ARRHYTHMIA INDUCED CARDIOMYOPATHY
FOCUS ON ATRIAL FIBRILLATION

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I have no disclosures

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Overview

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ARRHYTHMIA INDUCED CARDIOMYOPATHY

- Potentially reversible condition in which left ventricular systolic dysfunction is induced or mediated by atrial or ventricular arrhythmias
- Early recognition of AIC and prompt treatment of the culprit arrhythmia results in symptom resolution and recovery of ventricular function
- Although index presentation may take months to clinically present – recurrent arrhythmia can result in a rapid decline in ventricular function with development of heart failure which suggests residual ultrastructure abnormalities

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- AIC is defined as sufficient supraventricular or ventricular arrhythmias to result in left ventricular systolic dysfunction
- The arrhythmia can be:
  - *Sustained*
  - *Paroxysmal*
  - *Highly frequent ectopic activity*
- The duration of the arrhythmia to induce LV systolic dysfunction is somewhat difficult to determine (symptom duration/etc.):
  - *In animal models, rapid atrial pacing can produce AIC in 1 – 2 months*
- When the inducing arrhythmia is corrected, restoration of normal LV systolic function usually occurs within 6 weeks

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- First described in 1913
  - *Gossage AM, Braxton Hicks JA. On auricular fibrillation. QJ Med. 1913;6:435–40*

- Discovered to be reversible in 1962
  - *Whipple GH, Sheffield LT, Woodman EG, et al. Theophilis C, Friedman S. reversible congestive heart failure due to chronic rapid stimulation of the normal heart. Proc N Engl Cardiovasc Soc 1962*

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- Type I AIC:
  - Arrhythmia induced –
    - *The arrhythmia is solely responsible for the AIC, and the LV function normalizes upon successful treatment of the arrhythmia*

- Type II AIC:
  - Arrhythmia mediated -
    - *Arrhythmia exacerbates the underlying cardiomyopathy and treatment of the arrhythmia results in partial resolution of the cardiomyopathy*

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Epidemiology

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- Epidemiology:
  - Atrial fibrillation is present in 10 – 50% of patients with congestive heart failure.

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Pathophysiology

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- Afib is the most common cause of TIC
  - The pathophysiologic mechanisms underlying development of progression of cardiomyopathy include:
    - *Tachycardia*
    - *Heart Rate*
    - *Irregularity*
    - *Loss of atrial systolic function*
    - *Genetic functions*

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- The genetic susceptibility:
  - Why a similar burden of arrhythmia can have such variable effects on systolic function in different individuals.
- Tachycardia at >100 bpm and >15% of the day has the potential to result in AIC.
- Timing of onset of arrhythmia to clinical presentation or LV deterioration can vary widely and depend on:
  - *Duration of sustained arrhythmia*
  - *Coexisting structural heart disease*
  - *Age*

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- It is likely that AF unmasks an underlying tendency and susceptibility to develop a cardiomyopathy in patients with AIC.
- More than 50 causative genes have been implicated in dilated cardiomyopathy and may be identified in up to 30% of patients.
- The four major genes:
  - *Titen (TTN)*
  - *Lamin A/C (LMNA)*
  - *B-myocin Heavy Chain (MYH7)*
  - *Cardiac Troponin T (TNNT2)*

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- Irregular contraction leads to adverse hemodynamic consequences that are independent of heart rate
  - Heart rate control in AF and noted LV systolic dysfunction improvement with restoration of sinus rhythm
  - AV dyssynchrony can impair diastolic filling which in turn worsens diastolic function thereby leading to increased left sided pressure and negative atrial remodeling, which in turn perpetuates atrial fibrillation

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- The mechanisms of AIC are not fully defined but include:
  - *Subclinical ischemia*
  - *Abnormalities in energy metabolism*
  - *Redox stress & calcium overload*

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- Pathophysiology:
  - Phase 1:
    - Compensatory phase (>7 days). During this phase, there is increased neurohormonal activation with early changes to the extra cellular matrix and preserved LV systolic function.
  - Phase 2:
    - LV dysfunction phase (1-3 weeks). Continued neurohormonal activation and upregulation of the renin angiotensin system. There is cellular remodeling, contractile dysfunction with LV systolic dysfunction and dilatation.
  - Phase 3:
    - LV failure phase (>3 weeks). Further adverse LV remodeling with pump failure, severe dilatation, and abnormal intracellular calcium handling.

