstein’s anomaly, severe tricuspid regurgitation, pulmonary atresia with VSD
  - "functional pulmonary atresia"
  (in pulmonary hypertension and / or failing right ventricle)
Goal: displaying cardiac and coronary anatomy with respect to the therapeutic goal of neonatal RV decompression

- membranous vs. infundibular atresia
- extent of RV hypoplasia and hypertrophy
  - absence of trabecular part and apex?
  - the size of the tricuspid valve (TV) correlates well with RV size:
    → tricuspid valve annulus diameter (TVA) \((\text{apical and subcostal 4-chamber view in end-diastole})\) including Z-score calculation; relation to mitral valve annulus diameter
    → degree of TR; calculation of RV pressure
- size of pulmonary valve annulus, pulmonary artery trunk and proximal branch arteries
- size and morphology of the arterial duct (potential ductal stenting!) and atrial septal defect (restriction?)
- extent of coronary anomalies:
  - myocardial sinusoids / small coronary fistulas
  - potential right ventricule dependent coronary circulation?
the size of the tricuspid valve (TV) correlates well with RV size:
→ tricuspid valve annulus diameter (TVA) (*apical and subcostal 4-chamber view in end-diastole*) including Z-score calculation; relation to mitral valve annulus diameter
→ for complete imaging, both echocardiography and additional catheterization are usually required

→ for practical purpose, diagnostic catheterization and first catheter palliation will be performed during one intervention in most centers
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**Diagnostics**

- **morphological classification**
  - (echocardiography / angiography)

- **group A**
  - **sufficient RV-size**
    - TV Z-score* > -2.5
    - membranous atresia with well developed infundibulum
    - variable TR
    - no major coronary sinusoids
  
  - * TV-annulus ≥ 8 mm

- **group B**
  - **Intermediate forms**
    - ‘borderline’-RV, often hypoplastic trabecular RV-component (‘bipartite’)
      - TV Z-score* -2.5 bis -5
      - patent infundibulum
      - +/- subvalvular stenosis
      - +/- hypoplastic PV-annulus
      - variable TR
      - +/- small sinusoids
  
  - * TV-annulus > 5 mm und < 8 mm

- **group C**
  - **severe RV-hypoplasia**
    - TV Z-score* ≤ -5
    - no trabecular RV
    - infundibulum subatretic / atretic
    - mostly no TR
    - often large sinusoids
    - +/- RV-pressure-dependent coronary perfusion
  
  - * TV-annulus ≤ 5 mm
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Therapy

Goal (group A & B):
biventricular repair with separation of systemic and pulmonary circulation

(echocardiography / angiography)

- membrane atresia with well developed infundibulum
  - variable TR
  - no major coronary sinusoids

- TV Z-score* > -2.5

- membranous atresia with well developed infundibulum
  - variable TR
  - no major coronary sinusoids

- TV Z-score* -2.5 bis -5

- patent infundibulum
  - +/- subvalvular stenosis
  - +/- hypoplastic PV-annulus
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    - +/- small sinusoids

- no trabecular RV
  - infundibulum subatretic / atretic
  - mostly no TR
  - often large sinusoids
  - +/- RV-pressure-dependent coronary perfusion

Initial therapy

- RF-perforation or surgical commissurotomy
- RF-perforation + ductal stenting or surgical valvotomy +/- RVOT-enlargement +/- AP-shunt +/- Atrioseptostomy
- Ductal stent + BAS or AP-shunt +/- BAS

- Neonatal RV decompression (interventional or surgical valvotomy)
  => prerequisite for subsequent RV growth
  → antegrade pulmonary blood flow
  → decreasing RV pressure
  → reducing pre-existing TR

- Additional pulmonary perfusion through the duct is still needed in some patients to allow for adaptation of the RV → low-dose PG infusion might be continued

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Case I

1st day of life, 2.4 kg
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Case I

1st day of life, 2.4 kg

Z-score – 2.1

Moderate TR

good sized main PA
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Case I

3rd day of life, 2.3 kg:
catheter valvotomy
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Case I

3rd day of life, 2.3 kg: catheter valvotomy
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case I

3rd day of life, 2.3 kg: catheter valvotomy
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case I

