Postnatal management of Tetralogy of Fallot
1st year of life

Damien Bonnet

Unité médico-chirurgicale de Cardiologie Congénitale et Pédiatrique
Hôpital Universitaire Necker Enfants malades – APHP, Université Paris Descartes, Sorbonne Paris Cité
IcarP Cardiology, Institut Hospitalo-Universitaire IMAGINE

Centre de Référence Maladies Rares
Malformations Cardiaques Congénitales Complexes-M3C
Centre de Référence Maladies Rares
Maladies Cardiaques Héréditaires- CARDIOGEN
Simple Fallot
### Prenatal diagnosis, pregnancy termination, perinatal and early neonatal mortality for selected (isolated) congenital heart anomalies

**Paris Registry of Congenital Malformations, 1983-2010**

<table>
<thead>
<tr>
<th></th>
<th>83-88%</th>
<th>89-94%</th>
<th>95-00%</th>
<th>00-10%</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ToF</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prenatal diagnosis</td>
<td>20.0</td>
<td>37.5</td>
<td>69.7</td>
<td>74</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Pregnancy termination</td>
<td>10.0</td>
<td>12.5</td>
<td>0</td>
<td>1.8</td>
<td>0.07</td>
</tr>
<tr>
<td>First week mortality</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.3</td>
<td>-</td>
</tr>
<tr>
<td>Perinatal mortality</td>
<td>0</td>
<td>7.1</td>
<td>2.9</td>
<td>2.0</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Recent studies show that prenatal diagnosis DOES NOT impact neonatal CHD mortality

Khoshnood B et al. BMJ open 2017
van Velzen CL et al. BJOG 2016;123:400–407

<table>
<thead>
<tr>
<th>CHD</th>
<th>Prenatal diagnosis</th>
<th>Infant mortality</th>
<th>Risk ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n*</td>
<td>n†</td>
<td>%</td>
<td>95% CI</td>
</tr>
<tr>
<td>Functionally univentricular heart‡</td>
<td>No</td>
<td>7</td>
<td>3</td>
<td>42.9</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>32</td>
<td>17</td>
<td>53.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.2</td>
</tr>
<tr>
<td>d-Transposition of the great arteries‡</td>
<td>No</td>
<td>24</td>
<td>1</td>
<td>4.2</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>57</td>
<td>5</td>
<td>8.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.1</td>
</tr>
<tr>
<td>Tetralogy of Fallot‡</td>
<td>No</td>
<td>18</td>
<td>2</td>
<td>11.1</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>36</td>
<td>1</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.3</td>
</tr>
<tr>
<td>Coarctation of the aorta‡</td>
<td>No</td>
<td>44</td>
<td>3</td>
<td>6.8</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>29</td>
<td>2</td>
<td>6.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.0</td>
</tr>
</tbody>
</table>

*N = number of live births (denominator data).
†n = number of deaths (numerator data).
‡Cases with the specific International Paediatric and Congenital Cardiac Code for the given CHD; whether or not other CHD codes were also included, all cases with chromosomal or others anomalies were excluded.

Khoshnood B et al. BMJ open 2017
van Velzen CL et al. BJOG 2016;123:400–407
Impact of preterm birth on infant mortality for newborns with congenital heart defects
The EPICARD Study Group

- Preterm birth is associated with an approximately four-fold higher risk of infant mortality for newborns with CHD.
- This excess risk appears to be mostly limited to newborns < 35 weeks of gestation and is disproportionately due to early deaths.
One third of fetuses with ToF had extra cardiac anomalies
15% had intra-uterine growth retardation

## Death before hospital discharge in prenatally diagnosed « in-born » CCHD

<table>
<thead>
<tr>
<th>Type of CHD/predicted physiology</th>
<th>Mortality before discharge n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>at risk for Rashkind</td>
<td>8 (2.3)</td>
</tr>
<tr>
<td>ductal-dependent pulmonary flow</td>
<td>13 (12.1)</td>
</tr>
<tr>
<td>potentially ductal-dependent pulmonary flow</td>
<td>3 (2.1)</td>
</tr>
<tr>
<td>ductal-dependent systemic flow</td>
<td>25 (39.6)</td>
</tr>
<tr>
<td>potentially ductal-dependent systemic flow</td>
<td>16 (5.2)</td>
</tr>
<tr>
<td>TAPVR</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td>AV block with CHD</td>
<td>0 (0)</td>
</tr>
<tr>
<td>a priori at no risk of early intervention</td>
<td>7 (6.5)</td>
</tr>
<tr>
<td><strong>ALL</strong></td>
<td><strong>73 (6.7)</strong></td>
</tr>
</tbody>
</table>

![Graph showing mortality over years with two lines representing No Extracardiac and Extracardiac anomalies](graph.png)
Prenatal diagnosis anticipates and prevents early demise

Is in utero transfer a valid option?

