The following sponsors have provided generous support for the 2017 Southeastern Critical Care Summit

Exhibitors:

Astute Medical (NephroCheck)  Hamilton Medical
Cheetal Medical  Janssen Pharmaceuticals, Inc.
Edwards Lifesciences  NXStage
Ethicon  Otsuka
Fresenius Kabi  Shire
Gilead  Southeast Chapter of the Society Of Critical Care Medicine
Halyard Health  Theravance
COURSE DIRECTORS

Micah Fisher, MD  
Assistant Professor, Pulmonary and Critical Care  
Emory University School of Medicine  
Section Chief, Emory University Hospital

Greg Martin, MD, MSc  
Professor, Pulmonary and Critical Care  
Associate Division Director for Critical Care  
Emory University School of Medicine  
Section Chief, Grady Memorial Hospital

Jenny Han, MD, MSc  
Assistant Professor, Pulmonary and Critical Care  
Emory University School of Medicine

Gabriel Najarro, MMSc, PA-C  
Lead Affiliate Provider  
Cardiac Critical Care Unit  
Emoryhealthcare

Ashish Mehta, MD, MSc  
Assistant Professor, Pulmonary and Critical Care  
Emory University School of Medicine  
Medical Director, MICU, Atlanta VA Medical Center

Mary D. Still, MSN, APRN  
Clinical Nurse Specialist Critical Care  
Emory University Hospital

Marina Rabinovich, PharmD, BCPS  
Critical Care Clinical Pharmacist Specialist  
President, SCCM Southeast Chapter

Adam Webb, MD  
Assistant Professor of Neurology and Neurosurgery  
Emory School of Medicine  
Medical Director, Neuroscience  
Grady Memorial Hospital
PLENARY LECTURERS

Dr. Jesus Villar  Dr. Jesus Villar is Group Chief for the Center for Biomedical Research in Respiratory Diseases in Madrid and Senior Scientist of the Research Unit at the Hospital Universitario Dr. Negrin in Las Palmas, Spain. He is the Coordinator of the Multidisciplinary Organ Dysfunction Evaluation Research Network (MODERN) in the Canary Islands, where he resides. Dr. Villar received his medical degree from the University of La Laguna in the Canary Islands, followed by a master’s degree for work on meningococcal sepsis and a PhD in Critical Care Medicine from the University of La Laguna. He has been a research fellow and associate scientist at the University of Toronto, and Professor at Mercer University in Macon, Georgia. Over three decades, Dr. Villar has been an international leader in understanding the acute respiratory distress syndrome (ARDS) and its most common causes. He has contributed seminal articles on the incidence of ARDS, the role of shock as a cause of ARDS, and demonstrated methods for improving care of these patients with strategies ranging from lung protective mechanical ventilation to the application of systemic hypothermia.

Dr. E. Wesley Ely will lecture on Liberation

Dr. Wes Ely completed his undergraduate and medical school at Tulane University, where he was elected to the Alpha Omega Alpha medical honors society. Dr. Ely is currently Professor of medicine at Vanderbilt University School of Medicine with subspecialty training in Pulmonary and Critical Care Medicine. Dr. Ely’s research has focused on improving the care and outcomes of critically ill patients with ICU-acquired brain disease (manifested acutely as delirium and chronically as long-term cognitive impairment), particularly those with sepsis, respiratory failure and the geriatric population. He has built the ICU Delirium and Cognitive Impairment Study Group, amassing several thousand patients into cohort studies and randomized trials that were used to build the methodology for ICU acquired brain disease research.
SUMMIT FACULTY

William Bender, MD
Assistant Professor, Pulmonary and Critical Care
Emory University School of Medicine

Azra Bihorac, MD, MS, FCCM
R. Glenn Davis Associate Professor of Medicine,
Surgery and Anesthesiology,
Division of Nephrology, Hypertension
and Renal Transplantation
University of Florida

Bruce Bray, RRT, RCP
Division Director, Department of Respiratory Care,
Emory ECMO Center
Emory University Hospital, Orthopedics and Spine Hospital

Stacey Campbell, PharmD, MPH, BCPS
Critical Care Clinical Coordinator, Emory University Hospital

Michael Connor, Jr., MD
Divisions of Nephrology and Pulmonary Critical Care
Emory University School of Medicine

Ashley DePriest, MS, RD, LD, CNSC
Nutrition Support Dietitian
Northside Hospital

Annette Esper, MD, MSc
Associate Professor, Pulmonary and Critical Care
Emory University School of Medicine

David Green, MD
Assistant Professor, Pulmonary and Critical Care
Atlanta VA Medical Center
Emory University School of Medicine

Casey L. Hall, MD, MAT
Neuroscience Critical Care, Neurology
Emory University School of Medicine

Carolyn Holder, RN, APRN-BC, CCRN, CCNS
Clinical Nurse Specialist Medical ICU,
Emory University Hospital

William R. Hunt, MD
Assistant Professor, Pulmonary and Critical Care
Emory University School of Medicine

Octavian Ioachimescu, MD
Associate Professor, Pulmonary and Critical Care
Emory University School of Medicine

Wissam A. Jaber, MD, FACC
Assistant Professor of Medicine
Interventional Cardiology
Emory Heart Center, Emory University School of Medicine

Jeffrey Javidfar, MD
Assistant Surgical Director,
Emory McKeelvey Lung Transplant Program
Assistant Professor of Surgery
Emory School of Medicine

Prem Kandiah MD
Assistant Professor of Neurology & Neurocritical Care
Fellowship Co-Director,
Emory University Hospital

Sheetal Kandiah, MD, MPH
Assistant Professor, Division of Infectious Diseases
Emory University School of Medicine

Munish Luthra, MD
Assistant Professor, Pulmonary and Critical Care
Emory University School of Medicine

Barbara McLean, MN, RN, CCNS-BC, NP-BC
Critical Care Clinical Specialist, Critical Care Division
Grady Health System

Tammie Quest, MD
Professor, Emergency Medicine
Emory University School of Medicine

Jayashree Raikhelkar, MD
Assistant Professor, Department of Anesthesiology
Emory University School of Medicine

Jonathan Ratcliff, MD
Assistant Professor, Emergency Medicine
Emory University School of Medicine

Alex Truong, MD
Assistant Professor, Division of Pulmonary, Allergy,
Critical Care and Sleep Medicine
Emory University School of Medicine

Reinetta Waldrop, PhD
Assistant Professor, Morehouse School of Medicine
Critical Care Former Patient

Rachael Williams, MHS, MD
Assistant Professor of Surgery, Grady Burn Unit
Emory University School of Medicine.
Disclosure statement

It is the intent of Emory University School of Medicine to assure that its educational mission, and continuing medical education activities in particular, not be influenced by the special interest of individuals associated with its programs. All faculty members participating in a sponsored activity are expected to disclose to the audience two important points:

- Any significant financial interest of other relationship with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in an educational presentation; Any significant financial interest with any commercial supporters of the activity. (Significant financial interest or other relationships can include such things as grants or research support, employee, consultant, major stock holder, member of speaker’s bureau, etc.).
- All disclosed financial relationships were reviewed for potential conflicts of interest. Actions were taken to resolve any identified conflicts. The following committee members and/or speakers have disclosed potential conflicts of interest.

The Ochsner Clinic Foundation relies upon invited speakers at all sponsored continuing medical education activities to provide information objectively and free from bias of conflict of interest. In accordance with ACCME and institutional guidelines pertaining to potential conflicts of interest, the faculty for this continuing medical education activity has been asked to complete faculty disclosure forms. In the event that some invited speakers indicate that they have a relationship which, in the context of the subject of their invited presentation, could be perceived as a potential conflict of interest, their materials have been peer reviewed in order to ensure that their presentations are free of commercial bias.

