Tetralogy of Fallot: Long-Term Outcomes In the Adult Patient

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No financial conflicts of interest
OBJECTIVES

1. Review long term survival trends and other cardiac and noncardiac outcomes for patients with repaired tetralogy of Fallot

2. Learn ACC/AHA class I guidelines for an adult patient with repaired tetralogy of Fallot in order to improve outcomes

3. Use evidence to improve patient selection and timing of pulmonary valve replacement
WHAT IS TETRALOGY OF FALLOT?
WHY IS TETRALOGY OF FALLOT IMPORTANT?

- Most common cause of cyanotic CHD
- Nearly all patients expected to survive to adulthood, but many will have long-term morbidity
- Higher risk of sudden death than average population (0.3% / year)
- More and more common in adult patients as children’s survival increases
OVERVIEW

• Tetralogy of Fallot was generally fatal until:
• Major milestones:
  – 1945 Blalock, Taussig, Thomas shunt
  – 1954 Complete repair: Lillihei & Varco
• Surgical mortality:
  – 1950s: 50%
  – Now: <2%
• Most patients now lead normal lives but survival lower than age matched controls
• Many will require repeat operations
HEMODYNAMIC SEQUELAE

- Progressive RV dilation from PR
- Residual ASD or VSD
- Tricuspid regurgitation
- RVOT aneurysm
- Pulmonary artery stenosis
- Sudden cardiac death
  - 1.5-4.5 deaths per 1000 patient years
  - Most commonly ≥4 years post repair

1 Silka et al. JACC 1998.
A VICIOUS CYCLE

TOF Repair

↑ Pulmonary regurgitation

PA dilation (↑ capacitance)

↑ PA pulse pressure/volume

RV dilatation

↑ RV compliance

↑ Pulmonary regurgitation

Tal Geva. JCMR 2011. 13:9
CARDIAC MORBIDITY AND MORTALITY

• Leading causes of death:
  1. Arrhythmia / sudden death
  2. Heart failure

• Other cardiac comorbidities:
  – Syncope or Symptomatic Arrhythmia
  – Endocarditis
  – Pulmonary hypertension
  – Exercise intolerance
  – Cyanosis from residual shunts
  – Aortic insufficiency / aortic dilation & dissection
CARDIAC MORBIDITY AND MORTALITY

• Leading causes of death:
  1. Arrhythmia / sudden death
  2. Heart failure

• Other cardiac comorbidities:

Will focus on:

- Pulmonary regurgitation / RV dysfunction
- Risk stratification of sudden cardiac death
- Aortic dilation and dissection
- Major Noncardiac Comorbidities
SURVIVAL TRENDS: USA

Pillutla, Priya, MD
Am Heart J 2009;158:874-9
Finland has a complete data set of all cardiac surgeries done since 1953.

Data analyzed for patients with surgery from 1953-1989, data analyzed in 1998.

N=6461 with cardiac surgery (7240 operations) < age 15 yr.

96% follow-up.

Mean age at time of data analysis: 27.6 years; mean follow-up 22.3 years.

Overall survival rate:

- CHD: 78%
- Gen. population: 93%
Many trials focused on a composite endpoint of multiple harmful outcomes:

- Death
- Sustained ventricular tachycardia
- Increase in NYHA class to III or IV

Recurring theme in papers – risk factors for bad outcomes:

- RV dilation & QRS duration
- Pulmonary regurgitation
- LV function
RV DILATION AND FUNCTION AS RISK FACTOR FOR SERIOUS ADVERSE EVENTS

