ARRHYTHMIA INDUCED CARDIOMYOPATHY
FOCUS ON ATRIAL FIBRILLATION

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I have no disclosures
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Overview
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• 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
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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 extracellular 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.
Mechanisms of tachycardiacmyopathy (TCMP). The molecular, microscopic, and structural effects of TCMP.
**Cellular and Molecular Events**

- **Initial tachyarrhythmia stimulus**
  - Myocyte
  - ECM

- **Extracellular matrix remodeling**

- **Cellular remodeling, contractile dysfunction, viability**

- **Defects in Ca^{2+} handling and severe contractile dysfunction**
  - Ca^{2+} ATPase
  - L-Type Ca^{2+} Channel

**Natural History**

- **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
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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)
"No, you back off! I was here before you!"
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Treatment
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

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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

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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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- **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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RATE CONTROL OR RHYTHM CONTROL

• 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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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