Electrophysiology update for the Non-Electrophysiologist

AKA: "You burn what? Where?" or "Who gets what and why?"

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Introduction

 There is a growing need within general internal medicine to understand electrophysiology

- The disease processes are rapidly expanding
- The treatment is rapidly evolving/changing
- Those where were once hopeless have hope
- There is a often gap between that which is now available and that which is often offered by physicians

Objectives

Review Prevalence of Atrial fibrillation

- Growing in population, cost, and danger
- Update on treatment options of atrial fibrillation (AKA: "You burn what? Where?")
- What do the guidelines say?
- What is the science behind the guidelines
- Review device based therapies of congestive heart failure (AKA "Who gets what? Why?")
- Electrophysiology and Heart failure partners

Atrial Fibrillation Prevalence Estimates

• AF is the most common form of arrhythmia¹

- 2.3 million people in the United States
- 4.5 million people in the European Union¹
- AF is associated with high rates of morbidity and mortality^{1,4}
 - 1 of every 6 strokes occurs in patients with AF¹

It is estimated that 10-30% of patients with CHF have AF⁵

1. Fuster V et al. J Am Coll Cardiol. 2006;48:e149-246. 2. Fuster V et al. Nature Clinical Practice Cardiovascular Medicine. 2005;2:225. 3.Go AS et al. JAMA. 2001;285:2370-2375. 4. Wattigney WA et al. Am J Epidemiol. 2002;155:819-826. 5 Stevenson W N Engl J Med 1999; 341:910-911

Atrial Fibrillation: Prevalence Estimates



Turpie A. New oral anticoagulants in atrial fibrillation. EHJ 2007; 29:155-65

Atrial Fibrillation: a growing problem



Feinberg W, et al. Arch Intern Med. 1995;155:469-473.

Atrial fibrillation is a deadly problem: Framingham Heart Study

- 40 year follow-up patients with and without atrial fibrillation.
- Adjustment for age, hypertension, diabetes, CHF, valvular disease & myocardial infarction.
- Odds ratio for death: 1.5 in men, 1.8 in women

Atrial Fibrillation & Risk of Death: Framingham Heart Study



Circ. 1998;98:946-52

Current strategies for atrial fibrillation

ACCF/AHA/HRS FOCUSED UPDATE

2011 ACCF/AHA/HRS Focused Update on the Management of Patients With Atrial Fibrillation (Update on Dabigatran)

A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

2011 WRITING GROUP MEMBERS

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² Fuster V, Ryden LE, Cannom DS, et al. J Am Coll Cardiol 2006;48:854-906

What are the cornerstones in the management of the patient with Atrial Fibrillation?

Stroke/Thromboembolism Prevention

ythm Control

Ventricular Rate Control



- No difference in mortality, stroke risk or quality of life
- More frequent hospitalization and adverse drug effects in Rhythm Control arm



AFFIRM - N Engl J Med 2002;347:1825-33

Rate Control for ALL halted progress in AF treatment options.....

Pate Control for ALL Clinical Application of AFFIRM applied to EVERYONE Halted Progress!!!!!

The Rate Control Strategy: Problems with AFFIRM

• Mean age: 69.7 +/- 9 years

- Young patients were underrepresented
- 45% of those screened declined enrollment
 - Were highly symptomatic patients underrepresented?
- AFFIRM was not a trial of sinus rhythm versus atrial fibrillation: It was a trial of the strategy
 - o 62% of "Rhythm Control" patients were in NSR
 - 35% of "Rate Control" patients were in NSR

Errors in Patient Management Due to Misinterpretation of AFFIRM Trial Results

- Dooming patient without heart disease to lifelong drug therapy and coumadin
- Not attempting cardioversion in patients with "New Onset" AF because rate control is "preferred therapy"
- Forcing patient to accept rate controlling drug side effects as " part of aging process" (fatigue, loss of mental clarity, insomnia, constipation)

AFFIRM did apply to

- Asymptomatic Patients
- Elderly Patients
- o No CHF
- In THIS population:
 - Rate and rhythm control strategies result in similar outcomes with respect to
 - o mortality
 - o stroke
 - o functional capacity*
 - quality of life*

Relationships Between Sinus Rhythm, Treatment, and Survival in the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) Study

The AFFIRM Investigators*

- *Background*—The AFFIRM Study showed that treatment of patients with atrial fibrillation and a high risk for stroke or death with a rhythm-control strategy offered no survival advantage over a rate-control strategy in an intention-to-treat analysis. This article reports an "on-treatment" analysis of the relationship of survival to cardiac rhythm and treatment as they changed over time.
- *Methods and Results*—Modeling techniques were used to determine the relationships among survival, baseline clinical variables, and time-dependent variables. The following baseline variables were significantly associated with an increased risk of death: increasing age, coronary artery disease, congestive heart failure, diabetes, stroke or transient ischemic attack, smoking, left ventricular dysfunction, and mitral regurgitation. Among the time-dependent variables,

Conclusions—Warfarin use improves survival. SR is either an important determinant of survival or a marker for other factors associated with survival that were not recorded, determined, or included in the survival model. Currently available AADs are not associated with improved survival, which suggests that any beneficial antiarrhythmic effects of AADs are offset by their adverse effects. If an effective method for maintaining SR with fewer adverse effects were available, it might be beneficial. (*Circulation.* 2004;109:1509-1513.)