Other risk factors:
LVEF < 55%
QRS > 180*

QRS > 180 correlated with RVEDV and was not a predictor on multivariate analysis

Knauth...Geva et al. Heart 2008;94:211-216
### Univariate analysis (controlling for time from baseline evaluation to most recent follow-up)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds ratio (95% CI)</th>
<th>Area under ROC curve</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at TOF repair ≥6 years</td>
<td>7.78 (2.26 to 26.7)</td>
<td>0.748</td>
<td>0.001</td>
</tr>
<tr>
<td>Era of repair before 1970</td>
<td>4.05 (1.11 to 14.8)</td>
<td>0.591</td>
<td>0.035</td>
</tr>
<tr>
<td>RV end-diastolic volume Z ≥7</td>
<td>4.98 (1.47 to 16.9)</td>
<td>0.688</td>
<td>0.01</td>
</tr>
<tr>
<td>RV end-systolic volume index &gt;50 ml/m²</td>
<td>5.82 (1.22 to 27.7)</td>
<td>0.708</td>
<td>0.027</td>
</tr>
<tr>
<td>RV ejection fraction &lt;45%</td>
<td>5.31 (1.59 to 17.8)</td>
<td>0.750</td>
<td>0.007</td>
</tr>
<tr>
<td>LV ejection fraction &lt;55%</td>
<td>7.13 (2.11 to 24.0)</td>
<td>0.760</td>
<td>0.002</td>
</tr>
<tr>
<td>LV mass/volume ratio &gt;1.5</td>
<td>4.56 (1.27 to 16.4)</td>
<td>0.688</td>
<td>0.02</td>
</tr>
<tr>
<td>QRS ≥180 ms</td>
<td>6.27 (1.86 to 21.1)</td>
<td>0.673</td>
<td>0.003</td>
</tr>
<tr>
<td>Diuretics at baseline evaluation</td>
<td>7.68 (2.03 to 29.1)</td>
<td>0.646</td>
<td>0.003</td>
</tr>
<tr>
<td>Digoxin at baseline evaluation</td>
<td>4.67 (1.30 to 16.8)</td>
<td>0.689</td>
<td>0.018</td>
</tr>
<tr>
<td>β-Blocker at baseline evaluation</td>
<td>6.88 (1.12 to 42.3)</td>
<td>0.654</td>
<td>0.037</td>
</tr>
<tr>
<td>NYHA class II or III at baseline evaluation</td>
<td>5.27 (1.55 to 17.9)</td>
<td>0.724</td>
<td>0.008</td>
</tr>
</tbody>
</table>

### Multivariate analysis (controlling for time from baseline evaluation to most recent follow-up)

**Model 1**
- LV ejection fraction <55%: 8.05 (2.14 to 30.2) | p = 0.002
- RV end-diastolic volume Z ≥7: 4.55 (1.10 to 18.8) | p = 0.037

Area under ROC curve for the model: 0.850

**Model 2**
- RV ejection fraction <45%: 5.60 (1.47 to 21.2) | p = 0.011
- RV end-diastolic volume Z ≥7: 4.00 (1.10 to 14.6) | p = 0.036

Area under ROC curve for the model: 0.807

Knauth et al. Heart 2008;94:211-216
Table 3  Test characteristics of selected cardiac MRI variables for predicting major adverse outcomes

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive predictive value (%)</th>
<th>Negative predictive value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV ejection fraction &lt;30%</td>
<td>28</td>
<td>96</td>
<td>63</td>
<td>24</td>
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<tr>
<td>RV ejection fraction &lt;40%</td>
<td>50</td>
<td>79</td>
<td>38</td>
<td>56</td>
</tr>
<tr>
<td>RV ejection fraction &lt;45%</td>
<td>67</td>
<td>66</td>
<td>33</td>
<td>88</td>
</tr>
<tr>
<td>RV end-diastolic volume Z ≥6</td>
<td>47</td>
<td>76</td>
<td>85</td>
<td>33</td>
</tr>
<tr>
<td>RV end-diastolic volume Z ≥7</td>
<td>41</td>
<td>88</td>
<td>85</td>
<td>88</td>
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<tr>
<td>RV end-systolic volume index ≥45 ml/m²</td>
<td>100</td>
<td>33</td>
<td>100</td>
<td>27</td>
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<tr>
<td>RV end-systolic volume index ≥50 ml/m²</td>
<td>88</td>
<td>43</td>
<td>94</td>
<td>88</td>
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<tr>
<td>LV ejection fraction &lt;50%</td>
<td>31</td>
<td>91</td>
<td>45</td>
<td>85</td>
</tr>
<tr>
<td>LV ejection fraction &lt;55%</td>
<td>56</td>
<td>84</td>
<td>45</td>
<td>89</td>
</tr>
<tr>
<td>LV ejection fraction &lt;60%</td>
<td>75</td>
<td>58</td>
<td>30</td>
<td>91</td>
</tr>
</tbody>
</table>

LV, left ventricular; RV, right ventricular.
Transannular patches formerly very commonly used
Many adults with free pulmonary insufficiency
Can lead to RV dilation and irreversible RV dysfunction
   Hard to quantitate RV volumes on echo
   Cardiac MRI now the “Gold standard”
A big problem for patients lost to follow-up
Will a new valve make every patient better?
RVEDVI = 212 ml / m²
Easily inducible monomorphic VT originating from LVOT
Went on for pulmonary valve replacement + ICD

RVEF 42%, severe PR RF 44%

“YOU’VE BEEN FIXED!”
ARE WE OPERATING TOO LATE? OR TOO SOON?

