Diagnosis/Treatment of Arrhythmias and Conduction Disorders

1. Ventricular tachycardia's and treatment
2. QT syndromes
3. Brugada syndrome
4. Acute MI and pacemaker concerns
5. Atrial fibrillation and treatment options
6. ICD considerations
7. Right ventricular arrhythmias
Polymorphic Ventricular Tachycardia

Monomorphic Ventricular Tachycardia

LBBB + Inferior Axis
What is your drug treatment?

1. Flecainide
2. Procainamide
3. Quinidine
4. MgSO4-answer
5. Ibutilide
Polymorphic VT

- **Etiologies**
  - Drug induced
  - Lytes abnormality
  - Ischemia related
  - Long QT Syndrome
    - Acquired or Congenital

- **Treatment options**
  - CPR
  - Drugs
    - MgSO4
    - BB
    - Worse-
      - Procainamide
      - Sotalol and others
  - Long QT
    - Pacing/Isuprel
Congenital QT Prolongation

- Diagnostic Criteria:
  - Asymptomatic patient, QTc>470msec
  - OR: Male with QTc>440 or female with QTc>460
  - PLUS:
    - Stress-related syncope
    - Torsade de pointes
    - Family history of early (<35yo) SCD
  - These criteria are neither totally sensitive or specific

Romano-Ward (autosomal dominant)
Jervell-Lange-Nielsen (autosomal recessive-no hearing)

- Beta-Blockers have proven effective in preventing syncope in 75-80% of LQTS patients.

- However, despite full dose beta-blockers, 20-25% of patients continue to have syncopal episodes and remain at a high risk for sudden cardiac death.

- For those unresponsive patients, high thoracic left sympathectomy have been used. Recently, an international prospective study provided evidence that left cardiac sympathetic denervation is a very effective therapy.

- AICD is now becoming more commonly used, especially if arrest

- Q-T interval in excess of 440msec, familial in 85% of cases
32 y/o male presents to ER after jogging 5 miles and getting CPR. Cardiac enzymes were normal, Lab neg, CXR normal, physical neg. What is your treatment?

1. Beta blocker
2. Amiodarone
3. Sotalol
4. AICD
5. Procainamide
32 y/o male presents to ER after jogging 5 miles and getting CPR. Cardiac enzymes were normal, Lab neg, CXR normal, physical neg. What is your treatment?

1. Beta blocker
2. Amiodarone
3. Sotalol
4. AICD-answer
5. Procainamide
Brugada syndrome

- Distinct form of idiopathic ventricular fibrillation
- RBBB and ST segment elevation in the anterior precordial leads
- No evidence of structural heart disease
- Accounts for 40 to 60 percent of all cases of idiopathic ventricular fibrillation
- Sudden unexplained nocturnal death syndrome occurring in apparently healthy young Southeast Asians (associated with nightmares sometimes)
Brugada syndrome

- Loss of the action potential dome in the right ventricular epicardium – Cause of ST elevation
- VF results from the electrophysiological heterogeneity in the right ventricle
- Sodium channel blockers can reproduce the EKG findings
  - Mutations in a gene responsible for the sodium channel (SCN5A) has been identified in some families with Brugada syndrome
  - Causing acceleration of sodium channel recovery or in nonfunctional sodium channels
- Treatment AICD
Right Bundle-Branch Block and ST-Segment Elevation in Leads $V_1$ Through $V_3$

A Marker for Sudden Death in Patients Without Demonstrable Structural Heart Disease

Josep Brugada, MD; Ramon Brugada, MD; Pedro Brugada, MD

**Background**—Five years ago, we described a specific ECG pattern of right bundle-branch block and ST-segment elevation in leads $V_1$ through $V_3$ associated with sudden death in patients without demonstrable structural heart disease. Information on long-term outcome has become available due to pooled data on a large cohort of patients with this syndrome who are followed at 33 centers worldwide.

**Methods and Results**—Data on 63 patients (57 men; mean age, 38±17 years) with the described ECG pattern were analyzed in terms of arrhythmic events and sudden death. Events were analyzed for patients with at least one episode of aborted sudden death or syncope of unknown origin before recognition of the syndrome (symptomatic patients, $n=41$) and for patients in whom the ECG pattern was recognized by chance or because of screening related to sudden death of a relative (asymptomatic patients, $n=22$). During a mean follow-up of 34±32 months, an arrhythmic event occurred in 14 symptomatic patients (34%) and 6 asymptomatic patients (27%). An automatic defibrillator was implanted in 35 patients, 15 received pharmacological therapy with β-blockers and/or amiodarone, and 13 did not receive treatment. The incidence of arrhythmic events was similar in all therapy groups (log-rank 0.86); however, total mortality was 0% in the implantable defibrillator group, 26% in the pharmacological group, and 31% in the no therapy group (log-rank 0.0005). All mortality was due to sudden death.