**Common indications for in utero transfer**

- Life threatening CHDs
  - *Ex: TGA, TAPVR, HLHS*
- Evolutive defects
  - *Ex: Coarctation of the aorta*
- Uncertain perinatal physiology
  - *Ex: Tetralogy of Fallot*
- Highly variable/unpredictable postnatal outcome
  - *Ex: Ebstein*
Interventions in prenatally diagnosed « in-born » CHD

2543 in-born

**TGA**

- 748 in born
- 21% early demise
- 87% intervention

**Suspected coarctation**

- 486 in born
- 35% intervention

**ToF**

- 287 in born
- 4% intervention
Repair of TOF & PA-VSD at one year is closely related to size of pulmonary artery branches

<table>
<thead>
<tr>
<th>PA branches Normal vs. absent/hypoplastic</th>
<th>Repair &lt; 1y %</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>86 vs. 55</td>
<td>0.001</td>
<td></td>
</tr>
</tbody>
</table>

| PA trunk present vs. absent               | 79 vs. 16    | 0.003 |
| MAPCAs present vs. absent                 | 76 vs. 50    | 0.17  |
Predictors of long term outcome
Pediatric Cardiac Care Consortium

3283 patients with simple TOF
Follow-up 18.5 years (maximum, 33 years; IQR, 14.6-22.4 years),
The median age at death was 1.0 years (IQR, 0.6-2.1 years), with range 3 days to 19.7 years.

25 years survival 94.5%
3283 patients with simple TOF
Follow-up 18.5 years (maximum, 33 years; IQR, 14.6-22.4 years),
The median age at death was 1.0 years (IQR, 0.6-2.1 years), with range 3 days to 19.7 years.

Predictors of long term outcome
Pediatric Cardiac Care Consortium

Smith CA et al. JAMA Cardiol 2018
Non modifiable factor: genetic condition

HR 3.64

Smith CA et al. JAMA Cardiol 2018
Predictors of long term outcome
Pediatric Cardiac Care Consortium

Repair strategy

TOF Repair type

Smith CA et al. JAMA Cardiol 2018
ToF is a **progressive disease** with a potential increase in severity with time.

**Optimizing the pulmonary blood flow** in the most physiologic fashion may halt this process,

With the objective to **normalize growth of the pulmonary arteries** during infancy.

Thus, **early repair** is thought to be the **optimal** management approach.

**Preserving the pulmonary valve** predicts a better long-term outcome.
Patients vs. Strategies & Alternative Techniques

REACH GOAL!
STICK TO IT
GET TO WORK
MAKE PLAN
SET GOAL

Toolbox with various tools
Patients characteristics

Different categories

Non modifiable
- underlying genetic conditions

Time-dependent
- age and weight
- symptoms

Anatomical characteristics

Non modifiable
- location of the VSD
- coronary artery anatomy

Time-dependent/modifiable
- pulmonary valve and annulus
- pulmonary artery branches (size, contiguity)
- anatomy of the arterial duct
Goal: closed VSD, preserved pulmonary valve without obstruction or regurgitation, normal growth of pulmonary artery branches, normal RV function, no aortic regurgitation

Make plan: elective repair or patient’s dependent repair (staged or one step)

Get to work: when ? and how ?

