M3C Academy

Postnatal management of Tetralogy of Fallot
1st year of life

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Malformations Cardiaques Congénitales Complexes-M3C

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European Reference Network for rare or low prevalence complex diseases
Network Heart Diseases (ERN GUARD-HEART)

European Reference Network for rare or low prevalence complex diseases
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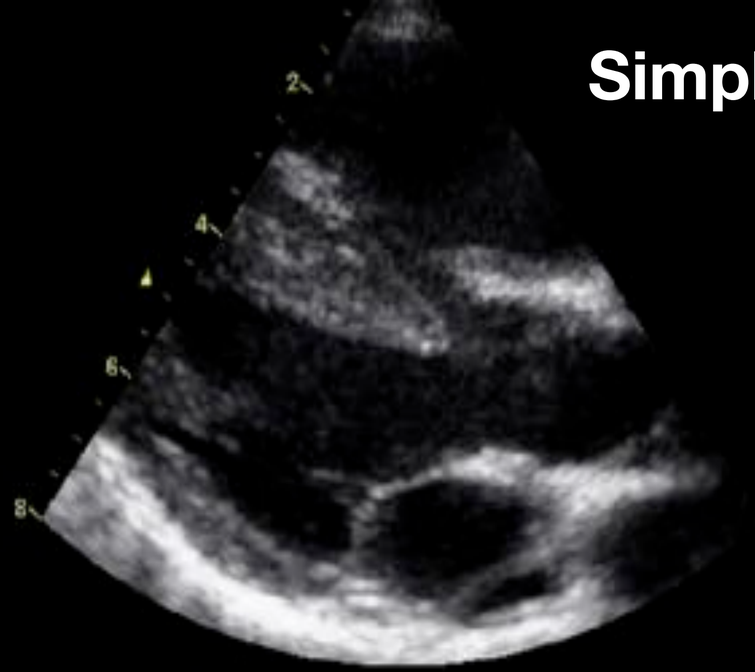
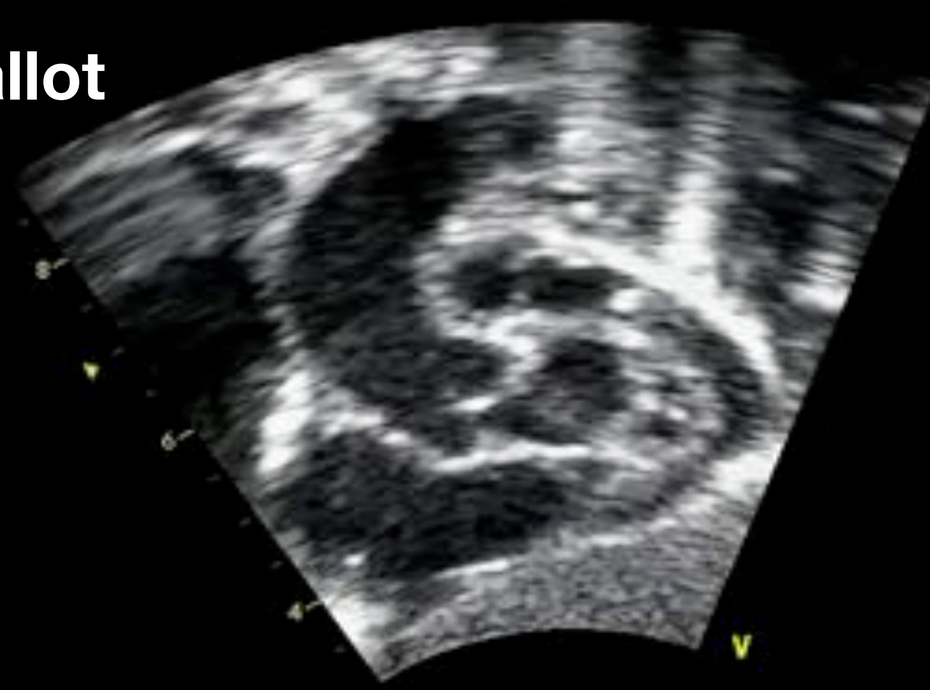
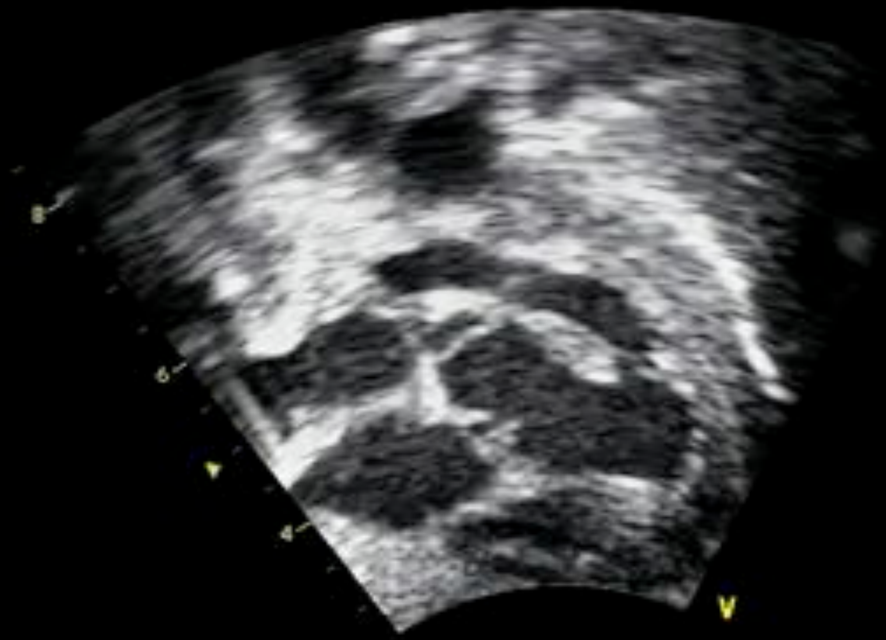
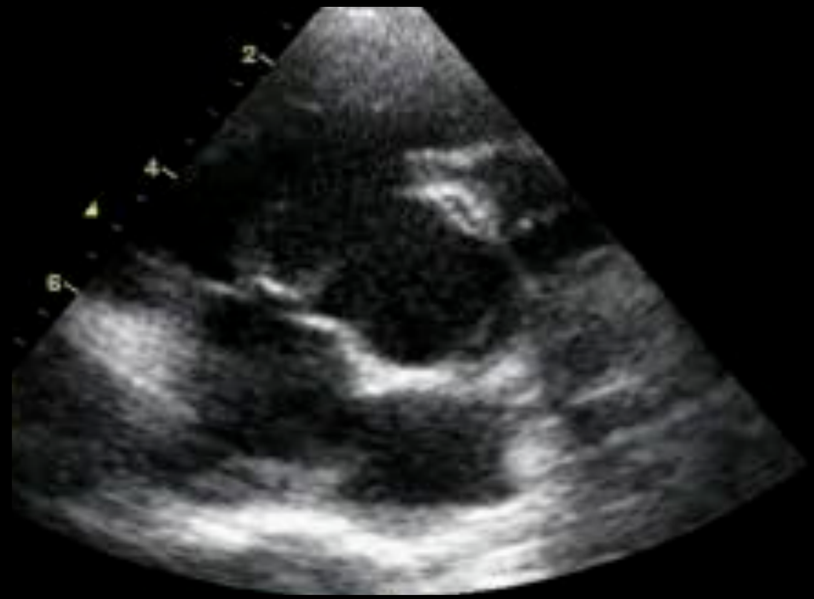
Simple Fallot









Prenatal diagnosis, pregnancy termination, perinatal and early neonatal mortality for selected (**isolated**) congenital heart anomalies

Paris Registry of Congenital Malformations, 1983-2010

ToF	83-88 %	89-94 %	95-00 %	00-10 %	p
Prenatal diagnosis	**20.0**	**37.5**	**69.7**	**74**	<0.005
Pregnancy termination	10.0	12.5	0	1.8	0.07
First week mortality	0	0	0	0.3	-
Perinatal mortality	0	7.1	2.9	2.0	0.63

Khosnood B et al. Pediatrics 2005;115:95-101

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

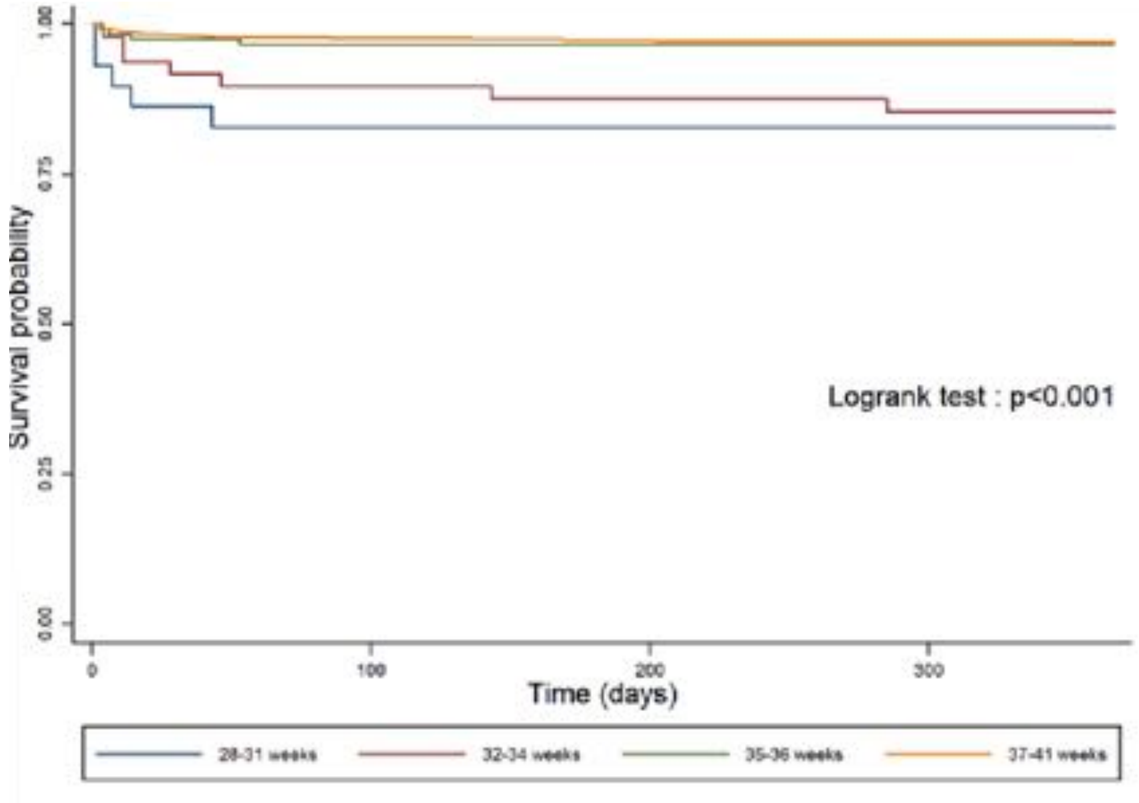
Table 3 Association between prenatal diagnosis and risk of infant mortality for four specific congenital heart defects (CHDs), EPIdémiologie des CARDiopathies congénitales (EPICARD) Population-Based Cohort Study

	Prenatal diagnosis	Infant mortality				
CHD		n*	n†	%	95% CI	Risk ratio	95% CI
Functionally univentricular heart‡	No	7	3	42.9	9.9 to 81.6		
	Yes	32	17	53.1	34.7 to 70.9	1.2	0.5 to 3.1
d-Transposition of the great arteries‡	No	24	1	4.2	0.1 to 21.1		
	Yes	57	5	8.8	2.9 to 19.3	2.1	0.3 to 17.1
Tetralogy of Fallot‡	No	18	2	11.1	1.4 to 34.7		
	Yes	36	1	2.8	0.07 to 14.5	0.3	0.02 to 2.6
Coarctation of the aorta‡	No	44	3	6.8	1.4 to 18.7		
	Yes	29	2	6.9	0.8 to 22.8	1.0	0.2 to 5.7

*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**.