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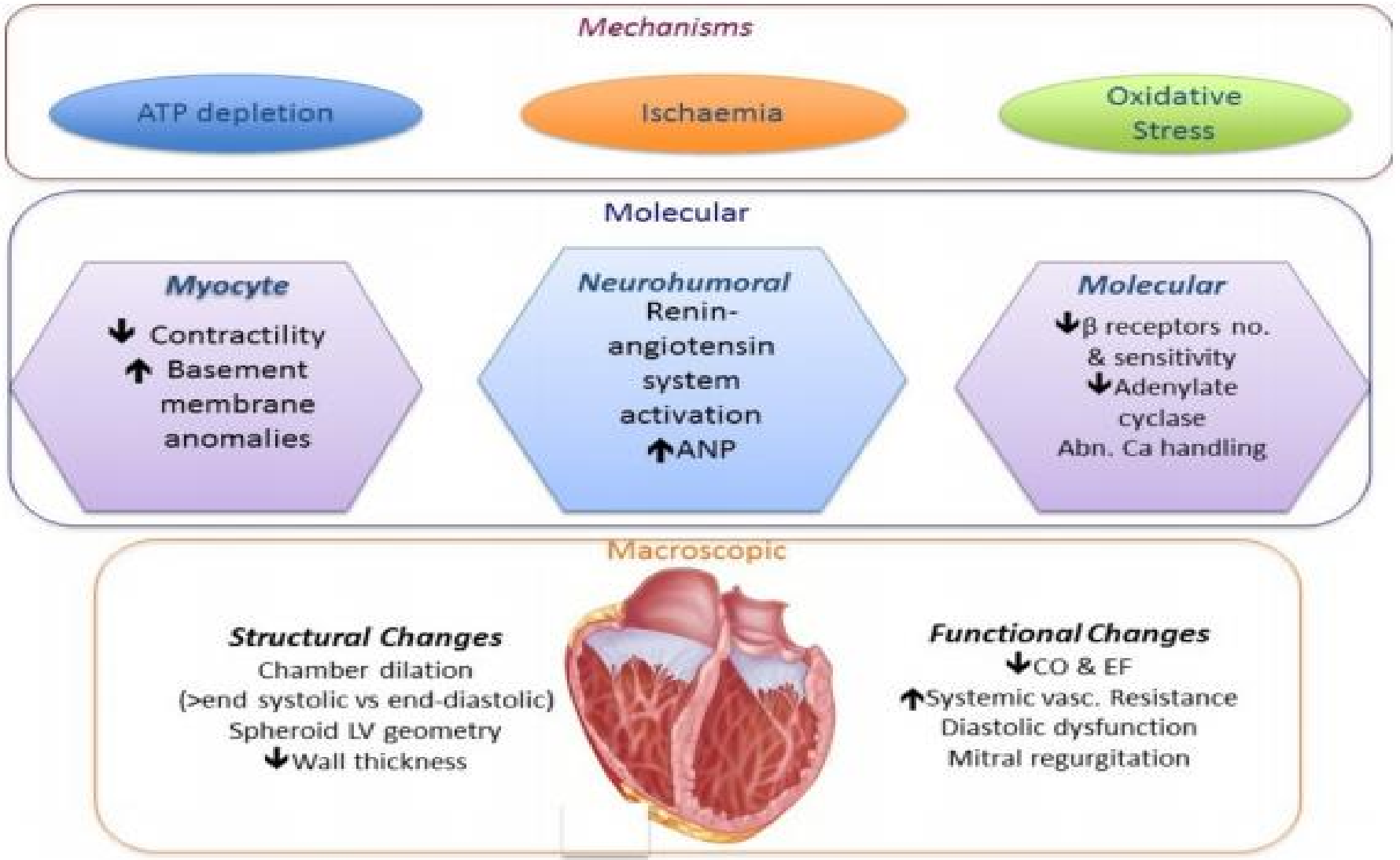
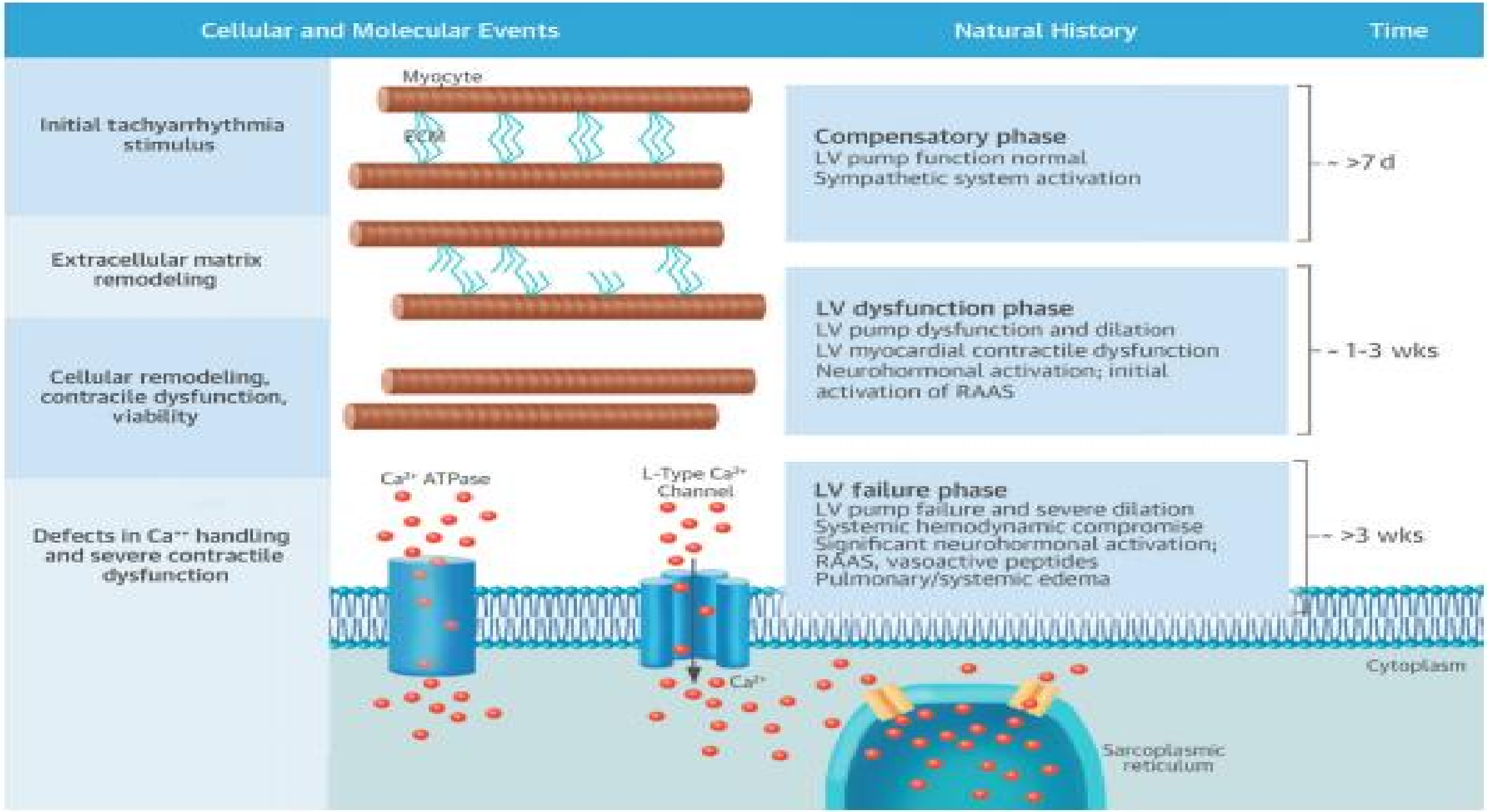


