Fundamentals of Critical Care: Hemodynamic Monitoring & Optimal Antibiotic Use

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Definitions and Principles

- The measurement and interpretation of biological systems that describe performance of the cardiovascular system
- Monitoring is NOT therapy
- Clinicians must know how to interpret the data
- Very few randomized controlled trials
Oxygen Delivery is the Goal

**Oxygen Delivery**

\[ DO_2 \text{ (mL O}_2\text{/min)} = \text{CO (L/min) x CaO}_2 \text{ (mL O}_2\text{/dL) x 10} \]

\[ \text{CO (L/min) = HR (beats/min) x SV (L/beat)} \]

\[ \text{CaO}_2 \text{ (mL O}_2\text{/dL) = [1.34 x (Hb)(g/dL) x SaO}_2] + [.003 x PaO}_2 \text{ mm Hg]} \]

**Oxygen Consumption**

\[ CVO_2 \text{ (mL O}_2\text{/dL) = [1.34 x (Hb)(g/dL) x SVO}_2] + [.003 x PVO}_2 \text{ mm Hg]} \]

\[ \text{VO}_2 \text{ (mL O}_2\text{/min) = CO x 3(CaO}_2 - \text{CVO}_2) x 10} \]
Determinants of Cardiac Performance

- **Preload**
  - Estimated by end-diastolic volume (pressure)
  - CVP for RVEDV, PAOP (wedge) for LVEDV

- **Afterload**
  - \[ SVR = \frac{[\text{MAP} - \text{CVP}]}{\text{CO}} \times 80 \]

- **Contractility**
Methods of Hemodynamic Monitoring

- Arterial Blood Pressure
  - Non-invasive
  - Direct arterial pressure measurement
- Central Venous Pressure
- The Pulmonary Artery Catheter
- Cardiac Output Measurement
- Tissue Oxygenation
Non-invasive Blood Pressure Monitoring
Non-invasive Blood Pressure Measurement

- Manual or automated devices
- Method of measurement
  - Oscillometric (most common)
    - MAP most accurate, DP least accurate
  - Auscultatory (Korotkoff sounds)
    - MAP is calculated
  - Combination
Limitations of Non-invasive Blood Pressure Monitoring

- Cuff must be placed correctly and must be appropriately sized
- Auscultatory method is very inaccurate
  - Korotkoff sounds difficult to hear
  - Significant underestimation in low-flow (i.e. shock) states
- Oscillometric measurements also commonly inaccurate (> 5 mm Hg off directly recorded pressures)
Direct Arterial Blood Pressure Measurement
Indications for Arterial Catheterization

- Need for continuous blood pressure measurement
  - Hemodynamic instability
  - Vasopressor requirement
- Respiratory failure
  - Frequent arterial blood gas assessments
- Most common locations: radial, femoral, axillary, and dorsalis pedis
Complications of Arterial Catheterization

- Hemorrhage
- Hematoma
- Thrombosis
- Proximal or distal embolization
- Pseudoaneurysm
- Infection
Pseudoaneurysm

Fig. 1 – Photography of colour Doppler result showing right axillary artery pseudoaneurysm
Limitations of Arterial Catheterization

- Pressure does not accurately reflect flow when vascular impedance is abnormal
- Systolic pressure amplification
  - Mean pressure is more accurate
- Recording artifacts
  - Underdamping
  - Overdamping
Waveform Distortion
Central Venous Catheterization

- Central venous pressure
  - Right atrial (superior vena cava) pressure
  - Limited by respiratory variation and PEEP

- Central venous oxygen saturation
  - $SCVO_2$
  - Correlates with $SMVO_2$ assuming stable cardiac function
  - Goal-directed resuscitation in severe sepsis and septic shock (Rivers, et al)
Central Venous Pressure Waveform
The Pulmonary Artery Catheter

- HJC Swan and sailboats
- Widespread use in critically ill patients
- Remains controversial
  - Lack of prospective, randomized trials
  - PAC data are only as good as the clinicians’ interpretation and application
- Measures CVP, PAP, PAOP, Cardiac Index and SVO$_2$
Pulmonary Artery Catheter
Indications for Pulmonary Artery Catheterization

