



# Tetralogy of Fallot - From Fetus to Adults: Management of Tachyarrhythmias in Complex Congenital Heart Disease

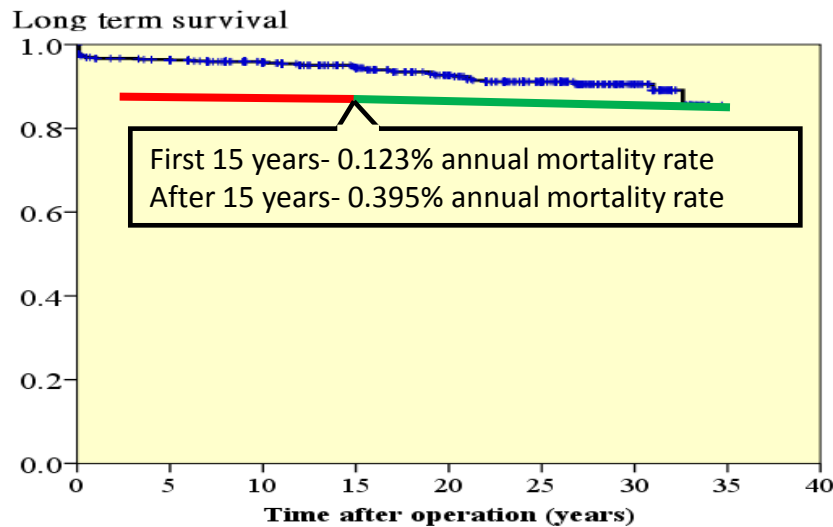
- ✓ TOF
- ✓ RAI

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**National Taiwan University Hospital, Taipei, Taiwan**



# Repaired TOF: problems and why arrhythmias matter

- National database 2000-6: TOF 0.63/1000 live births
- NTUH : 819 TOF repaired during 1970-2002\*
  - early death 27 (3.3%)
  - Mean follow up 17 years, late death 29 (3.6%)



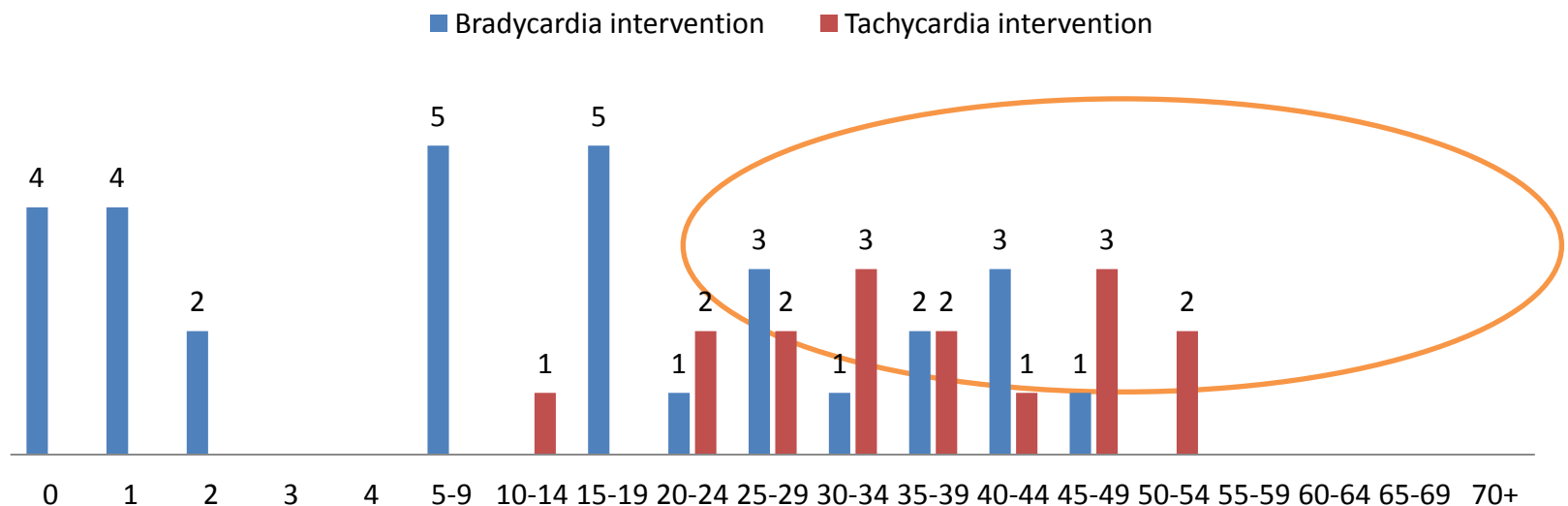
| Cause of death                          | Number (%) |
|---|------------|
| Cardiovascular origin                   | 15 (51.7%) |
| Heart failure or pulmonary hypertension | 7 (24.1%)  |
| Sudden cardiac death                    | 5 (17.2%)  |
| Arrhythmia                              | 3 (10.3%)  |
| Accident or suicide                     | 8 (27.6%)  |
| Hepatic or gastrointestinal cause       | 3 (10.3%)  |
| Infection                               | 2 (6.9%)   |
| Stroke                                  | 1 (3.4%)   |