- Therrien et al prospectively studied MRI pre and postop in 17 patients
- At mean follow-up of 21 months, statistically significant decrease in RV dimensions but no change in RVEF
- No patients “normalized” if preop dimensions:
  - RVEDV > 170 ml/m²
  - RVESV > 85 ml/m²
- Are symptoms reliable?

Therrien et al. Am J Card 2005
WILL RV DIMENSIONS NORMALIZE AFTER A LONGER FOLLOW-UP PERIOD?

Therrien et al. Am J Card 2005

Indiana University Health
TIMING OF PULMONARY VALVE REPLACEMENT: ROLE OF BNP

- Prospective study of NT-proBNP as predictor of RV dilation and dysfunction (n=21, avg 12 y.o.)
- All patients had echo, MRI, and NT-proBNP level
- Mean RVEDVi 148±64 ml/m2; mean RVEF 35±10%
- Categorical variables:
  - RV dilation if RVEDVi > 108 ml/m2
  - RV dysfunction if RVEF < 40%

Khositseth et al. 2007
## RV Size and Function vs. ProBNP

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV dilation</td>
<td>71%</td>
<td>100%</td>
</tr>
<tr>
<td>RV dysfunction</td>
<td>71%</td>
<td>71%</td>
</tr>
<tr>
<td>Both dilation and dysfunction</td>
<td>83%</td>
<td>78%</td>
</tr>
</tbody>
</table>

Using ROC cut-off NT-proBNP of 115 pg/mL

Khositseth et al. 2007
TIMING OF PULMONARY VALVE REPLACEMENT: ROLE OF BNP

• Study in Zurich 2004-2005
• 18 patients with no or minimal symptoms and RVEDVI > 150 proceeded with PVR
• NT-proBNP preop, 1 & 6 months post
• RVEDVI, proBNP, and PR fraction decreased significantly
• proBNP correlated with RVEF but NOT RVEDVI
• Would a low proBNP help delay surgery in asymptomatic patients?

Several standard surgical options exist

- Biologic valves preferred
- Pulmonary homograft
- Bovine pericardial
- Porcine aortic root (stentless “Freestyle” valve)

Since 2009, transcatheter valve approved by FDA

- Medtronic Melody valve
1\textsuperscript{st} Transcatheter valve replacement approved in US
Can be implanted in patients with an adequate “landing zone”
Approximately 80\% of TOF patients don’t have good landing zone
Research underway to develop cath-implantable valve for the other 80\%
Arrhythmias & Sudden Cardiac Death

Arrhythmias are #1 cause of death in repaired TOF

Sudden death rate ~0.3% / year

Both ventricular and supraventricular arrhythmias are common

Several studies have evaluated risk factors for arrhythmias

Improving risk stratification important area of ongoing research
Implantable Cardioverter-Defibrillators in Tetralogy of Fallot
Paul Khairy, Louise Harris, Michael J. Landzberg, Sangeetha Viswanathan, Amanda Barlow, Michael A. Gatzoulis, Susan M. Fernandes, Luc Beauchesne, Judith Therrien, Philippe Chetaille, Elaine Gordon, Isabelle Vonder Muhll and Frank Cecchin

*Circulation* 2008;117:363-370; originally published online Jan 2, 2008;
DOI: 10.1161/CIRCULATIONAHA.107.726372

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MANY PRIMARY PREVENTION ICDs ALREADY PLACED WITHOUT GREAT EVIDENCE

Khairy et al. 2008

N=121; 11 centers
### Table 2. Predictors of Appropriate ICD Shock in Primary Prevention

