Two Decades of Managing Myocarditis

Peter C. Laussen MB.BS., FCICM
• No disclosures
Etiology

• Viral infections
  – Epidemiologic change over time:
    • Enteroviruses: 1970’s & 80’s Coxsackie group
    • Adenovirus: 1990’s
    • Parvovirus, herpesviruses (CMV, EBV), influenza: 2000’s,
  – Geographical & seasonal variation

• Bacterial / fungi, parasites and protozoa
  – Borrelia / Lyme disease
  – Mycobacteria and others

• Toxins / drugs
• Immune-mediated
Pathogenesis

Direct myocyte injury

Immunological activation

Autoimmune mediated

(Magnani JW, Dec GW. “Myocarditis: current trends in diagnosis and treatment.” Circulation. 2006 Feb 14;113(6):876-90.)
Pediatric Health Information System (PHIS) 1997-2007:
- Variable presentation
- No unique phenotype identified
Characteristics

Ghelani S. et al; Circ Cardiovascul Qual Outcomes 2012
Frequency histogram of time to ventricular recovery

Outcomes of Paediatric Myocarditis
Z.M. Eini, Alejandro A. Floh, Stephen B. Freedman, Tilman Humpl, Steven M. Schwartz, V. Ben Sivarajan
## Baseline Clinical Features (N=60)

<table>
<thead>
<tr>
<th></th>
<th>AFM (n = 35)</th>
<th>AM (n = 25)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>6</td>
<td>15.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>57%</td>
<td>76%</td>
<td>NS</td>
</tr>
<tr>
<td>Abnormal vital signs</td>
<td>94%</td>
<td>40%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Predominant complaint</td>
<td>GI (65%)</td>
<td>CV (80%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Abnormal CXR</td>
<td>84%</td>
<td>27%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Abnormal ECG</td>
<td>87%</td>
<td>86%</td>
<td>NS</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>46%</td>
<td>24%</td>
<td>NS</td>
</tr>
<tr>
<td>Abnormal Troponin T/I</td>
<td>96%</td>
<td>100%</td>
<td>NS</td>
</tr>
</tbody>
</table>

All values are depicted as median and n(%); *p-value < 0.001
AM- acute myocarditis; AFM- acute fulminant myocarditis
Arrhythmia on admission predicted need for ECMO

Transfer early
Diagnostic and prognostic validity of different biomarkers in patients with suspected myocarditis

Christian Ukena · Michael Kindermann · Felix Mahfoud · Jürgen Geisel · Philipp M. Lepper · Reinhard Kandolf · Michael Böhm · Ingrid Kindermann

A  hs-TnT  

B  NT-proBNP

![Graph showing the levels of hs-TnT and NT-proBNP in acute, chronic, and no myocarditis groups.](#)
Biomarkers

* All serum troponin levels were taken within 24 hrs of admission
** All patients had abnormal serum troponin levels on admission
Imaging: ECHO

- Wall motion abnormalities
- Thickness (septum)
- AVVR
- LVEDD dimension

<table>
<thead>
<tr>
<th>LVEDD Z-Score at Presentation</th>
<th>Early recovery</th>
<th>Late / no recovery</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.67 (-0.50, 0.67)</td>
<td>4.7 (3.7, 5.6)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

• Caution: direct observation and monitoring

Z.M. Eini, Alejandro A. Floh, Stephen B. Freedman, Tilman Humpl, Steven M. Schwartz, V. Ben Sivarajan
LVEDD Z-score over time

Median follow-up: Early recovery 5.4m; late/non recovery 69.6m
Imaging: cMRI

- Hemodynamic assessment:
- Gadolinium enhancement:
  - Myocardial edema
  - Early: Hyperemia, non specific
  - Late: Fibrosis: more specific
- Consensus criteria for suspected diagnosis of myocarditis: 2 of 3 + (78% correlation with Bx)

Kindermann I JACC 2012
Endomyocardial Biopsy

• Remains the gold standard for diagnosis
• Worse longer term outcomes:
  - Lymphoctye dominant myocarditis
  - Presence of fibrosis

Detailed pathologic evaluation on endomyocardial biopsy provides long-term prognostic information in patients with acute myocarditis

Jong-Chan Youn a, Hyo Sup Shim b,*, Jae Seok Lee b, Ah-Young Ji a, Jaewon Oh a, Namki Hong a, Hye Sun Lee c, Sungha Park a, Sang-Hak Lee a, Donghoon Choi a, Namsik Chung a, Seok-Min Kang a,d,**

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The International Society for Heart and Lung Transplantation Guidelines for the management of pediatric heart failure: Executive summary

Richard Kirk, MA, FRCP, FRCPCH,a Anne I. Dipchand, MD, FRCPC,b David N. Rosenthal, MD,c Linda Addonizio, MD,d Michael Burch, MD,e Maryanne Chrisant, MD,f Anne Dubin, MD,c Melanie Everitt, MD,g Robert Gajarski, MD,h Luc Mertens, MD,b Shelley Miyamoto, MD,i David Morales, MD,j Elfriede Pahl, MD,k Robert Shaddy, MD,l Jeffrey Towbin, MD,j and Robert Weintraub, MDm