<table>
<thead>
<tr>
<th>Speaker/committee member</th>
<th>Role/Type</th>
<th>Name of Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azra Bihorac, MD</td>
<td>Research grant</td>
<td>Astute Medical</td>
</tr>
<tr>
<td>Wes Ely, MD</td>
<td>Research grant</td>
<td>NIH and VA funding</td>
</tr>
<tr>
<td></td>
<td>Honoraria</td>
<td>Pfizer/Abbott/Orion</td>
</tr>
<tr>
<td>Greg Martin, MD</td>
<td>Research grant</td>
<td>NIH, Bristol-Myers Squibb</td>
</tr>
<tr>
<td></td>
<td>Consultant</td>
<td>Bard, Cheetah, Edwards, Grifols</td>
</tr>
<tr>
<td>Barbara McLean, RN</td>
<td>Research grant</td>
<td>Cheetah (co PI)</td>
</tr>
<tr>
<td></td>
<td>Speaker</td>
<td>Edwards Lifesciences</td>
</tr>
<tr>
<td>Adam Webb, MD</td>
<td>Consultant</td>
<td>Bard Medical</td>
</tr>
<tr>
<td>Rachael Williams, MD</td>
<td>Consultant</td>
<td>Integra</td>
</tr>
</tbody>
</table>
7:30 - 8:00  CONTINENTAL BREAKFAST

8:00 - 8:10  WELCOME AND INTRODUCTION – J. Han

8:10 - 9:20  FIRST MORNING SESSION
- Lessons from a critical care survivor – R. Waldrop
- Surviving Sepsis 3 - Merging SSC and the new sepsis – M. Still

9:20 - 9:30  FIRST MORNING BREAK AND POSTER VIEWING

9:30 - 10:40  SECOND MORNING SESSION
- Sepsis 3 turns 1 - Updates and controversies – G. Martin
- Weaning mechanical ventilation - does the mode matter? – B. Bray
- Update on sedation – S. Campbell

10:40 - 11:00  SECOND MORNING BREAK AND POSTER VIEWING

11:00 - 12:00  DAY 1 PLENARY LECTURE
Lung Protective Mechanical Ventilation in Patients - State of the Art 2017 – J. Villar

12:00 - 1:00  LUNCH

1:00 - 2:10  FIRST AFTERNOON SESSION
- Antibiotic stewardship in the ICU – S. Kandiah
- Updates on feeding the critically ill – A. Depriest
- Ketamine for sedation in the ICU: A one man pro-con debate – P. Kandiah

2:10 - 3:30  FIRST AFTERNOON BREAK

2:20 - 3:30  SECOND AFTERNOON SESSION
- Palliative care – T. Quest
- Avoiding intubation – Role of NIV and high-flow oxygen systems – W. Bender
- Post intensive care syndrome and clinics – A. Truong

3:30 - 3:40  SECOND AFTERNOON BREAK

3:40 - 4:40  ROUNDTABLE DISCUSSION
Current approaches to massive and sub-massive PE – M. Fisher, W. Jaber, J. Javidfar

4:40 - 5:00  Wrap-up and raffle drawing – G. Martin
Lessons from a Critical Care Survivor
Reinetta Waldrop, PhD, MSHS
Assistant Professor Morehouse School of Medicine, Master of Public Health Program
Surviving Sepsis
Merging Concepts in a Multi-Hospital System!!

MARY D STILL APRN ACNS-BC CCRN FCCM (MDSTILL@EMORY.EDU)
CLINICAL NURSE SPECIALIST
EMORY UNIVERSITY HOSPITAL
ATLANTA, GEORGIA

Objectives
1. Describe initial process for incorporating elements of sepsis management into daily care.
2. Identify key elements needed for success and sustainment of care during the revision in both definition and recommendations for sepsis management.
   - Common Vision
   - Teamwork
   - System support
   - Provider/staff engagement
   - Clear Goals
3. Describe transition process from SEP1, CMS requirements and SEP3. How can these be incorporated into care.

No conflicts of interest to disclose

We began with:
SURVIVING SEPSIS CAMPAIGN BUNDLES 2012

Common Vision: of what it can be! And How it should be?
Leaders: How best to start initiative
Goals: What to accomplish and When?
Recognition of Barriers: Value stream mapping to determine current state.
What were the challenges/opportunities?
Time line for success
How do we measure success? Data/ Metrics( SCCM Recommendations)
Continuous re evaluation of process!!!!!!
Clinical Effectiveness: Summary of Initiatives

Teamwork Critical!!!!!!

<table>
<thead>
<tr>
<th>Initiative Description</th>
<th>Overall Risk Level</th>
<th>Ease to Implement</th>
</tr>
</thead>
<tbody>
<tr>
<td>IT Optimization</td>
<td>Medium</td>
<td>3</td>
</tr>
<tr>
<td>Lab</td>
<td>High</td>
<td>3</td>
</tr>
<tr>
<td>Standardization of Supplies and Equipment</td>
<td>Low</td>
<td>3</td>
</tr>
<tr>
<td>Education: Staff, Provider, Patient and Family</td>
<td>Medium</td>
<td>2</td>
</tr>
<tr>
<td>Care Process Standardization</td>
<td>Medium - High</td>
<td>4</td>
</tr>
<tr>
<td>Antibiotics (Resuscitation and Management Phase)</td>
<td>Medium</td>
<td>2-3</td>
</tr>
<tr>
<td>Patient care transitions across continuum of care</td>
<td>Low</td>
<td>1</td>
</tr>
</tbody>
</table>

TOTAL EXPECTED BENEFIT

Clinical Effectiveness: Summary of Initiatives

Teamwork Critical!!!!!!

Barriers to Sepsis Management

System Support Critical!!!!!!!

Sepsis Bundle Management Metrics

To be accomplished as soon as possible and scored over first three hours:

- Serum lactate measured
- Blood cultures obtained prior to antibiotics administered
- Administer broad-spectrum antibiotics
- For hypotension and/or lactate > 2 mmol/L:
  - Deliver an initial minimum of 30 ml/kg of crystalloid

To be accomplished as soon as possible and scored over first six hours:

- Apply compensatory hyperventilation if respiratory rate > 25
- In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate > 4 mmol/L:
  - Measure CVP
  - Measure SaO2
  - Re-measure lactate if initial lactate is elevated >2

Source: Sepsis and Septic Shock

Drews C, Angus, D.C., D.P., and Tom van der Poll, M.D., Ph.D.

**Question: Sepsis, is it a Clear/ Clean Definition?**

**Staff:**
- Had issues with screening (SIRS criteria could fit many clinical situations)
- Concerns about diagnosis vs symptom identification
- Concerns by some if the bedside nurse could make these decisions (lack of clear defined roles and responsibilities)

**Coders, CDI specialists and Physicians:**
- Had challenges because it can be difficult to diagnose (no specific marker like AMI)
- How do you diagnose and initiate treatment for sepsis with negative blood cultures?
- Since sepsis carries a high mortality cost, CDI and Coders may query for sepsis too quickly?
- The solution?
  - Need clear process for screening
  - Providers need to be sure sepsis is correctly identified and documented early and start bundle treatment.
  - CDI specialists need to know what a septic patient looks like
  - Coders need to know the guidelines and when it is appropriate to code sepsis (documentation with correct language and timing)

---

**Sepsis Alert Notification Pop Up**

(Based on electronic trigger)

---

**Three Phases of Management**

**Phase I:** Sepsis Power Plan, including the “Suspected Sepsis” and “Antibiotics” Phases introduced in both the ED and ICU

*June 4, 2013*
DEFINITIONS
Sepsis: SIRS + suspected source of infection
Severe sepsis: sepsis + end organ damage
Septic shock: hypotension despite adequate fluid resuscitation

Changes/Decisions!
Sepsis: Syndrome with dysregulated host response + presence of organ dysfunction
Septic shock: subset of patients with circulatory and cellular/metabolic abnormalities that highly increases mortality

2016: New Sepsis Definition

What has changed and How does it impact our process?