Reach goal: initial strategy and long-term outcomes
Alternative techniques

**Palliate:**
- Blalock
- or Stenting the arterial duct
- or surgical right ventricle to pulmonary connection
- or stenting the right outflow tract

**Repair:**
- Trans-annular patch
- Preserve pulmonary valve
- RV-PA conduit
- Limit right ventriculotomy
Simple ToF(s) or one patient/one ToF

Patient population

Treatment

Standard approach
Low mortality
Tolerated morbidity (early and late)

Tailored approach
Reduced mortality?
Reduced morbidity (early and late)
Improve patients reported outcomes
Initial strategy in symptomatic neonates with ToF

Non elective intervention

Blalock shunt

1-Patients characteristics
- good sized pulmonary arteries rather than small
- with potentially preservable pulmonary valve

2-Strategy
- avoid lesion of pulmonary valve
- avoid neonatal conduit (coronary anomaly)
- limit/avoid right recurrent right ventriculotomy
  +/- avoid bypass

3-Alternative techniques
- vs. stenting of the arterial duct
- vs. complete repair in neonatal period
Initial strategy in symptomatic neonates with ToF

Non elective intervention

1- Patients characteristics
- good sized pulmonary arteries rather than small
- with potentially preservable pulmonary valve

2- Strategy
- avoid lesion of pulmonary valve
- avoid neonatal conduit (coronary anomaly)
- limit/avoid right recurrent right ventriculotomy
+/- avoid bypass

3- Alternative techniques
- vs. stenting of the arterial duct
- vs. complete repair in neonatal period

Outcomes of BT shunts

In hospital mortality (4-5%)
Inter-stage mortality (3.6%)

24% of acute post-operative events
including shunt thrombosis, pulmonary overcirculation, shunt stenosis, and pulmonary artery stenosis

Initial strategy in symptomatic neonates with ToF

Non elective intervention

**Stenting of arterial duct**

1- **Patients characteristics**
   - Tendency for complex PDA–pulmonary artery morphology.

![Images of heart structures](image)

- LPA coarctation
- Tortuous
- Underneath the aortic arch
- From innominate artery Right aortic arch
Initial strategy in symptomatic neonates with ToF

Non elective intervention

Stenting of arterial duct

2-Strategy
- avoid surgery

Axillary access

Carotid access
Initial strategy in symptomatic neonates with ToF

Non elective intervention

Stenting of arterial duct

2-Strategy
- avoid surgery

Outcomes of PDA stenting in ToF
Aggravation of PA branch stenosis
Poor growth of vessel 'jailed' by stent
Shorter duration of palliation vs. BT shunt
Acute stent thrombosis

Tortuous PDA with multiple bends is NOT an indication

Rehman R et al. Future Cardiol 2018
Initial strategy in symptomatic neonates with ToF

Non elective intervention

Surgical right ventricle to pulmonary connection

1- Patients characteristics
   - small sized pulmonary arteries or LPA stenosis or disconnected PA
   - with very diminutive RVOT

2- Strategy
   - promote symmetrical growth of PA
   - more physiological than shunt

3- Alternative techniques
   - vs. stenting of the RVOT
   - vs. complete repair in neonatal period
Initial strategy in symptomatic neonates with ToF

Non elective intervention

Neonatal right ventricle to pulmonary connection

A

Survival

Overall survival
1 year 90%
5 years 84%
10 years 81%

Time (years) after RV-PA connection

B

Freedom for reinterventions following complete repair

Patch enlargement
Prosthetic conduit

89 ± 1%
84 ± 1%

Log-rank test = ns

Patients at risk (n)

34 (15) (10) (5) (3)
(34) (15) (10) (5) (2)

(Patch enlargement)
(Prosthetic conduit)

Age after complete repair (years)

Gerelli et al. EJTC 2013
Lenoir M et al. EJTC 2017
Initial strategy in symptomatic neonates with ToF
Non elective intervention

Neonatal right ventricle to pulmonary connection

Outcomes of surgical RV-PA connection
In hospital mortality (2-3%)
Inter-stage mortality (0%)
The main event is PA branch stenosis (10%)
Initial strategy in symptomatic neonates with ToF

Non elective intervention

Stenting of right ventricle outflow tract

1- Patients characteristics
   - small sized pulmonary arteries
   - with very diminutive RVOT

2- Strategy
   - promote symmetrical growth of PA
   - more physiological than shunt

3- Alternative techniques
   - vs. complete repair in neonatal period
Initial strategy in symptomatic neonates with ToF

Non elective intervention

Stenting of right ventricle outflow tract

IDEAL: elective repair > 3 months
CATH: Stenting
EARLY: repair before 3 months

Wilder TJ et al. JTCVS 2017
Initial strategy in symptomatic neonates with ToF
Non elective intervention

Stenting of right ventricle outflow tract vs. BT shunt

More reinterventions in stent
No mortality
Severe complications in 4-5%
No difference in late survival
Reduced ICU LOS
Better oxygenation?
Better growth of PA branches

Quandt D et al. J Am Coll Cardiol Intv 2017;10:1774–84
Non elective primary repair vs. shunt in infants < 3 months

BT patients were significantly younger (14 vs 25 days, \( P < .0001 \)), had a higher incidence of extracardiac congenital abnormalities (41% vs 33%, \( P .02 \)), had a higher rate of prematurity (17% vs 12%, \( P .04 \)), and more frequently received PGE1.