Wu MH, et al. J Pediatr, 2010

Chiu SN, et al. Circ-CV quality and outcome, 2012

# Repaired TOF in Taiwan: national database 2000-2010

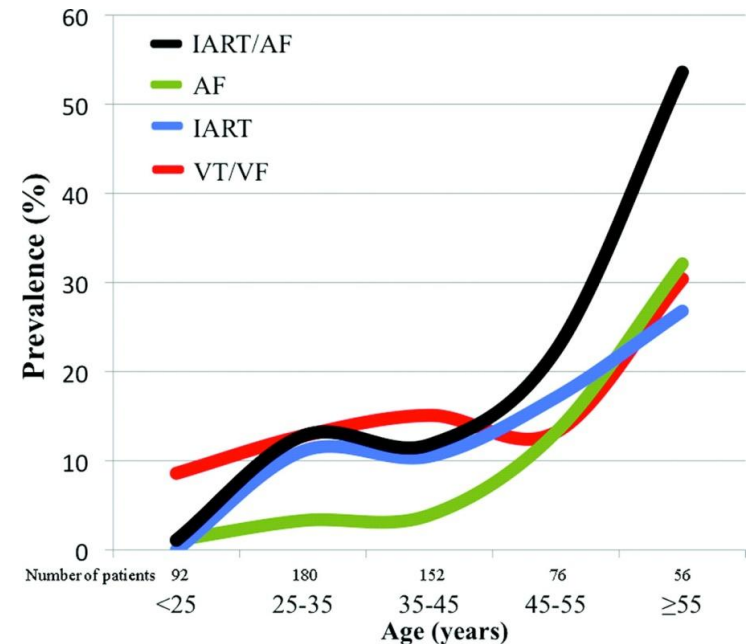
- 6003 TOF patients received medical care.
- Receiving medical care for tachyarrhythmias
  - 165 (2.75%) patients
  - The chance of arrhythmia intervention was 3.78% per patient-year, including 7 ICD for SD prevention.



# Adults with repaired TOF: arrhythmia burden

Khairy et al (Alliance for Adult Research in Congenital Cardiology, AARCC):  
556 adult rTOF, -- **43%** (Circulation, 2010)

|                                  |              |
|----------------------------------|--------------|
| <b>Sustained tachyarrhythmia</b> | <b>29.9%</b> |
| Atrial tachyarrhythmia           | 20.1%        |
| IART 11.5%, AF 7.4%              |              |
| Ventricular tachyarrhythmia      | 14.6%        |
| VT 14.2%, VF 0.5%                | 14.2%        |

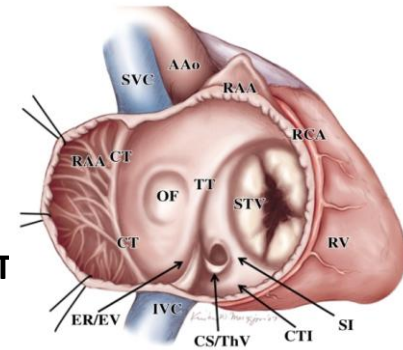
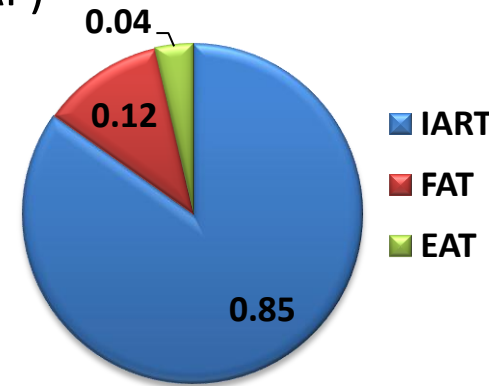


# Repaired TOF: atrial tachyarrhythmia

## Subtypes:

- Intra atrial reentrant tachycardia (IART, AF)
- Focal atrial tachycardia (FAT)
- Ectopic atrial tachycardia (EAT)

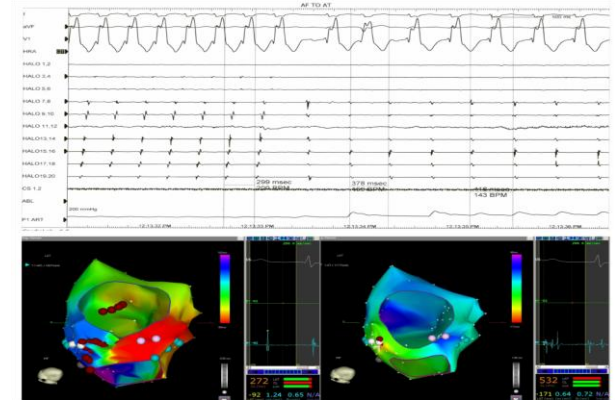
127 AT in 58 TOF and DORV



## Pharmacological control: unsatisfactory

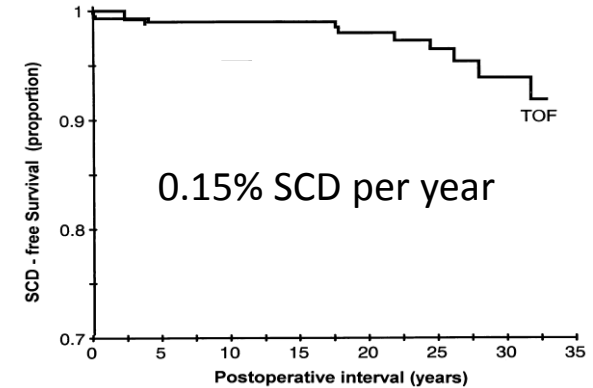
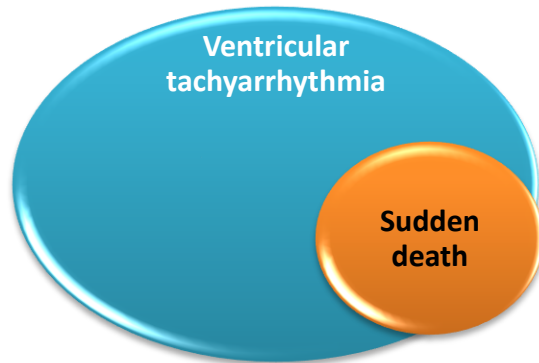
### RF Catheter Ablation

- Electroanatomical guidance: 76-98% success
- Recurrences are common, sometimes turning to EAT.
- Post-ablation pharmacological modification may be helpful.
- Pacemaker for tachy-brady syndrome (6% of AARCC patient cohort)
- Maze operation as a concomitant surgery



- Gatzoulis et al. Lancet. 2000
- Khairy et al. Circulation 2010
- Hallioglu et al. Ann Noninvasive Electrocardiol. 2004
- Mah DY et al, JCE 2011