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior palliative shunt</td>
<td>2.6</td>
<td>0.7–0.4</td>
<td>0.12</td>
</tr>
<tr>
<td>Left ventricular end-diastolic pressure ≥12 mmHg</td>
<td></td>
<td></td>
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<tr>
<td>Non-sustained ventricular tachycardia</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Ventriculotomy incision</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>QRS duration ≥180 ms</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Inducible sustained ventricular tachycardia</td>
<td></td>
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<tr>
<td>Moderate or severe tricuspid regurgitation</td>
<td></td>
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<tr>
<td>Time from corrective surgery ≥30 years</td>
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<tr>
<td>Palpitations</td>
<td></td>
<td></td>
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<tr>
<td>Prior palliative shunt</td>
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<td></td>
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<tr>
<td>Transannular patch</td>
<td></td>
<td></td>
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<tr>
<td>Moderate or severe pulmonary regurgitation</td>
<td></td>
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<tr>
<td>Syncope</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Moderate or severe RV systolic dysfunction</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| LVESD ≥12 mmHg                                    | 4.8  | 1.9–10.7     | 0.023 |
| Nonsustained ventricular tachycardia              | 3.7  | 1.2–11.3     | 0.0233|
APPROPRIATE SHOCK RISK SCORE

Khairy et al. 2008
Rate of Inducible Ventricular Arrhythmia in Adults With Congenital Heart Disease

Shane F. Tsai, MD\textsuperscript{a,b,c,*}, David P. Chan, MD\textsuperscript{a,b}, Pamela S. Ro, MD\textsuperscript{a,b}, Bethany Boettner, MA\textsuperscript{a}, and Curt J. Daniels, MD\textsuperscript{a,b,c}
DOES ROUTINE EPS HELP RISK-STRATIFY

- Data from study in Ohio
- 80 ACHD patients 2005-2009 with preop or preinterventional cath undergoing screening EPS (mean age 30 years)
- 37 patients with TOF; 32 % with inducible VT/VF
- Risk factors for inducible VT/VF:
  + Male sex
  + Increasing QRS duration
  + Decreasing VO2 max
  + Ventricular Fibrosis on CMR
  + Fibrosis + VO2 < 80% predicted = 100% sensitivity for VT/VF
  + Fibrosis: great NPV (96%) poor PPV (58%)

Tsai et al. 2010
STILL SEARCHING FOR BETTER RISK STRATIFICATION...

- 21% of NCH cohort high risk per Khairy’s risk score from ICD
- only 2 high risk patients had VT/VF
- In contrast, 29% of low-risk patients had VT/VF
- Excluding the patients with TOF, VT/VF still found in 26% of low-to-intermediate risk patients

Tsai et al. 2010
Timing of Surgery

Some patients survive to adulthood despite no surgery

Is it still necessary to undergo repair? What are the risks?

Are outcomes worse with a shunt before repair?

Are outcomes really worse with a transannular patch?
Late risk of outcomes for adults with repaired tetralogy of Fallot from an inception cohort spanning four decades

Edward J. Hickey, Gruschen Veldtman, Timothy J. Bradley, Aungkana Gengsakul, Cedric Manlhiot, William G. Williams, Gary D. Webb, Brian W. McCrindle

Division of Cardiovascular Surgery, Department of Surgery, University of Toronto, The Hospital for Sick Children, Toronto, Canada
Division of Cardiology, Department of Pediatrics, University of Toronto, The Hospital for Sick Children, Toronto, Canada
Division of Cardiology, Department of Medicine, University of Toronto, Toronto General Hospital, Toronto, Canada

Received 4 September 2007; received in revised form 12 June 2008; accepted 23 June 2008; Available online 9 October 2008

- Toronto group evaluated all TOF born before 1984 and evaluated data from 2003-2006
- N = 1181; median 20 years post repair
- Repair stretching from 1960 to 1998
Massive improvement in 1-year mortality
1965: 27% mortality at 1 year
1985: 2% mortality at 1 year
Potts and Waterston shunt had much higher early mortality than other groups
Authors predict 88% 40 year survival for those repaired post 1985
RISK OF REOPERATION

- Anatomic variants increase risk:
  - Branch PA stenosis
  - AVSD
  - RV-PA conduit
  - Fewer than 10% will be free of repeat surgery over 30 years

- Children with favorable anatomy repaired >1985
- Expected that >50% will be alive and not require reoperations 40 years later

Hickey et al 2009
WHAT IF 1st REPAIR IS IN ADULTHOOD?

