Tetralogy of Fallot
&
Pacing

Saeed Oraii MD, Cardiologist
Interventional Electrophysiologist
Tehran Arrhythmia Clinic
April 2016
Tetralogy of Fallot

• Tetralogy of Fallot (TOF) is the most common form of cyanotic congenital heart disease.

• The first cardiac repair of TOF was successfully performed in 1955 in the United States.


Improving Survival

• Patients with congenital heart disease (CHD) are living longer.

• Surgical repair of TOF is highly successful.

• In the United States, a 40% reduction in annualized death rates for TOF was reported between 1979 and 2005.

Growing Population

- The population of adults with repaired TOF and other CHD is growing rapidly.

Arrhythmias, Leading Cause of Death

Late Death in Repaired Tetralogy

793 adult pts (1985-95)
33 pts died (4.2% mortality)

Gatzoulis et al. Lancet 2000
Conduction Abnormalities

• Right bundle branch block (RBBB) is almost universal in patients after TOF repair

• Approximately 15% of these patients, have also left anterior hemiblock.

• Many patients have slower atrioventricular (AV) conduction as well.

Conduction System Injury

• Tremendous advances in the surgical management of CHD have been achieved over the past half century.

• Nevertheless, conduction system injury continues to be a leading cause of long-term postoperative cardiac morbidity.
Incidence

• The incidence of postoperative AV conduction block has declined significantly since it was first explored in detail in a landmark paper by Lillehei et al in 1963.

• Still, heart block continues to complicate approximately 1% to 3% of operations performed at major CHD surgical centers.

Spontaneous Resolution

- Postoperative heart block is variably reported to resolve spontaneously in 43% to 92% of cases.

- The large degree of variation among studies is attributable to a variety of factors, such as the era, case identification and inclusion criteria, and follow-up duration.

Spontaneous Recovery

- Spontaneous recovery usually does take place within 7 to 10 days.

Timing of Pacemaker Implant

- There is uncertainty regarding optimal timing of permanent pacemaker (PPM) implantation
  - Long-term risks associated with nonintervention, vs. the morbidity of lifelong pacemaker therapy
- The concept that transient, spontaneously resolving heart block does not require permanent pacing is widely accepted, but its application is less clear considering the possibility of late recovery of heart block vs. late recurrence.
Late Recovery

• Late recovery is well recognized.

• Recovery of AV conduction was reported in about 10% of cases of postoperative heart block persisting beyond 14 days.

• Recovery was noted at postoperative times ranging up to 113 days (median 41 days).

Very Late Recovery

• Even very late recovery of AV conduction has been reported up to 20 years (median 5.5 years) after onset of heart block in 14 (32%) of 44 patients who had undergone PPM implantation.

Against Delay in Implant

• Despite the possibility of a late return of AV conduction, two contemporary considerations weigh against protracted delay in the decision to proceed with PPM implantation.
  – The ongoing improvement in longevity and miniaturization of pacing systems available for infants and children, reducing concerns over pacing-related morbidity
  – The cost-driven pressure for reductions in hospital length-of-stay
Recurrence of AV Block

• Although the decision to proceed with PPM implant is largely made by the immediate time course of recovery from postop AV block, the risk of late recurrence of heart block is a more ominous and poorly defined problem with potentially life-threatening implications.

• The very concept of “recurrence” is challenged by the observation that heart block can appear, presumably de novo, long after CHD surgery.
Early vs. Late Onset

• In a report, 114 CHD patients undergoing PPM implantation for postoperative AV block were divided into “early”- and “late”-onset groups – Those whose heart block was initially detected either less than 30 days or at least 30 days after surgery.

• Fully 36% of the patients fell into the “late” group, with heart block identified at a mean of 4.7 years after CHD surgery in that group.

Association with Sudden Death

• The incidence of late sudden death is correlated strongly with transient postop heart block.

• Among 20 patients with postop heart block lasting more than 3 days, 8 (40%) subsequently died suddenly.

• The sudden death rate among 55 patients with heart block of shorter duration was 7.3%, similar to the 6.1% noted in the 196 patients who had no documented heart block.

Site of Block

• Several investigators have attempted to identify additional prognostic predictors in the early postop heart block.

• Attention has focused on the anatomic site of conduction system disruption (above or below His bundle).

• The location and degree of conduction system injury likely do carry prognostic significance in patients with transient heart block.

Residual Fascicular Block

• The risk increases dramatically when transient heart block recovered with residual bifascicular block.