- Identification of the type of shock
  - Cardiogenic (acute MI)
  - Hypovolemic (hemorrhagic)
  - Obstructive (PE, cardiac tamponade)
  - Distributive (septic)
  - Many critically ill patients exhibit elements of more than 1 shock classification

- Monitoring the effectiveness of therapy
## Normal Hemodynamic Values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>SVO2</td>
<td>60-75%</td>
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<tr>
<td>Stroke volume</td>
<td>50-100 mL</td>
</tr>
<tr>
<td>Stroke index</td>
<td>25-45 mL/M²</td>
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<tr>
<td>Cardiac output</td>
<td>4-8 L/min</td>
</tr>
<tr>
<td>Cardiac index</td>
<td>2.5-4.0 L/min/M²</td>
</tr>
<tr>
<td>MAP</td>
<td>60-100 mm Hg</td>
</tr>
<tr>
<td>CVP</td>
<td>2-6 mm Hg</td>
</tr>
<tr>
<td>PAP systolic</td>
<td>20-30 mm Hg</td>
</tr>
<tr>
<td>PAP diastolic</td>
<td>5-15 mm Hg</td>
</tr>
<tr>
<td>PAOP (wedge)</td>
<td>8-12 mm Hg</td>
</tr>
<tr>
<td>SVR</td>
<td>900-1300 dynes·sec·cm⁻⁵</td>
</tr>
</tbody>
</table>
## Hemodynamic Profiles in Shock

<table>
<thead>
<tr>
<th>Class of Shock</th>
<th>CVP</th>
<th>PAOP</th>
<th>CO/CI</th>
<th>SVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiogenic</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Hypovolemic</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Hyperdynamic septic</td>
<td>↑</td>
<td>↔</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Hypodynamic septic</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
</tbody>
</table>
Pulmonary Artery Catheter Placement
Complications of Pulmonary Artery Catheterization

- General central line complications
  - Pneumothorax
  - Arterial injury
  - Infection
  - Embolization
- Inability to place PAC into PA
- Arrhythmias (heart block)
- Pulmonary artery rupture
The Pulmonary Artery Catheter Controversy

- Accuracy of data affected by many conditions common in critically ill patients
- Lack of prospective randomized data supporting better outcomes with PAC
- Limited by the ability of the clinician to accurately interpret PAC data
Cardiac Output Measurement

- Multiple techniques
  - Thermodilution – most common
  - Transpulmonary
  - Pulse contour analysis
  - Esophageal Doppler

- Newer pulmonary artery catheters offer continuous cardiac output measurement
Thermodilution Method of Cardiac Output Measurement
Tissue Oxygenation

- Despite advances, our ability to monitor the microcirculation and tissue perfusion is limited
- Laboratory tests for metabolic acidosis are global and insensitive
- Newer technology on the horizon
  - Gastric tonometry
  - Sublingual capnometry
Conclusions

- Multiple different methods of hemodynamic monitoring

- Keys to success
  1) Know when to use which method
  2) Technical skills for device placement
  3) Know how to interpret the data

- Remember the limitations of the technology
Q: Why is hemodynamic monitoring really important?

A: To ensure that the antibiotics get to the tissues......
Optimal Antibiotic Use

- Antimicrobial prophylaxis for surgery
- Empiric antimicrobial therapy
- Challenges of therapeutic antibiotics
  - Correct antibiotic(s)
  - Correct dosing
  - Length of therapy
- Ventilator-associated pneumonia
- Antimicrobial resistance
  - Strategies against resistance
- Bad bugs
Antimicrobial Prophylaxis for Surgery: NSIPP

- First dose of antibiotics within 60 minutes of surgical incision
- Prophylactic antibiotics should be discontinued within 24 hours of surgery
- Specific antibiotic should be chosen based on activity against bacteria likely to be encountered and having smallest possible impact on normal flora
Principles of Empiric Antimicrobial Therapy

- Vigilance and high index of suspicion
  - Local and systemic signs
  - Laboratory and radiographic findings