Laas E et al. 2018

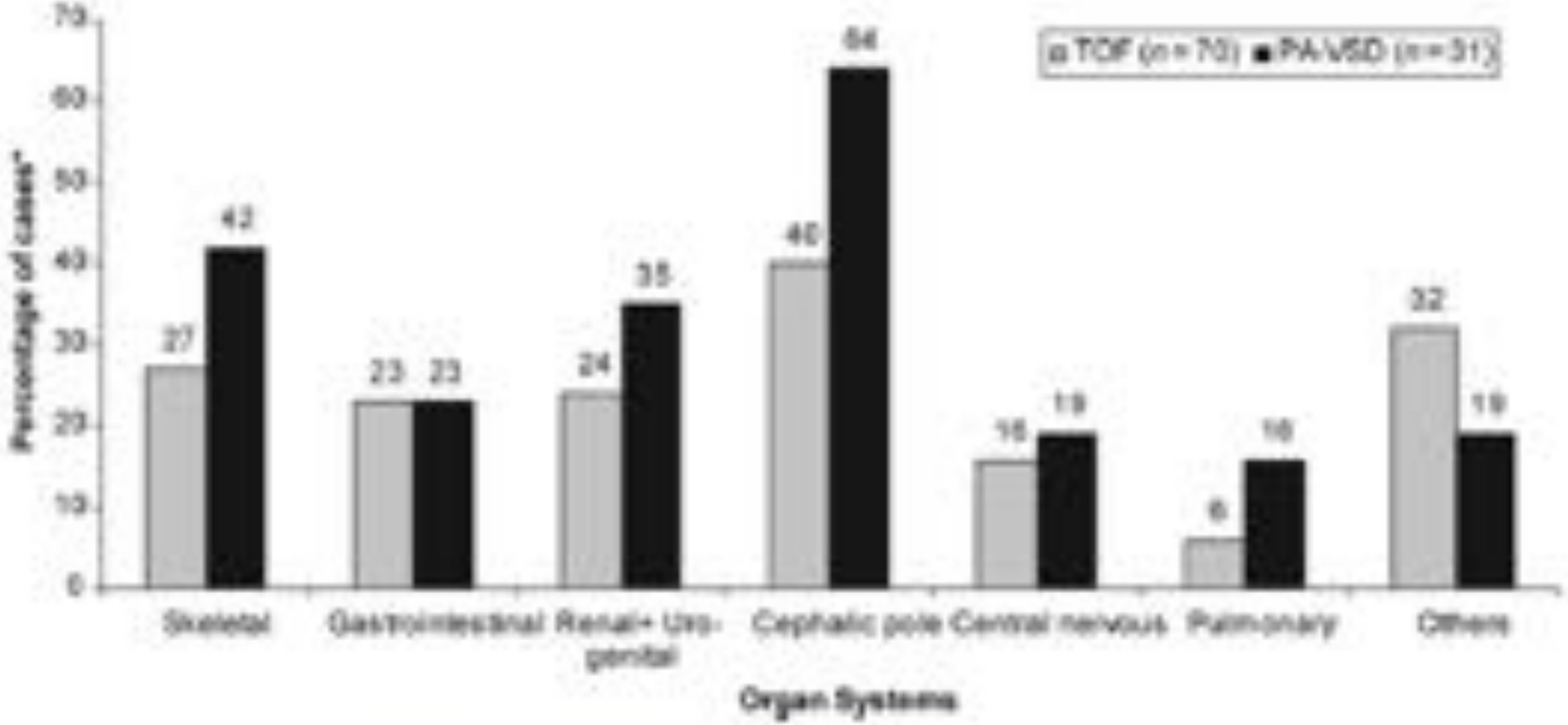


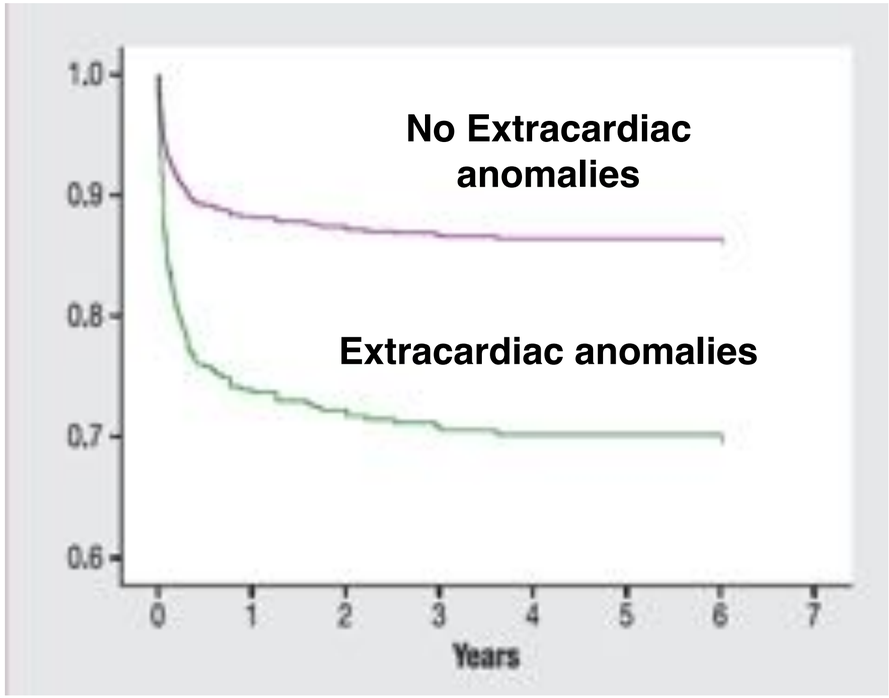
Figure 2 Details on extracardiac anomaly in foetal TOF and PA-VSD. Others, growth and endocrinological abnormalities, mental retardation, ophtalmological anomalies, uniс umbilical artery, cystic hygroma; TOF, tetralogy of Fallot; PA-VSD, pulmonary atresia with ventricular septal defect; the asterisk indicates the number of abnormalities by system/number of foetuses with associated extracardiac malformations per type of CHD (TOF or PA-VSD).

One third of fetuses with ToF had extra cardiac anomalies
15% had intra-uterine growth retardation

Kaguelidou F, Bonnet D. Eur Heart J. 2008 Jun;29(11):1432-8.

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

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



Bensemlali M et al. CiTY 2016
Bensemlali M et al. Arch Cardiovasc Dis 2016

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

Bensemlali M et al. CiTY 2016
Bensemlali M et al. Arch Cardiovasc Dis 2016

Is information on probability of complete repair individualized ?

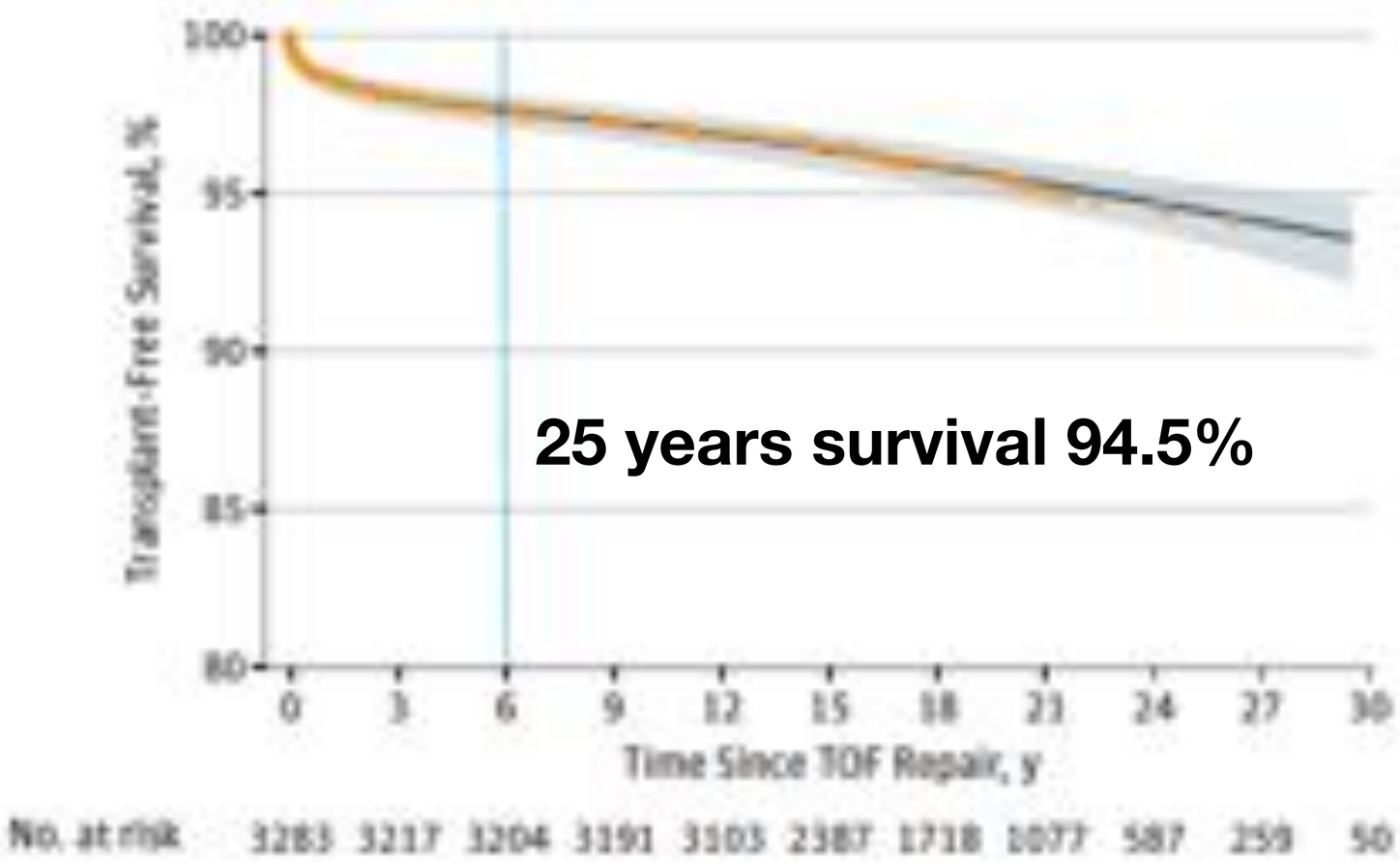
Repair of TOF & PA-VSD at one year is closely related to size of pulmonary artery branches

	Repair < 1y %	p
PA branches Normal vs. absent/hypoplastic	86 vs. 55	<0.001
PA trunk present vs. absent	79 vs. 16	0,003
MAPCAs present vs. absent	76 vs. 50	0.17

Kaguelidou F et al. Eur Heart J. 2008

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.



Smith CA et al. JAMA Cardiol 2018

Predictors of long term outcome
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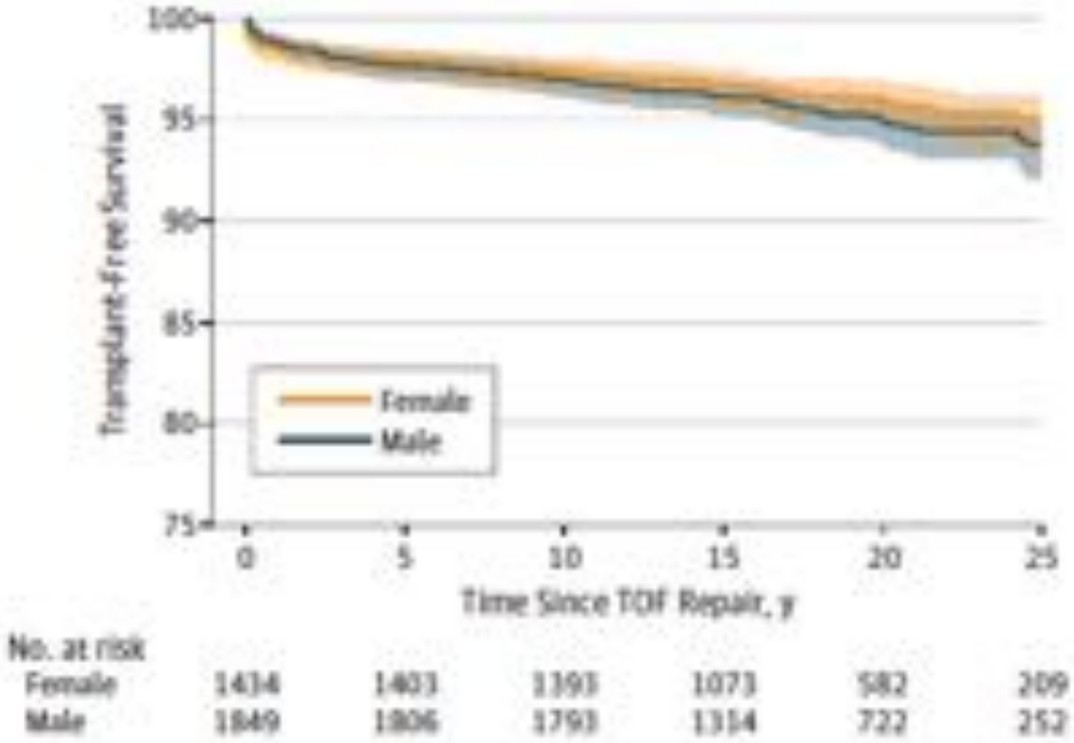
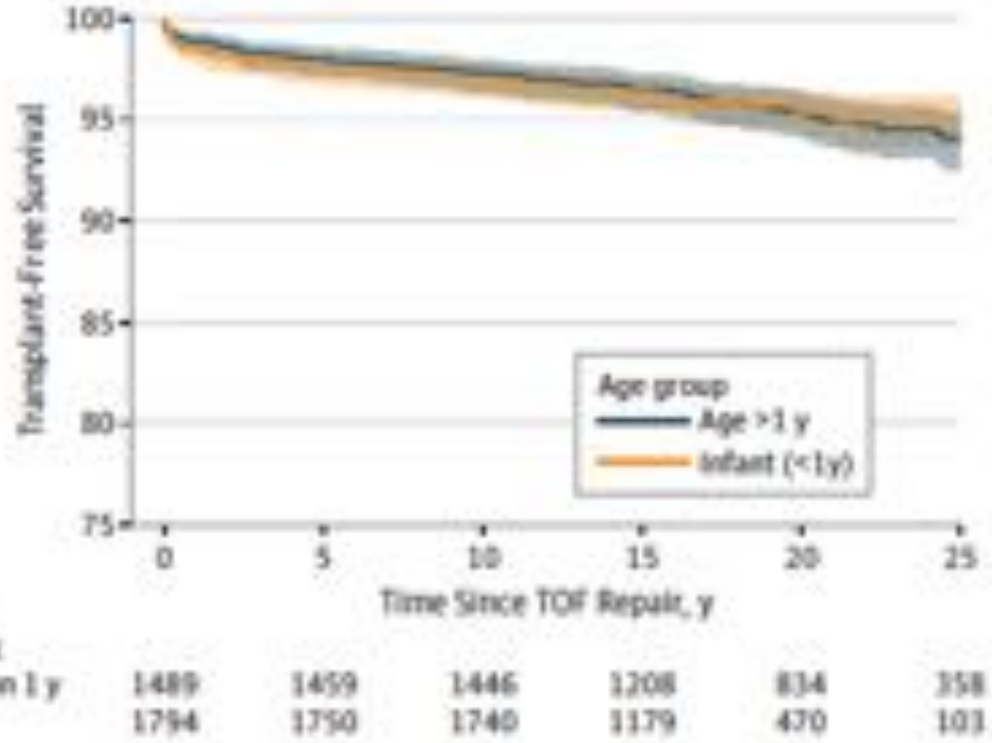
SEX



No. at risk						
Female	1434	1403	1393	1073	582	209
Male	1849	1806	1793	1314	722	252