- 33 died in 1st year (25 perioperative)
- 1 year survivors with same life expectancy as patients without CHD
- Causes of death: CHF (3), MI (2), SCD (2)
- 80% of survivors NYHA I-II; 95% improved NYHA class after surgery

1st Repair in Adulthood

- Dos et al (Toronto): 116 patients – mean 36 yo
- 118 PVRs; 95% required additional procedures
- 30-day mortality: 2.5%
- 40% with post-op complications
  - Arrhythmias (19%)
  - Respiratory (13%)
  - Reoperation (13%)
- Post-op complications ➔ longer hospital stay:
  - 14 ± 12 vs 7 ± 3 days (p=.001)

PATIENT VARIABLES AND PREDICTORS OF COMPLICATIONS

- Mean QRS: 170 ± 24 msec (42% > 180 msec)
- RVEDVI = 192 ± 49 ml/m²
- RVEF = 37 ± 7%
- PR fraction: 38 ± 12%
- VO2 max: 20 ± 6 ml/kg/min (54 ± 14% pred.)
- Prior sternotomies: 1.2 ± 0.5
- Prior ventricular arrhythmia: 19%
- Prior SVT: 30%
- Prior syncope: 15%

• Multivar. predictors of prolonged hospitalization:
  – Age at operation > 45 years (OR 6.1)
  – # of prior sternotomies (OR 3.8)
  – Need for urgent surgery (OR 5.7)
    • 10% urgent: sustained VT in 8, endocarditis 3, RHF in 1
• Risk score (1 point for each predictor) for risk of >14 days in hospital post-op
  – 0 factors = 3%
  – 1 factor = 15%
  – 2 factors = 64%
Proximal aorta often enlarged in TOF
First case report of dissection in 2005, total of 4 now reported
When, or if, to intervene?
Management of the Aortic Root in Adult Patients With Conotruncal Anomalies

Joseph A. Dearani, Harold M. Burkhart, John M. Stulak, Thoralf M. Sundt, and Hartzell V. Schaff

Conotruncal anomalies such as tetralogy of Fallot, double outlet right ventricle, truncus arteriosus, and transposition of the great arteries are a group of congenital heart defects with abnormalities of the outflow tracts and great vessels. It is common for the ascending aorta and aortic root to be significantly dilated following initial repair of the conotruncal anomaly, and little information is available on the management of this increasing problem. Although there are few case reports of aortic dissection and rupture in the literature, it appears to be rare in the setting of a conotruncal anomaly and may be related to the absence of hypertension and smoking in many of these patients. The timing of operation with regard to the size of the aortic root is difficult. In the absence of a family history of aortic dissection or aneurysm, or documented rapid growth of the ascending aorta, we proceed with replacement of the ascending aorta when the size is $\geq 55$ mm. When the size of the ascending aorta is 5.0-5.5, treatment is individualized depending on the associated anomalies that need to be addressed, patient comorbidities, and life expectancy. In this group of patients we consider a simple reduction ascending aortoplasty. We generally proceed with root replacement and coronary reimplantation when there is effacement of the sinotubular junction, or when there is severe dilatation of the aortic root with an intact sinotubular junction. If the ascending aorta is $\geq 55$ mm with an intact sinotubular junction and the sinuses are $\leq 4$ cm, then we use a supracoronary tube graft.

Semin Thorac Cardiovasc Surg Pediatr Card Surg Ann 12:122-129 © 2009 Elsevier Inc. All rights reserved.

KEYWORDS Tetralogy of Fallot, Ascending aortic aneurysm, Conotruncal anomaly
16 year period (1993-2008)

Patients with conotruncal defects

n = 53 with aortic root operations

Indications for surgery:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic regurgitation</td>
<td>41 (77%)</td>
</tr>
<tr>
<td>AAo aneurysm</td>
<td>12 (23%)</td>
</tr>
<tr>
<td>Root aneurysm</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>5 (9%)</td>
</tr>
<tr>
<td>AS and AR</td>
<td>4 (8%)</td>
</tr>
</tbody>
</table>

Dearani et al. 2009
If there is severe aortic insufficiency, recommendations are to follow guidelines for aortic dilation in bicuspid aortic valve.