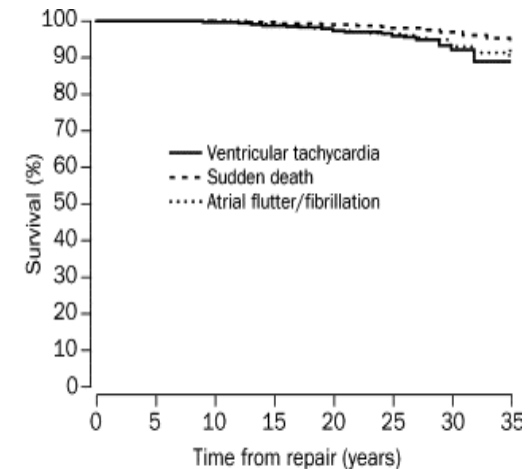
# Repaired TOF: Ventricular tachyarrhythmia



Silka MJ et al. JACC 1998

## Risk factors:

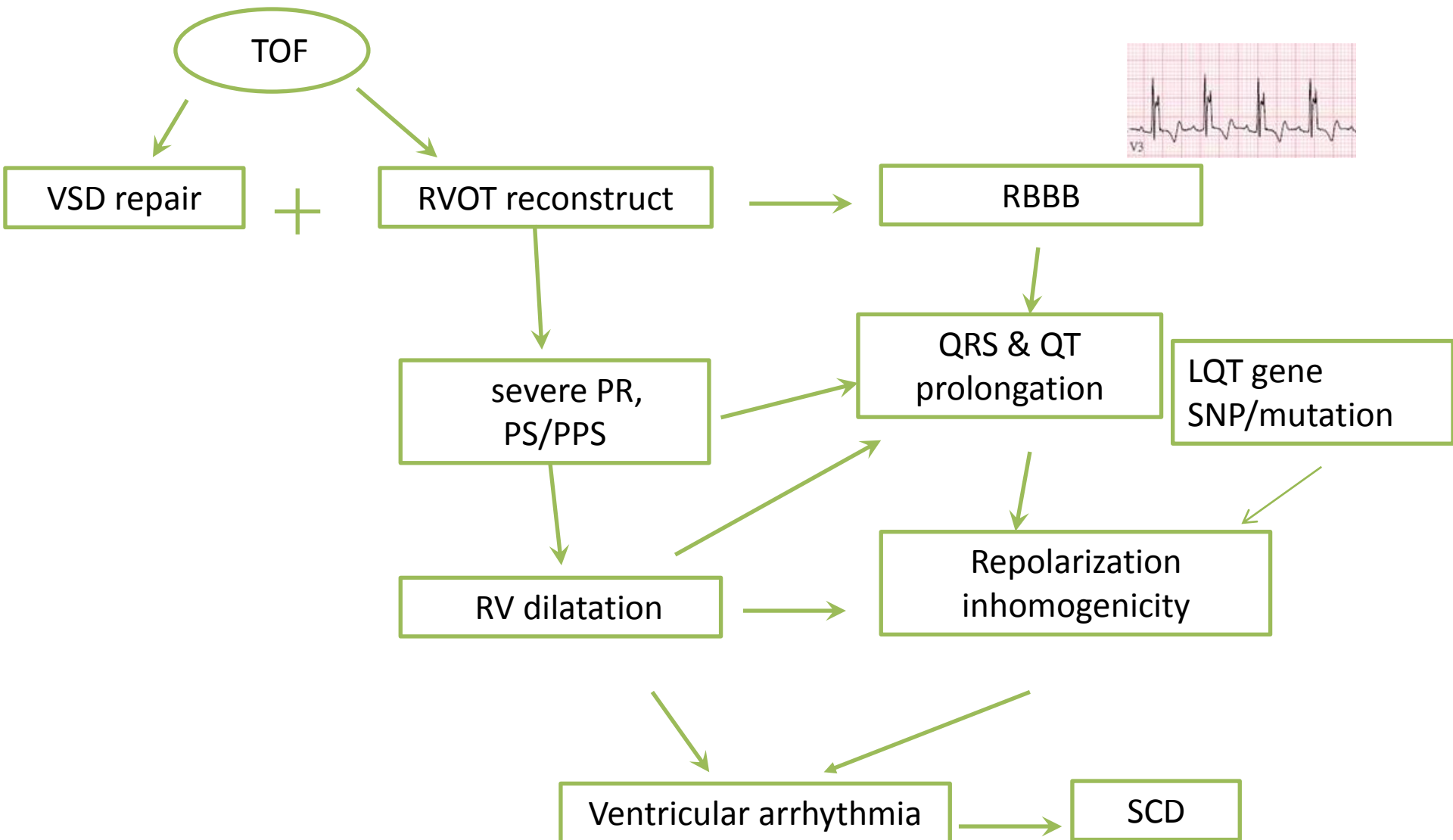
- a QRS duration  $> 180$  ms was predictive of VT and SCD.
- SCD patients showed late hemodynamic characteristics similar to the VT group, but had TOF repair at a much later age than those in the VT group.
- Very late repair  $\rightarrow$  myocardial substrate with different responses and a different outcome once VT occurred—ie, early degeneration to ventricular fibrillation and death.