Key Words: antiarrhythmia agents ■ anticoagulants ■ arrhythmia ■ fibrillation

Management of the patient with Atrial Fibrillation

Stroke/Thromboembolism Prevention

Ventricular Rate Control

Rhythm Control

Management of Atrial Fibrillation: Rhythm Control

- Antiarrhythmic drugs +/- DC cardioversion
- AF catheter ablation (PVAI)
- o Atrial Segmentation
 - o Surgical Maze procedure
 - o Catheter Maze procedure: "Linear AF ablation"
- o Pacing
 - o Prevention/Suppression algorithms
 - o Treatment (termination) algorithms

2011 AF Guidline Antiarrhythmic Updates



Problem? They aren't that effective

Time to recurrence of atrial fibrillation: Sotalol versus class I drugs



The AFFIRM First Antiarrhythmic Drug Substudy Investigators, J Am Coll Cardiol 2003;42:20-29

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Problem? They aren't that safe



Epstein, et al, Circ, 2004

You' re going to burn What? Where?



What is all this ablation about?

Dual Substrate Model of Atrial Fibrillation



Pulmonary Vein Triggers Initiating Atrial Fibrillation





Pulmonary Veins Antrum Isolation (PVAI):Circular Mapping





Pulmonary Veins Antrum Isolation: Circular Mapping Technique



Before PV Antrum Isolation

After PV Antrum Isolation















Impact of type of atrial fibrillation (AF) and repeat catheter ablation on long term freedom from AF: Results from a Multicenter Study

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AF Ablation: Long term data

 \circ N = 1,404 patients

- 728 PAF
- 676 non-PAF
 - o 293 Persistent
 - 383 Long standing (chronic)
- 12 operators at 4 different centers
- Technique: intracardiac echo (ICE) guided circular mapping radiofrequency catheter ablation

Table 2: Freedom from Al	after initial and repeat	catheter ablations
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SN	Variable	Paroxysmal (1)	NPAF (2)	P-value (1 vs. 2)	Persistent (3)	Long lasting persistent (4)	P-value (1 vs. 3 vs. 4)
1	Primary recurrence	163/728	222/676	/	71/293	151/383	7
2	Primary freedom from AF	77.6%	67.2%	<0.001	75.8%	60.6%	<0.001
3	Redo ablation done	121(74.2%)	166(74.8%)	0.904	51(71.8%)	115(76.2%)	0.782
4	Recurrence after redo (Sec)	13/121	52/166	1	15/51	37/115	T.
5	Total recurrence (Sec)*	57/728	114/676	7	36/293	78/383	Ť.
6	Secondary freedom from AF	92.2%	83.1%	<0.001	87.7%	79.6%	<0.001

Bhargava M, Cummings JE, Natale A et al. Heart Rhythm. 2009 Jun 9.



Bhargava M, Cummings JE, Natale A et al. Heart Rhythm. 2009 Jun 9.

So what are the risks?


Atrial Fibrillation Ablation Complications Perforation / Tamponade

- Intracardiac
 Echocardiography
- Rapid diagnosis
- Evaluate for RA / RV collapse



Pulmonary Vein Stenosis

- o 1-2% Incidence
- CT Scans
 - o 3 months
 - 6 months if stenosis seen at 3 months
- Angioplasty / Stenting warranted in cases
 >70% or if Significant decrease in perfusion
 <25% in affected lung¹
- Complete occlusion can be asymptomatic¹



Stroke

- 1-2% Incidence
- Char and/or Thrombus
- Intra-procedure echo
- Anticoagulation

0

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Radiation Exposure

- Procedures are long (especial second procedures) requiring significant amounts of fluoroscopy
- Increased risk for both physician and patient
- Especially if additional imaging performed prior procedure

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CONFERENCE REPORT

Developing an Action Plan for Patient Radiation Safety in Adult Cardiovascular Medicine

Proceedings From the Duke University Clinical Research Institute/ American College of Cardiology Foundation/American Heart Association Think Tank Held on February 28, 2011

Participating societies include the American College of Cardiology Foundation, American College of Radiology, American Heart Association, American Society of Nuclear Cardiology, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society of Nuclear Medicine

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*See Appendix for Writing Committee disclosure information.

