Cardiac Dysfunction & Sepsis

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10/31/18
Disclosure statement

I have no actual or potential conflict of interest in relation to this program/presentation.
Cardiologist at a Sepsis Talk ?!
EVOLUTION OF THE CARDIAC CARE UNIT
“..times they are a changin’ ” B Dylan

1980s
Resuscitation
- Rapid Defibrillation
- Post MI Care
- STEMI
- Gen ICU RN

1990s
Intervention
- Rapid Defibrillation
- Antiarrhythmics
- All ACS
- CHF
- IABP
- Specialized RN

Today
Comprehensive Critical Care
- TTM
- MCS
- Advanced CHF
- Pul HTN
- Multidisciplinary
- Performance Tracked
CENTRAL ILLUSTRATION: Impact of Noncardiovascular Illness in the CICU

In 100 CICU Patients:

50 without acute kidney injury, acute respiratory failure, or sepsis

Only 1 will die

50 with acute kidney injury, acute respiratory failure, or sepsis

11 will die

MultiOrgan Dysfunction Drives Mortality
Case R.C.

30 year old admitted with ARDS

• One week of severe viral prodrome

• Admitted with pulmonary infiltrates, “septic shock”
  – Cold and clammy with SvO2 >70%
  – Progressive renal failure, CVVHD, rising lactate
  – Liver failure (TB > 30) → Listing for transplant x 2

• High dose pressors x 3 → Cards Consult

• Stat echo / RHC
EF 10%, PCWP 35mmHg, CI 1.4, SVR >1500
Pitfalls of data...
“Cardiac Sepsis”

- Significant overlap of Cardiogenic and Septic Shock

- Various Phenotypes that can change with time
  - Sepsis with normal heart
  - Sepsis with cardiomyopathy
  - Sepsis with Stress Cardiomyopathy / Takotsubo
  - Sepsis-induced Cardiomyopathy

- Diagnosis can be difficult
  Biomarkers
  Labs of metabolism
  PA catheters
Labs: Troponin

- Elevation common in septic patients (45-85%)
- Associated with a higher risk of death
- It is **Prognostic**, but not **Diagnostic**
- Elevation Day 7 > Day 1, rise is important
- Pitfalls in the ICU…other Dx (myocarditis, APS)
Sepsis: Antibody Interference

- “True” **heterophilic antibodies**: produced against poorly defined antigens, are weak, with multispecific activities
  - Infection from rubella, measles, adeno-, entero- and varicella-zoster viruses

- **HAMA antibodies**: develop after treatment with animal immunoglobulins, generated against well-defined antigens, characterized by strong avidities
cTnI Assays

**True +**

**False +**

Figure 2. Principle of automated, sandwich Troponin immunoassay. Troponin forms a bridge between one antibody bound to a solid particle and another carrying a light-emitting label (left hand panel). Anti-animal antibodies in serum that bind the antibodies used in the immunoassay can also form a bridge between the two antibodies producing a false positive result (right hand panel, A). Anti-Troponin antibodies can produce false negative results (right hand panel, B).
Labs: False Positive Troponin

- Interference from spurious hemolysis
- Hyperbilirubinemia
- Fibrin clots
- Presence of microparticles or immunocomplexes
- Calibration bias
- Reagent deterioration
- Analyzer malfunction
- Inappropriate sample dilution

- **Antibody interference:**
  - Heterophile antibodies
  - Human anti-murine antibodies (HAMA)
  - Autoantibodies against cTNT or cTnI
  - Rheumatoid factor

* No true troponin present.
* No characteristic rise and fall in troponin.
Case R. M.

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<td>PROTEIN, TOTAL</td>
<td>8.2 g/dL</td>
<td>H</td>
<td>6.1-8.1</td>
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<td>INTERPRETATION</td>
<td>See Below</td>
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<td>Decreased albumin and polyclonal increase in gamma globulins, suggesting chronic inflammation and/or liver disease.</td>
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<td>BETA GLOBULINS</td>
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<td>0.8-1.4</td>
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<td>ALPHA-2-GLOBULINS</td>
<td>0.4 g/dL</td>
<td>L</td>
<td>0.5-1.0</td>
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<td>ALPHA-1-GLOBULINS</td>
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<td>0.1-0.3</td>
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<td>ALBUMIN</td>
<td>2.8 g/dL</td>
<td>L</td>
<td>3.5-4.7</td>
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<td>GAMMA GLOBULINS</td>
<td>3.7 g/dL</td>
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<td>0.6-1.6</td>
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Simultaneous Troponin Levels

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<tr>
<th>Date</th>
<th>Time</th>
<th>Value</th>
<th>Instrument</th>
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<tr>
<td>17Dec2014</td>
<td>12:13 PM</td>
<td>0.01</td>
<td>UMass Beckman</td>
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<tr>
<td></td>
<td>10:53 AM</td>
<td>0.172</td>
<td>Leominster Siemens</td>
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### R.M.