Gatzoulis et al. Lancet. 2000

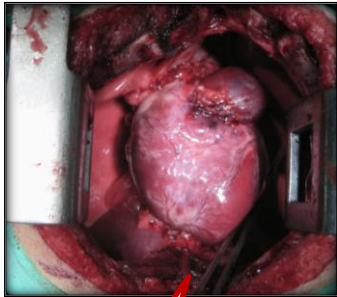
# Mechanism of ventricular arrhythmias in repaired TOF

## Electro-mechanical interaction and genetic disposition



# Animal model for rTOF

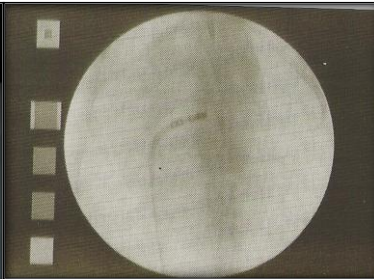
- Effective animal model for rTOF (PR and CRBBB)
- Hemodynamic and electrophysiologic factors both important: the EKG parameters change and VT events are most significant in combined factors group.
- Pharmacological testing shall be feasible



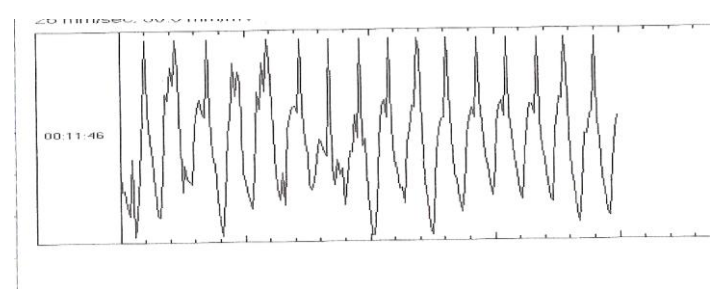
PR



Loop recorder



CRBBB





# Mechanism of ventricular arrhythmias in repaired TOF

## Electro-mechanical interaction and genetic disposition

Acquired Long QT syndrome: (LQT gene SNP/mutation plus secondary repolarization abnormality from RBBB)



