Cardiac management in the Neuromuscular Patient

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Cardiac involvement in NMD

- Myotonic dystrophies
- Muscular dystrophies
- Mitochondrial disorders
- Congenital myopathies
- Myofibrillar myopathies
- Limb girdle muscular dystrophies
How should Cardiac care be delivered?

- Who?
- What?
- How often?
Myotonic dystrophy

- Autosomal dominant
- Cardiac manifestations present in ~ 80% DM1
- Respiratory and Cardiac complications are the primary cause of death in DM1
• Optimal approach to diagnosis and treatment of arrhythmias is unclear.

• The effect of therapeutic interventions on the risk of sudden death is unclear.

• Frequency of surveillance is unclear
Tachyarrhythmia

Atrial Fibrillation

Ventricular Tachycardia and Fibrillation
Bradyarrhythmia

Heart block

PR interval = AV delay

QRS duration = ventricular delay
What causes SCD?

- Ventricular arrhythmia
- AV block
Can we predict SCD?

Electrocardiographic Abnormalities and Sudden Death in Myotonic Dystrophy Type 1

William J. Groh, M.D., M.P.H., Miriam R. Groh, M.S., Chandan Saha, Ph.D., John C. Kincaid, M.D., Zachary Simmons, M.D., Emma Ciafalon, M.D., Rahman Pourmand, M.D., Richard F. Otten, M.D., Deepak Bhakta, M.D., Girish V. Nair, M.D., M.S., Mohammad M. Marashdeh, M.D., Douglas P. Zipes, M.D., and Robert M. Pascuzzi, M.D.

NEJM 2008

- 406 adults. 5.7 years follow-up
- ECG characteristics:
  - Non SR, PR > 240ms, QRS > 120ms, advanced AV block
- 81 deaths (27 SD, 32 respiratory, 5 cardiac not SD, 17 other)
Incidence and predictors of sudden death, major conduction defects and sustained ventricular tachyarrhythmias in 1388 patients with myotonic dystrophy type 1

- 6 French sites; 10 year follow-up
- 253 deaths (18%) - SCD 39 (3.6%)

<table>
<thead>
<tr>
<th>Event</th>
<th>Predictors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudden death (n=39)</td>
<td>Age, FH of SD</td>
</tr>
<tr>
<td>Conduction defects (n=143)</td>
<td>Age, male, syncope, AF, abnormal ECG</td>
</tr>
<tr>
<td>Sustained VT (n=26)</td>
<td>Previous NSVT</td>
</tr>
</tbody>
</table>
Can we detect fibrosis?

Hermans et al. JCMR 2012
Myotonic Dystrophy in GG&C

110 patients
- 18 devices
- 2 deceased
- 6 non-attenders

84 patients
- ECG: N=84, Mean 0.9 years
- Echocardiogram: N=64, Mean 1.4 years
- Holter Monitor: N=63, Mean 1.2 years
Abnormal ECG in 22/81

- PR interval 200ms = 13 (16%)
  (1 had SR < 50 bpm)
- QRS duration > 120ms = 6 (7%)
- Both PR > 200 & QRS > 120 = 2

Data from Fernando Loo FY1 Cardiology
Other investigations

• Echocardiography (n=63)
  • 8 Mild LVSD (12.5%)

• No echocardiogram (n=19)
  • 2 had QRS > 120 ms
  • 3 had PR > 200 ms
  • 1 had both

• Ambulatory ECG (n=64)
  • 3 in AF
  • 1 PAF detected

• No Ambulatory ECG (n=18)
  • 3 had QRS > 120 ms
  • 2 had PR > 200 ms
  • 1 had both
## Muscular Dystrophies

<table>
<thead>
<tr>
<th>Condition</th>
<th>Gene</th>
<th>Cardiomyopathy</th>
<th>Arrhythmia</th>
<th>Conduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duchenne</td>
<td>Dystrophin</td>
<td>Common</td>
<td>Common (late)</td>
<td>Rare (late)</td>
</tr>
<tr>
<td>Becker</td>
<td>Dystrophin</td>
<td>Common</td>
<td>Common</td>
<td>Rare (late)</td>
</tr>
<tr>
<td>Emery-Dreifuss</td>
<td>Emerin</td>
<td>Rare</td>
<td>Common</td>
<td>Common (SD)</td>
</tr>
</tbody>
</table>

- X-linked recessive
  - Affected males
  - Female carriers
Cardiac involvement in DMD/BMD

• Historically not referred to cardiology until late stage

• Specific challenges:
  • Classification of heart failure symptoms
  • Small evidence base for treatment
    • ACEi and ARB
    • Epleronone
  • Variable access to some imaging modalities e.g. CMR
International DMD Care Consensus

Lancet Neurology 2018

**Diagnosis**
- Baseline evaluation at diagnosis
- Consultation with cardiologist
- Cardiac medical history
- Family history
- Physical examination
- Electrocardiogram
- Non-invasive imaging:
  - Echocardiogram (<6-7 years old)
  - Cardiovascular MRI (≥ 6-7 years old)

**Annual assessment**
- Annual cardiovascular assessment
  - Cardiac medical history
  - Physical examination
  - Electrocardiogram
  - Non-invasive imaging

**Assessment of female carriers**
- Cardiac assessment in early adulthood
- Cardiovascular MRI
- If symptomatic or imaging positive, increase assessment frequency on the basis of cardiologist recommendation
- If negative, repeat evaluation every 3-5 years

**Ambulatory and early non-ambulatory stage**
- Conduct cardiac assessment at least annually
- Initiate angiotensin-converting enzyme inhibitors or angiotensin receptor blockers by age 10

**Late non-ambulatory stage**
- Monitor closely for signs and symptoms of cardiac dysfunction; symptomatic heart failure can be difficult to diagnose in this stage
- Monitor for rhythm abnormalities
- Treat with known heart failure therapies

**Symptomatic**
- Increase assessment frequency on the basis of cardiologist recommendation
- Initiate pharmacological treatment

**Surgery**
- Assess with electrocardiogram and non-invasive imaging before major surgery
- Make anaesthetist aware of Duchenne muscular dystrophy diagnosis; patients have increased anaesthesia risks
Case

- 46 year old
- Affected son age 4.5

- First cardiac assessment
  - Fatigue, SOB
  - Overweight
  - Calf hypertrophy
Case

• Echo
  • Infero septal hypokinesis
  • Normal LVEF

• CMR
  • LVEF 52%
Female carriers

• Current practice
  • 5 yearly ECG and echocardiogram

• 2016 study
  • 36 female carriers (age 44 +/- 14)
    • 20 DMD, 16 BMD
  • 47% had CMR abnormalities
    • Reduced LVEF 14%
    • LGE 44%
Dilated cardiomyopathy

- Neuromuscular examination is routine
- CK measurement
- LGMD and congenital myopathies
- Lamin A/C
  - Distinct cardiac phenotype
Lamin A/C Cardiomyopathy

- Nuclear envelope protein
- 5% DCM
- Age dependent penetrance (nearly 100% 7th decade)
- Arrhythmias precede/supercede HF
- Heart failure progression

- Potential therapy
  - Mitogen activated protein kinase inhibitors
Lamin A/C Cardiomyopathy

Kumar et al. JACC, 68 (21), 2016, 2299–2307
Conclusions

• Consensus guidelines on cardiac surveillance
  • Annual ECG in DM1, yield low from additional investigations
  • Annual ECG, Echo/CMR in DMD/BMD
  • Considerable variation in practice

• Decisions around devices remain challenging
  • Which patients benefits from pacemakers/ICDs
  • Does a device reduce mortality?

• New tools to monitor cardiac function