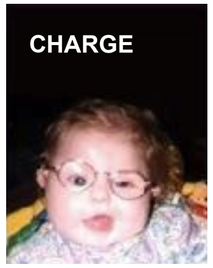
AGE GROUP



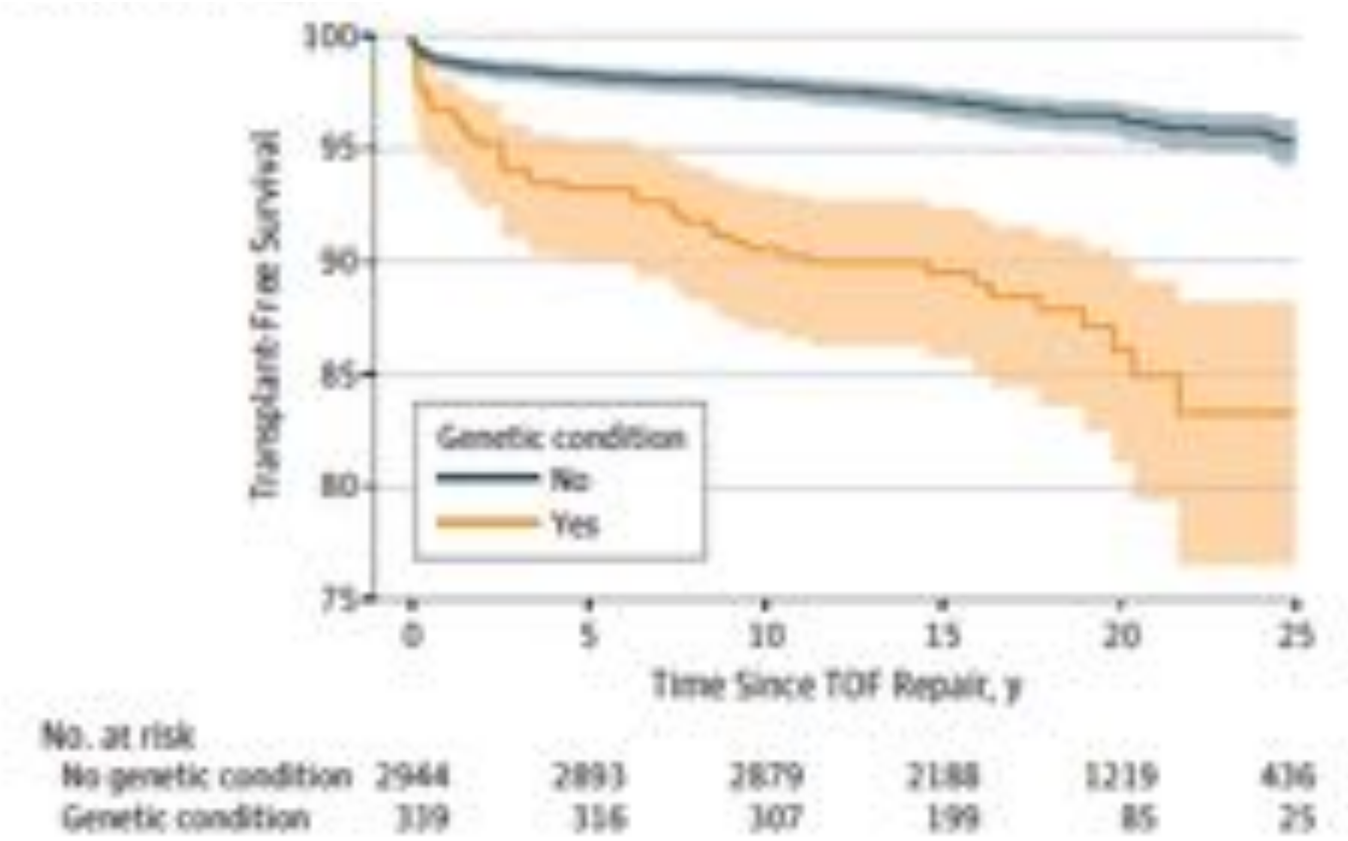
No. at risk						
Older than 1 y	1489	1459	1446	1208	834	358
Infant	1794	1750	1740	1179	470	103

Smith CA et al. JAMA Cardiol 2018

Predictors of long term outcome
Pediatric Cardiac Care Consortium



Non modifiable factor : genetic condition

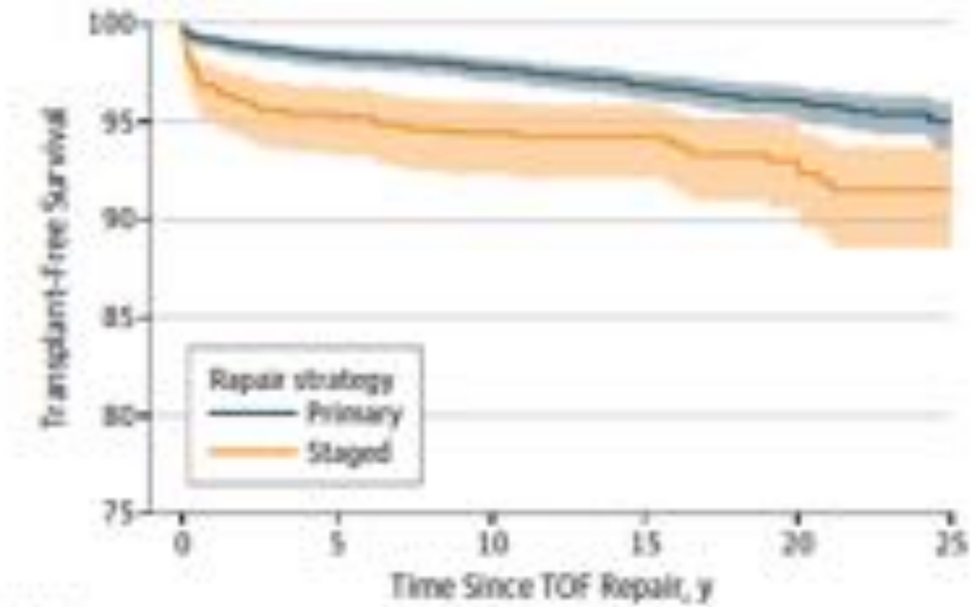


HR 3.64

Smith CA et al. JAMA Cardiol 2018

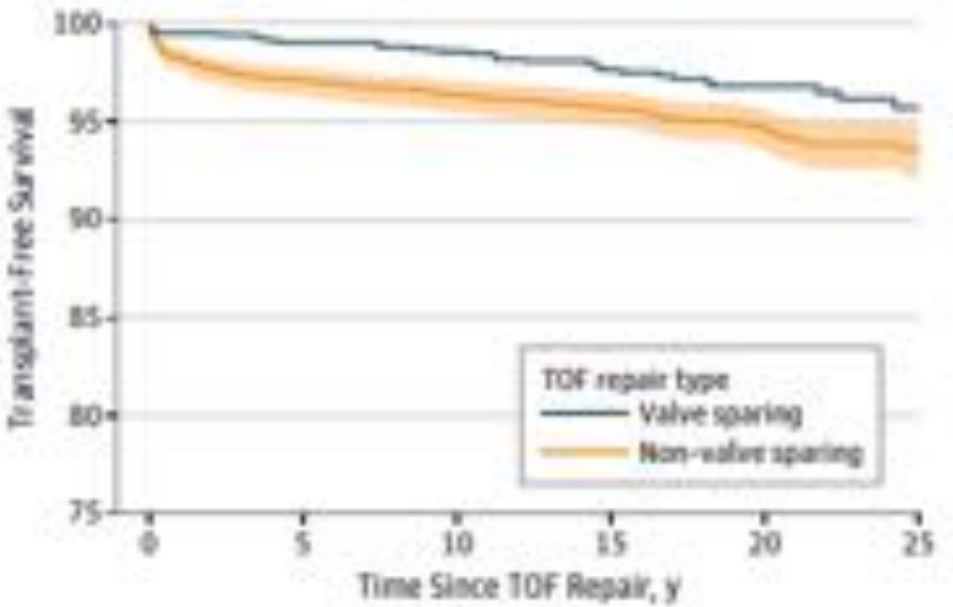
Predictors of long term outcome
Pediatric Cardiac Care Consortium

Repair strategy



No. at risk						
Primary	2672	2627	2610	1952	1041	365
Staged	611	582	576	435	263	96

TOF Repair type



No. at risk						
Valve sparing	1058	1048	1043	778	424	155
Non-valve sparing	2201	2137	2119	1587	866	301

Smith CA et al. JAMA Cardiol 2018

Perinatal strategy in simple ToF
What is the plan during infancy ?

ToF is a **progressive disease** with a potential increase in severity with time.

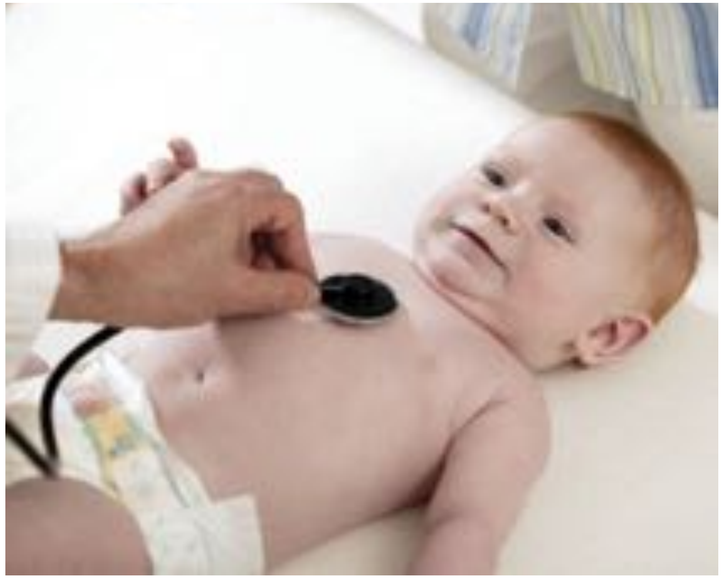
Optimizing the pulmonary blood flow in the most physiologic fashion may halt this process,

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



Patients characteristics

Different categories

Non modifiable

-underlying genetic conditions

Time-dependent

-age and weight

-symptoms

Anatomical characteristics

Non modifiable

-location of the VSD

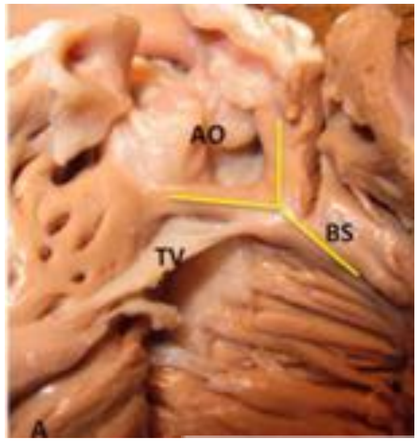
-coronary artery anatomy

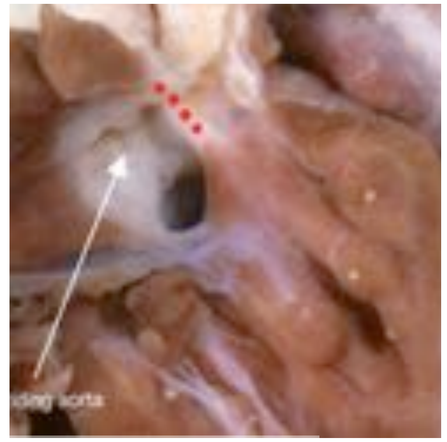
Time-dependent/modifiable

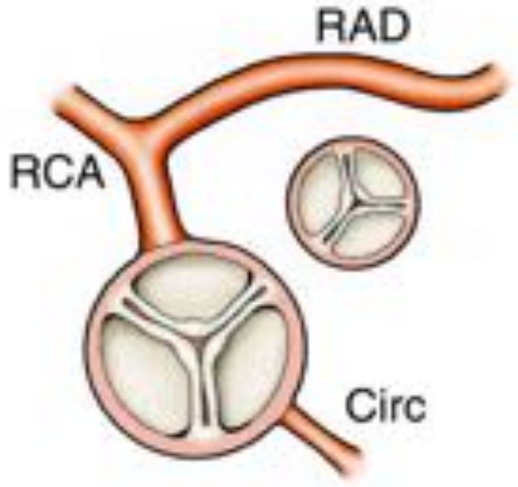
-pulmonary valve and annulus

-pulmonary artery branches (size, contiguity)

-anatomy of the arterial duct







Strategy
Different options

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:

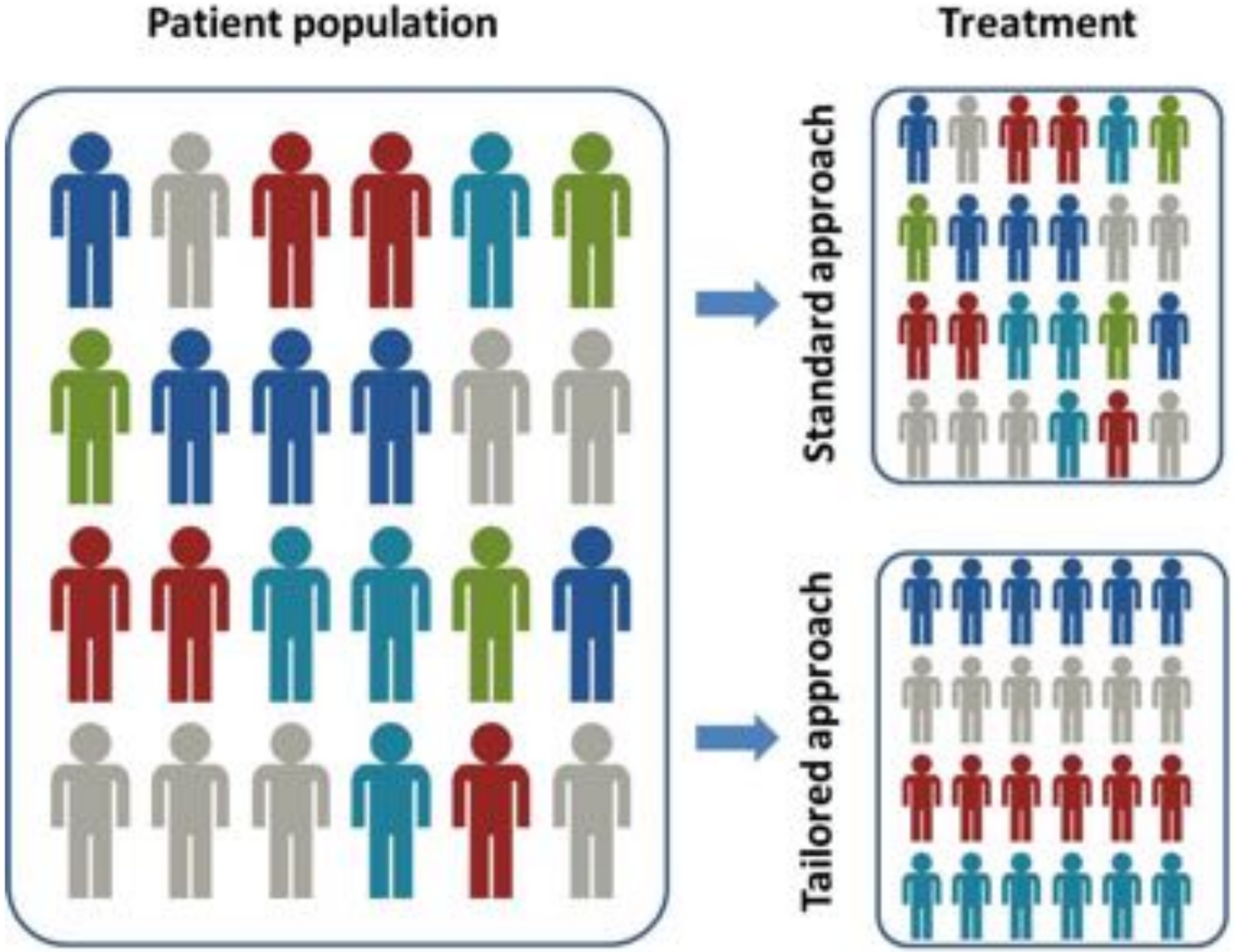
Trans-annular patch

Preserve pulmonary valve

RV-PA conduit

Limit right ventriculotomy

Simple ToF(s) or one patient/one ToF

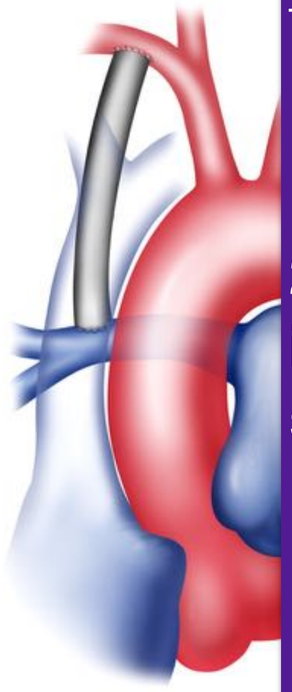


Low mortality
Tolerated morbidity (early and late)

Reduced mortality?
Reduced morbidity (early and late)
Improve patients reported outcomes

Initial strategy in symptomatic neonates with ToF

Non elective intervention



<u>Outcomes of BT shunts</u>

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

Hobbes B et al. Ann Thorac Surg 2017;104:1365–70

-vs. complete repair in neonatal period

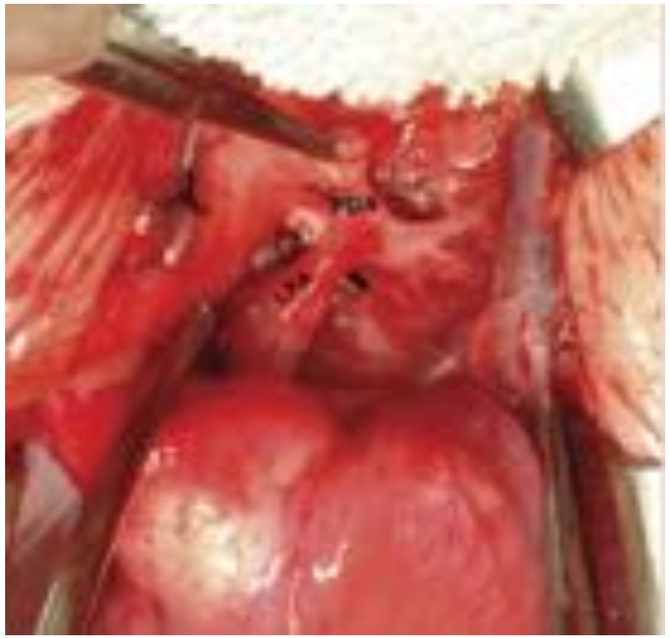
Initial strategy in symptomatic neonates with ToF

Non elective intervention

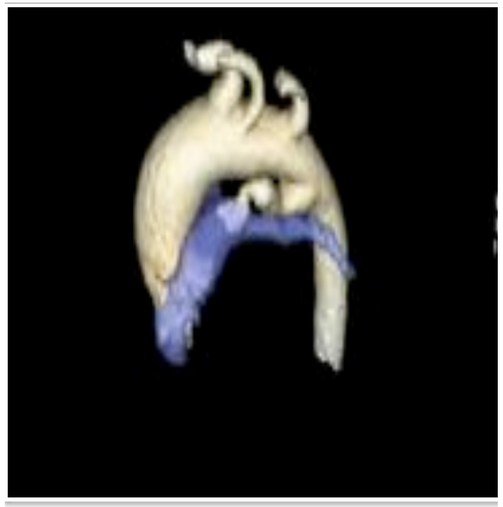
Stenting of arterial duct

1-Patients characteristics

-Tendency for complex PDA–pulmonary artery morphology.

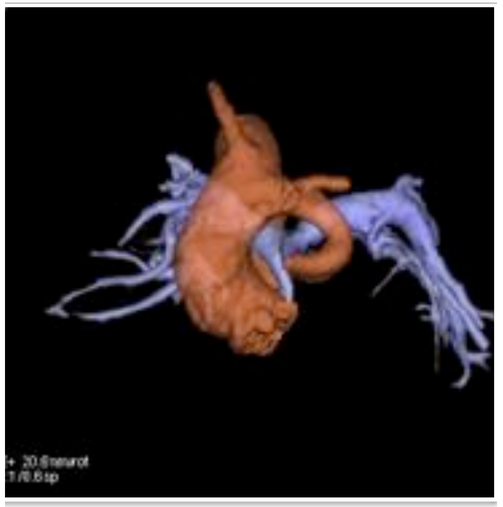


LPA coarctation



Tortuous

Underneath
the aortic arch



From innominate artery
Right aortic arch

Initial strategy in symptomatic neonates with ToF

Non elective intervention

Stenting

2-Strategy

-avoid sur

cess

Outcomes of PDA stenting in ToF

Aggravation of PA branch stenosis

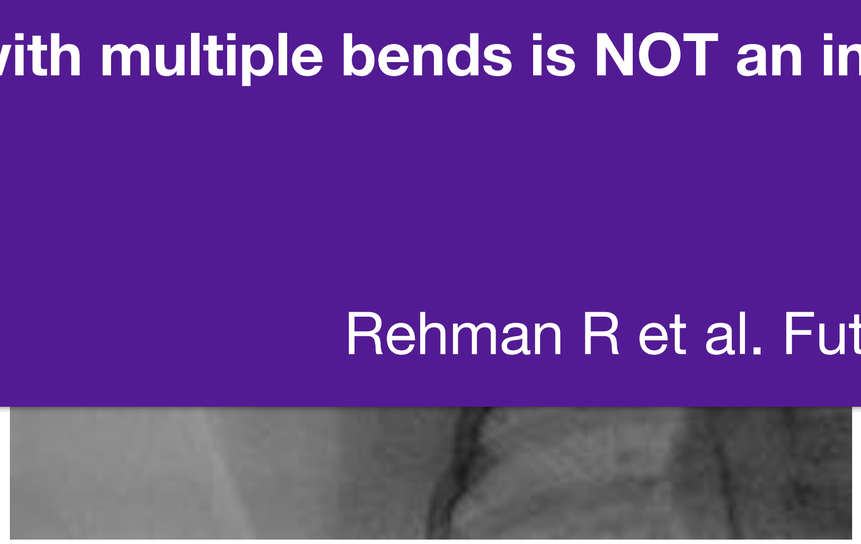
Poor growth of vessel ‘jailed » by stent

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

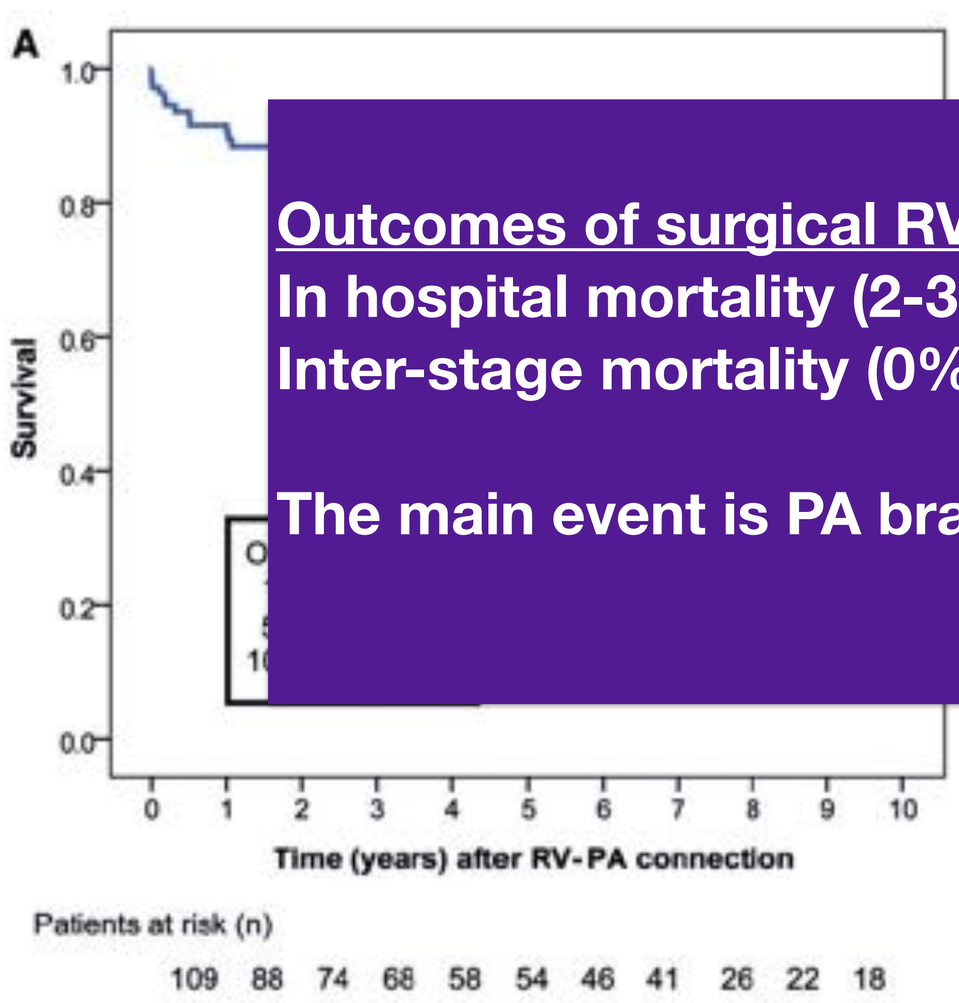
-vs. stenting of the RVOT

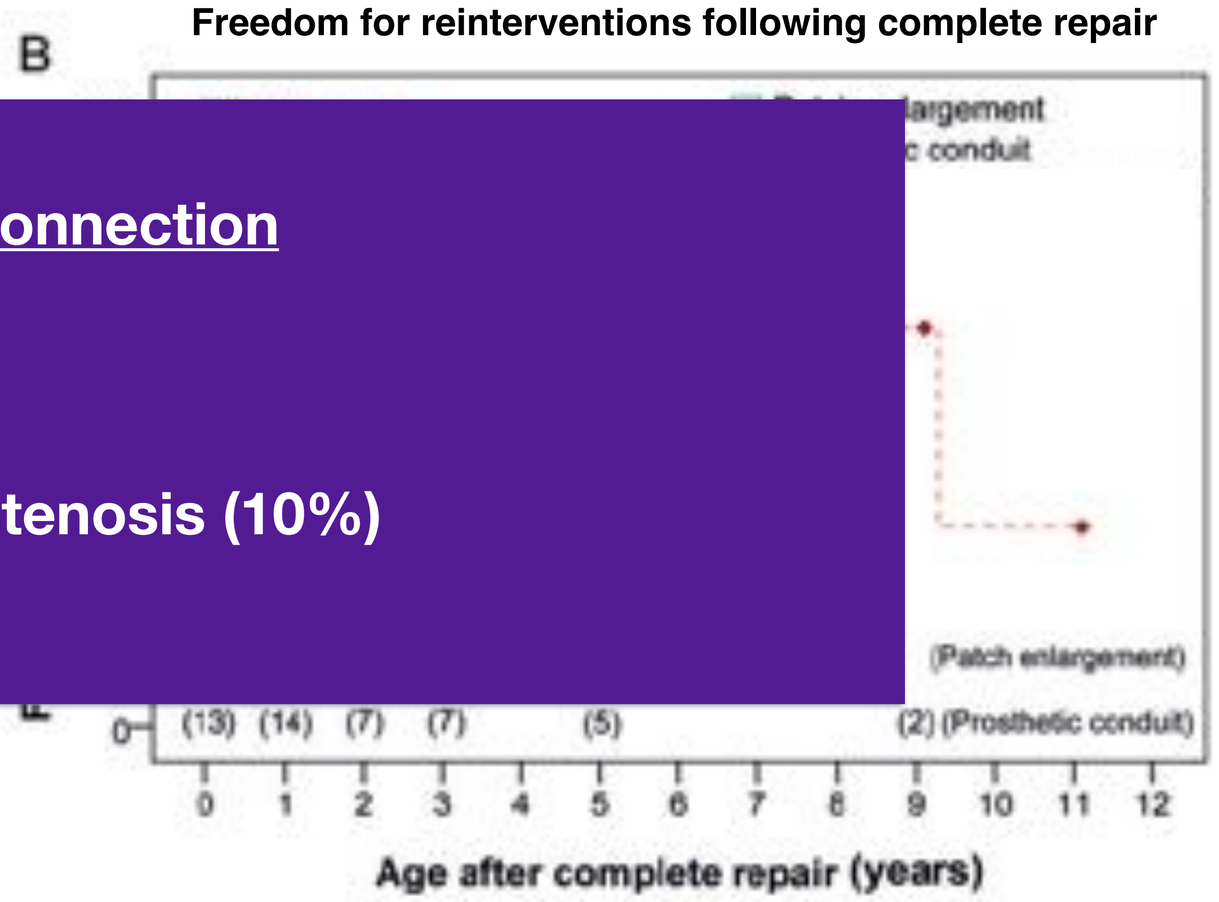
-vs. complete repair in neonatal period

Initial strategy in symptomatic neonates with ToF

Non elective intervention

Neonatal right ventricle to pulmonary connection





<u>Outcomes of surgical RV-PA connection</u>

In hospital mortality (2-3%)