**Conclusions**—Patients without demonstrable structural heart disease and an ECG pattern of right bundle-branch block and ST-segment elevation in leads $V_1$ through $V_3$ are at risk for sudden death. Amiodarone and/or β-blockers do not protect them against sudden death, and an implantable defibrillator seems to be the present treatment of choice. (*Circulation*. 1998;97:457-460.)
86 y/o/w female presents with Acute inferior wall MI and nurses call about patients sudden change in EKG below...what is your suggested treatment BP 85/60 patient pain free after lytics 4 hours ago
What is your diagnosis and Treatment?

1. RBBB with posterior hemiblock s/p inferior MI and needs a pacemaker now.
2. Inferior MI few hours old and is stable even though she has new RBBB
3. Patient requires only monitoring
4. Patient has PVC and needs lidocaine
What is your diagnosis and Treatment?

1. RBBB with posterior hemiblock s/p inferior MI and needs a pacemaker now.
2. Inferior MI few hours old and is stable even though she has new RBBB
3. Patient requires only monitoring
4. Patient has PVC and needs lidocaine
Guidelines for **Temporary Pacing** in AMI

- **Class I**
  - Sinus bradycardia (<50) with SBP < 80 unresponsive to drugs
  - Mobitz II 2 degree AV block
  - 3rd Degree AV block
  - Bilateral BBB (Regardless of Age)
    - Alternating BBB
    - RBBB with LPFB
  - New or age undetermined LBBB, LAFB or LPFB with RBBB*
    - Transcutaneous patches for quick access
  - RBBB or LBBB with first degree AV block
  - Asystole

- [Transcutaneous pacing until transvenous placed](Heart Rhythm Vol 5, June 2008:e1)
Guidelines for **Permanent Pacemaker after AMI**

- **Class I**
  - Persistent 2\textsuperscript{nd} Degree AV block in His Purkinje system (wide QRS) with bilateral BBB (RBBB and LBBB)
  - CHB
  - Symptomatic AV Block at any level
  - Transient advanced (2\textsuperscript{nd} or 3\textsuperscript{rd} degree)AV block at AV Node level (narrow QRS)
NOT Indicated after AMI

1. Permanent ventricular pacing is not indicated for transient AV block in the absence of intraventricular conduction defects. *(Level of Evidence: B) (75)*
2. Permanent ventricular pacing is not indicated for transient AV block in the presence of isolated left anterior fascicular block. *(Level of Evidence: B) (77)*
3. Permanent ventricular pacing is not indicated for new bundle-branch block or fascicular block in the absence of AV block. *(Level of Evidence: B) (48,75)*
4. Permanent ventricular pacing is not indicated for persistent asymptomatic first-degree AV block in the presence of bundle-branch or fascicular block. *(Level of Evidence: B) (75)*

Heart Rhythm Vol 5, June 2008:e1
Atrial Fibrillation

Medical Treatment
- Correct Underlying Etiology
- Cardioversion
- Rate Control

Atrial Remodeling
The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Study

- Randomized, multicenter comparison of these two treatment strategies in patients with atrial fibrillation and a high risk of stroke or death
  - Rate control
  - Rhythm control
- Primary end point: All cause mortality
- N=4060
- F/U 9 years

Selected Patient Characteristics
- HT 70%
- CAD 38%
- Enlarged LA 64%
- Reduced EF 26%

JACC March 1, 2001;37:691–704
Treatment Groups

Rate Control
- Digoxin – 70%
- Beta-blocker - 68%
- Diltiazem - 46%
- Verapamil - 16%
- Amiodarone - 10%

Rhythm Control
- Amiodarone - 62.8%
- Sotalol - 41.4%
- Propafenone - 14%
- Procainamide - 8.5%
- Quinidine - 7.4%
- Flecainide - 8.3%

P=All Significant

<table>
<thead>
<tr>
<th></th>
<th>Rate</th>
<th>Rhythm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Torsades</td>
<td>2 pts</td>
<td>12 pts</td>
</tr>
<tr>
<td>Cardiac Arrest</td>
<td>1 pts</td>
<td>9 pts</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>73%</td>
<td>80%</td>
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</table>

RACE II study shows that lenient-rate control <110 bpm is not inferior to strict-rate control <80 bpm.