3rd day of life, 2.3 kg: catheter valvotomy
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case I

TTE nach 6 Mo

TV-Ring 12 mm
Z-score -1.3
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case II

PA-IVS; 4 kg; PG E – infusion; severe TR (IV°); subsequent massive RA-dilatation

- HF-perforation and balloon dilation (3 & 8 mm balloons)
- PG E continued for 5 days
- rapid regression of TR after successful catheter valvotomy
- no further intervention during f/u (8.5 y)
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case III

PA-IVS; 2.8 kg; 'good sized' RV, TV Z-score -1.1; moderate TR;

ductal stenosis despite PG E, decreasing SO₂

=> RF perforation + balloon;
PG E continued
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case III

antegrade ductal stenting with coronary stent

rationale for ductal stenting:
40 % of pts after interventionally perforated atresia and nearly 50 % of pts after surgical valvotomy need a second intervention to secure sufficient pulmonary blood flow before hospital discharge
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Follow-up / case III

2 y after valvotomy: mild PR, stented duct with residual flow

4.5 y after valvotomy; TV Z-score: 0.4
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case IV

PA-IVS; 4.3 kg; severe RV-hypertrophy; good sized TV annulus; good sized PV annulus

- RF perforation + balloon
- ductal stenting (2 stents)
- persistent muscular RVOTO
- redilation RVOT (balloon)
- surgical RVOT augmentation

- no further intervention for the next 6 y;
  normal exercise capacity
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**Therapy**

<table>
<thead>
<tr>
<th>Group A: sufficient RV-size</th>
<th>Group B: Intermediate forms</th>
<th>Group C: severe RV-hypoplasia</th>
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<tbody>
<tr>
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<td>ductal stent + BAS or AP-shunt +/- BAS</td>
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<td>▪</td>
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<tr>
<td><strong>reintervention</strong></td>
<td><strong>sufficient RV-growth</strong></td>
<td><strong>insufficient RV-growth</strong></td>
</tr>
<tr>
<td>▪ rare!</td>
<td>▪ no cyanosis =&gt; no reintervention</td>
<td>▪ cyanosis =&gt; interventional ASD/PFO closure</td>
</tr>
<tr>
<td>• RVOT-redilatation</td>
<td>• CPA (1½ ventricle)</td>
<td></td>
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<tr>
<td>• RVOT-augmentation (fixed subvalvular stenosis)</td>
<td>• w/o additional RVOT augment. (subvalv.stenosis / small PV-annulus)</td>
<td></td>
</tr>
<tr>
<td>• TV-reconstruction (severe TR)</td>
<td>• TV-reconstruction (severe TR)</td>
<td></td>
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<tr>
<td>▪</td>
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<td></td>
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<td><strong>group A</strong>: sufficient RV-size</td>
<td><strong>group B</strong>: Intermediate forms</td>
<td><strong>group C</strong>: severe RV-hypoplasia</td>
</tr>
<tr>
<td><strong>reinterventions during follow-up</strong> focus on</td>
<td></td>
<td></td>
</tr>
<tr>
<td>→ residual RVOT stenosis</td>
<td>→ surgical treatment of severe TR</td>
<td></td>
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<tr>
<td>→ ASD closure to achieve separation of systemic and pulmonary circulation</td>
<td></td>
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<tr>
<td>→ pulmonary valve replacement [in the long-term]</td>
<td></td>
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<tr>
<td><strong>Insufficient RV growth</strong> =&gt; ‘1½-ventricle repair’</td>
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<tr>
<td>→ surgical removal of residual RVOT obstruction combined with a bidirectional RVOT obstruction continous with a bidirectional cavo-pulmonary anastomosis</td>
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<td></td>
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<tr>
<td>→ closure of the ASD</td>
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<tr>
<td><strong>severe RV hypoplasia</strong> =&gt; univentricular palliation according to the ‘Fontan principle’</td>
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</tbody>
</table>
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Follow-up

- life-long follow-up by pediatric cardiologists and subsequently specialists for adult congenital heart disease is mandatory

- besides tricuspid valve regurgitation and pulmonary valve regurgitation, regular follow-up visits should assess growth and function of RV and TV (Z-scores, identical reference group!)