DEFINITIONS
Sepsis: SIRS + suspected source of infection
Severe sepsis: sepsis + end organ damage
Septic shock: hypotension despite adequate fluid resuscitation

Changes/Decisions!
Sepsis: Syndrome with dysregulated host response + presence of organ dysfunction
Septic shock: subset of patients with circulatory and cellular/metabolic abnormalities that highly increases mortality
CMS Introduces recommendation for compliance!

Why do Core Measures Matter????

- Designed to hold hospitals accountable for "standards of care"
- Many measures come from the National Quality Foundation (NQF)
- Challenges!!
- One of the Most difficult disease to diagnose
- Wide spectrum of disease
- Definitions have undergone change
- Don't have accurate estimates of disease incidence

Hospital documentation policies for sepsis have real world financial impacts

Example of financial impact of documenting sepsis versus SIRS

How to determine what we need to change based on the new definition?

1. What role does CMS play in the final process?

   - 2009 Agency for Healthcare Research and Quality (AHRQ) included sepsis as part of its programs
   - Sepsis carries high mortality compared to other diagnosis
   - Rising hospitals stays related to sepsis
   - Frequent cause of re-hospitalizations
   - Medicare covered 58.1% of sepsis-related hospital stays

Federal Register / Vol. 79, No. 163 / Friday, August 22, 2014 / Rules and Regulations
FY17:

Plan for Improvement:
New recommendations, SCCM, ESCCM and CMS
Revision and implementation for early recognition trigger
Interdisciplinary decision to maintain SIRS criteria as trigger for assessment
New Dashboard developed based on core metrics.
Back to the basics: Re-education for all!
Code Sepsis implemented
Focus on Entity issues and common defects assessed from CMS reviews!
Power Plan updated to reflect minor changes and prevent duplication of Orders
Determine impact on patient outcomes and savings
Sepsis protocol utilization, cont.

Initial sepsis protocol initiation (%)
Definition: The percent of all sepsis encounters with documentation of initial sepsis protocol initiation during their hospitalization.

Entity EUH EUHM ESJH EJCH EHC
Jan 2017 YTD 43 18 45 44 72 66 50 13 51 36
Feb Mar Apr May Jun Jul 2016 2017 0 20 40 60 80 100%

Sepsis management protocol initiation (%)
Definition: The percent of severe sepsis encounters with documentation of sepsis management protocol initiation during their hospitalization.

Entity EUH EUHM ESJH EJCH EHC
Jan 2017 YTD 20 6 30 24 52 41 33 8 31 19
Feb Mar Apr May Jun Jul 2016 2017 0 20 40 60 80 100%
### Patient outcome: Mortality Rate By FY

<table>
<thead>
<tr>
<th>Discharge Fiscal Year</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12.00%</td>
<td>11.41%</td>
</tr>
<tr>
<td>2014</td>
<td>2.00%</td>
<td>4.00%</td>
</tr>
<tr>
<td>2015</td>
<td>4.00%</td>
<td>6.00%</td>
</tr>
<tr>
<td>2016</td>
<td>6.00%</td>
<td>8.00%</td>
</tr>
<tr>
<td>2017</td>
<td>8.00%</td>
<td>10.00%</td>
</tr>
<tr>
<td>2018</td>
<td>10.00%</td>
<td>12.00%</td>
</tr>
</tbody>
</table>

### TAKE HOME MESSAGES
- Sepsis is an evolving disease state.
- Sepsis-3 definitions aimed to identify those patients at highest risk morbidity and mortality.
- Clinicians are hyperaware of sepsis yet still no clear marker.
- Making a sepsis management system as “one size fits all” is challenging.
- Regulatory mandates will continue playing catchup as new definitions evolve.
- Systems must remain flexible and open for continuous re-evaluation.

### References
Vasopressors: What’s Hot, What’s Not, and What’s New

Marina Rabinovich, PharmD, BCPS
Clinical Pharmacy Specialist – MICU
Grady Health System
mrabinovich@gmh.edu

Objectives and Disclosures

• Review updated recommendations for vasopressors use in septic shock based on 2016 Surviving Sepsis Guidelines
• Analyze the evidence behind the type and order of vasopressor to be selected in septic shock
• Discuss future and ongoing research in new vasopressor development

• Disclosures: None

Vasopressors

• Catecholamines
  – Norepinephrine
  – Epinephrine
  – Dopamine
  – Phenylephrine
• Vasopressin analogues
  – Vasopressin
  – Terlipressin
  – Selepressin
• Angiotensins
  – Angiotensin II
Surviving Sepsis Guideline Recommendations

2004
- Either norepinephrine or dopamine is the first choice vasopressor agent (Grade D)
- Vasopressin use may be considered in patients with refractory shock despite adequate fluid resuscitation and high-dose conventional vasopressors (Grade E)

2008
- Norepinephrine or dopamine is the first-choice vasopressor (Grade D)
- Vasopressin use may be considered in patients with refractory shock despite adequate fluid resuscitation and high-dose conventional vasopressors (Grade E)

2012
- Norepinephrine is the first-choice vasopressor (Grade 1C)
- Epinephrine, phenylephrine, or vasopressin should not be administered as the initial vasopressor in septic shock (Grade 2C)
- Vasopressin may be added to norepinephrine with anticipation of an effect equivalent to norepinephrine alone (Grade 2C)
- Use epinephrine as the first alternative agent in septic shock when blood pressure is poorly responsive to norepinephrine or dopamine (Grade 2B)

2016
- Norepinephrine is the first choice vasopressor (strong recommendation, moderate quality of evidence)
- Add vasopressin to raise MAP to target or decrease norepinephrine dose (weak recommendation, moderate quality of evidence)
- Dopamine as a alternative vasopressor to norepinephrine only in highly selected patients (weak recommendation, low quality of evidence)
- Phenylephrine is not recommended in the treatment of hypotension except in certain circunstances (Grade 2C)

What about Phenylephrine?

Decreased NE use by > 20% was associated with increased odds of in-hospital mortality (35.9% vs 39.4%; absolute mortality difference = 3.7% [95% CI, 1.3%–6.0%]; adjusted odds ratio = 1.15 [95% CI, 1.01–1.30]; P = .03)

Current Situation

- Catecholamines
  - Norepinephrine
  - Epinephrine
  - Dopamine
  - Phenylephrine
- Vasopressin analogues
  - Vasopressin
  - Terlipressin
  - Selepressin
- Angiotensins
  - Angiotensin II
How Did We Get Here

• No study to date has demonstrated a statistically significant survival benefit of one vasopressor over another
• Choice of vasopressor in septic shock is rather empiric
• Norepinephrine remains to be the front runner

Meta-analysis of 28 studies

Vasopressors and Mortality
Norepinephrine vs Dopamine
Sepsis Occurrence in Acutely Ill Patients (SOAP II) trial

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Dopa</th>
<th>Norepi</th>
<th>Odds Ratio (95%CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>28-day</td>
<td>52.5</td>
<td>48.5</td>
<td>1.17 (0.97-1.42)</td>
<td>0.10</td>
</tr>
<tr>
<td>ICU</td>
<td>50.2</td>
<td>45.9</td>
<td>1.19 (0.98-1.46)</td>
<td>0.07</td>
</tr>
<tr>
<td>Hospital</td>
<td>58.4</td>
<td>56.6</td>
<td>1.12 (0.92-1.37)</td>
<td>0.24</td>
</tr>
<tr>
<td>6-month</td>
<td>63.8</td>
<td>62.9</td>
<td>1.05 (0.86-1.31)</td>
<td>0.71</td>
</tr>
<tr>
<td>12-month</td>
<td>65.9</td>
<td>63.0</td>
<td>1.15 (0.91-1.46)</td>
<td>0.34</td>
</tr>
</tbody>
</table>

Adverse Events (%)