• Late-onset complete heart block occurs in almost 33% of such patients.

• At another report, 16 (29%) of these patients experienced either late-onset complete heart block or sudden cardiac death.

Transient AV Block

- A pacemaker should, therefore, be considered in patients with postoperative transient AV block and residual bifascicular block (IIb indication).

- However, there is currently no evidence to support routine pacemaker implantation for bifascicular block in asymptomatic adults with CHD who did not have transient complete AV block.
Atrial Arrhythmias

• Despite congenital or postop AV block, atrial fibrillation and intra-atrial reentrant tachycardia remain an ongoing concern in patients with CHD and can complicate effective utilization of dual-chamber pacing.

• Dual-chamber pacing is preferred over VVI pacing in adults with CHD and intrinsic or postop heart block.

Optimal Lead Implant Site

• It is now well recognized that right ventricular pacing, especially the free wall, can have deleterious effects on ventricular function.

• Although ventricular septal pacing has been advocated as preferential to the apex, surgical patch materials can prevent septal implant.

AV Valve Flow Pattern

• Standard RV pacing without careful manipulation of the AV interval may be insufficient to shorten the QRS duration in patients with TOF and RBBB.

• Concomitant echocardiographic evaluation of AV valve inflow patterns with pacemaker programming of AV intervals may allow for identification of the longest possible diastolic filling time for maximal cardiac output.

Late Postoperative Problems

• Despite high surgical success rates, long-term mechanical problems after surgical repair include pulmonary regurgitation, right ventricular (RV) dilation due to residual RV outflow tract obstruction and/or pulmonary regurgitation, tricuspid valve regurgitation, residual ventricular septal defect, and left ventricular (LV) dysfunction.


Redo Surgeries

• Although the timing of primary repair has also changed toward repair at presentation or symptom appearance, most adult patients with repaired TOF currently have undergone trans-annular patching.
RV Dysfunction

• Right heart failure is due to the combined effects of pressure and volume overloads and of the myocardial lesions inflicted during and after the operation.

• The resulting RV dysfunction may lead to fibrosis, which, in itself, begets RV dysfunction and is accompanied by delay in electrical activation of myocardial tissue.
RV Dysfunction

• RV dysfunction and right heart failure in patients with TOF often are multifactorial in origin:
  – Chronic pressure overload,
  – Volume overload,
  – Myocardial injury associated with cardiopulmonary bypass during surgical repair,
  – RBBB and electrical dyssynchrony, or
  – A combination of these factors.

RBBB

- RBBB almost invariably develops after surgical repair of TOF.
- Besides the direct interruption of conduction pathways and various hemorrhagic, edematous, or ischemic complications, the duration of operation, the performance of a ventriculotomy, and the repair of an interventricular septal defect or of the muscular outflow tract are all contributing factors.

RBBB & Hemodynamics

• The hemodynamic consequences of RBBB might play a predominant role in the long-term clinical outcomes of these patients.

• A relationship probably exists between electrical and mechanical dysfunction, as well as links between myocardial remodeling, rhythm disturbances, and electromechanical dyssynchrony.

RBBB & Prognosis

• Depressed contractility and remodeling may be promoted by mechanical dyssynchrony, which, therefore, may be a desirable therapeutic target.

• Furthermore, a wide QRS is prognostically important, and QRS duration and risk of developing ventricular arrhythmias are closely correlated.

The Level of Block

- Postoperative RBBB is classified as **proximal** when near the His bundle, **distal** when at the level of the moderator band, and **terminal** when due to injury to the Purkinje network.

- No electrocardiographic criterion is capable of precisely locating the level of block.

Level of Block

• It could be important to know the level of block for several reasons.

• The risk of complete AV block is considerably higher when the block is proximal than when it is distal, since conduction depends only on the left bundle branch.

From the perspective of Cardiac Resynchronization Therapy (CRT), which tries to correct the dispersion of segmental electromechanical activation, it might be critical to pinpoint the site of block.

The characteristic activation sequence of proximal RBBB, which is most likely to complicate the repair of an interventricular septal defect, is markedly different from terminal block.
Proximal vs. Terminal Block

• In Proximal block the entire ventricular mass is activated via the left bundle, and the RV is activated by continuity, with important delays among the septal, apical, outflow, and free wall segments.