- **Prompt initiation of therapy**

- Appropriate choice of empiric coverage
  - Suspected site of infection
  - Most likely microbial etiologies
  - Likelihood of antimicrobial resistance – institution specific
  - Patient-specific toxicity and allergic concerns

- Modification of empiric coverage after 48-72 hours
The Risks of Inadequate Empiric Antimicrobial Treatment

- Prospective cohort study of 2000 ICU patients
  - Hospital mortality rate greater (52% vs. 12%) in patients who received inadequate antimicrobial treatment
  - Most important independent determinant of hospital mortality by logistic regression

- 655 patients infected
  - 169 (25.8%) received inadequate antimicrobial treatment
    - Risk factors: prior antibiotic use, presence of bloodstream infection, higher APACHE II scores, decreasing age
  - Infection-related mortality rate 42% vs. 17.7%

The Risks of Inadequate Empiric Antimicrobial Treatment: Bloodstream Infections

- Prospective cohort study of 492 patients with documented bloodstream infections
- 147 (29.9%) received inadequate antimicrobial therapy
- Hospital mortality rate 61.9% vs 28.4%
- Risk factors for inadequate antimicrobials:
  - Candida bloodstream infection
  - Prior antibiotic use during same hospitalization
  - Decreasing serum albumin
  - Increasing central catheter duration

Modification of Empiric Coverage

- Based on clinical condition and culture results
- 48-72 hours after empiric antimicrobials initiated
- Interpret all results with caution
  - Negative cultures drawn after antibiotics initiated
  - Cultures with high incidence of false positives (tracheal aspirates)
  - Contaminants
Therapeutic Antimicrobials: Choosing the Right Drug(s)

- **Gram-positive infections**
  - β-lactam antibiotics (penicillins, cephalosporins, carbapenems)
  - Fluoroquinolones
  - Vancomycin
  - Linezolid, Daptomycin

- **Gram-negative infections**
  - β-lactam antibiotics
  - Fluoroquinolones
  - Aminoglycosides
Therapeutic Antimicrobials: Choosing the Right Drug(s)

- Anaerobic infections
  - Penicillins
  - Carbapenems
  - Second-generation cephalosporins
  - Metronidazole

- Fungal infections
  - Amphotericin
  - Triazoles
  - Echinocandins
Therapeutic Antimicrobials: Bactericidal vs. Bacteriostatic

- **Bactericidal**
  - Penicillins*
  - Cephalosporins
  - Carbapenems
  - Monobactams
  - Vancomycin*
  - Quinolones
  - Aminoglycosides
  - Quinupristin-dalfopristin
  - Metronidazole

- **Bacteriostatic**
  - Trimethoprim-sulfamethoxasole
  - Clindamycin
  - Linezolid
  - Macrolides
  - Chloramphenicol
  - Tetracyclines
Therapeutic Antimicrobials: Correct Dosing

- Important variables in critically ill patients:
  - Target organism
  - Site of infection
  - MIC
  - Host defenses
  - Volume of distribution
  - Hepatic and/or renal impairment

- Concentration-dependent vs. Time-dependent killing
Therapeutic Antimicrobials: Duration of Therapy

- Very controversial
- Factors to consider:
  - Severity of infection
  - Presence of prosthetic material, abscess, necrotic tissue
  - Rapidity of clinical and microbiological response
  - Status of host defenses
- Balancing adequacy of therapy with prevention of resistance
Ventilator Associated Pneumonia

- Most frequent nosocomial infection in ICU
  - 80% of hospital-acquired pneumonia
  - 21-fold increased risk with artificial airway
  - Cumulative risk is 1% per day of mechanical ventilation
  - > $40,000 cost per patient (1999)

- Risk factors
  - Burns
  - Trauma
  - Male gender
  - Central nervous system disease
  - Aspiration
Diagnosis of Ventilator Associated Pneumonia

- Johanson criteria
  - Chest X-ray
    - Sensitive but not specific
  - Leukocytosis/leukopenia
  - Purulent secretions

- Clinical Pulmonary Infection Score
  - Adds fever, oxygenation, and culture results
  - Sensitivity and specificity are highly variable

- Bacteriologic data
  - Different methods of quantitative cultures seem equivalent
Strategies to Prevent Ventilator Associated Pneumonia