- Arrhythmias (Atrial): 24.1 vs 12.4, <0.001


---

Norepinephrine vs Dopamine

- No difference in MAP, time or max dose needed to achieve goal MAP
- No difference in severe adverse events (tachyarrhythmias)
- No difference in 28 or 90-day mortality

---

Marik PE et al. JAMA 1994;272:1354
Patel GP et al. Shock 2010;33:375
Mathur. Indian J Crit Care Med 2007;11:186
Martin C et al. Chest 1993;103:1826

---

Norepinephrine vs Epinephrine
CAT Study Group

- No difference in MAP, time or max dose needed to achieve goal MAP
- No difference in severe adverse events (tachyarrhythmias)
- No difference in 28 or 90-day mortality

Norepinephrine vs Epinephrine

<table>
<thead>
<tr>
<th>Side effect</th>
<th>Illustrative comparative risks (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No. of participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-term mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study population</td>
<td>62 of 1,000 (340)</td>
<td>0.77 to 1.21</td>
<td>4 (4 studies)</td>
<td>moderate</td>
</tr>
<tr>
<td>Serious adverse events - supraventricular arrhythmias</td>
<td>46 of 1,000</td>
<td>0.82 to 1.06</td>
<td>3 (3 studies)</td>
<td>low</td>
</tr>
<tr>
<td>Serious adverse events - ventricular arrhythmias</td>
<td>86 of 1,000</td>
<td>1.27 to 1.31</td>
<td>3 (3 studies)</td>
<td>low</td>
</tr>
</tbody>
</table>

* Grade reduced for imprecision.
* Outcome reported only in one of four trials.

Norepinephrine vs Vasopressin

Vasopressin And Septic Shock Trial (VASST)

No difference days alive free of organ failure, length of stay (ICU and hospital), or adverse events

VASST

Post-hoc Analysis

- Vasopressin may be more effective at preventing deterioration in renal function.
- Vasopressin + steroids led to lower mortality compared with norepinephrine + steroids.
Vasopressin and Steroids in Septic Shock

- steroid treatment significantly increased vasopressin levels by 33% (6 hours) and by 67% (24 hours; p 0.006 and p 0.025, respectively)
- levels were extremely low and were not altered by steroids in the norepinephrine group

Russell JA et al. Crit Care Med 2009 Vol. 37, No. 3

• steroid treatment significantly increased vasopressin levels by 33% (6 hours) and by 67% (24 hours; p 0.006 and p 0.025, respectively)

Norepinephrine vs Vasopressin

VAso pressin vs Noradrenaline as Initial therapy in Septic shock (VANISH) study

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Vasopressin</th>
<th>Norepinephrine</th>
<th>Significant?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survivors who never developed kidney failure (%)</td>
<td>57</td>
<td>59.2</td>
<td>No</td>
</tr>
<tr>
<td>Kidney failure free days</td>
<td>9</td>
<td>13</td>
<td>No</td>
</tr>
<tr>
<td>Use of RRT (%)</td>
<td>25.4</td>
<td>35.3</td>
<td>Yes</td>
</tr>
<tr>
<td>28-day mortality (%)</td>
<td>30.9</td>
<td>27.5</td>
<td>No</td>
</tr>
<tr>
<td>ICU mortality (%)</td>
<td>28.4</td>
<td>25</td>
<td>No</td>
</tr>
</tbody>
</table>

No difference in rate of:
- Organ failure
- Time to shock reversal
- Open-label inotrope use
- Adverse events


Norepinephrine vs Vasopressin

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Vasopressin</th>
<th>Norepinephrine</th>
<th>Significant?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-term mortality</td>
<td>60 (9 to 101)</td>
<td>80 (13 to 600)</td>
<td>No</td>
</tr>
<tr>
<td>Serious adverse events - supraventricular arrhythmias</td>
<td>10 (0.32 to 10)</td>
<td>10 (1.8 to 60.4)</td>
<td>No</td>
</tr>
<tr>
<td>Serious adverse events - ventricular arrhythmias</td>
<td>8 (0.5 to 5)</td>
<td>10 (1 to 60.4)</td>
<td>No</td>
</tr>
<tr>
<td>Serious adverse events - stroke</td>
<td>0 (0 to 2)</td>
<td>1 (1 to 6)</td>
<td>No</td>
</tr>
<tr>
<td>Serious adverse events - acute coronary events</td>
<td>0 (0 to 2)</td>
<td>1 (1 to 6)</td>
<td>No</td>
</tr>
<tr>
<td>Serious adverse events - limb ischemia</td>
<td>2 (0.3 to 10)</td>
<td>1 (0.3 to 10)</td>
<td>No</td>
</tr>
</tbody>
</table>

1 Variations in type of molecule (vasopressin vs terlipressin) and in dose.
2 Some studies have compared vasopressin with norepinephrine, and some studies have compared vasopressin plus norepinephrine versus norepinephrine.
3 Unclear risk of bias in some studies (methods for allocation concealment, blinding).
4 Imprecision with wide confidence intervals spanning harm and benefit.
5 Imprecision. Only 21 events.
What’s left?
Do we need new vasopressors?

• Catecholamines
  – Norepinephrine
  – Epinephrine
  – Dopamine
  – Phenylephrine

• Vasopressin analogues
  – Vasopressin
  – Terlipressin
  – Selepressin

• Angiotensins
  – Angiotensin II

What’s New
Selepressin – V1a selective agonist

• Unlike vasopressin that activates V1a, V1b, V2, and oxytocin receptors
• Animal studies suggest lower mortality, less lung edema, improved urine output and free water clearance as well as less vascular leak compared to vasopressin and norepinephrine

Selepressin

Better Water Clearance
Less Lung Edema
Selepressin Evaluation Programme for Sepsis Induced Shock – Adaptive Clinical Trial

SEPSIS-ACT

- Double blind, randomized, placebo controlled phase 2b/3 clinical trial
  - Safety and efficacy
  - Multiple-dose regimens
- 50-60 sites in Europe and US
- 1800 patients with estimated completion April 2019
- Primary outcome
  - Vasopressor and mechanical ventilator-free days up to day 30
- Secondary Outcomes
  - All-cause mortality at 90 days
  - Renal replacement therapy-free days up to day 30
  - Intensive care unit-free days up to day 30

https://clinicaltrials.gov/ct2/show/NCT02508649

What’s New (or Old)

- Angiotensin II
  - First described in 1961 as treatment for shock
- Theory of septic kidney
  - Increased renal blood flow
  - Decreased GFR
  - Intraglomerular hypotension
- “Angiotensin II insufficiency”
  - Loss of ACE activity in ALI → inability to convert ANG I to ANG II → catecholamine resistance and AKI


ACE: angiotensin converting enzyme; ANG I: angiotensin I; ANG II: angiotensin II; AKI: acute kidney injury
Angiotensin II
Intravenous Angiotensin II for the Treatment of High Output Shock (ATHOS) trial

• Pilot study, 20 patients
• Low doses of ANG II can cause catecholamine sparing effect
  – Rescue vasopressor?
• ANG II may be more useful in ARDS patients
  – Pulmonary capillary endothelium damage can restrict conversion of ANG I to ANG II

Chawla LS et al. Critical Care 2014;18:534

A Phase 3 Study of LJPC-501 in Patients With Catecholamine-Resistant Hypotension (ATHOS-3)

• Completed April 2017
  - Double-blind, randomized, placebo-controlled, multi-center (US, 42 Europe, 15 Canada, 20 ANZICs)
  - N=344

  Titration of LJPC-501 (2-200 ng/kg/min) or Placebo to achieve and maintain MAP 75 mmHg at 3 hrs

  Placebo + Standard of Care Vasopressors
  LJPC-501 + Standard of Care Vasopressors

  Outcomes:
  - Increase in MAP at 3 hrs
  - Change in SOFA score at 48 hrs
  - Mortality at 7 and 28 days