• In contrast, in the presence of terminal block, usually caused by ventriculotomy or myocardial resection, the activation delay is confined to the anterior outflow tract.
Distal RBBB

• Distal block, intermediate between proximal and terminal and usually caused by the direct section of the moderator band, is characterized by:
  – Preserved activation of the anteroseptal and apical RV via right bundle fibers, which penetrate the RV myocardial tissue ahead of the moderator band
  – Delayed activation of the RV posterior wall.
Mapping the Level of Block

• In contrast to the weak contributions of the surface electrocardiogram, invasive or noninvasive mapping may facilitate the localization of the level of block.

• A normal activation of the RV apex excludes the presence of proximal block.
Ventricular Activation Pattern

• Marked differences observed in the ventricular electrical mapping of two patients whose surface electrocardiogram showed the same RBBB pattern after surgical repair of TOF.

Proximal block

Distal block

Level of Block & Dyssynchrony

• Remodeling leading to RV dilatation and dysfunction varies as a function of the level of block.

• A relationship between electrical dyssynchrony and mechanical dysfunction is distinctly more likely in the presence of proximal than terminal block, since the hemodynamic consequences of delayed outflow tract (OT) activation are small.
A Wide QRS

- RV dysfunction and dilatation of chambers promote the development of myocardial fibrosis, which is electrophysiologically manifested by fragmented and low-amplitude endocardial electrograms.

- The presence of a >180-ms QRS duration is not simply due to the section of a conduction pathway and is invariably the expression of a widespread disorder of intramyocardial conduction.
Wide QRS & Dyssynchrony

• In all echocardiographic studies conducted in this patient population, electrical dyssynchrony has invariably been associated with mechanical dyssynchrony.

• Differences were observed, however, in the sites of ventricular activation delays and types of dyssynchrony.

Practical Implications

• In the case of major activation delays in the RV chamber, the implantation of an RV lead may be appropriate.

• In contrast, in the case of disturbances confined to the OT, the hemodynamic effects of implanting a lead in the RV chamber or in the OT are uncertain, because of the marked electrical and mechanical abnormalities encountered in that region.
TOF & LV Dyssynchrony

• A 50%–90% prevalence of LV dyssynchrony has been observed in echocardiographic studies of TOF.

• The mechanical interaction between a dilated and pressure-overloaded RV and an a priori functionally and structurally normal LV stresses the septal surface and causes LV activation delays.


Furthermore, perioperative ischemia and variable operative techniques may contribute to LV dyssynchrony.

The presence of contractile dysfunction associated with a left-sided conduction disturbance is a major determinant of the mode of stimulation recommended for these patients.
A Vicious Circle

- Pulmonic insufficiency causes a progressive increase in RV volumes, which, in turn, increases the activation time and causes segmental dyssynchrony of activation.

- The conduction disorder may then promote remodeling and further chamber dilatation.

- Deleterious effect and adverse outcome persist even after pulmonary valve replacement.

Current Therapies

• Current therapies for chronic RV failure are largely empiric, and their effectiveness is not known.

• All treatment approaches for RV failure considered together have been studied in fewer than 500 subjects.

• This contrasts markedly with left ventricular failure, for which multiple therapeutic strategies have been evaluated, often in mega-trials of thousands of subjects.
CRT & LV Failure

- Cardiac Resynchronization Therapy has been shown to be effective in addressing the fundamental problems of left heart failure, improving quality of life and exercise capacity and prolonging survival in patients with electrical dyssynchrony and cardiomyopathy.
CRT in Children

• Unlike LV failure, RV failure is poorly understood and its management remains largely empirical.

• In contrast to the vast experience with CRT in adults with LV dysfunction and LBBB, studies of the CRT in patients with CHD and RV dysfunction are limited to case reports and retrospective analyses of heterogeneous populations.
Application to RV Failure

• Some application of CRT to the problem of RV failure has already been made, but we are only in the very early stages of this process.

• Among the important obstacles to be addressed are the inadequacies of current assessments of RV function, the heterogeneity of diseases that lead to RV failure, and the difficulty of identifying appropriate clinical endpoints for assessing efficacy of treatment.
CRT in Children

- The heterogeneous patient population, technical limitations from patient size, vascular access issues, and unique forms of ventricular dyssynchrony make it difficult to determine risks and benefits of this procedure in children.

Assessment of RV Function

- Echocardiography is much less accurate for global RV function than it is for LV function.
- Echocardiography can also offer a limited information about timing of RV regional contraction, a problem that results from the complex anatomy of the RV.
- Assessment of global RV function now can be reliably performed using cardiac magnetic resonance imaging (MRI).
Indolent Nature

• Finally, the clinical picture of right heart failure poses unique challenges to implementation of CRT.