Esophageal Complications: Esophageal-Atrial Fistula

- o <50 reported in the world</p>
- First reported in surgical literature (open atrial ablation)
- First case reports in following percutaneous procedures were in 2005-2006
- Injury presumed to be thermal in nature





Esophageal complications





²Donaldson D et al Heart Rhythm Vol 7 no 2 Feb 2010

- The damage is presumed to be thermal
- The esophagus is clearly in the way of placing lesions in the regions NECESSARY to achieve pulmonary vein isolation
- So the dilemma will be where to ablate successfully with <u>minimal risk</u>



Esophageal Complications

- Blinded surveys from active atrial fibrillation centers
- Collected information on 9 cases
 - Insidious onset presenting 10-16 days post procedure
 - Presented as:
 - o Sepsis
 - o Stroke
 - o GI bleed

Mortality nearly 100%

Table 1. Characteristics of Patients

Characteristic	Value
Male sex, n	4
Mean time to presentation (range), d	12.3 (10–16)
Deaths, n/n	9/9
Presenting symptoms, <i>n/n</i>	
Sepsis	9/9
Neurologic symptoms	8/9
Myocardial infarction or ischemia	2/9
Overt gastrointestinal bleeding	3/9
Computed tomography performed, n/n	4/9
Diagnosis by computed tomography, n/n	3/4
Diagnosis confirmed by autopsy, <i>n/n</i>	9/9
Diagnosis only by autopsy, <i>n/n</i>	6/9

Summary: AF Catheter Ablation Candidates

- Symptomatic AF (paroxysmal or persistent)
- At least one antiarrhythmic medication failure
- Younger patients with "lone" paroxysmal AF are the best candidates, but patients with persistent AF, older patients and those with co-morbidities such as structural heart disease and heart failure may also be appropriate candidates

Summary: AF Catheter Ablation: Potentially Poor Candidates

- Asymptomatic or minimally symptomatic AF
- No trial of antiarrhythmic drug
- Left atrial cardiomyopathy
- Goal of undergoing ablation is to get off warfarin
- Frail, elderly patients
- Severe structural heart disease, mechanical mitral valve, etc.

Device Based Therapies of Congestive Heart Failure

 The evolution of devices in the treatment of congestive heart failure



CHF and EP: The chicken and the egg.....

- Heart failure is a chronic, progressive, debilitating disease in which the heart muscle weakens and gradually loses the ability to pump blood effectively. It can result from any structural or functional cardiac disorder that impairs the ability of the ventricles to fill with or eject blood.
- CHF leads to high risk electrophysiologic abnormalities: Sudden Cardiac Death
- EP Conduction changes contribute to CHF

How does CHF affect EP? Risk of Sudden Cardiac Death (SCD)

- SCD claims an estimated 325,000 lives each year
 - 1,000 lives every day, one life every two minutes
- In people with CHF, SCD occurs at 6-9 times the rate of the general population ¹

¹ American Heart Association, American Stroke Association. Heart Disease and Stroke Statistics. 2008 Update At-a-Glance. 2008.



He died at 6:11 a.m. on the golf course ¹.

Heart Failure Mortality Sudden Cardiac Death



Device Therapy in CHF: Can we prevent Sudden Death

Internal Cardiac Defibrillators (ICD)











23%

Reduction in the risk of all-cause mortality when using an ICD, in combination with conventional drug therapy, when compared to CDT alone (*p value:0.007*)¹

Clinical Question

Does ICD therapy, used in combination with conventional drug therapy (CDT), significantly improve mortality for patients with NYHA Class II/III heart failure and EF <35%, versus either CDT + amiodarone or CDT + placebo? ¹



ACC/AHA Guidelines 2005:

ICD Recommendations الله الله

 Recommended as secondary prevention to prolong survival in patients with current or prior symptoms of HF and reduced LVEF who have a history of cardiac arrest, VF, or hemodynamically unstable VT

 Recommended for primary prevention to reduce total mortality by a reduction in SCD in patients with ischemic heart disease who are at least 40 days post-MI, with LVEF less than or equal to 30-35%, and with NYHA functional class II or III symptoms*

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 Recommended for primary prevention to reduce total mortality by a reduction in SCD in patients with nonischemic cardiomyopathy, LVEF less than or equal to 30-35%, and NYHA functional class II or III symptoms*

*While undergoing chronic optimal medical therapy with reasonable expectation of survival with good functional status >1 year. VF=ventricular fibrillation; VT=ventricular tachycardia; SCD=sudden cardiac death.

Underlining represents changes from 2001 guidelines.

Hunt SA, et al. ACC/AHA 2005 Practice Guidelines. Available at: http://www.acc.org.

Is preventing sudden death enough? Can we improve CHF symptoms?