LQT gene SNP/mutation

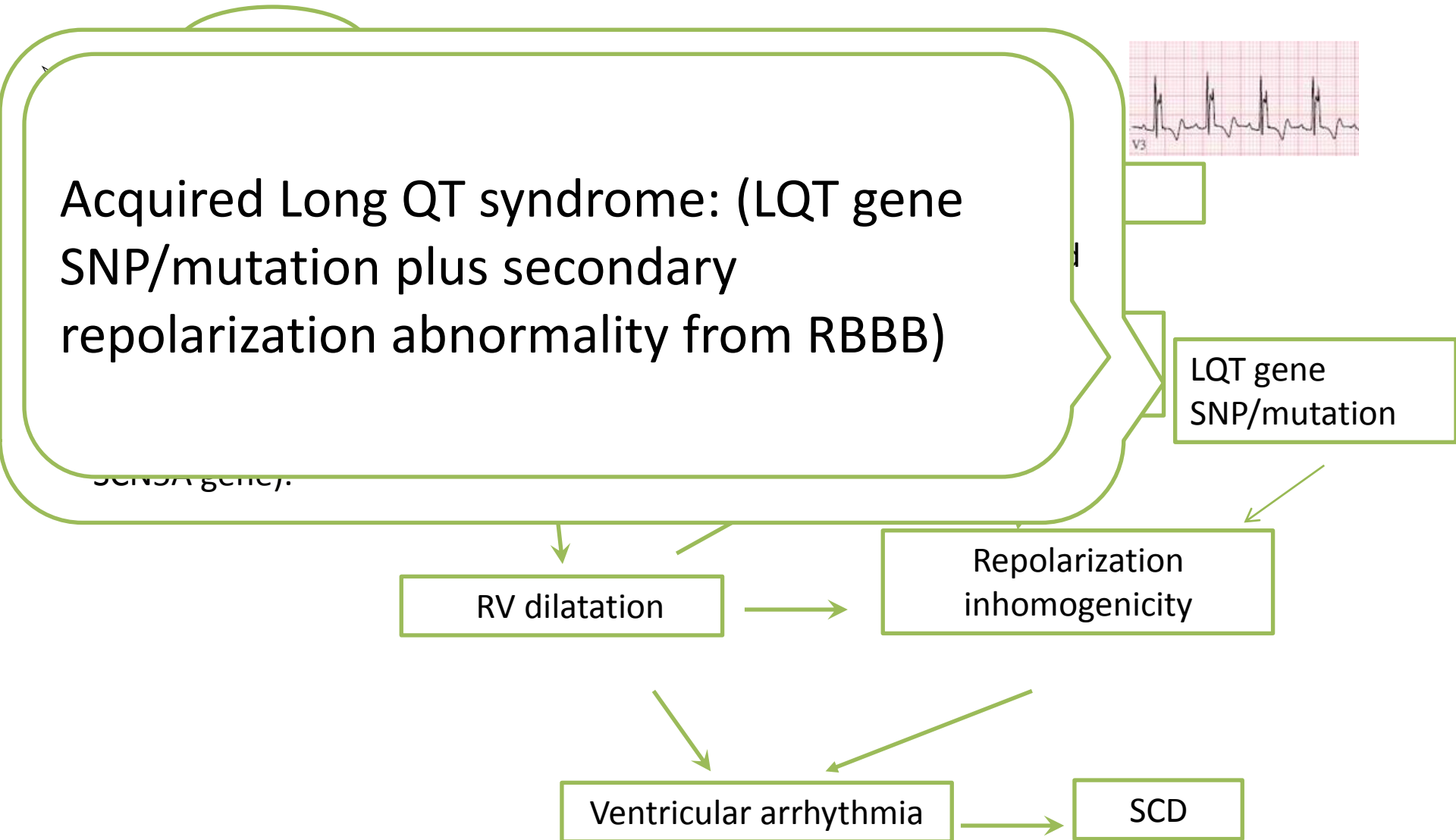
RV dilatation

Repolarization inhomogeneity

Ventricular arrhythmia

SCD

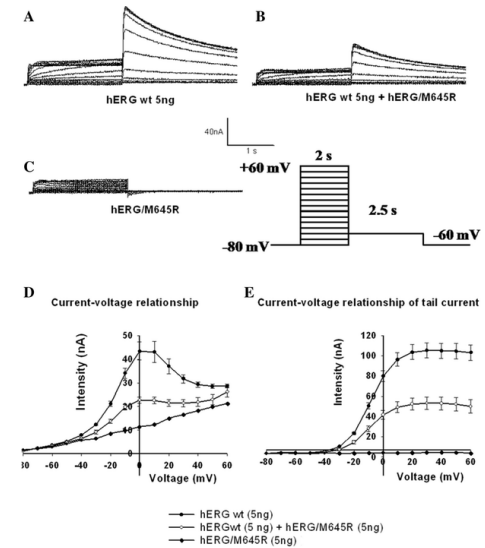
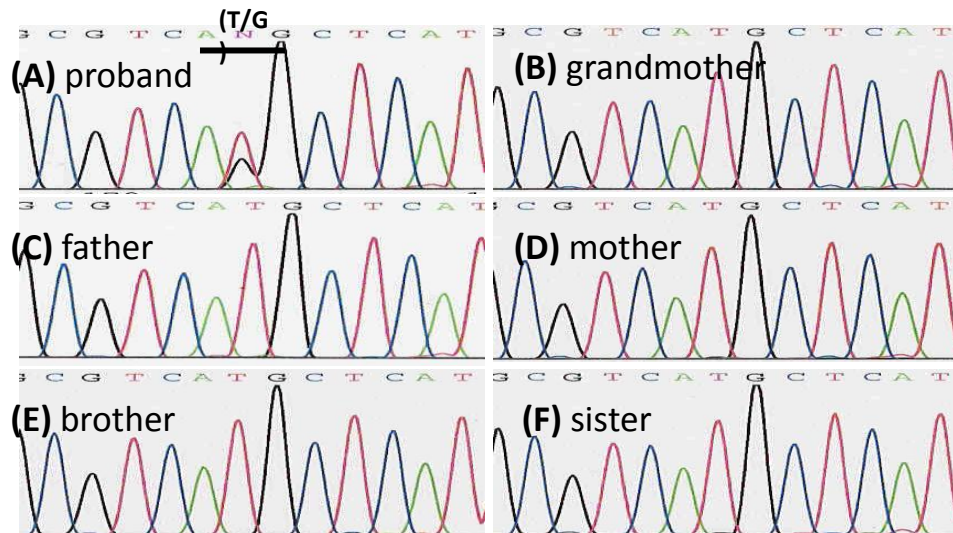
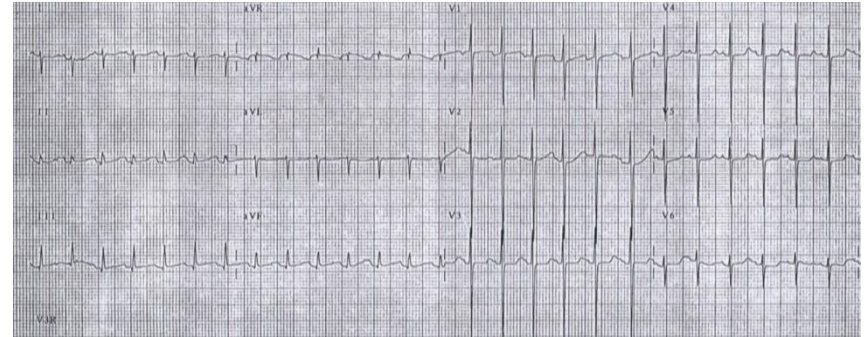
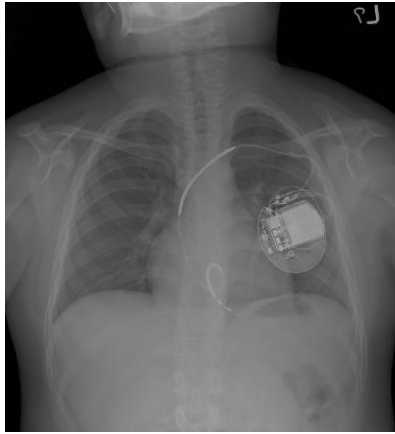
SCD gene.



A 6 y/o boy with TOF operated at 3 y/o.

HERG mutation, p.M645R<sup>M</sup>

I<sub>Kr</sub> pore region , dominant negative effect on I<sub>Kr</sub>



# Pharmacological modification for SCD prevention in rTOF

- Class II AADs ( $\beta$ -blockers)
- Class III AADs: Amiodarone
- ACE inhibitor
- Aldosterone antagonist
  
- Sotalolo: decrease DFT



SCD prevention  
in adults

## Repaired TOF?

33 patients (mean age: 30.9 years) with NYHA class 1 or 2, with 1) BNP >100 pg/ml and 2) reduced peak uptake of oxygen less than 25 ml/kg/min.

$\beta$ -blockade with Bisoprolol has no beneficial effects on right ventricular dysfunction secondary to repaired TOF. Norozi K et al. *Cardiol Young*. 2007

Ramipril (ACEI) is a well tolerated therapy, improves biventricular function in patients with rTOF and may have a particular role in patients with restrictive RV physiology.

Babu-Narayan SV et al. *Int J Cardiol* 2012

31 TOF elevation of BNP in patients after TOF repair could reflect volume and pressure load in the RV end-diastolic phase, and ACEI (11 patients) may reduce BNP levels in a dose-dependent manner Furukawa et al. *Ped Cardiol* 2012

# Repaired TOF: ventricular tachyarrhythmia and SD

## Treatments:

### ➤ Drugs:

#### Anti-arrhythmic drugs:

- $\beta$ -blockers
- amiodarone if QT not too much prolonged
- sotalol aduvant (decrease DFT)
- avoid class Ia and Ic if either ventricular dysfunction

#### Non-antiarrhythmic agents:

ACEI to improve RV dysfunction  
Spironolactone may be helpful

# Repaired TOF: ventricular tachyarrhythmia and SD

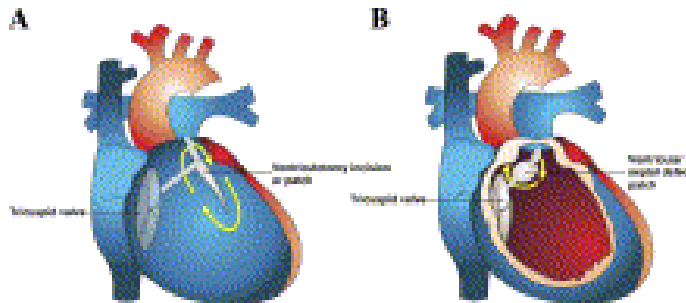
## ➤ Interventions:

### Ablation:

- 11% of VT patients in AARCC cohort received RFCA
- Success rate may be improved (to around 80%) with noncontact mapping
- VT ablation with PVR surgery

### Ablation targets:

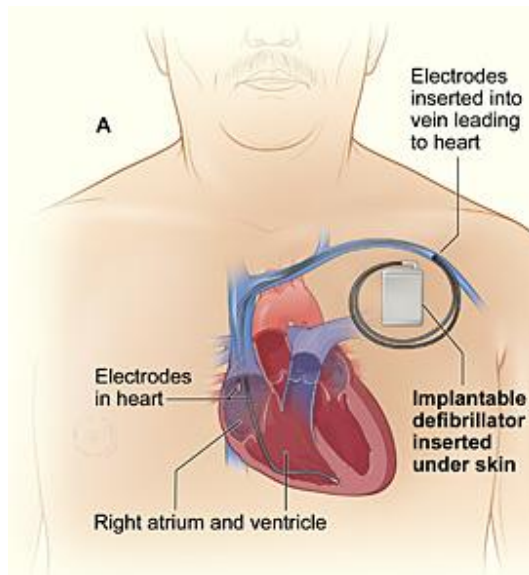
- Potential arrhythmia circuits of VT are along the RV free wall and septum.
- RFCA could target on the 4 potential critical isthmuses.
- Guided by electroanatomic mapping techniques, diastolic potentials and regions with concealed entrainment mapping with short postpacing intervals



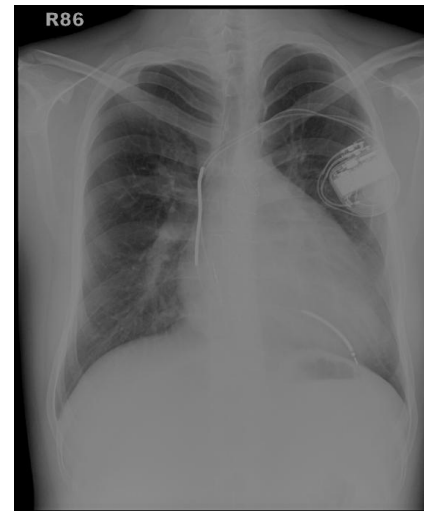
Khairy et al. Circulation 2010  
Kriebel et al. JACC 2007  
Khairy et al. Heart Rhythm 2009  
Kanter et al. JCE 2010

# Timing for ICD in TOF: secondary prevention

- Appropriate shock: 9.8% per year <sup>1</sup>
- Appropriate shocks were more common in patients who received an ICD for secondary prevention (32%) compared with primary prevention (18%,  $p < 0.001$ )<sup>2</sup>

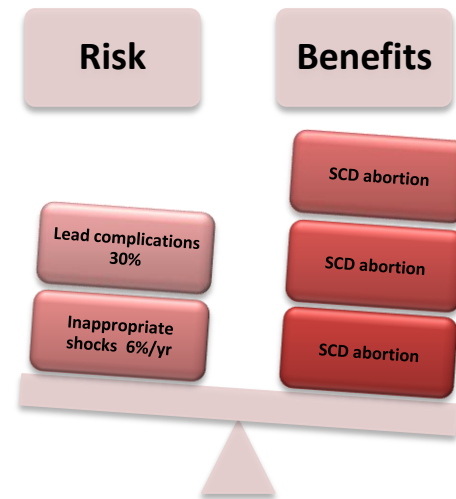


A 20 y/o r-TOF



1 Khairy et al. Current Opinion in Cardiol 2011  
2 Berul et al. JACC 2008

# Timing for ICD in TOF: primary prevention



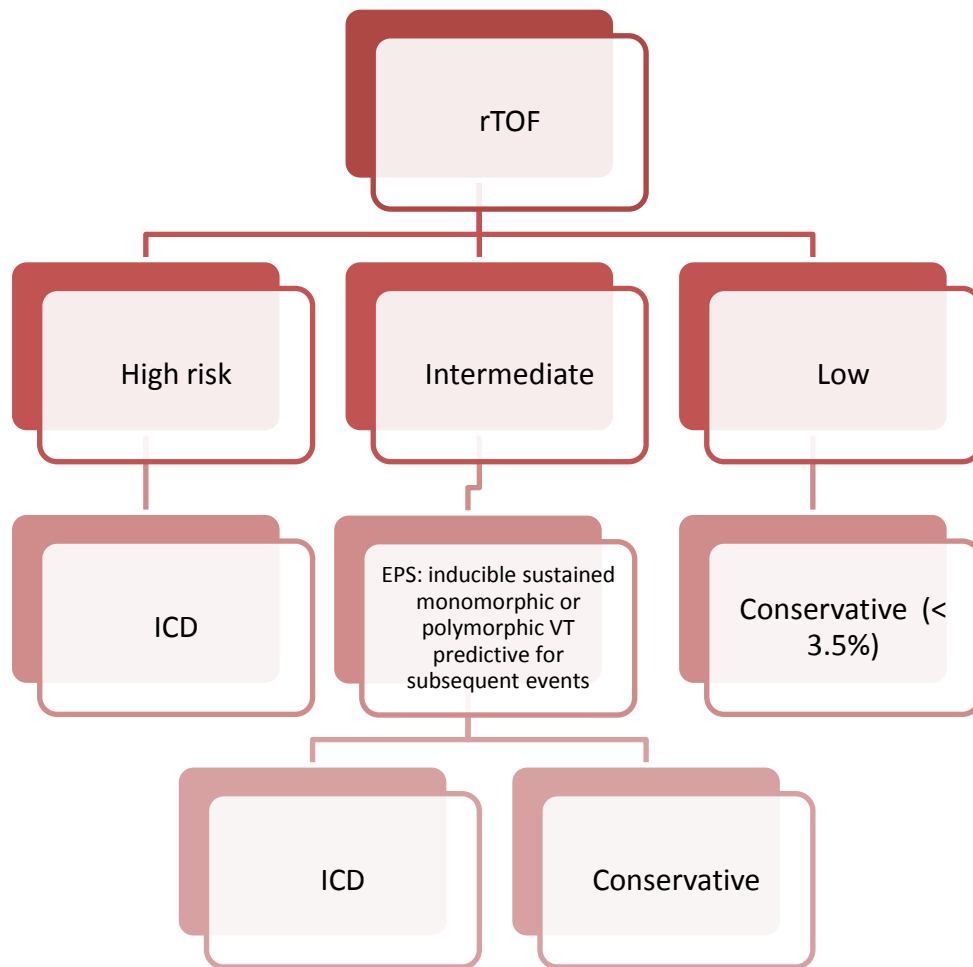
- From adult ICD studies, benefit from ICDs has been demonstrated if the baseline population risk for SCD is  $> 3.5\%$  per year.