Conclusion

• Vasopressor choice and order is still unclear and should be patient-specific
• Norepinephrine remains the first choice vasopressor
• Multiple vaspressors with different mechanisms of action might be needed to achieve goal
• Need for additional vaspressors with more targeted activity
Sepsis-3 Turns 1

Greg Martin, M.D., M.Sc.
Professor of Medicine
Section Chief, Grady Memorial Hospital
Pulmonary, Allergy, Critical Care and Sleep
Director of Research, Emory Center for Critical Care
greg.martin@emory.edu

Southeastern Critical Care Summit
May 4, 2017

---

<table>
<thead>
<tr>
<th>Relationship</th>
<th>Company Name</th>
<th>Role</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equity, stock, or options in biomedical industry companies or publications</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Board of Directors or Officer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Society of Critical Care Medicine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Project Hope</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Council (Board of Directors)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Chick Medical Advisory Board</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Royalties</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. NIH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Bristol-Myers Squibb</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Funds or other support to Emory for research</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Astute Medical</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Bard</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Cheetah Medical</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Edwards</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Grifols</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Regeneron</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

Sepsis-3 Turns 1

- Review prior and current sepsis definitions
- Discuss evidence for SEPSIS-3 application
- Review current knowledge for validity of the SEPSIS-3 definition
Sepsis: A Historical Perspective

• “Small creatures invisible to the eye, fill the atmosphere, and breathed through the nose cause dangerous diseases.”
  – Marcus Terentius Varro, c. 100 BC

• “Hectic fever, at its inception, is difficult to recognize but easy to treat; left unattended it becomes easy to recognize and difficult to treat.”
  – Niccolo Machiavelli, The Prince, 1513

ACCP / SCCM Consensus Definition (Sepsis-1)

- Infection
  - Invasion of normally sterile tissues, or
  - Inflammatory response to microorganisms
- Systemic Inflammatory Response Syndrome (SIRS)
  - Systemic response to a variety of processes
- Sepsis
  - Infection with ≥ 2 SIRS criteria
- Severe Sepsis
  - Sepsis with consequent acute organ dysfunction
- Septic shock
  - Sepsis with refractory hypotension or hypoperfusion
- Multiple Organ Dysfunction Syndrome (MODS)
  - Altered organ function, requiring intervention, in an acutely ill patient


‘Sepsis-2’

Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection.
**QUICK BEDSIDE PROMPT OF AT-RISK INFECTED PATIENT**

3 simple bedside clinical criteria
- Low systolic BP (≤100 mmHg)
- Tachypnea (≥22 / min)
- Altered mentation

**Assessment of criteria**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>SIRS</th>
<th>SOFA</th>
<th>LODS</th>
<th>qSOFA</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU Encounters</td>
<td>0.64 (0.62, 0.66) AUROC in hospital mortality</td>
<td>0.74 (0.73, 0.76)</td>
<td>0.20</td>
<td>0.75 (0.73, 0.76)</td>
</tr>
</tbody>
</table>

SIRS and LODS superior in the ICU
qSOFA similar to complex scores outside the ICU

**Familiar with SOFA Score?**

<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIRS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOFA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LODS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AUROC in-hospital mortality:
- SIRS: 0.76 (0.75, 0.77) <0.01
- SOFA: 0.79 (0.78, 0.80) <0.01
- LODS: 0.81 (0.80, 0.82) <0.01

**Outside the ICU encounters**

N = 66,522

qSOFA similar to complex scores outside the ICU
1991 Septic Shock definitions

1991
• Sepsis-induced hypotension, persisting despite adequate fluid resuscitation, along with the presence of hypoperfusion abnormalities or organ dysfunction

2001
• State of acute circulatory failure characterized by persistent arterial hypotension unexplained by other causes

Neither definition proposed explicit criteria

Septic Shock – Defined

• Definition
  – Septic shock is defined as a subset of sepsis in which underlying circulatory, cellular and metabolic abnormalities are associated with a greater risk of mortality than sepsis alone

• Clinical criteria
  – Hypotension requiring use of vaspressors to maintain MAP ≥65 mmHg and having a serum lactate >2 mmol/L persisting despite adequate fluid resuscitation

How Does SEPSIS-3 Perform in Real Life?
Performance of qSOFA

- Freund compared SIRS, SOFA and qSOFA in 879 ED patients with suspected infection
  - Mortality: qSOFA < 2 = 3%, qSOFA ≥ 2 = 24%
  - AUC qSOFA = 0.80, SOFA = 0.77, SIRS = 0.65
- Raith compared SIRS, SOFA and qSOFA in 184,875 infected ICU patients in Australia & New Zealand from 2000-2015
  - For the 90% of patients with SOFA > 2, 87% were SIRS positive and 54% were qSOFA positive
  - AUC qSOFA = 0.61, SOFA = 0.75, SIRS = 0.59

Performance of qSOFA

- Chen compared qSOFA and CRB-65 for 1641 Chinese ED patients with pneumonia between 01/2012 and 05/2014
  - Mortality AUROC qSOFA = 0.66, CRB-65 = 0.66
  - Mortality by qSOFA score
    - qSOFA 1 = 16.3%
    - qSOFA 2 = 24.4%
    - qSOFA 3 = 48.2%
    - qSOFA 4 = 68.4%
- Wang compared qSOFA, SOFA, MEDS and APACHE II among infected ED patients
  - AUROC for 28-day mortality greatest for MEDS (0.75) compared to SOFA (0.73), APACHE (0.73), qSOFA (0.67)

Conclusions

- Organ dysfunction can be identified as an acute change in total SOFA score ≥ 2 points consequent to the infection.
  - The baseline SOFA score can be assumed to be zero in patients not known to have preexisting organ dysfunction.
- A SOFA score ≥ 2 reflects an overall mortality risk of approximately 10% in a general hospital population with suspected infection. Even patients presenting with modest dysfunction can deteriorate further, emphasizing the seriousness of this condition and the need for prompt and appropriate intervention, if not already being instituted.
Conclusions

• The new SEPSIS-3 definition has important changes from the original sepsis definition
  – Elimination of “severe” sepsis
  – Use of qSOFA for screening outside the ICU
  – Use of SOFA for identifying organ dysfunction as a diagnostic requirement for sepsis
  – For septic shock, requirement for vasopressor requirement and lactic acidosis

• Subsequent studies have shown qSOFA performs as expected, by predicting adverse outcomes among infected patients outside the ICU

Thank you!
WEANING FROM MECHANICAL VENTILATION

DOES THE MODE REALLY MATTER?

Bruce Bray, RRT, RCP
Division Director
Departments of Respiratory Care, Emory ECMO Center,
EKG, Pulmonary & Blood Gas Laboratories
Emory University Hospital
Emory University Orthopaedics and Spine Hospital
Emory Rehabilitation Hospital

Bruce.bray@emoryhealthcare.org

No conflicts with this presentation
Mechanical Ventilation and Weaning

- **Mechanical ventilation** is a life-supporting modality that is used in a significant proportion of patients in ICUs. Most patients are extubated quite readily. However, as many as 20% will fail their first attempt at weaning and more than 40% of the total duration of MV is spent in the weaning process.[1,2]

Modern electronic ventilators possess a myriad of Modes to choose from:

- **From Traditional**
  - Assist Control, SIMV, PVC, APRV,
  - Spontaneous with Pressure Support Ventilation

- **to Newer Dual Modes**
  - Adaptive Support Ventilation (ASV),
  - Pressure Regulated Volume Control (PRVC)

**Assist Control Ventilation - A/C**

**AKA-Synchronous Control Mechanical Ventilation - (S)CMV**

- **Characteristics:** The CONTROL Factor
  - Set volume with every breath
  - Set minimum rate with ability for patient assist to increase total rate
    - Set flow rate
    - Set flow pattern
A/C
(S)CMV

- **Pros:** Offers full ventilatory support with control of Vt, rate, flow pattern and flow rate (ARDS friendly)
- **Con:** No variability in the above parameters which can cause P-V asynchrony, patient discomfort, hyperventilation, hyperinflation, muscle atrophy

Synchronous Intermittent Mechanical Ventilation - SIMV

**Characteristics:**
- Set ventilator rate - additional patient initiated efforts are spontaneous
- Set ventilator volumes – additional patient initiated breaths with/without Pressure Support Ventilation (to augment volume and/or decrease WOB).
- Strategy is to decrease SIMV rate to allow patient to increase spontaneous rate and volume.