How does electrophysiology contribute to heart failure: Dyssynchrony





Mechanical Dyssynchrony

- Mechanical dyssynchrony means that the heart does not contract as an efficient, unified whole unit
 - The left and right ventricles may contract at slightly different times
 - The left ventricle may contract in segments instead of as one unit

Heart Failure Mortality

Mechanism of Death in Heart Failure¹



The likely mechanism of death in heart failure patients moves from SCD to pump failure (CHF) as the disease progresses ¹

Can we take the ICD from preventing SCD to preventing CHF

Cardiac Resynchronization Therapy (CRT)



Cardiac Resynchronization: The BiV ICD



COMPANION: Providing New Access to CRT Therapies



Trials Have Proven CRT Safety & Efficacy in NYHA Class III/IV Total Enrolled Patients = Nearly 4,000!



*O'Connell JB, Bristow MR. Economic impact of heart failure in the United States: time for a different approach. J Heart Lung Transplant. 1994 Jul-Aug;13(4):S107-12.

Cardiac Resynchronization Therapy* in Patients With Severe Systolic Heart Failure



For patients who have left ventricular ejection fraction (LVEF) less than or equal to **35%**, a QRS duration greater than or equal to **0.12 seconds**, and sinus rhythm, cardiac resynchronization therapy (CRT) with or without an ICD is indicated for the treatment of New York Heart Association (NYHA) functional **Class III or ambulatory Class IV heart failure symptoms** with optimal recommended medical therapy.



For patients who have LVEF less than or equal to 35%, a QRS duration greater than or equal to 0.12 seconds, and AF, CRT with or without an ICD is reasonable for the treatment of NYHA functional Class III or ambulatory Class IV heart failure symptoms on optimal recommended medical therapy.



For patients with LVEF less than or equal to 35% with NYHA functional Class III or ambulatory Class IV symptoms who are receiving optimal recommended medical therapy and who have frequent dependence on ventricular pacing, CRT is reasonable.

*All primary SCD prevention ICD recommendations apply only to patients who are receiving optimal medical therapy and have reasonable expectation of survival with good functional capacity for more than 1 year.

The next evolution: Can we prevent CHF?



MADIT-CRT

Size: 1820 patients

Endpoint: All-cause mortality or non-fatal heart failure event Published: NEJM 2009

41%

Reduction in the risk of heart-failure events (primarily in QRS duration of 150msec or more)¹

reduce the risk of death or heart failure events in patients with mild cardiac

symptoms, a reduced EF and a wide

Clinical Question

Does CRT with biventricular pacing

QK2



lo. at Risk (Probability of Survival)

No. at Kisk (Flobability of Sulvival)							
ICD only	731	621 (0.89)	379 (0.78)	173 (0.71)	43 (0.63)		
CRT-ICD	1089	985 (0.92)	651 (0.86)	279 (0.80)	58 (0.73)		

Figure 2. Kaplan–Meier Estimates of the Probability of Survival Free of Heart Failure.

There was a significant difference in the estimate of survival free of heart failure between the group that received cardiac-resynchronization therapy plus an implantable cardioverter–defibrillator (CRT–ICD) and the group that received an ICD only (unadjusted P<0.001 by the log-rank test).

¹ Moss AJ, et al, NEJM, 2009 ; 361:1329-1338

MADIT-CRT- Endpoints

Kaplan-Meier Estimate of Heart Failure Free Survival Probability





MADIT-CRT: Pre-specified Subgroups



Women v. Men in the MADIT-CRT Probability of Heart Failure or Death



Arshad et al. JACC 2011;57(7);813-20.

MADIT-CRT

- Although men received significant benefit from CRT-D women had significantly better results
 - 72% reduction in all-cause mortality
 - Even greater reduction in those with LBBB and QRS >150ms
- There were significant differences in baseline characteristics between women and men that could have contributed
 - A greater proportion of the female cohort had
 - Non-ischemic Cardiomyopathy
 - o LBBB
 - Higher utilization of beta-blockers

In Conclusion: DBT of CHF

- Device based therapies of congestive heart failure has evolved significantly over the last several years. We have gone from
 - Preventing sudden cardiac death
 - Improving morbidity and mortality in patients with severe CHF
 - Preventing morbidity and mortality in patients with mild CHF
- Cause of death in patients with CHF is SCD early on in patients but as the CHF progresses pump failure is more common
- Early data has demonstrated that female gender may predict a better response to CRT-D

In Conclusion: Atrial Fibrillation

- Atrial fibrillation ablation remains a viable option in symptomatic patients who have failed at least one antiarrhythmic therapy
- Complication risk is higher as the patients cormorbidities (age, LA size, previous stroke etc) increase and thus decision for ablation still is made on a patient by patient basis.
- Over the last several years we have gone from
 - Rate control and pacemaker as an only option
 - Surgical ablation and isolation of the pulmonary veins
 - Percutaneous ablation as an option for potential cure of atrial fibrillation