Inter-stage mortality (0%)

The main event is PA branch stenosis (10%)

Gerelli et al. EJTCS 2013

Lenoir M et al. EJTCS 2017

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

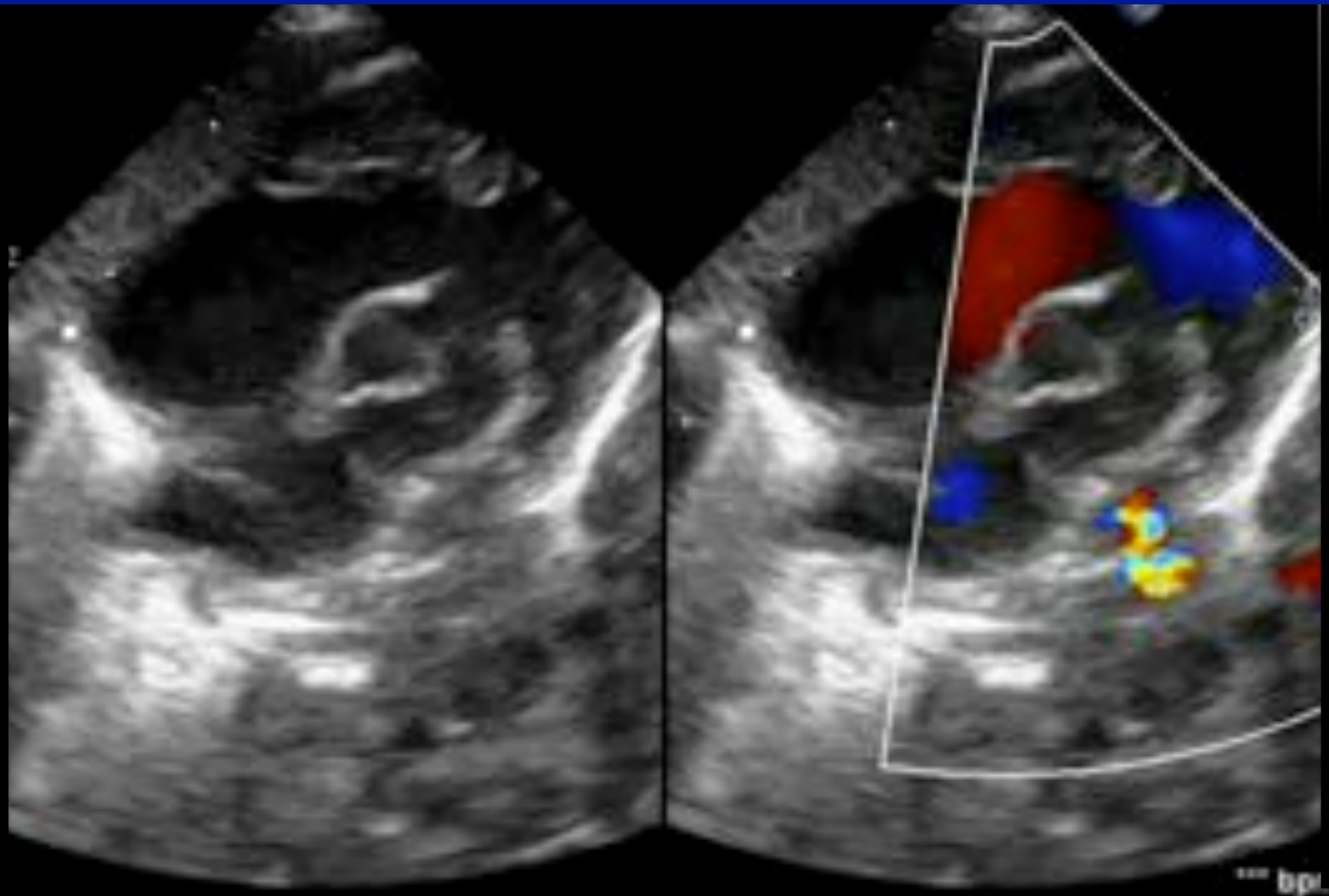
-more physiological than shunt

3-Alternative techniques

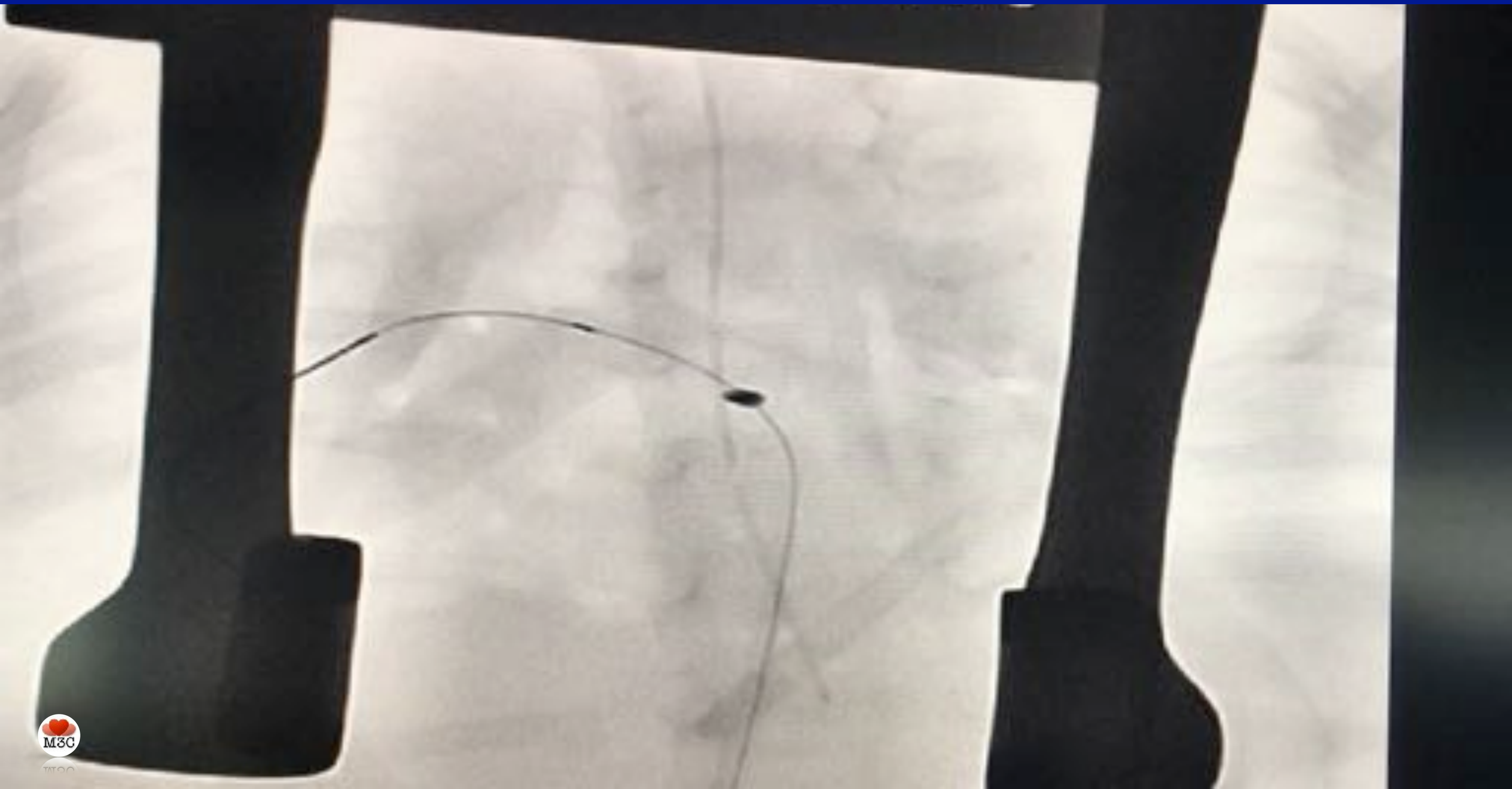
-vs. complete repair in neonatal period

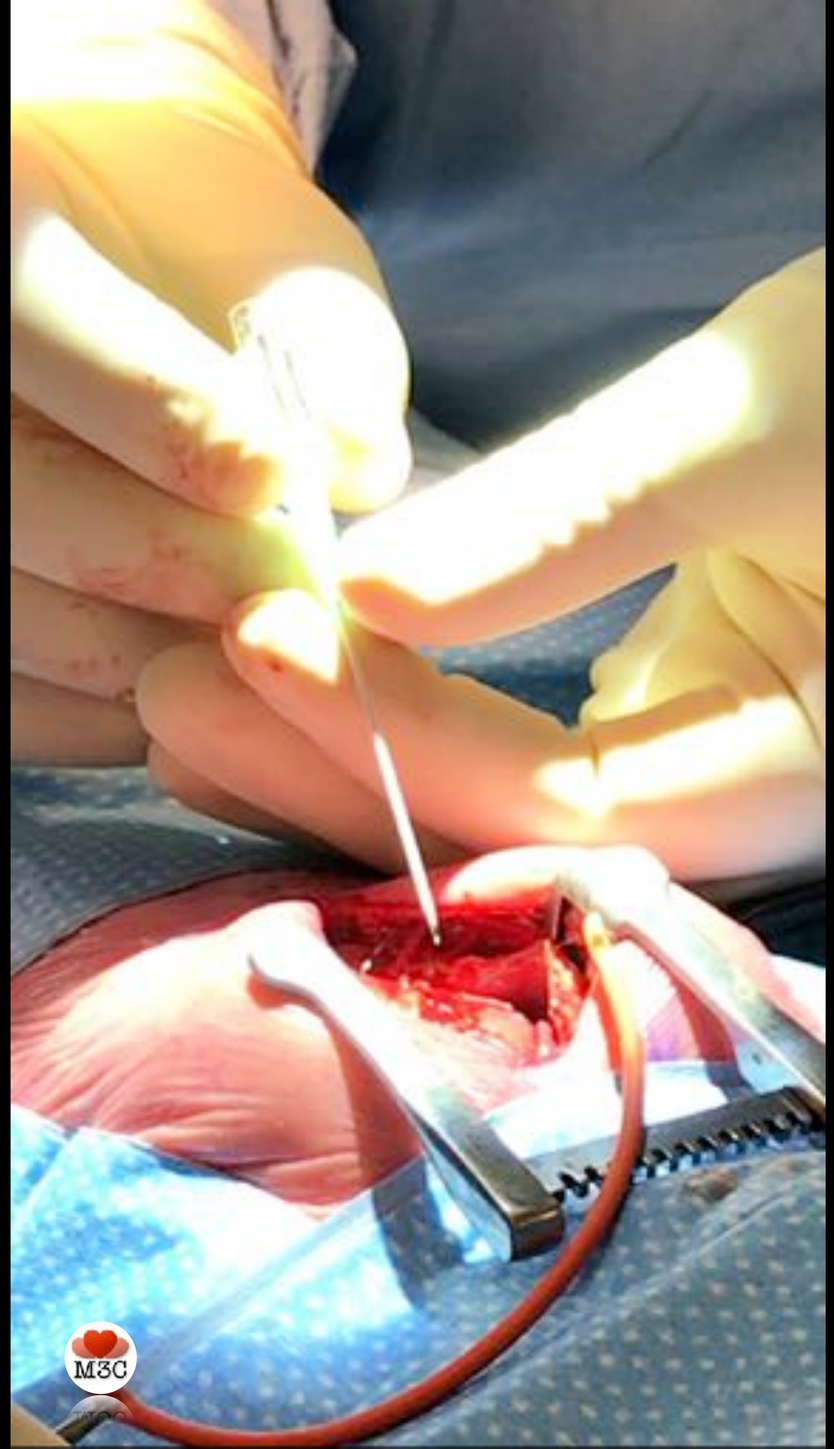
Hybrid Stenting of the RVOT in symptomatic neonates with ToF