• RV failure is an indolent disease, characterized by long-term consequences of cirrhosis, cachexia, and effort intolerance but not associated with high rates of short-term mortality.
Disease Course

- Unlike LV failure, chronic RV failure does not have high rates of mortality over a period that a clinical trial could reasonably study.

- Therefore, the clinical endpoints for a trial of RV CRT are difficult to define.
RBBB & CRT

• More than 70% of CRT in the pediatric age group has been in the setting of CHD, 30% to 40% involving the RV.

• In the setting of RBBB, Vogel et al first demonstrated abnormal regional wall motion in the RV free wall and interventricular septum using tissue Doppler techniques, offering an early suggestion of a substrate for resynchronization.


Postoperative Trials

• The immediate postoperative effects of cardiac resynchronization were initially studied in mixed populations of patients presenting with congenital heart disease, as well as in patients with TOF.

• Atrial synchronized RV stimulation with optimized AV delays was performed using temporary RV wires placed during the operation.
Short term Effects

• Although their endpoints were variable, all studies reported hemodynamic improvements and alleviation of postoperative heart failure.

• Ventricular stimulation immediately increased the systemic blood pressure, enabled a decrease in inotropic support and volume replacement, and stabilized hemodynamic function during the first postop 48 hours, after which stimulation could be uneventfully discontinued.

Long term Stimulation

• Studies of the clinical outcomes of patients with TOF who underwent long-term cardiac stimulation for hemodynamic indications are few.

• A few case reports, or isolated patients presenting with TOF, who were included in single- or multicenter studies of CRT in patients with CHD.
RV only Pacing

• In one study, RV pacing improved RV function without affecting LV function.

• These findings paved the way to the idea of RV resynchronization by RV pacing in patients with TOF.

Single RV Pacing

• Singe-sided RV pacing is generally regarded as detrimental in the long term in patients with anti-bradycardia pacing and normal ventricular conduction.

• It may, however, be beneficial in patients with TOF, heart failure and wide QRS complex due to RBBB.

• This beneficial effect could be attributed entirely to resynchronization of the RV by RV pacing.
Single Sided RV Pacing

• Single sided RV pacing, as it resynchronizes the RV with RBBB, may be considered analogous to LV pacing in LBBB.

• Ventricular pacing also can be helpful in correcting prolonged AV conduction, thereby optimizing filling.

Long Term Studies

• A prospective study evaluated RV resynchronization therapy in outpatients with TOF and right heart failure who already had an ICD in place.
  – A single-blinded crossover design
  – Improvement in RV ejection fraction
  – Improvement in self-reported quality of life.
  – No decrease in left ventricular ejection fraction

Long Term Studies

• In another study in adults with TOF they failed to demonstrate improved cardiac index using RV CRT.

• At this time, RV CRT can be considered as unproven, but its use should be considered in patients who have failed other options.

Biventricular Pacing

• One study in seven children with congenital heart disease and a RBBB pattern found that resynchronization therapy by biventricular (BiV) pacing resulted in small, but statistically significant, acute improvements in cardiac output and right ventricular \( dp/dt \).

Biventricular Pacing

- A single-center experience with CRT in 60 consecutive children demonstrated benefit in the majority of patients, although there were significant challenges associated with implantation.

Biventricular Pacing

- Bleasdale et al showed that in patients with heart failure and elevated central venous pressure, LV preexcitation can improve LV function, even in the absence of resynchronization, by reducing external constraint of the LV.

Heart Failure without RBBB

• The fact that not all failing RV can be improved by RV pacing is actually demonstrated by the animal data, which showed that in failing RV in the absence of a proper RBBB, RV pacing was harmful to RV function.

• Resynchronization therapy should always be focused on restoring or optimizing ventricular synchronous electrical activation with single-sided LV pacing, single-sided RV pacing, or BiV pacing.
CRT & Narrow QRS

• Failure of studies such as RethinQ (Cardiac-Resynchronization Therapy in Heart Failure with Narrow QRS Complexes) indicate that CRT is useless in patients with narrow QRS complexes.

• After all, in hearts with normal impulse conduction, even BiV pacing creates, rather than reduces, asynchrony and thus can worsen patients' condition.