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<th>Goal</th>
<th>29Sep2014</th>
<th>10Aug2014</th>
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<tr>
<td>RHEUMATOID FACTOR QUANT</td>
<td>31.5 IU/mL</td>
<td>RHEUMATOID FACTOR</td>
<td>New</td>
<td>11:37 AM</td>
<td>12:19 PM</td>
</tr>
<tr>
<td>ANA SCREEN, MULTIPLEX</td>
<td></td>
<td>ANA SCREEN, MULTIPLEX</td>
<td>New</td>
<td>41</td>
<td>*Negative</td>
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<tr>
<td>CYCLIC CITRUL PEPTIDE IGG AB</td>
<td></td>
<td>CYCLIC CITRUL PEPTIDE IGG AB</td>
<td>New</td>
<td>*&lt;16 UNITS</td>
<td>*&lt; 16</td>
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### Test Results

<table>
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<th>Test</th>
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<tr>
<td>Mitochondrial Antibody Screen</td>
<td>NEGATIVE</td>
</tr>
<tr>
<td>SMOOTH MUSCLE AB SCR</td>
<td>Negative U</td>
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Elevations of Troponin in the Absence of Overt Ischemic Heart Disease

Cardiac contusion, or other trauma including surgery, ablation, pacing, etc.

*Congestive heart failure—acute and chronic*

Aortic dissection
Aortic valve disease
Hypertrophic cardiomyopathy
Tachy- or bradyarrhythmias, or heart block
Apical ballooning syndrome
Rhabdomyolysis with cardiac injury

*Pulmonary embolism, severe pulmonary hypertension*

*Renal failure*

*Acute neurological disease*, including stroke or subarachnoid haemorrhage

Infiltrative diseases, e.g. amyloidosis, haemochromatosis, sarcoidosis, and scleroderma

Inflammatory diseases, e.g. myocarditis or myocardial extension of endo-/pericarditis

Drug toxicity or toxins

*Critically ill patients, especially with respiratory failure or sepsis*

Burns, especially if affecting 30% of body surface area

Extreme exertion
Labs: BNP/proBNP

- Along with troponin, often above the reference range
  84% for troponin T
  98% for proBNP

- Sign of wall stress, prognostic in sepsis

- Not diagnostic for sepsis-induced CM

- Adequacy of fluid resuscitation
  Cannot use for titration of therapy
Non-HF Factors that Affect NP Levels

**Increase levels:**
- Age
- **Female gender**
- Ascites/liver failure
- Renal failure* (proBNP renal clearance)
- Thyrotoxicosis
- COPD / PE
- HTN/LVH
- Sepsis

**Decrease levels:**
- Obesity
- Diabetes
- Hypothyroidism
- Post CABG
(Was) Controversial in cardiogenic shock
Shock mortality predictor ≠ CI, CO, SVR, PCWP but rather *reserve pumping capacity*.

Heart pump dependent on preload and resistance circuit, function can be variable (i.e. what do you want the EF to be?)

Cardiac Power (or reserve) = pressure x flow
MAP x CO/451
Resistance is not futile! Importance of SVR

Classic Cardiogenic Shock
↑ SVR
Low perfusion
Cool
MODS

Classic Vasodilatory Shock
↓ SVR
High demand
Warm
MODS
Mortality Risk with Inotrope Dosing

Adequate Oxygen delivery?

\textbf{SvO}_2: mixed venous oxygen saturation
Consumption and \textit{Delivery}

\textbf{Lactate}: the demand and need for oxygen
Consumption and \textit{Demand}
Mixed Venous Oximetry

SvO₂ is the averaged end-capillary oxygen content

SvO₂ is a useful parameter of hemodynamic status in specific conditions

→ If SvO₂ < 60% some capillary beds ischemic
→ In sedated, paralyzed patient SvO₂ parallels CO
**IMPROVED END ORGAN PERFUSION WITH pVAD**

Changes in Sublingual Microcirculation

- **Baseline prior to Impella support**
- **After 48hrs of Impella support**

Lam, et. al., Clin Res Cardiol, 2009,
55 yo diabetic/ trop 70
No fever
SVR high
IABP
Monomorphic VT

64 yo/ trop 70
No fever
SVR mildly up
Just meds
Walked out in 3 days

42 yo/ trop 70
38.5 at hour 36 then
SVR 400
Mechanical Support
LOS 12 days
**Inflammation / NOS**