No difference in mortality between the two techniques

Irrespective of the surgical approach, younger patients (OR 1.03, \( P .007 \)), patients with noncardiac congenital anomalies (OR 2.48, \( P .016 \)), and those with prematurity (OR 3.28, \( P .007 \)) had a higher risk of mortality.
Initial strategy in Asymptomatic neonates with ToF

*Elective neonatal repair*

**Metanalysis**

3858 patients in 8 studies with 724 (19%) having undergone neonatal repair (6-20 days) and 3134 (81%) having undergone non-neonatal repair (60-220 days).
Initial strategy in Asymptomatic neonates with ToF

**Elective neonatal repair**

**Metanalysis**

3858 patients in 8 studies with 724 (19%) having undergone neonatal repair (6-20 days) and 3134 (81%) having undergone non-neonatal repair (60-220 days).

- Elective neonatal repair should be avoided when possible
- In hospital mortality (6%)
- Higher cost
- More trans-annular patch anticipating more late morbidity

Loomba RS et al. Pediatr Cardiol 2017;38:893–901
Elective repair 6 kgs/3 months

1-Patients characteristics
- acceptable sized pulmonary arteries
- pulmonary valve ?
- coronary artery epicardial course ?
- multiple VSD ?

2-Strategy
- limit late complications

3-Alternative techniques
- None
Outcomes ToF
Parisian experience (07-17): 923 ToF (PA-VSD excluded)

46%
51%
3%

Reintervention after complete repair

Freedom from reintervention (%)

Years

p < 0.001
p < 0.001

TOF without transannular patch
TOF/TOF-PA with transannular patch
TOF-PA with RVOT tube

Mostefa-Kara M et al. in preparation
Outcomes ToF
Parisian experience (07-17): 923 ToF (PA-VSD excluded)

Risk factors for reintervention (surgical or cath) after repair:
- Initial staged strategy
- Trans-annular patch and conduit
- Pulmonary branch stenosis

Mostefa-Kara M et al. in preparation
Can we have an algorithm in simple ToF?

Non elective

- Normal PA branches
- PV can be preserved
  - PDA anatomy simple
    - PDA-Stenting
  - PDA anatomy complex
    - BT-shunt

Elective or Staged repair

- Small PA branches
- PV cannot be preserved
  - Non elective repair
    - RVOT stenting
    - RV-PA surgical connection
  - PV can be preserved
    - Non trans-annular patch
    - Trans-annular patch
  - PV cannot be preserved
Can we have an algorithm in simple ToF?

- **Non elective**
  - Normal PA branches → PV can be preserved
  - Small PA branches → PV cannot be preserved

- **PDA anatomy**
  - Simple → PDA-Stenting
  - Complex → BT-shunt

- **Non elective repair**
  - RVOT stenting
  - RV-PA surgical connection
Can we have an algorithm in simple ToF?

- Non elective repair
  - PV cannot be preserved
  - PDA anatomy complex
  - RVOT stenting
  - RV-PA surgical connection

- Non elective
  - PV can be preserved
  - PDA anatomy simple
  - PDA-Stenting
  - BT-shunt

- Normal PA branches
- Small PA branches
ToF is a **progressive disease** with a potential increase in severity with time.

**Repair in infancy is the common goal** when feasible.

**Elective repair before 3 months/5-6 kgs** should **not be preferred**.

**Non elective palliation** should

- be adapted to anatomy and patient’s non-modifiable characteristics
- optimize pulmonary blood flow in the most physiologic fashion
- promote symmetric growth of pulmonary arteries
- preserve long-term outcome

**Tailored management** is the optimal strategy

Local skills and preferences have an important role (are an important bias)
Helen Taussig  
Alfred Blalock and Eileen Saxon  
Vivien Thomas

Thank you