Lenient-rate control may be adopted as a reasonable strategy in patients with permanent AF.
Atrial Fibrillation and Anticoagulation

- **Dabigatran**-RE-LY trial reduces strokes in Afib vs warfarin (direct thrombin inhibitor)

- **New agents**
  - **Factor Xa inhibitors**
    - Rivaroxaban (Xarelto)-approved
      - Bayer/J&J
      - ROCKET-AF
        - Stroke prevention study
        - AHA Nov 2010
    - Apixaban
      - Bristol-Myers Squibb/Pfizer
      - FDA application on file
      - **ARISTOTLE**
        - 2011
        - AVERROES trial
          - Lower strokes and systemic embolic events vs ASA

FXa and its co-factor FVa form the prothrombinase complex, which activates prothrombin to thrombin
### Molecular differences

<table>
<thead>
<tr>
<th>Factor Xa inhibitor</th>
<th>Factor IIa inhibitor</th>
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<tbody>
<tr>
<td>Gatekeeper of the coagulation cascade</td>
<td>Final common pathway</td>
</tr>
<tr>
<td>Block thrombin generation</td>
<td>Block thrombin activity</td>
</tr>
<tr>
<td>Preserve hemostatic mechanisms</td>
<td>Block contact activation</td>
</tr>
<tr>
<td></td>
<td>Block platelet activation</td>
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</table>
# New drugs for atrial fibrillation patients

<table>
<thead>
<tr>
<th>Medication</th>
<th>Action</th>
<th>Phase 3 Trial</th>
<th>Comparator</th>
<th>Design</th>
<th>n</th>
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</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>Direct thrombin inhibitor</td>
<td>RE-LY</td>
<td>Warfarin</td>
<td>Non-inferiority</td>
<td>18,113</td>
</tr>
<tr>
<td>Apixaban</td>
<td>AntiXa</td>
<td>AVERROES</td>
<td>Aspirin</td>
<td>Superiority</td>
<td>5600</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>AntiXa</td>
<td>ARISTOLE</td>
<td>Warfarin</td>
<td>Non-inferiority</td>
<td>18,201</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>AntiXa</td>
<td>ROCKET AF</td>
<td>Warfarin</td>
<td>Non-inferiority</td>
<td>14,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ENGAGE AF</td>
<td>Warfarin</td>
<td>Non-inferiority</td>
<td>16,500</td>
</tr>
</tbody>
</table>
Predicting Sudden Cardiac Death After Myocardial Infarction

“Time Dependent…sudden death occurs late”

% Sudden Death

N=700 post MI patients 95% on BB

Sudden Cardiac Death

Non Sudden Cardiac Death

No ICD --90 grace period after MI with EF <35% (lifevest?)

Huikuri J Am Coll Cardiol 2003; 42: 652-8
Time Dependence of Mortality Risk in MUSTT

MUSTT inclusion criteria: CAD/post-MI, LVEF ≤ 40% and NSVT on EPS

MADIT II
“How to Pick Your ICD Patient”

- N=1232
- Post MI
- EF<30
- Randomized ICD/Medical
- F/U 20 months
- Severe renal dysfunction to be the most powerful predictor of all-cause mortality

Risk Factors
- Age >70
- NYHA functional class>II
- BUN>26
- Atrial fibrillation-Yes
- QRS duration>120

Goldenberg J Am Coll Cardiol 2008;51:288–96
1. ICD therapy is indicated in patients who are survivors of cardiac arrest due to VF or hemodynamically unstable sustained VT after evaluation to define the cause of the event and to exclude any completely reversible causes. (Level of Evidence: A) (16,319–324)

2. ICD therapy is indicated in patients with structural heart disease and spontaneous sustained VT, whether hemodynamically stable or unstable. (Level of Evidence: B) (16,319–324)

3. ICD therapy is indicated in patients with syncope of undetermined origin with clinically relevant, hemodynamically significant sustained VT or VF induced at electrophysiological study. (Level of Evidence: B) (16,322)

4. ICD therapy is indicated in patients with LVEF less than 35% due to prior MI who are at least 40 days post-MI and are in NYHA functional Class II or III. (Level of Evidence: A) (16,333)

5. ICD therapy is indicated in patients with nonischemic dilated cardiomyopathy who have an LVEF less than or equal to 35% and who are in NYHA functional Class II or III. (Level of Evidence: B) (4,139–141)