**RV vs. BiV Pacing**

- Although long-term single-chamber RV pacing for bradycardia in the presence of normal ventricular function is considered detrimental, it may be beneficial in patients presenting with heart failure and RBBB.

- On the other hand, BiV stimulation seems preferable in the presence of concomitant LV dysfunction.

For Whom, When, and How?

• The presence of a wide QRS in patients with ventricular dysfunction indicates an increased risk of heart block and sudden death that may suggest, at a minimum, the implantation of a dual-chamber ICD.

• Once a decision has been made for ICD, one must decide whether to add CRT to improve a hemodynamic status that is often the main presenting problem.
For Whom?

• The surface ECG might not be the most reliable means of identifying candidates for CRT.

• Various echocardiographic studies and invasive or noninvasive mapping techniques, which more accurately detect inter-individual variations, are more likely to identify the best candidates for CRT.

• This, however, has not been reproduced in clinical trials by now.
When?

• Equally uncertain is the optimal timing of CRT system implantation in these patients.

• From the studies published so far, it is unclear when CRT should be prescribed?
  – In combination with an ICD upon the development of arrhythmias or ventricular dysfunction or
  – Earlier, with a view to prevent the adverse effects of remodeling due to prolonged electrical dyssynchrony, which creates the substrate for ventricular tachyarrhythmias.
How?

• Ventricular dysfunction in TOF is initially limited to the right heart.

• The observations made thus far in this patient population suggest that the implant of a standard dual-chamber pacemaker is promising.

• However, RV stimulation might adversely impact LV activation. Thus, an ideal solution would favor a fusion with the spontaneous wavefront to preserve normal LV activation.
BiV vs. RV Stimulation

- BiV stimulation is unequivocally more challenging technically, although it seems most appropriate in the presence of concomitant LV dysfunction.

Thambo J, et al. Electrical dyssynchrony and resynchronization in tetralogy of Fallot. Heart Rhythm Volume 8, Issue 6, Pages 909-914
Design of Trials

• The evaluation of hemodynamic effects conferred by CRT warrant the organization of a multicenter study of the effects of long-term stimulation in patients with TOF.

• The contributions made by CRT must be examined separately for each congenital disease, as the only link between patients with TOF, systemic RV, idiopathic dilated cardiomyopathy, or single ventricle is the physician who takes care of them.
MRI-compatible Pacing Leads

• Looking to the future, the problems previously preventing accurate evaluation of RV function will largely resolve to the emergence of MRI-compatible pacing leads, which allow accurate quantitative measurement of RV function in patients with implanted devices.
TOF & Tachyarrhythmias

- Tachyarrhythmias are common in adults with repaired TOF.
- In a multicenter cohort followed up for 35 years after corrective surgery, sustained atrial and ventricular tachyarrhythmias occurred in 10% and 12% of patients, respectively.

Mechanism of Arrhythmias

• Macro-reentrant right atrial tachycardia is the most common atrial arrhythmia.

• However, in a multicenter cohort of adults with TOF, atrial fibrillation was the most prevalent one over the age of 55 years.

• The mechanism for monomorphic ventricular tachycardia in the young adult with surgically repaired TOF is most often macro-reentry.

Arrhythmia-induced cardiomyopathy

• When confronting a patient with heart failure and any kind of tachyarrhythmias, whether atrial or ventricular, one should think about:
  – Arrhythmia-induced Cardiomyopathy
  or
  – Arrhythmia-aggravated Cardiomyopathy

• They should be corrected before any decision about device implantation.
Incisional Macro-reentrant VT

Focal Atrial Tachycardia

36 yrs. old male
TOF
3 Previous surgeries,
ICD for syncopal VT
Almost incessant VT
Refractory to multiple anti-arrhythmic drugs
Worsening functional class
Clinical VT 1
Clinical VT 2
Incessant VT
Large scars at RVOT and RV free walls
Ablation lines transecting scars ineffective
Entrainment with presystolic potential, RVOT free wall
Termination of VT during Burn at RVOT free wall
Final ECG
Incisional Right Atrial Tachycardia
Final Messages

• Conduction disturbances are common in patients with repaired TOF and are a major source of morbidity and mortality.

• CRT is a viable option in patients with RV or biventricular dysfunction.

• Ultimately, the best strategy is unequivocally preventive.

• Every effort must be made intraoperatively to preserve the integrity of the conduction system.
Keep in Mind

Think about

**Arrhythmia Induced Cardiomyopathy**

before any decision about CRT or ICD implantation.