SIMV

- **Pros:** Guarantees a certain number of ventilator breaths. Mandatory breaths are synchronized to coincide with spontaneous respirations.
- **Con:** Increased WOBI and a tendency to reduce cardiac output, which may prolong ventilator dependency.[1]
Adaptive Support Ventilation - ASV

Characteristics:

- Tidal Volume set to IBW
- Rate, I:E, Insp. Time and Exp. Time established through measuring respiratory mechanics.
- All Ventilator Tidal volumes use Pressure Control with a Volume Target
- All Spontaneous volumes use Pressure Support with a Volume Target
- Ventilator rate decreases as Spontaneous rate increases

Do the Newer Dual Modes offer clinical benefit over Traditional Modes?

- ASV is based on the minimal WOB concept, which suggests that the patient will breathe at a Tidal Volume and Respiratory frequency that minimizes the elastic and resistive loads while maintaining oxygenation and acid base balance.[2]

Newer Techniques to Reduce WOBi and/or Patient-Ventilator asynchrony

Proportional Assist Ventilation (PAV)
Neurally Adjusted Ventilatory Assist (NAVA)

- Studies have shown a decrease in P-V asynchrony with PAV and NAVA[2]
- PAV allows for distributing work % using PSV
- NAVA tailors the level of assistance to electromyographic activity of the diaphragm
Do the Newer Dual Modes offer clinical benefit over Traditional Modes?

- Decreased WOBi may be due to a more sensitive and responsive patient trigger (such as Flow Trigger vs Pressure Trigger)
- Targeted Tidal Volumes set to IBW
- Tidal Volumes also monitored in cc/Kg IBW allowing clinician to keep volumes <8cc/Kg or 4-6cc/Kg for ARDS patients.
- Variable Inspiratory Flow to meet pt. demands

Do the Newer Dual Modes offer clinical benefit over Traditional Modes?

- Newer modes offer “Lung Protective Strategies” but appropriate clinician input is necessary for patient to realize protection against Barotrauma, Volutrauma, Patient-Ventilator asynchrony and increased WOBi.

Newer modes can help incorporate Lung Protective Strategies, but have not demonstrated superiority to Sedation Vacation, Daily Weaning Assessment and Standard Breathing Trial.

- Two large multicenter studies have demonstrated the MV can be discontinued abruptly in approximately 75% of mechanically ventilated patients whose underlying cause of respiratory failure has either improved or resolved.[7,8]
- Several studies have shown that a direct method of assessing readiness to maintain spontaneous breathing is simply to initiate a trial of unassisted breathing.[7,8,9,10,11]
Protocol driven practice sets the Standard

- Evidence-based practice now supports early attempts at weaning in a protocol-driven fashion.\(^{[8,12,13,14]}\)
- About 70-80% of patients who require MV for respiratory failure will be extubated after a trial of spontaneous breathing trial once the precipitating process has been corrected.\(^{[15]}\)

Respiratory Therapist Driven Protocol AKA Ely’s TDP

- Implementation of a validated weaning strategy is feasible as a Respiratory Therapist Driven Protocol without daily supervision from a weaning physician or team. RCPs can appropriately perform and interpret Daily Screen data more than 95% of the time…\(^{[16]}\)

Consistency and a Standard Approach are keys to decrease time to extubation

These three steps have made a positive difference at EUH:

- A daily Sedation Awakening Trial
- A Daily Weaning Assessment (or Daily Screening)
- A Spontaneous Breathing Trial
In Summary - Modes

• Newer modes offer methods to “ventilate” patients in a safer and more comfortable fashion.

• However using smaller Vt, limiting Plateau Pressures to <30 cmH2O, and use of PEEP related to FiO2 has demonstrated lower incidence of Lung Injury.

In Summary - Wean to Extubation

• After an extensive review of modes, methods, practices, and protocols;

  A standardized approach towards a Spontaneous Breathing Trial is the most efficient method to extubation in 76-81% of ventilated patients.

References

References


Update on Sedation: Focus on Prevention of Post Intensive Care Syndrome

Stacey L. Campbell, PharmD, MPH, BCPS
Clinical Pharmacy Specialist, Medical ICU
Emory University Hospital
stacey.Campbell@emoryhealthcare.org
No conflicts of interest to disclose

Objectives

• Review risk factors and proposed mechanism of transition from acute to chronic post-ICU pain
• Discuss use of nonopioid analgesics as adjunctive therapy to manage ICU pain
• Review literature related to use of dexmedetomidine and ketamine as potential or alternative sedative options

Definition of Post Intensive Care Syndrome (PICS)

New or worsening impairments in physical, cognitive, or mental health status arising after critical illness and persisting beyond acute care hospitalization
Sedative Use and PICS

- PTSD more likely with sedative-induced delusional memories
- Adverse mental health effects of sedatives persist for months after hospital discharge
- Reducing sedative drug exposure may improve cognitive function

Strategies for Managing Pain and Agitation

- We suggest that analgesia-first sedation be used in mechanically ventilated adult ICU patients
- We suggest that sedation strategies using nonbenzodiazepine sedatives may be preferred over sedation with benzodiazepines

Acute to Chronic Pain Transition

- Activated Nociceptive Fibers
- Sensitized Nociceptive Fibers
- CNS Neuroplasticity
Risk Factors

• ICU length of stay
• Shorter time in the hospital
• Prolonged sedation
• Lack of treatment of acute pain
• Genetic and patient related predisposition
• Psychosocial factors
• Uncontrolled pain, pain of high intensity, and pain of longer duration

Medication Management to Avoid Withdrawal

• N-methyl-D-Aspartate (NMDA) receptor antagonists
  – Ketamine
  – Methadone
• Alpha-2 agonists
  – Dexmedetomidine
  – Clonidine
• Multimodal analgesia
Clonidine significantly decreased hemodynamic, metabolic, and respiratory demands, induced mild sedation and facilitated patient cooperation with the ventilator.
Multimodal Analgesic Techniques

- Nonopioid analgesics
  - Acetaminophen
  - NSAIDS
- Anticonvulsants

Summary

- Providing sufficient analgesia to ICU patients is essential to promote comfort
- Large doses of opioids may increase risk of opioid dependence and withdrawal
- NMDA receptor antagonists and/or alpha-2 agonists may be considered as adjunctive agents to facilitate opioid and sedative weaning
- Multimodal analgesia in conjunction with slow weaning of opiates and sedatives may help with recovery
Lung-Protective Mechanical Ventilation:
State of the ART 2017

Jesús Villar, MD, PhD, FCCM
CIBER de Enfermedades Respiratorias, Instituto de Salud Carlos III, Madrid, Spain
Research Unit, Hospital Universitario Dr. Negrín, Las Palmas, Spain

Hickling et al (ICM 1990, 16:372)
- 50 ARDS patients
- Hospital mortality: actual 16%, predicted 40%
- SIMV, volume targeted
- PIP <40 cmH₂O
- VT as low as 5 mL/kg
- PaCO₂ averaged about 60 mmHg
- PEEP 9 ± 6 cmH₂O, FIO₂ ≤ 0.60

Mechanical Ventilation

- Biochemical Injury
- Biophysical Injury
- Distal Organs Affected
- MSOF

Slutsky, Tremblay (AJRCCM 1998;157:1721)
ARDSnet: Improved Survival with Lower $V_T$

A $V_T$ of 6 mL/Kg PBW results in a lower mortality than a $V_T$ of 12 mL/Kg PBW (31% vs. 39.8%, p<0.01).