If no family history of dissection or aneurysm, and no rapid growth:

+ AAo > 5.5 = replace
+ AAo 5.0-5.5 = replace if benefits outweigh risks, weighted on co-morbidities, life expectancy, etc.

## TABLE 1. Aorta: Biopsy Specimens

<table>
<thead>
<tr>
<th>Disease</th>
<th>Normal</th>
<th></th>
<th></th>
<th>Grade 1</th>
<th></th>
<th></th>
<th>Grade 2</th>
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<th>Grade 3</th>
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</thead>
<tbody>
<tr>
<td>Controls</td>
<td>21</td>
<td>21</td>
<td>21</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>10</td>
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<tr>
<td>Marfan</td>
<td>10</td>
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<td>0</td>
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<tr>
<td>Annuloaortic ectasia</td>
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<tr>
<td>Bicuspid aortic stenosis</td>
<td>12</td>
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<td>0</td>
<td>2</td>
<td>3</td>
<td>6</td>
<td>5</td>
<td>4</td>
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<tr>
<td>Bicuspid aortic regurgitation</td>
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<td>0</td>
<td>2</td>
<td>4</td>
<td>3</td>
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<tr>
<td>Paracoarctation aorta</td>
<td>12</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>7</td>
<td>8</td>
<td>5</td>
<td>4</td>
<td>4</td>
<td></td>
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<tr>
<td>Fallot’s tetralogy, pulmonary stenosis or atresia</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>10</td>
<td>6</td>
<td>5</td>
<td>5</td>
<td></td>
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<tr>
<td>Truncus arteriosus type I</td>
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<tr>
<td>Initial operation</td>
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<td>Double aortic arch, DAR</td>
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SoV: 3.6 +/- 0.6 cm (2.4 – 5.2)
AAo: 3.1 +/- 0.6 cm (1.9 – 5.1)

n = 87 pts

Kay, Cook, Daniels – IJC 2012
RESULTS: PATTERNS OF ENLARGEMENT

- Sinuses are larger than the ascending in the majority of patients
- AA > SOV in 17% of our cohort
- > 70% enlarge over time at one segment
- Over a mean follow up of 3.3 years, only 1/55 patients enlarged from < 4.5 to > 4.5 cm

Kay, Cook, Daniels – AHA 2010
RESULTS BASELINE
PREDICTORS OF AORTIC ENLARGEMENT

Multivariate analysis: (p < 0.05)

SoV
- Right aortic arch
- Late age at first repair

AAo
- Pulmonary atresia
- Hypertension

Kay, Cook, Daniels – AHA 2010
Multivariate Predictors for Increasing Size SoV:

- Right aortic arch (trend, $p=0.055$)
- Pregnancy (trend, $p=0.052$)
- Late age at initial repair ($p < 0.001$)
- Smoking ($p < 0.02$)

AAo: No Predictors
A significant number (~30%) of rTOF patients have aortic dilation compared to expected size. Risk factors for aortic enlargement include older age, smoking, hypertension, TOF-PA, and late age at initial TOF surgery. In rTOF, the aorta may undergo progressive dilation at the SoV and/or AAo, but the rate appears to be slow.
A subset of rTOF patients dilate at the AAo, thus echo alone may not provide adequate surveillance.

A reasonable approach to surveillance to consider includes routine aortic MRAs at baseline and every 3 years.

Further studies are needed to determine appropriate timing of prophylactic aortic root replacement.
Class I recommendations:
Before pregnancy or if a genetic syndrome is identified, consultation with a geneticist should be arranged for patients with tetralogy of Fallot. (Level of Evidence: B)
PREGNANCY OUTCOMES IN TOF

TOF-PS: No CV events in 222 pregnancies
TOF-PA: 20% CHF in 40 pregnancies

ZAHARA Investigators: JACC 2007;49:2303–11
CURRENT AHA / ACC GUIDELINES (2008)

- Class I
  - Benefit >>> Risk
  - Standard of care, should be offered

- Class IIa
  - Benefit >> Risk, may need further studies
  - It is reasonable to offer

- Class IIb
  - Benefit > Risk
  - May be considered

- Class III
  - CONTRAINDUCTED, likely to be harmful
LEVELS OF EVIDENCE

• A – multiple populations analyzed
  – Multicenter or multiple randomized control trials
  – Metanalisys
  – No LOE A guidelines for rTOF
• B – limited population but with robust methods
  – Single RCT
  – Multiple robust nonrandomized studies
  – Only 11 LOE B guidelines
• C – expert opinion based on limited data
A pilot study of exercise training in adult patients with repaired tetralogy of Fallot

Judith Th
© 2009 Wiley Periodicals, Inc.