- Fever, leukocytosis, Big temp (38.5+) typically hour 24-30

- Nitric Oxide (neuronal, endothelial, *inducible*)
  - Low levels (eNOS) is cardioprotective, increases contractility
  - High levels (iNOS) in inflammatory conditions ↓ Contractility
    - Suppression of mitochondrial respiration in nonischemic myocardium
    - Alters substrate metabolism (glucose)
    - Reduced efficacy of catechols
    - Vasodilation
    - Interaction at high levels with free radicals causes cell death/toxicity
# Shock Phenotypes

<table>
<thead>
<tr>
<th></th>
<th>Wet</th>
<th>Dry</th>
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<tr>
<td><strong>Cold</strong></td>
<td>Classic Cardiogenic Shock</td>
<td>Euvolemic Shock</td>
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<tr>
<td></td>
<td>↓CI; ↑SVRI</td>
<td>↓CI; ↑SVRI</td>
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<tr>
<td><strong>Warm</strong></td>
<td>Vasodilatory Cardiogenic Shock or Mixed Shock</td>
<td>Vasodilatory Shock</td>
</tr>
<tr>
<td></td>
<td>↓CI; ↓/↔SVRI</td>
<td>↑CI; ↓SVRI</td>
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Sepsis-Induced CM

• No formalized definition

• 2-fold Increase in mortality

1) Reversible in 7-10 days

2) Left ventricular dilation at normal filling pressures
   – Change in Ventricular compliance, Ca2+ handling

3) Reduced $Biventricular$ EF with global dysfunction
   – MRI with edema, no necrosis, ?hibernating
Septic Cardiomyopathy

Metabolic changes

Changes of coronary microvasculature and blood flow

Mitochondrial dysfunction

Nitric oxide and peroxynitrite (NO and ONOO)

Cardiosuppressing circulating mediators

Perturbances of Calcium flux and cardiomyofilament interactions

Apoptosis

Autonomic Dysfunction
Sepsis-triggered Takotsubo / Stress CM

Catechol response only
Left Ventricle only
Reversible
Not global HK
May involve LVOT
Beta blockers and Sepsis: Block adrenergic overstimulation?

- Adrenergic stimulation mediates much of cardiac dysfunction
- Persistent sympathetic stimulation deleterious
- Potential modulate overall catabolic state, an impairment of glucose metabolism and a derangement of the physiologic inflammatory state
- Concept-β-blockers can decrease tissue oxygen consumption and attenuate effects of stimulation
- Data is conflicting…likely due to various hemodynamic profiles
- Timing likely a key factor
- Atrial fibrillation prominent in sepsis
- ? Role for levosimendan?
Don’t ignore The RV!

- RV empties when relaxing
- Very sensitive to afterload
- Prolongs isovolumetric time increases O2 cost
- Several opportunities for compromise in sepsis (ARDS, PEEP, PNA, PE)

1 Ejection (opened PV)
2 Relaxation
3 Close of pulmonic/aortic valve end of ejection
Comparison of Dopamine and Norepinephrine in the Treatment of Shock

Daniel De Backer, M.D., Ph.D., Patrick Biston, M.D., Jacques Devriendt, M.D., Christian Madl, M.D., Didier Choctrand, M.D., Cesar Aldecoa, M.D., Alexandre Brasseur, M.D., Pierre Defrance, M.D., Philippe Gottignies, M.D., and Jean-Louis Vincent, M.D., Ph.D., for the SOAP II Investigators

Figure 2. Kaplan–Meier Curves for 28-Day Survival in the Intention-to-Treat Population.

Figure 3. Forest Plot for Predefined Subgroup Analysis According to Type of Shock.

A total of 1044 patients were in septic shock (542 in the dopamine group and 502 in the norepinephrine group), 280 were in cardiogenic shock (135 in the dopamine group and 145 in the norepinephrine group), and 263 were in hypovolemic shock (138 in the dopamine group and 125 in the norepinephrine group). The P value for interaction was 0.87.
Rx considerations:

SVR is important and determines Shock Phenotype

“Normal Heart” – fluid resuscitation

Reduced EF- Often underfilled/resuscitated (low SVR)...then overfilled (high SVR)

Reduced EF- “Honeymoon period” (low SVR) of sepsis until crash (lactate!)

Sepsis-triggered CM- is it global? Is it predominantly Right or Left Ventricle? Is it Takutsubo or Stress CM?

Is it changing?!?
Recommendations

• Labwork: Know the pitfalls, check trop and Naturietic peptides for prognostic purposes

• Lactate often!

• Consider addition of MVo2 to lactate

• Echocardiogram is a must! If change in status, or worsening after a period of stability, ? SVR has changed, cardiac situation evolving… sepsis triggered events (direct or indirect)

• Don’t discount PA cath or even Mechanical Help