Mechanisms of tachycardiomyopathy (TCMP). The molecular, microscopic and structural effects of TCMP.


Cellular and Molecular Events
Natural History
Time
Initial tachyarrhythmia stimulus
Extracellular matrix remodeling
Cellular remodeling, contractile dysfunction, viability
Defects in Ca++ handling and severe contractile dysfunction
Myocyte
ECM
Compensatory phase
LV pump function normal
Sympathetic system activation
~ >7 d
LV dysfunction phase
LV pump dysfunction and dilation
LV myocardial contractile dysfunction
Neurohormonal activation; initial activation of RAAS
~ 1-3 wks
LV failure phase
LV pump failure and severe dilation
Systemic hemodynamic compromise
Significant neurohormonal activation; RAAS, vasoactive peptides
Pulmonary/systemic edema
~ >3 wks
Ca2+ ATPase
L-Type Ca2+ Channel
Ca2+
Cytoplasm
Sarcoplasmic reticulum

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Diagnosis

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- Atrial fibrillation is a very common arrhythmia
- Congestive Heart Failure is a very common diagnosis
- The needed heart rate for this to develop is not well defined
  - *Likely lower than initially suspected*
- Beat to beat variability plays a role in this disorder
  - *May supersede heart rate*
- Lack of persistent tachycardia from autonomic influences and resultant slower rates during sleep likely explains why AIC are rare or non-existent with inappropriate sinus tachycardia or postural tachycardia syndrome (POTS)

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Treatment

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RATE CONTROL OR RHYTHM CONTROL IN AIC

- Catheter ablation of atrial fibrillation in patients with concomitant left ventricular impairment: a systematic review of efficacy and effect on ejection fraction.