**Bayesian perspective** with pretest probability, post-test probability, (+)/(-)likelihood:

- TOF revealed a  $0.15\%$  annual incidence of SCD. To have a positive post-test probability of  $3.5\%$ , the minimum pretest probability for SCD should be  $0.95\%$ . We need a risk factor with (+) likelihood ratio of 24. ---- composite risk scores

# Timing for ICD in TOF: primary prevention

| <u>Variable</u>         | <u>Points</u> |
|-------------------------|---------------|
| Prior palliative shunt  | 2             |
| Inducible sustained VT  | 2             |
| QRS >180 ms             | 1             |
| Ventriculotomy incision | 2             |
| Nonsustained VT         | 2             |
| LV EDP >12mmHg          | 3             |
| <b>Total point</b>      | <b>0-12</b>   |



| Risk score | Risk         | Rate of appropriate shock |
|------------|--------------|---------------------------|
| 0-2        | Low          | 0                         |
| 3-5        | Intermediate | 3.8%                      |
| 6-12       | High         | 17.5%                     |

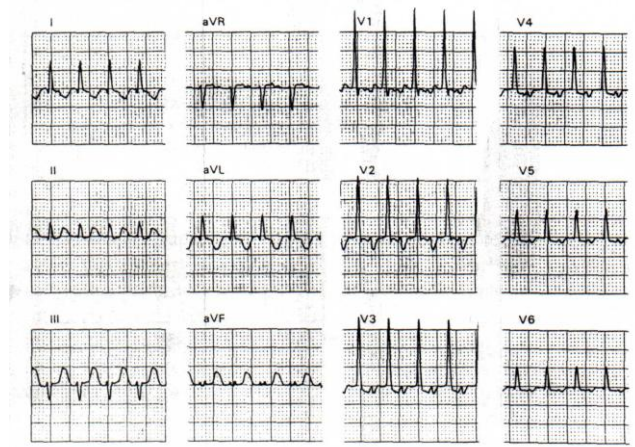
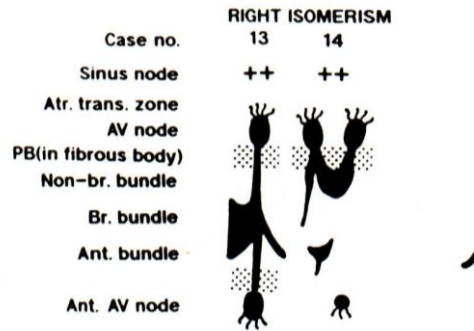
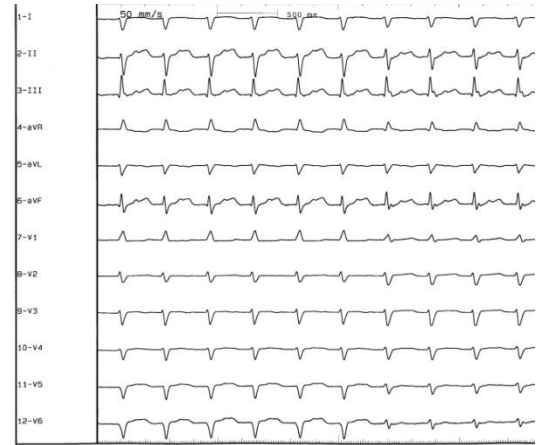
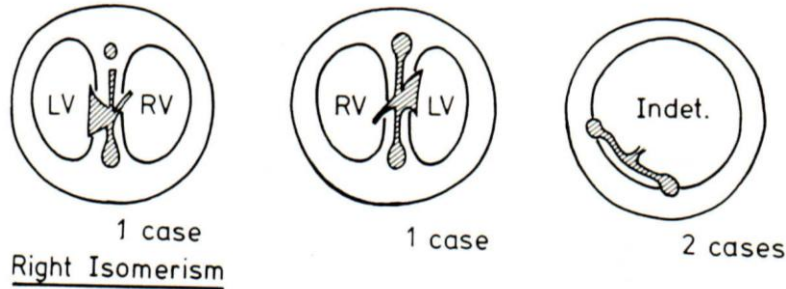
Khairy et al.  
Current Opinion in Cardiol 2011



# Summary for rTOF

1. Arrhythmias are common in repaired TOF after quiescent 10-15 postoperative years, and account for one-fourth of late death.
2. Medical treatment and ablation for atrial tachyarrhythmias are feasible but need to be optimized.
3. Medical treatment and ablation for ventricular tachyarrhythmias are not stand-alone therapy. The development of medical strategy in rTOF with RBBB need to consider the scenario of acquired LQTS.
4. Composite risk scores are helpful to identifying patients requiring ICD as primary SD prevention therapy.