Single center
N = 18

CONGENTIAL HEART DISEASE

Effect of Captopril on Pulmonary Artery Pressure Following Corrective Surgery for Tetralogy of Fallot

Zeng-Shan Ma, M.Sc., M.D.,* Sheng-Jun Ma, M.D.,* Ming-Feng Dong, M.D.,* Jian-Tang Wang, M.D.,* and Le-Xin Wang, M.D., Ph.D.†

*Department of Cardiac Surgery, Liaocheng People’s Hospital, Taishan Medical University, Liaocheng, Shandong, China
†School of Biomedical Sciences, Charles Sturt University

Single center
N = 76

Original Article

A prospective, randomized, double-blind, placebo controlled trial of beta-blockade in patients who have undergone surgical correction of tetralogy of Fallot

Kambiz Noroozi,¹ Jens Bahlmann,² Björn Raab,³ Valentin Alper,⁴ Jan O. Arnhold,⁵ Titus Kuchne,⁵ Katrin Klimes,³ Monika Zoeger,² Siegfried Geyer,² Armin Wesser,² René Buchhorn³

Single center
N = 33
• Adults with repaired tetralogy of Fallot should have at least annual follow-up with a cardiologist who has expertise in ACHD (LOE C)
• Screening for heritable causes of their condition (e.g., 22q11 deletion) should be offered to all patients with tetralogy of Fallot. (LOE C)
• Adult patients with tetralogy of Fallot should have echocardiographic examinations and/or magnetic resonance imagings (MRIs) performed by staff with expertise in ACHD. (LOE C)
• Patients with unrepaired or palliated forms of tetralogy should have a formal evaluation at an ACHD center regarding suitability for repair. *(Level of Evidence: B)*

• Comprehensive echocardiographic imaging should be performed in a regional ACHD center to evaluate the anatomy and hemodynamics in patients with repaired tetralogy of Fallot. *(Level of Evidence: B)*
Catheterization of adults with tetralogy of Fallot should be performed in regional centers with expertise in ACHD. *(Level of Evidence: C)*

Coronary artery delineation should be performed before any intervention for the right ventricular outflow tract (RVOT). *(Level of Evidence: C)*
Electrophysiology Guidelines

- All level of evidence C
- Class I
  - For patients with cardiac rhythm devices:
  - Annual history, ECG, assessment of RV function
  - Periodic exercise testing
- Class Ila
  - Periodic Holter monitoring; frequency individualized based on hemodynamics and clinical suspicion of arrhythmias
- Class Ilb
  - EP study in an ACHD center may be reasonable to define suspected arrhythmias in adult with rTOF
NONCARDIAC MORBIDITY

- Stroke
- Brain Abscess
- Gallstones
- Gout
- Hemoptysis
GALLSTONES

- Prolonged periods of cyanosis can lead to calcium bilirubinate gallstones
- ACHD patients at risk, even after repair, but risk reduced by earlier age at repair
- Study in Japan of 114 consecutive congenital patients with prospective abdominal ultrasound
  - 27% of patients rendered acyanotic by surgery found to have noncholesterol gallstones (1/12 required surgery after screening)

Nine cases found out of 400 patients with cyanotic congenital heart disease

At least 5x the incidence of general population

Most patients male and had onset < 40 years of age

Somerville J, 1960

Fig. 2.—Relationship of haemoglobin to serum uric acid in patients with cyanotic congenital heart disease over 16 years of age.
GROWING NUMBER OF ACHD CENTERS
1. Survival is improving in TOF
2. There is still room to improve patient selection for pulmonary valve replacement
3. LVEDP essential for risk stratification
4. AHA/ACC guidelines based on sparse evidence
5. Better TOF-specific aortic root guidelines needed
6. Lifelong follow-up by CHD clinicians is essential
7. Patient registries essential for tracking and improving long-term outcomes