Stenting of the RVOT in symptomatic neonates with ToF



Stenting of the RVOT in symptomatic neonates with ToF

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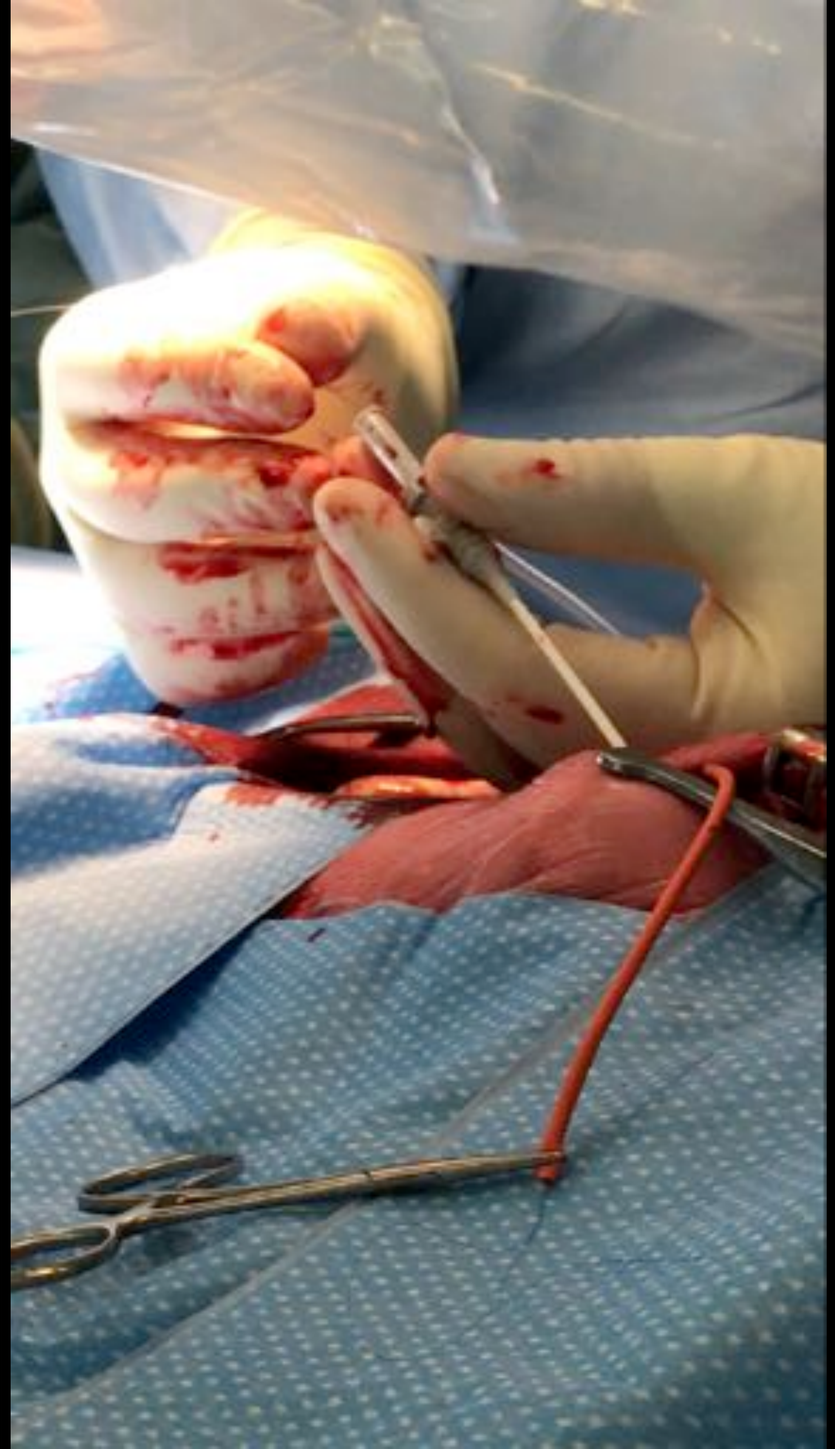
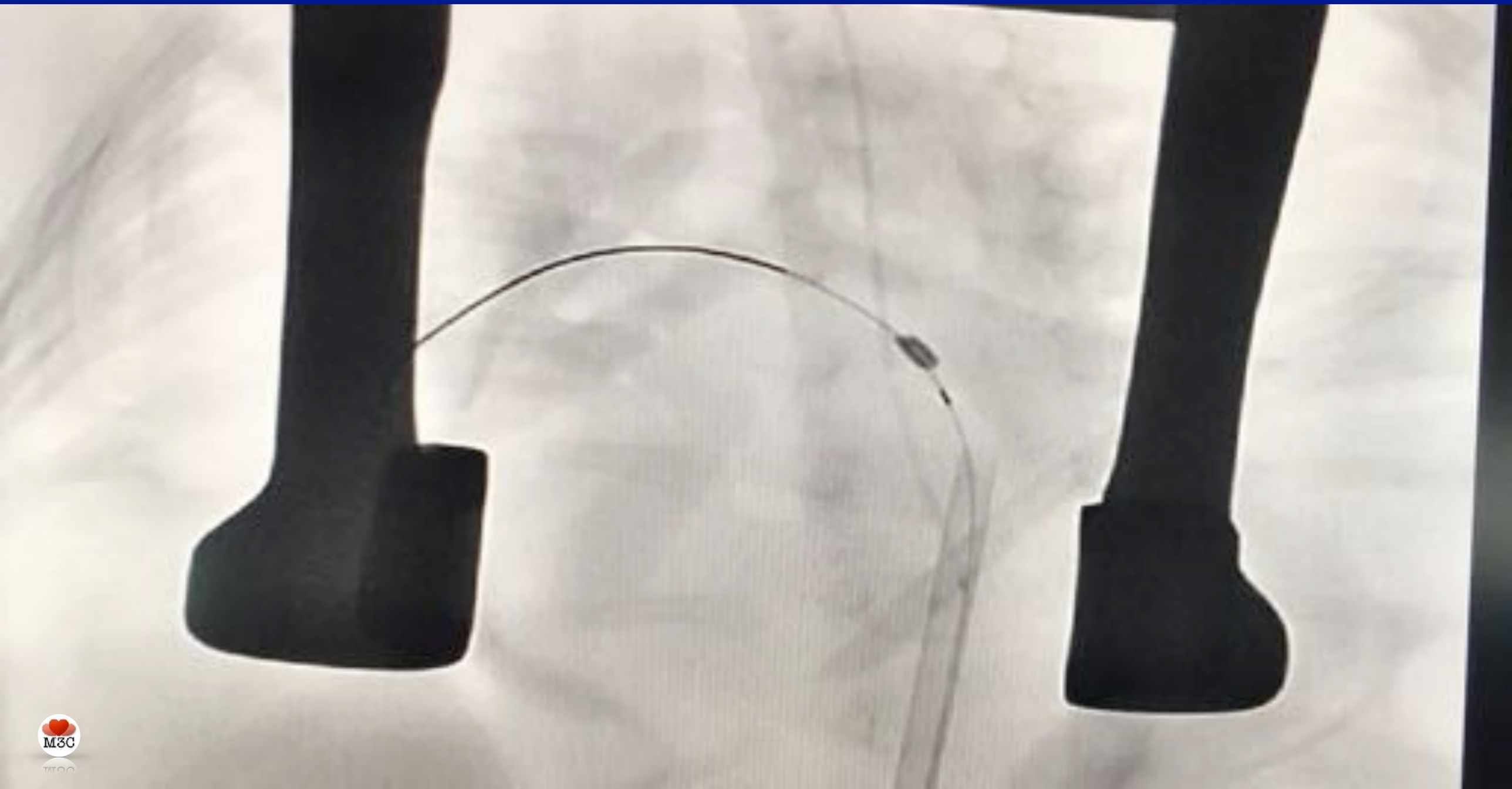
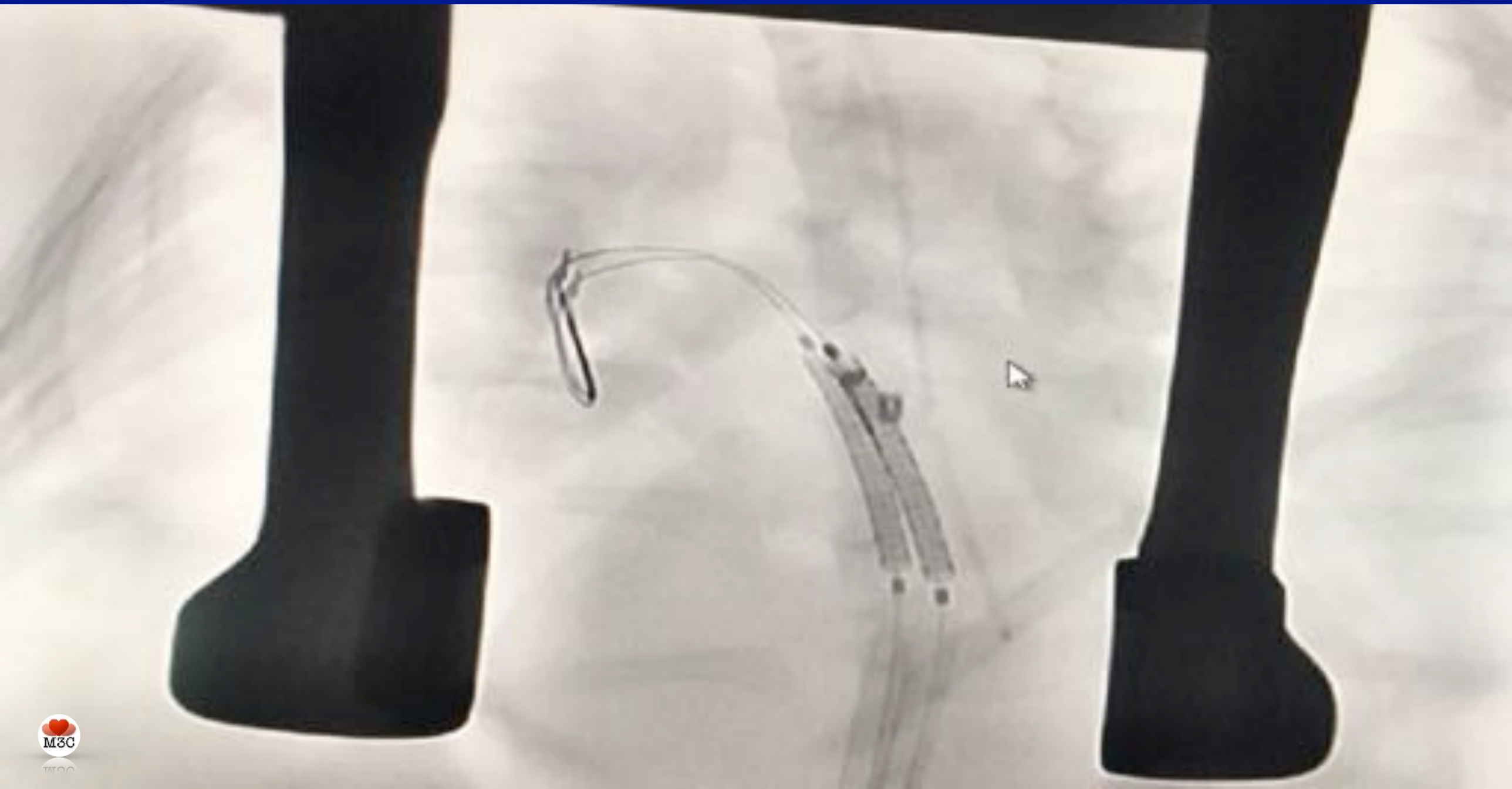


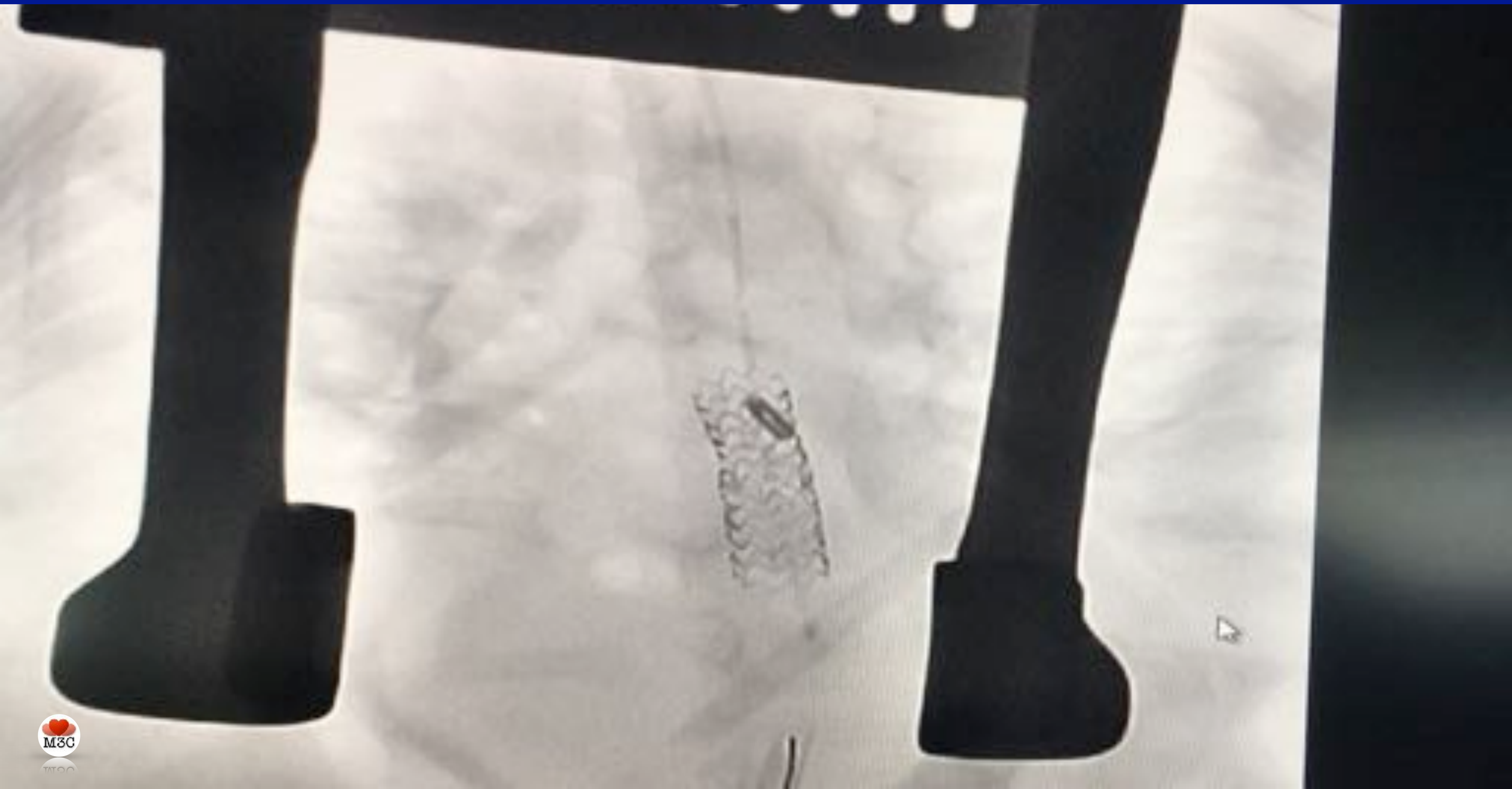
Stenting of the RVOT in symptomatic neonates with ToF