# AV node-to-AV node in RAI



Ho et al. JACC 1992  
 Dickinson et al. Circ 1979

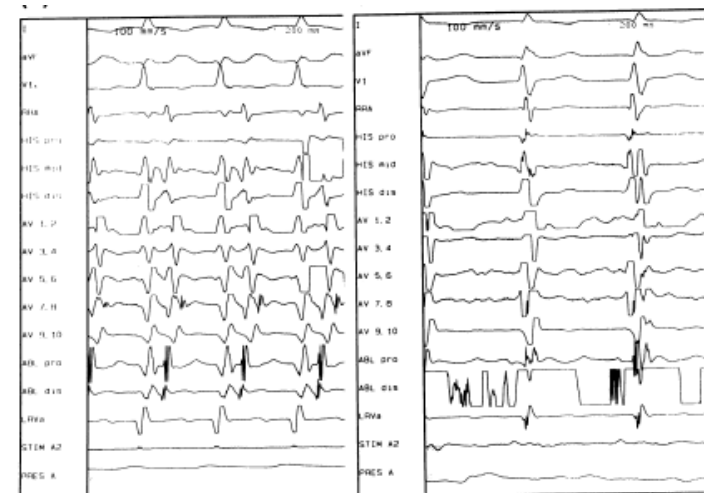
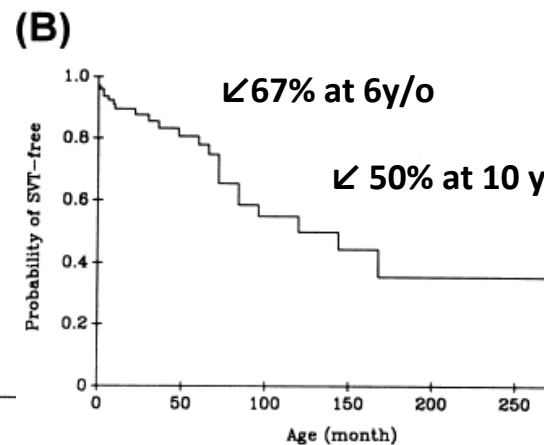
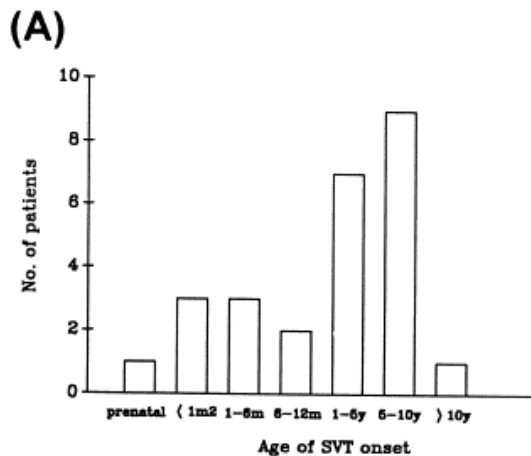
The 2 patients report form NTUH  
 Electrophysiological properties of dual  
 atrioventricular nodes in patients with right atrial  
 Isomerism. Wu MH, et al, Br Heart J 1995

## Supraventricular Tachycardia in Patients With Right Atrial Isomerism

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- 101 RAI patients & 4 fetuses
- SVT incidence: 24.8 % for kids, 25% for fetus
- SVT onset: prenatal to 14 yrs, median 4 yrs
- RF ablation given at tachycardia, aiming the earliest A during tachycardia or second His potential of the sinus rhythm.
- Successful site was associated with the development of junctional ectopic tachycardia.



# Twin AV Node Reentrant Tachycardia

Report of 7 (5 with EPS) cases from  
Boston Children's Hospital,  
Epstein et al. JCE 12;671-9, 2001

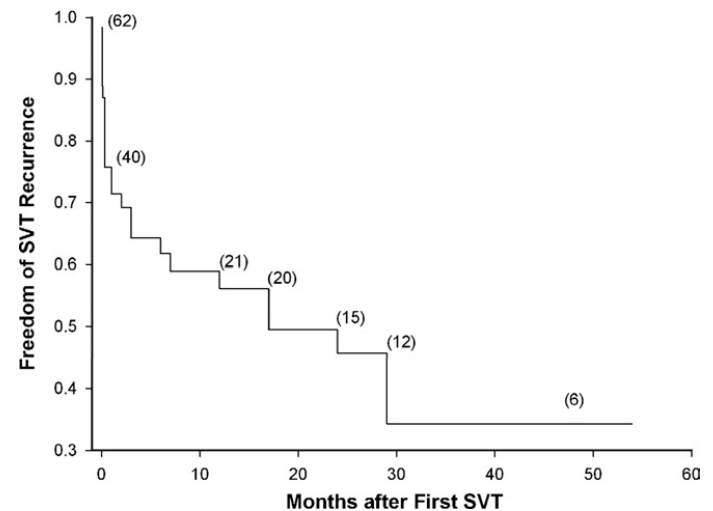
- Existence of 2 discrete non-preexcited QRS morphology with His electrogram
- Decremental and adenosine sensitive antegrade and retrograde conduction
- Inducible AV reciprocating tachycardia with antegrade through one AVN and retrograde through another AVN

# Long-term outcome of twin atrioventricular node and supraventricular tachycardia in patients with right isomerism of the atrial appendage

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*From the Departments of \*Pediatrics and †Internal Medicine, National Taiwan University Hospital, College of Medicine, National Taiwan University, Taipei, Taiwan.*

- 257 RAI patients
- SVT incidence: 26 %
- Two QRS morphology: 64% (>2 EKG)
- Recurrence of SVT: 40%, 1 day to 4.5 years after the first episode.
- The occurrence or recurrence of SVT was not associated with increased all-cause mortality.
- Treatment: medication ( $\beta$  blocker etc), ablation



# Summary for RAI

1. Twin AV nodes (2 discrete QRS pattern) is common if serial EKG is taken.
2. SVT, particularly, twin AV node reentrant tachycardia, may occur from fetal stage and the probability free from SVT is around half by the age of 10 years.
3. EPS and RFCA in those with history of tachycardia may be considered before the completion of TCPC, because the venous access will be limited after the completion.
4. If it is difficult to eliminate the substrates of TAVRT, medical control for the SVT is still helpful.

Thank you!  
THANK YOU!



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