- Systematic review of 19 studies (914 patients)
  - 13.3 -16% LVEF improvement in patients who underwent catheter ablation to restore sinus rhythm

Ganesan AN, Nandal S, Luker J, et al. Catheter ablation of atrial fibrillation in patients with concomitant left ventricular impairment: systemic review of efficiency and effect on ejection fraction. Heart Lung Circ. 2015;24(3):270-80

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RATE CONTROL OR RHYTHM CONTROL

- **AATAC-AF trial**
  - Randomized 203 persistent AF patients with HF and cardiomyopathy (LVEF<40%) to either amiodarone or catheter ablation
    - *70% of patients in the ablation arm were free of AT/AF*
    - *34% in the amiodarone arm*
    - *LVEF improved 9.6% ±7.4% in the ablation arm*
    - *4.2% ±6.2% in the amiodarone arm*

Di Biase L, Mohanty P, Mohanty S, et al. Ablation Versus Amiodarone for treatment of Persistent Atrial Fibrillation in Patients with Congestive Heart failure and an implanted device: results from the AATAC Multicenter Randomized Trial. Circulation 2016;133:1637–44.

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RATE CONTROL OR RHYTHM CONTROL

- **Camera-MRI trial:**
  - 68 patients with persistent AF and DCM (EF <45%)
    - Rate control vs Catheter Ablation
    - F/U 6 months
    - CAD/other structural heart disease patients excluded
      - *Average age 60*
      - *Average LVEF 33%*
      - *Average Chads-vasc score 2.4*
    - Arrhythmic burden followed with implantable loop recorder

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Journal of the American College of Cardiology Oct 2017, 70 (16) 1949-1961; DOI: 10.1016/j.jacc.2017.08.041

Simple Man (Skynyrd)
Suzy Q
A Fool for your Stockings (ZZ top)
La Grange
Cheap Sunglasses *new

Fire - Hendrix *new
Ain't No Sunshine *new
Honey Bee (Tom Petty) *New

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- **Camera-MRI trial:**
  - 18.3% LVEF improvement in the catheter ablation arm
  - 4.4% LVEF improvement in the medical rate control arm
    - 58% catheter based arm normalized their LVEF
    - 9% medical rate control arm normalized their LVEF

  - Absence of late gadolinium enhancement (LGE) portended better outcomes
    - 22% improvement: no LGE
    - 11% improvement: + LGE

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- **CASTEL-AF Trial:**
  - Multi-center international study
  - Randomized 363 patients to ablation vs medical therapy (included rate or rhythm control)
  - Included both persistent and PAF patients
  - LVEF <35% (ischemic (40 – 50%) or non-ischemic)
  - All patients had ICDs or Bi-v ICDs
  - Mean follow-up 37 months

- Primary end point: Composite of death or CHF admission
  - Ablation Group: 51 patients (28.5%)
  - Medical Therapy group: 82 patients (44.6%)
  - At 60 months – absolute EF improved 8% in the ablation group vs 0% in the medical treatment group
  - *Subgroup analysis showed a greater benefit in the 25-35% LVEF group vs the < 25% group*

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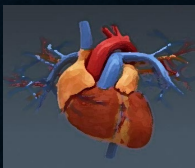
Marrouche NF, et al. "Catheter Ablation for Atrial Fibrillation with Heart Failure". *The New England Journal of Medicine*. 2018. 378(5):417-27.



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Future Focus

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- There is a subset of AIC patients who have experienced SCD
  - Either after the initial diagnosis and prior to normalization of LVEF
    - *How do we identify these patients?*
  - SCD may be more common in patients with recurrent AIC
    - Genetic assessment ?
    - Cardiac MRI ?
      - *Does LGE define this population*
      - *Would other markers of regional wall motion abnormalities such as strain imaging with echocardiography be useful*

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- Recurrence of TIC:
  - There is evidence to suggest that recurrent tachycardia in patients who have previously had TIC may result in a faster and more severe onset of TIC than the initial presentation.
  - In one study of 24 patients with TIC, 5 had recurrent tachycardia associated with a rapid drop in EF and symptoms of clinical HF occurring within 6 months
  - This suggests that there must be some structural cardiac abnormalities that persist after an apparent recovery in function.
    - Therefore, maintenance of a HF treatment regimen after normalisation of EF, and continued monitoring of patients for recurrence of arrhythmia may a prudent strategy in some patients –
      - But which patients – how do we identify them?
      - Genetic assessment ?

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Take Home Points

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- There has to be a high clinical suspicion for this diagnosis in patients with CHF and Atrial Fibrillation:
  - Prompt Recognition
  - Especially if either is a new diagnosis
  - Standard Heart Failure treatment protocols should be followed
  - Rate Control may result in improvement of left ventricular systolic dysfunction – but restoration of NSR has been linked to the best short and long term outcomes
    - *Restoration of NSR also helps answer the question of the chicken vs. egg issue*

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