- Patient-oriented
  - Gown and glove use
  - Avoiding gastric distention
  - Head-of-bed elevation
  - Minimizing stress-ulcer prophylaxis

- Microorganism-oriented
  - **HAND WASHING**
  - Clorhexidine oral rinse
  - Selective gut decontamination

- Device-oriented
  - Subglottic drainage
  - Humidification
Management of Ventilator Associated Pneumonia

- Prompt initiation of adequate empiric therapy is the most important concept

- Considerations:
  - Prior antibiotic exposure
  - Comorbidities
  - Length of hospitalization
  - Local microbial epidemiology and susceptibilities

- Key questions:
  - Is the patient at risk of MRSA?
  - Is *A. baumannii* a problem at the institution?
  - Is the patient at risk of *P. aeruginosa*?
Antimicrobial Resistance

Pssst! Hey kid! Wanna be a Superbug...?
Stick some of this into your genome...
Even penicillin won't be able to harm you...

It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.
Antimicrobial Resistance: CDC Programs

- National Nosocomial Infections Surveillance (NNIS) System
- Project ICARE (Intensive Care Antimicrobial Resistance Epidemiology)
- Higher rates of resistance in the ICU correlate with more antibiotic use:
  - *Enterobacter* - 3rd-generation cephalosporins
  - Enterococci - vancomycin
  - *P. aeruginosa* - antipseudomonal penicillins and 3rd-generation cephalosporins
- Higher rates of resistance in the ICU that do not correlate with more antibiotic use:
  - MRSA and MR-CNS
Strategies to Minimize Antimicrobial Resistance: Individual Patient

- Use antimicrobials with highest potency
- Appropriate dose and dosing intervals
- Avoid known inducers of chromosomal resistance
- Choose agents with good penetration to site of infection
- Avoid antagonistic antimicrobial combinations
- Appropriate treatment duration
- Achieve therapeutic drainage and/or device removal
Strategies to Minimize Antimicrobial Resistance: ICU-based

- **HAND-WASHING**
  - Appropriate glove and gown use
  - Surveillance monitoring for resistant strains
    - MRSA
    - VRE
    - ESBL
  - Appropriate patient isolation policies
  - Antimicrobial cycling
  - Computer-assisted antimicrobial prescription
Antimicrobial Resistance
Reasons for Antimicrobial Failure

- Undrained infected material
- Underlying host defenses
- Infected prosthetic material
- Poor tissue penetration
- Superinfection with (new) pathogen
- Evolved resistance
- Inadequate dosing
- Antagonistic antimicrobial combination
Bad Bugs

- Vancomycin-resistant Enterococci
- Methicillin-resistant S. aureus
- *Pseudomonas aeruginosa*
- ESBL strains
  - *Enterobacter*
  - *Klebsiella*
  - *Serratia*
- *Acinetobacter baumannii*
Vancomycin-resistant Enterococci

- Predominantly *E. faecium*
- Usually resistant to ampicillin
- Can be contaminant but bloodstream infections and purulent closed-space collections in symptomatic patients must be treated
  - Linezolid
  - Quinupristin/dalfopristin
  - Daptomycin
Methicillin-resistant *S. aureus*

- Vancomycin remains useful, but be aware of limitations
  - Slow bactericidal activity
  - Poor lung and CNS penetration
  - Poor activity in biofilms
- Emergence of vancomycin-resistance
- Linezolid
- Quinupristin/dalfopristin
- Daptomycin
**Pseudomonas aeruginosa**

- **Virulent:** infection-associated mortality as high as 70% despite therapy
- **Intrinsic and acquired resistance:**
  - Chromosomal-mediated β-lactamase
  - Aminoglycoside modifying enzymes
  - Mutations of outer membrane porin channels
- **Piperacillin-tazobactam**
- **Meropenem**
- **Aminoglycosides**
- **Colistin**
ESBL strains

- Plasmid-mediated production of β-lactamases
- Resistance to aztreonam, piperacillin, and later generation cephalosporins
- ESBL strains commonly coexpress aminoglycoside and/or quinolone resistance
- Carbapenems are the most proven antimicrobial