Stenting of the RVOT in symptomatic neonates with ToF



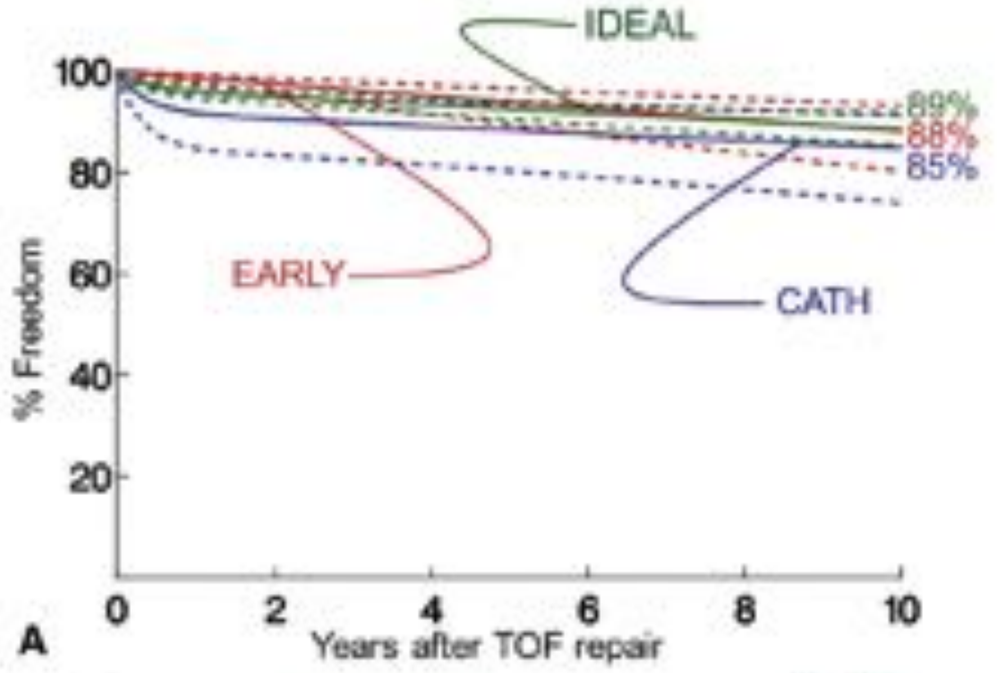
Stenting of the RVOT in symptomatic neonates with ToF

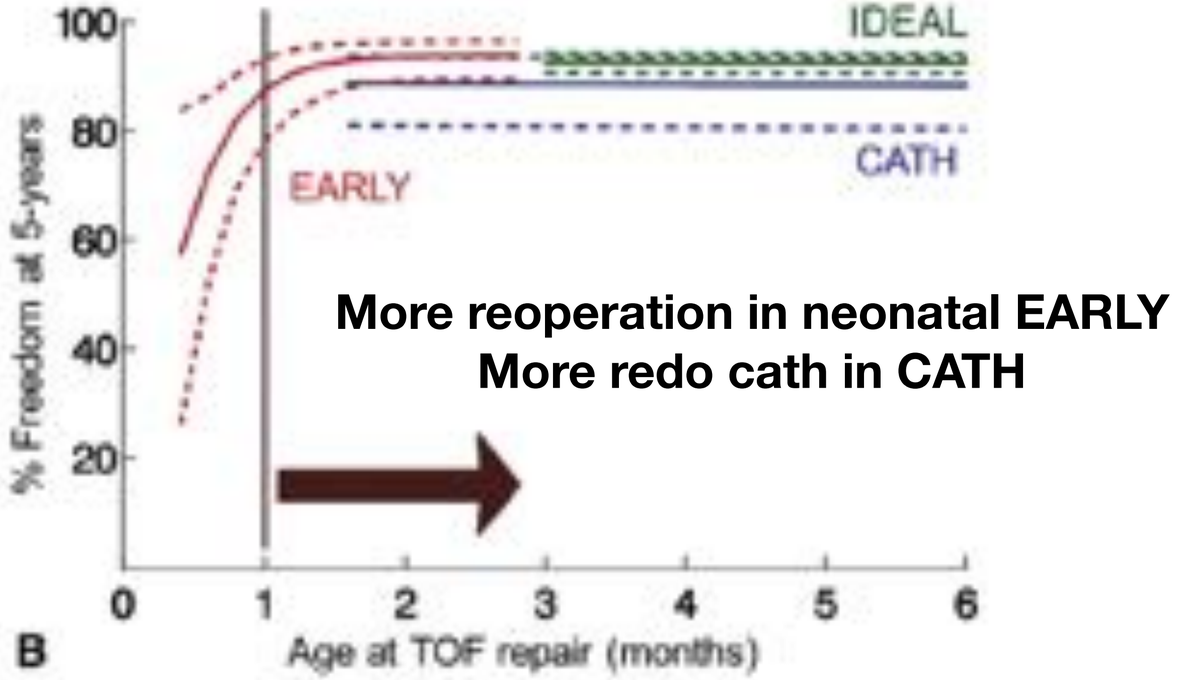


Initial strategy in symptomatic neonates with ToF

Non elective intervention

Stenting of right ventricle outflow tract





More reoperation in neonatal EARLY
More redo cath in CATH

IDEAL : elective repair > 3 months

CATH: Stenting

EARLY: repair before 3 months

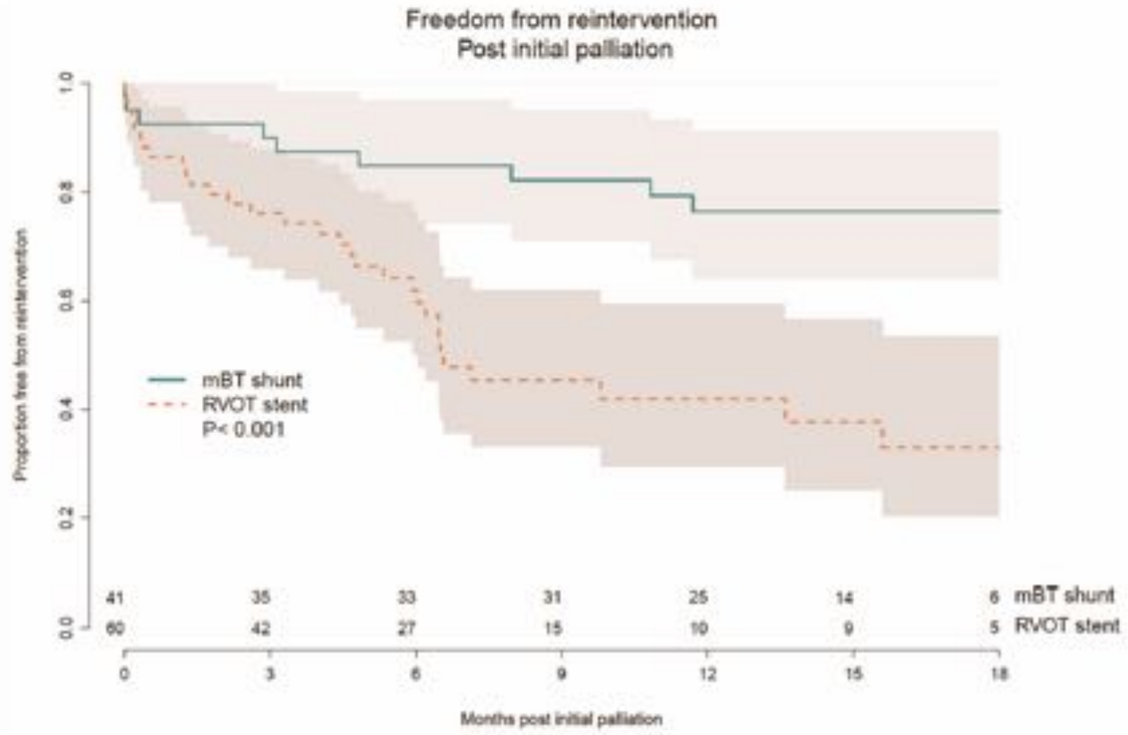
Wilder TJ et al. JTCVS 2017

Sandoval JP et al. Circ Cardiovasc Interv 2016

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)
Quandt D et al. Heart 2017;103:1985–1991

Initial strategy in symptomatic neonates with ToF

Non elective intervention

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 (OR3.28, P .007) had a higher risk of mortality.

Ramakrishnan KV et al. World Journal for Pediatric and Congenital Heart Surgery 2018, Vol. 9(5) 539-545

Initial strategy in Asymptomatic neonates with ToF

Elective neonatal repair

Metanalysis

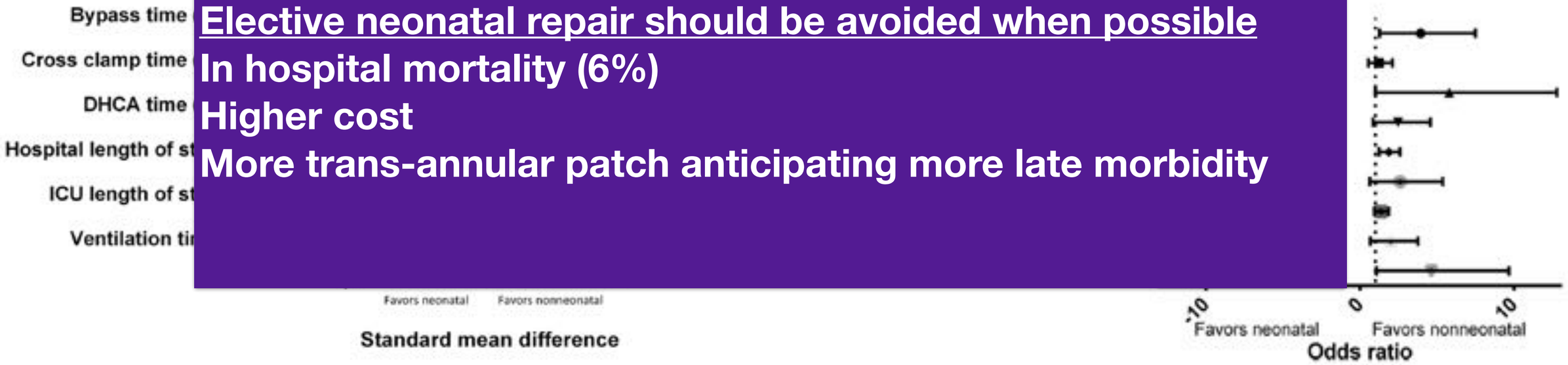
3858 patients in 8 studies with 724 (19%) having undergone neonatal repair (6-20 days) and 3134 (81%) having undergone non-neonatal repair (60-220 days)

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

Strategy in Asymptomatic infants > 3 months with ToF

Elective repair

Elective repair 6 kgs/3 months

1-Patients characteristics

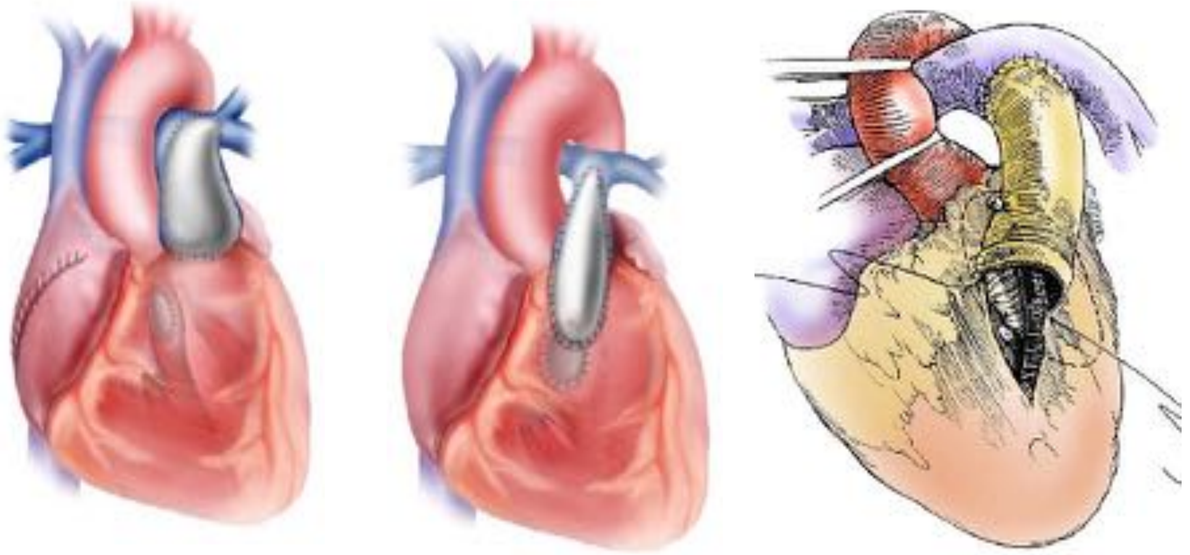
-acceptable sized pulmonary arteries
-pulmonary valve ?
-coronary artery epicardial course ?
-multiple VSD ?