The Journal of Heart and Lung Transplantation, Vol 33, No 9, September 2014
Recommendations for Cath and EMB

• EMB *not indicated* if clinical diagnosis with minimal symptoms, mild dysfunction or rapid normalization (Class IIa, Level of evidence C)

• *Reasonable* to perform EMB in setting of new-onset heart failure associated with hemodynamic compromise, ventricular arrhythmia or heart block, and failure to respond to medical therapy (IIb B)

• Cardiac cath and EMB is *reasonable* in pediatric patients presenting with heart failure when a specific diagnosis is suspected that would influence therapy (IIb, C)
Risk of procedures : Benefit of diagnosis

• cMRI
  – Environment

• Risk of catheterization
  – Arrhythmia, arrest
  – Perforation
  – Limited biopsy site
Management of Acute Myocarditis: Supportive with critical observation

Reduce $\text{VO}_2$
- Temperature management: core hyperthermia
- Fretful, agitated: cautious sedation

Manage Pre-Load:
- Diuresis / fluid restrict

Monitor for Response:
- Non-invasive Vs. invasive: Risk of obtaining access
- End-organ function & Biomarkers: Risk of blood draw

Respiratory support
- NIV and PPV
Mx with NIV, diuretic, milrinone then epi. Increase WOB, grunting and diaphoretic
Intubation: Anticipation

• Risk on induction and with PPV
• Cascade of events leading to PEA or VT/VF from which it is can be difficult to achieve ROSC with conventional resuscitation
• **Possibly preventable event**, therefore:
  Experienced personnel / briefing & time out
  ECLS stand-by
  If ROSC, still consider cannulation for mech support
Management of Acute Myocarditis: Escalation of support

Enhance Contractility:
  - Considerations for access
Reduce Afterload (if no hypotension):
  - PDE Inhibition
Manage Rhythm:
  - CAUTION !!
Mechanical support
## Survival for Myocarditis Supported with ECMO

<table>
<thead>
<tr>
<th>Author</th>
<th>Years</th>
<th>No: patients</th>
<th>Age</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duncan, BW</td>
<td>1990 -1997</td>
<td>15</td>
<td>4.6 y</td>
<td>87%</td>
</tr>
<tr>
<td>Lin, CH</td>
<td>1999 – 2003</td>
<td>6</td>
<td>12 y</td>
<td>50%</td>
</tr>
<tr>
<td>Mani, A</td>
<td>2002 – 2008</td>
<td>8</td>
<td>6 y</td>
<td>63%</td>
</tr>
<tr>
<td>Rajagopal, SK</td>
<td>1995 – 2006</td>
<td>255</td>
<td>17 m</td>
<td>61%</td>
</tr>
<tr>
<td>Madden, K</td>
<td>1995 – 2006</td>
<td>24</td>
<td>11 d</td>
<td>33%</td>
</tr>
<tr>
<td>Teele, SA</td>
<td>1996 – 2008</td>
<td>10</td>
<td>13 y</td>
<td>70%</td>
</tr>
<tr>
<td>Wilmot, I</td>
<td>2001 – 2008</td>
<td>6</td>
<td>0.7 y</td>
<td>67%</td>
</tr>
</tbody>
</table>
MCS Devices to support Myocarditis

Acute Myocarditis

- Fulminant Myocarditis
  - Lung Injury
  - CPR

- ECMO

Heart Failure / DCM

- Slow Deterioration
- Increasing Support

- Short Term VAD
- Durable VAD

Type of MCS in Myocarditis

- ECMO
- ECMO+VAD
- VAD

Limited data:
- No recovery of ejection by 72 hours
- Inability to wean by day ~ 7 of support

Ghelani S. Circ Cardiovascul Qual Outcomes 2012
ECMO Support for Myocarditis

Timely ECMO deployment

Early LV decompression
   Promotes Myocardial Recovery
      ↓Lung Injury due to ↑LAp

Timely transition to VAD & Heart Transplantation evaluation
Immunomodulation

Class IIb

1. The evidence in the literature does not support the routine use of corticosteroids in children with myocarditis. Level of Evidence C

2. The evidence in the literature does not support the routine use of intravenous immunoglobulin in children with myocarditis. Level of Evidence C

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What have we learned in 20 years of managing acute myocarditis

• Fragile but high transplant-free survival (mortality ~10%)
• Clinical, ECG, echo diagnosis and value of troponin
  – Risk: Benefit trade-off for cMRI and biopsy (infants)
• Outcome predicted by LVED dimensions on admission
• Supportive therapy is the mainstay of management:
  – Immunomodulation not recommended
  – Beware arrhythmias
  – Early mechanical support