- objective examinations of exercise capacity and Holter ECGs every 2-3 years (school age)

- residual findings, which might require further diagnostic imaging (MRI, re-cath) and potential treatment:
  - RVOT reobstruction
  - tricuspid regurgitation
  - high-grade pulmonary regurgitation
  - ASD
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Follow-up / Reinterventions

Chubb et al. JACC 2012
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Prognosis

- Perioperative morbidity and mortality is considerable in infancy (highest in patients with low birth weight, concomitant Ebstein's anomaly, dilated thin-walled RV, and RVDCC)

- Positive prognostic factors to achieve biventricular repair with separation of systemic and pulmonary circulation (~ 50 % of cases) are:
  - larger initial TV and PV annulus diameter
  - a ratio of TVA / MVA of > 0.5
  - tcSO₂ > 90 % at the age of one year

- Despite absolute growth of TV and RV, a real catch-up growth (increase in tricuspid valve Z-score of > 2 points) is observed in only 10-15 % of cases

- Exercise capacity will be reduced in most patients even after biventricular repair due to the ongoing restrictive RV physiology with diastolic RV-dysfunction
Z = \frac{\text{measured value} - \text{mean of the population}}{\text{standard deviation of the normal population}}

- The Z-value quantifies the position of an individually measured size within a sample population; the measurement unit is the standard deviation above (+) or below (-) the population’s mean value.
- The validity of the values is limited to:
  - a comparable normal population with normal distribution of the data
  - the **same measurement method** for the definition of the mean and standard deviation

- To be used in the clinical setting, the **sample size** should have been large enough (especially in young infants!).
- Mean and standard deviation may vary between the various investigators or with body size.
- For observational studies the **same reference data** and the **same method of measurement** should be used throughout.

Chubb et al. Annals of Pediatric Cardiology 2012
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Dealing with Z-scores / Z-values


Zilberman et al. Ped Cardiol
2005

782 pts; 125 pts < 1 y
in a normal sized newborn (0,2 m²), a measured TV-diameter of X mm corresponds to a TV Z-score of

<table>
<thead>
<tr>
<th>reference</th>
<th>graphik</th>
<th>parameterz</th>
<th>nomogramm boys</th>
<th>parameterz boys</th>
<th>nomogramm girls</th>
<th>parameterz girls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detroit data, Pettersen</td>
<td>-3</td>
<td>-2,5</td>
<td>-3,93</td>
<td>-2,42</td>
<td>-1,8</td>
<td>-0,3</td>
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<tr>
<td>J Am Soc Echocard</td>
<td>-7,59</td>
<td>-6,07</td>
<td>-4,98</td>
<td>-3,12</td>
<td>-2,42</td>
<td>-1,24</td>
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<td>Cincinatti data, Zilberman</td>
<td>-6,3</td>
<td>-3,5</td>
<td>-2,75</td>
<td>-2,06</td>
<td>-1,43</td>
<td>-0,86</td>
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<tr>
<td>Ped Cardiol 2005</td>
<td>-11,9</td>
<td>-6,3</td>
<td>-3,5</td>
<td>-1,2</td>
<td>-0,2</td>
<td>0,5</td>
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<td>Wessex data</td>
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<td>-4,6</td>
<td>-4</td>
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<td>Daubeney 1999</td>
<td>-9,7</td>
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<td>-4,7</td>
<td>-3,41</td>
<td>-2,23</td>
</tr>
<tr>
<td>Rowlatt-Daten (Patho)</td>
<td>-5,3</td>
<td>-4,6</td>
<td>-4</td>
<td>-3,3</td>
<td>-2,1</td>
<td>-0,8</td>
</tr>
</tbody>
</table>
Implications for the PA-IVS guideline:

- most of the (older) surgical publications use reference data of inadequately small autopsy series, which should no longer be applied today

- the best validated reference data for the calculation of TV Z-scores are from Pettersen et al. ['Detroit data'], which are available for online calculation under www.parameterz.com
Guideline PA-IVS
Dealing with Z-scores / Z-values

modified from Chubb et al. JACC 2012, using Z-scores from Pettersen 2008