2-Strategy

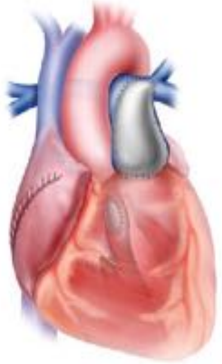
-limit late complications

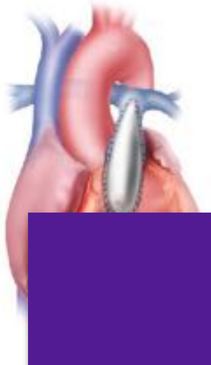
3-Alternative techniques

-None

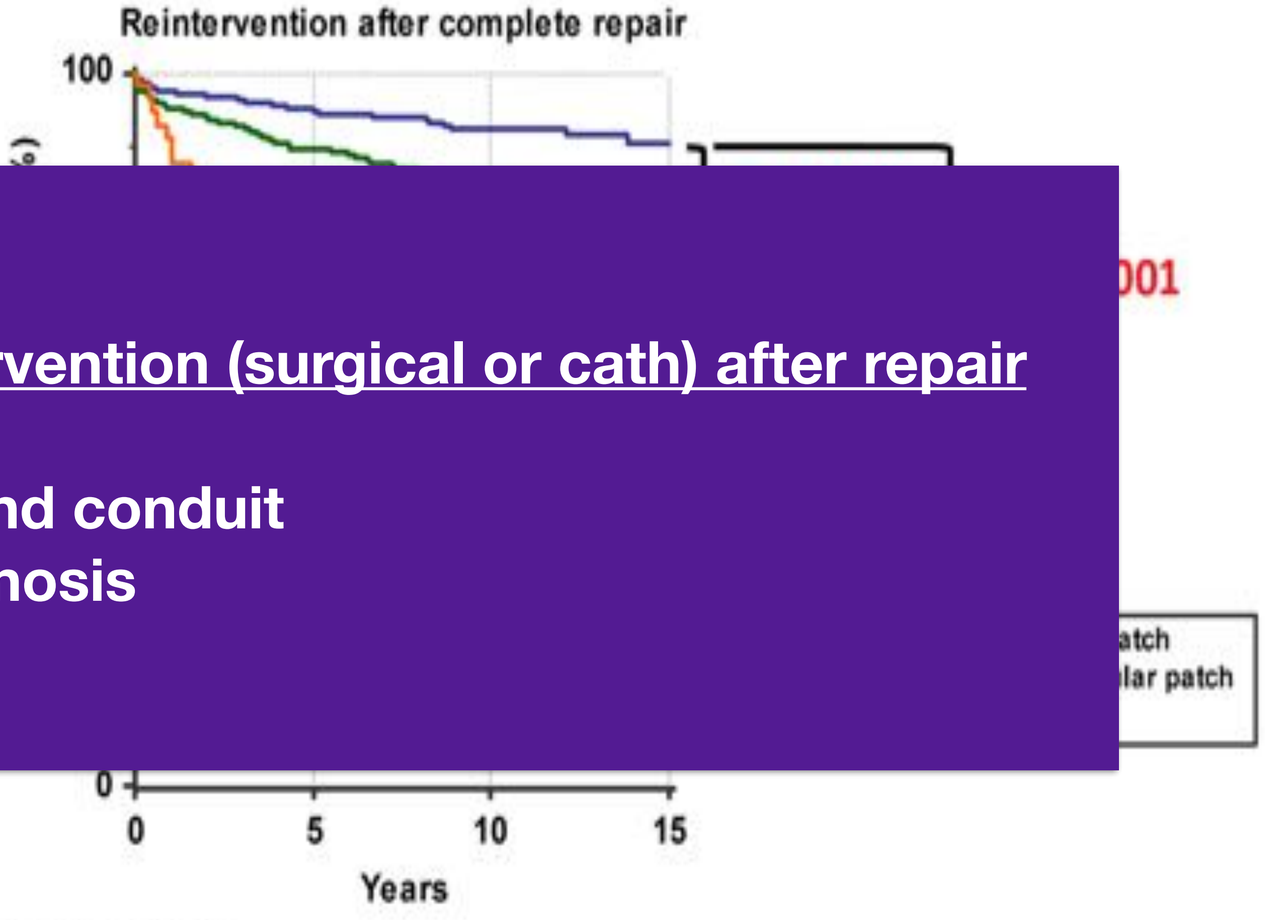


Outcomes ToF
Parisian experience (07-17): 923 ToF (PA-VSD excluded)





46%



Risk factors for reintervention (surgical or cath) after repair

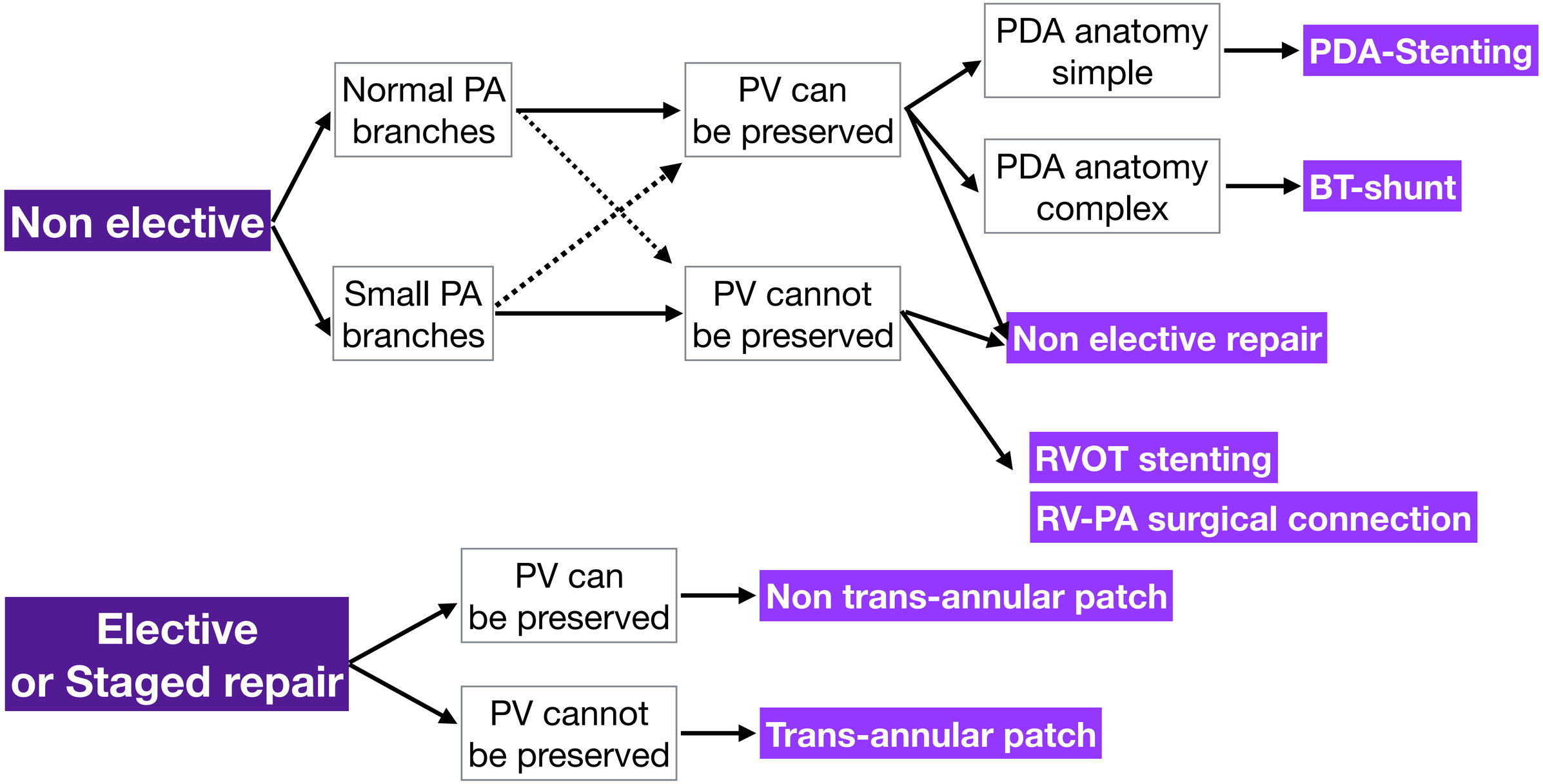
Initial staged strategy

Trans-annular patch and conduit

Pulmonary branch stenosis

Mostefa-Kara M et al. in preparation

Can we have an algorithm in simple ToF ?



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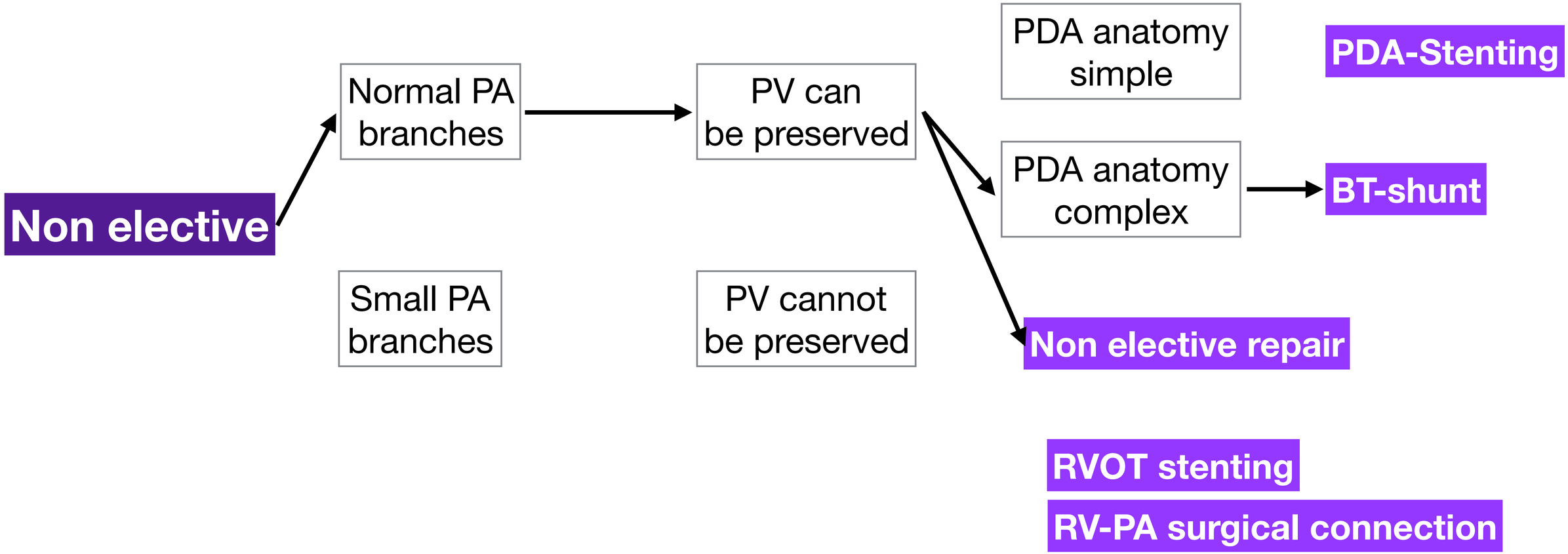

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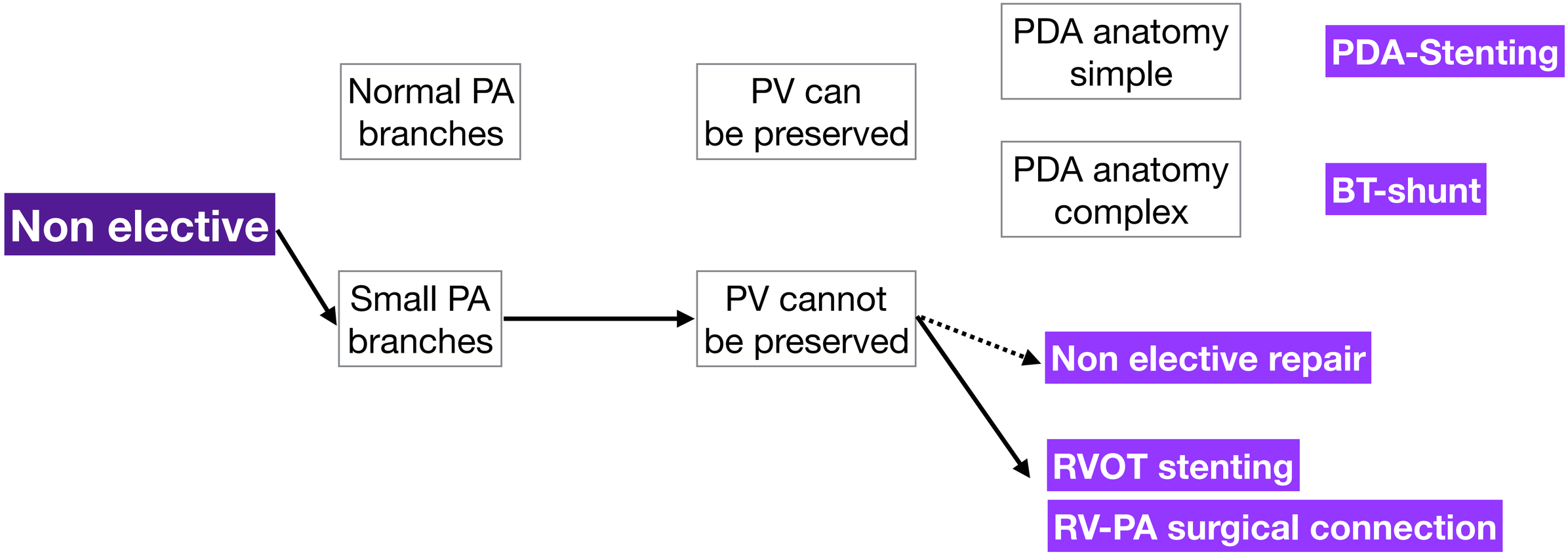

Conclusion

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