6. ICD therapy is indicated in patients with LV dysfunction due to prior myocardial infarction who are at least 40 days post-myocardial infarction, have an LVEF less than 30%, and are in NYHA functional Class I. (Level of Evidence: A) (4,132)

7. ICD therapy is indicated in patients with nonsustained VT due to prior myocardial infarction, LVEF less than 40%, and inducible ventricular fibrillation or sustained VT at electrophysiological study. (Level of Evidence: B) (4,131,142)
Arrhythmogenic right ventricular dysplasia

- Cardiomyopathy-childhood appear normal hearts
- Diffuse or localized RV dilatation
- Presence of fatty tissue predisposing to ventricular tachycardia and sudden cardiac death
- VT that generally has **a left bundle branch block** contour (since the tachycardia arises in the right ventricle) & right-axis deviation and T waves inverted over the right precordial leads
- A terminal notch in the QRS (called an **epsilon wave**) may be present as a result of slowed intraventricular conduction (50% of patients)

This is described as a terminal notch in the QRS complex. It is due to slowed intraventricular conduction.
RV fat replacing muscle
Left Ventricular Involvement in Arrhythmogenic Right Ventricular Cardiomyopathy

MRI showing RV compatible with fat infiltration

Fat saturation over the anterior and inferior myocardium

Circulation. 2002;105:1394
# Arrhythmogenic right ventricular dysplasia/cardio myopathy diagnostic criteria

<table>
<thead>
<tr>
<th>Group</th>
<th>Major criteria</th>
<th>Minor criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural or functional RV abnormality</td>
<td>Severe RV dilation and reduction of RV ejection fraction with little or no LV involvement</td>
<td>Mild global RV dilation and/or ejection fraction reduction with normal LV</td>
</tr>
<tr>
<td></td>
<td>Localized RV aneurysm</td>
<td>Mild segmental dilation of the right ventricle</td>
</tr>
<tr>
<td></td>
<td>Severe segmental dilation of the right ventricle</td>
<td>Regional RV hypokinesia</td>
</tr>
<tr>
<td>Tissue characterization</td>
<td>Infiltration of RV myocardium by fibrofatty replacement tissue</td>
<td>No criteria listed</td>
</tr>
<tr>
<td>Electrocadio gram depolarization/ conduction abnormality</td>
<td>Epsilon waves or localized prolongation (&gt;110 ms) of the QRS complex in right precordial leads (V1–V3)</td>
<td>Late potentials on signal-averaged electrocardiogram</td>
</tr>
<tr>
<td>Electrocadio gram repolarization abnormality</td>
<td>No criteria listed</td>
<td>Inverted T waves in electrocardiogram leads V1–V3, aged &gt;12 years, without RBBB</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>No criteria listed</td>
<td>LBBB-type ventricular tachycardia (sustained or nonsustained)</td>
</tr>
<tr>
<td>Family history</td>
<td>Family history of ARVD/C confirmed on autopsy or surgery</td>
<td>Frequent premature ventricular contractions (&gt;1,000 per 24 h)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Family history of ARVD/C clinically and independently diagnosed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Familial history of premature sudden death (&lt;35 years) owing to suspected ARVD/C</td>
</tr>
</tbody>
</table>

Abbreviations: ARVD/C, arrhythmogenic right ventricular dysplasia/cardio myopathy; LBBB, left bundle branch block; LV, left ventricular; RBBB, right bundle branch block; RV, right ventricular. Permission obtained from the BMJ Publishing Group © McKenna W et al. (1994) 71: 215–218.

2 major criteria, or 1 major and 2 minor criteria, or 4 minor criteria, with each criterion coming from a different group.

Cardiac Desmosome &
Electrical Conductivity Through Regulation of Gap Junctions

1. Desmosome gene mutations
2. RV enlargement and dysfunction
3. Fibrofatty scar formation

A. Age-dependent onset of ARVD/C, screening starts at age 12 then every 2- to 3-year intervals

B. Families with earlier onset disease or sudden cardiac death in children, earlier clinical screening should be performed

Arrhythmogenic RV dysplasia

Abbreviations: Dsc2, desmocollin-2; Dsg2, desmoglein-2; Dsp, desmoplakin; Pkg, plakoglobin; Pkp2, plakophilin-2; PM, plasma membrane.

Chromosomes 1 and 14q23-q24 and, most recently, chromosome 10
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