SCALING OF THE LUNG IN MAMMALS

Lung Volume = 6.3% BW
Tidal Volume = 6.3 ml/kg

Adapted from Tenney & Remmers, Nature 1963;197:54-6

Plateau Pressure and $V_T$

- End-inspiratory overdistension: primary cause of VILI
- Transpulmonary pressure: best indicator of overdistension
  \[ TPP = P_{plat} - P_{pleural} \]
- The best clinical indicator of TPP is plateau pressure not just VT.
ALVEOLI: FiO₂ and PEEP Table

<table>
<thead>
<tr>
<th>FiO₂</th>
<th>Low PEEP</th>
<th>High PEEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3</td>
<td>5 8</td>
<td>5 8</td>
</tr>
<tr>
<td>0.4</td>
<td>10 8</td>
<td>10 8</td>
</tr>
<tr>
<td>0.5</td>
<td>10 10</td>
<td>12 12</td>
</tr>
<tr>
<td>0.6</td>
<td>10 10</td>
<td>14 14</td>
</tr>
<tr>
<td>0.7</td>
<td>10 12</td>
<td>14 14</td>
</tr>
<tr>
<td>0.8</td>
<td>8 10</td>
<td>12 14</td>
</tr>
<tr>
<td>0.9</td>
<td>8 10</td>
<td>14 16</td>
</tr>
<tr>
<td>1.0</td>
<td>5 8</td>
<td>5 8</td>
</tr>
</tbody>
</table>

- Lack of physiological basis!
- Based in surveys of clinicians' practice!

End-Expiratory Transpulmonary Pressure

- Normal Spontaneous breathing:
  - about 1-2 cmH₂O end-expiratory transpulmonary pressure (TPP) maintains alveoli open.

\[ TPP = \text{PEEP} - \text{Ppl} \]

1 cmH₂O = 0 cmH₂O – (-1 cmH₂O)

- A negative end-expiratory TPP results in alveolar collapse at end exhalation.
End-Expiratory Transpulmonary Pressure

- End-expiratory esophageal pressure (surrogate for pleural pressure) used to determine the correct setting of PEEP.

\[
TPP = PEEP - Ppl
\]

\[-3 \text{ cmH}_2\text{O} = 5 \text{ cmH}_2\text{O} - 8 \text{ cmH}_2\text{O}\]

\[
TPP = PEEP - Ppl
\]

\[2 \text{ cmH}_2\text{O} = 10 \text{ cmH}_2\text{O} - 8 \text{ cmH}_2\text{O}\]

28-d mortality: 17% vs. 39%, \( p=0.055 \) (\( p<0.001 \), adjusted)

Open Lung Approach for ARDS

- N = 200 persistent ARDS (PaO\(_2\)/FiO\(_2\)≤300 on PEEP≥10).
- 99 OLA vs. 101 ARDSnet.
- OLA was associated with a trend for
  - lower 60-day mortality: 29% vs. 33%
  - ICU mortality: 25% vs 30%
  - and greater VFDs

- Multi-regression analysis of 9 RCT on ARDS: Variable Vₜ and Variable PEEP.
- VT not the primary variable associated with mortality.
- Plateau pressure not the primary variable associated with mortality.
- PEEP not the primary variable associated with mortality.
- Driving Pressure (DP) on 1st day of randomization: the primary variable associated with mortality!!!

\[ \text{DP} = \text{Plateau Pressure} - \text{PEEP} \]


A Quantile Analysis of Plateau and Driving Pressures: Effects on Mortality in Patients With Acute Respiratory Distress Syndrome Receiving Lung-Protective Ventilation

- Jesús Villas, MD, PhD, FCCM, GA, Carmen Martín-Rodriguez, MD, Ana M. Domínguez-Berrio, MD, Lorenz Fernandez, MD, Carlos Fernández, MD, PhD, Juan A. Solé, MD, PhD, Ana M. Oliva-Lara, MD, Elena Gilabert-Higueras, MD, PhD, Laura Negredo, MD, PhD, Alfredo Añó, MD, PhD, Domingo Caramelo, MD, PhD, Mónica Fernández, MD, PhD, and Javier Martínez, MD

(Crit Care Med 2017; XX:00–00)
Ventilator-related causes of lung injury: the mechanical power
Gattinoni et al (ICM 2016, 42:1567-75)

- Reanalysis of Chiumello data (AJRCCM 2008;178:346): 30 pts normal lungs, 50 pts ARDS
- Defining the impact of various ventilator variables on the development of VILI - increased mechanical power of the ventilator applied to the lungs.

\[
\text{Power}_{iH} = \text{RR} \cdot \left( \frac{\Delta V^2}{2} \cdot \frac{1}{E_{\text{air}}} + \text{RR} \cdot \frac{(1 + f \cdot P)}{60 - f \cdot E} \cdot \text{Pipel} \right) + \Delta V \cdot \text{PEEP}
\]

- RR, Vₜ, Flow, I:E, PEEP, Pplat, PIP, Respiratory System Elastance and Airways Resistance, all affect the development of VILI in normal and ARDS lungs!!!!

Lung Protective Ventilation 2017

- Driving Pressure <19 cmH₂O, LOWER better!
- \( P_{\text{PLAT}} < 29 \text{ cmH}_2\text{O}, \text{ LOWER better!} \)
- \( P_{\text{PLAT}} \geq 29 \text{ cmH}_2\text{O}, \; V_T \; 4.5 \text{ ml/kg} \)
- \( P_{\text{PLAT}} \geq 25 \text{ cmH}_2\text{O}, \; V_T \; 6 \text{ ml/kg} \)
- \( P_{\text{PLAT}} \leq 25 \text{ cmH}_2\text{O}, \; V_T \; 6-8 \text{ ml/kg} \)
- RR limit based on auto-PEEP, LOWER better?
- ARDS: PEEP set by Best Compliance/positive TPP
  - moderate/severe ARDS: PEEP 12 to 20 cmH₂O
  - mild ARDS: PEEP 10 to 15 cmH₂O
- Normal lungs: 5 to 10 cmH₂O
ANTIMICROBIAL STEWARDSHIP IN THE ICU

Sheena Kandiah MD MPH
Assistant Professor of Medicine
Division of Infectious Diseases
Emory University School of Medicine
Medical Director, Antimicrobial Stewardship
Grady Health System
sheetal.kandiah@emory.edu
No conflicts of interest to disclose

OBJECTIVES

• To discuss the role of antimicrobial stewardship in the ICU
• To illustrate how rapid diagnostics can be leveraged to decrease antibiotic use and improve clinical outcomes in the ICU
• To review data on the use of procalcitonin to decrease antibiotic use and improve clinical outcomes in the ICU

OUTLINE

• Antimicrobial stewardship in the ICU
• Rapid diagnostics
• Procalcitonin
National Action Plan
March 2015 (CARB)

• Reduce inpatient use of antibiotics by 20% by 2020
• Reduce outpatient use of antibiotics by 50% by 2020
• 95% participation in the CDC AU and AUR module by 2020
• Monitoring ambulatory usage of antibiotics
• Establishment of quality measures that assess excessive or inappropriate antibiotic use in PQRS
• Patient education - social/behavioral factors that drive demand for and inappropriate prescribing of antibiotics

ICU – Antibiotic Stewardship

• 30-60% of antibiotic utilization are unnecessary, inappropriate, or suboptimal
• Stewardship activities in the ICU
  • rapid identification of patients with bacterial infections
  • better empirical treatment selection,
  • using pharmacokinetic-pharmacodynamic (PK-PD) characteristics to optimize antibiotic dosing and administration modalities
  • de-escalation once culture results become available
  • shortening therapy duration
  • reducing the numbers of patients treated unnecessarily

Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America

<table>
<thead>
<tr>
<th>Program</th>
<th>Guideline practice</th>
<th>Recommendation</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal care: ASP</td>
<td>General practitioners</td>
<td>Low quality evidence</td>
<td></td>
</tr>
<tr>
<td>Discharge education</td>
<td>Weak recommendation</td>
<td>Moderate evidence</td>
<td></td>
</tr>
<tr>
<td>Antimicrobial stewardship</td>
<td>Weak recommendation</td>
<td>Moderate evidence</td>
<td></td>
</tr>
<tr>
<td>Stewardship guidelines</td>
<td>Weak recommendation</td>
<td>Low quality evidence</td>
<td></td>
</tr>
<tr>
<td>Stewardship surveillance</td>
<td>Strong recommendation</td>
<td>Good quality evidence</td>
<td></td>
</tr>
<tr>
<td>CIP targeted interventions</td>
<td>Strong recommendation</td>
<td>Good quality evidence</td>
<td></td>
</tr>
<tr>
<td>Precautions and avoidance of anti-aspergillus</td>
<td>Weak recommendation</td>
<td>Moderate evidence</td>
<td></td>
</tr>
<tr>
<td>QRB systems</td>
<td>Weak recommendation</td>
<td>Moderate evidence</td>
<td></td>
</tr>
</tbody>
</table>

### Impact of Regular Collaboration Between Infectious Diseases and Critical Care Practitioners on Antimicrobial Utilization and Patient Outcome*

**Kamal R. Rimawi, MD et al.**

*Crit Care Med. 2013 Sep;41(9):2099-107*

- 3-month retrospective chart review
- 3-month prospective intervention – ID fellow
- 246 charts were reviewed
  - Guideline compliance
  - Demographics
  - Microbiologic results
  - Severity scores
  - Documented diagnosis
- 24 bed MICU – tertiary care center – north carolina

#### Outcome Statistical significance p-value

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Statistical significance</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days on the ventilator</td>
<td>Decreased</td>
<td>0.0053</td>
</tr>
<tr>
<td>LOS</td>
<td>Decreased</td>
<td>0.0188</td>
</tr>
<tr>
<td>All cause mortality</td>
<td>Decreased (MICU)</td>
<td>0.0167</td>
</tr>
<tr>
<td>All cause mortality</td>
<td>Decreased (hospital)</td>
<td></td>
</tr>
<tr>
<td>DOT</td>
<td>Decreased (except cephalosporins, tetracyclines and aminoglycosides)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>C. Diff</td>
<td>Increased</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Page 53
RAPID DIAGNOSTICS

- MALDI – TOF (Mass spectrometry)
- FilmArray – PCR based
- FISH – Fluorescence In situ hybridization

Integrating rapid diagnostics and antimicrobial stewardship improves outcomes in patients with antibiotic resistant Gram-negative bacteremia

- Pre and a post-intervention study
- Gram negative bacteremia
  - Time to positivity
  - Time to susceptibility
  - Time to optimal therapy
  - Hospital costs
  - Mortality
  - Length of stay
Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults
S Jain et. al., N Engl J Med. 2015 Dec 10;373(24):2382

• 3 Chicago hospitals
• 2 Nashville Hospitals
• 2 years: 2010-2012
• 2,320 patients with radiographic evidence of pneumonia
Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults
S Jain et. al., N Engl J Med. 2015 Dec 10;373(24):2382

Limitations
• Age>65 less likely to be enrolled
• Ventilated less likely to be enrolled
• No asymptomatic controls
• Sensitivity and specificity of tests not great
• Subjective radiographic results

Effectiveness and safety of procalcitonin evaluation for reducing mortality in adults with sepsis, severe sepsis or septic shock (Review)
• Multiple studies demonstrating a reduction in antibiotic use for patients with LRTI
• Emerging data for other conditions such as meningitis and COPD exacerbations
• Established data about use of antibiotic reduction in the LRTI group which historically showed non-inferiority with regards to pneumonia (PRORATA)
• Use in sepsis reviewed by Cochrane in 2017, but did NOT include SAPS study

Cochrane Database Syst Rev. 2017 Jan
### Cochrane review

- 486 articles
- 12 articles chosen
- 10 studies chosen
- 59 variables

### Effectiveness and safety of procalcitonin evaluation for reducing mortality in adults with sepsis, severe sepsis or septic shock

<table>
<thead>
<tr>
<th>Primary Outcome</th>
<th>Standard vs PCT</th>
<th>Relative effect (95% CI)</th>
<th>Number of participants (studies)</th>
<th>Quality of the evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality at longest follow up</td>
<td>Std: 261 per 1000</td>
<td>RR 0.81 (0.65 to 1.01)</td>
<td>1156 (10 RCT)</td>
<td>LOW</td>
</tr>
<tr>
<td>Mortality at 28 days</td>
<td>Std: 250 per 1000</td>
<td>RR 0.89 (0.61 to 1.21)</td>
<td>316 (9 RCT)</td>
<td>LOW</td>
</tr>
<tr>
<td>Mortality at ICU discharge</td>
<td>Std: 57 per 1000</td>
<td>RR 1.25 (0.50 to 2.91)</td>
<td>516 (3 RCT)</td>
<td>LOW</td>
</tr>
<tr>
<td>Mortality at hospital discharge</td>
<td>Std: 189 per 1000</td>
<td>RR 0.88 (0.75 to 1.27)</td>
<td>805 (7 RCTs)</td>
<td>MODERATE</td>
</tr>
<tr>
<td>Time receiving anti microbial therapy (days)</td>
<td>Std: 8.09 days</td>
<td>RR 0.88 (0.61 to 1.21)</td>
<td>313 (4 RCT)</td>
<td>VERY LOW</td>
</tr>
</tbody>
</table>

### Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial

- Prospective, multicentre, randomised, controlled, open-label intervention trial
- 15 hospitals in the Netherlands
- ICU Age >18
- Antibiotic 1st dose >24 hours for presumed or proven infection
- PCT guided antibiotic discontinuation
- Standard of care antibiotic discontinuation
- PCT group (n=761)
  - Guidance provided
  - PCT decrease by 80% or < 0.2
  - Standard of care (n=785)
  - Antibiotic protocols

- Primary endpoint
- Antibiotic DDD
- Duration of antibiotic treatment
- Analysis
  - Intention to treat
  - Mortality
- Safety endpoints
- Reinstitution of antibiotics
- Recurrent inflammation measured by CRP (measured in population adhering to rules)
Table 3: Laboratory and hematological parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Procalcitonin-guided group</th>
<th>Standard of care group</th>
<th>Difference (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature (°C)</td>
<td>37.3 (36.5)</td>
<td>37.0 (36.5)</td>
<td>-0.3 (p=0.008)</td>
</tr>
<tr>
<td>Time to resolution of fever (days)</td>
<td>3.5 (3.5)</td>
<td>5.0 (5.0)</td>
<td>-1.5 (p=0.008)</td>
</tr>
<tr>
<td>Time to defervescence (days)</td>
<td>3.0 (3.0)</td>
<td>5.0 (5.0)</td>
<td>-2.0 (p=0.008)</td>
</tr>
<tr>
<td>Time to normalization of leucocyte count (× 10^9/L)</td>
<td>5.5 (5.5)</td>
<td>6.0 (6.0)</td>
<td>-0.5 (p=0.008)</td>
</tr>
<tr>
<td>Time to normalization of platelet count (× 10^4/L)</td>
<td>5.0 (5.0)</td>
<td>6.0 (6.0)</td>
<td>-1.0 (p=0.008)</td>
</tr>
<tr>
<td>Mean platelet count (× 10^9/L)</td>
<td>200 (180)</td>
<td>250 (250)</td>
<td>50 (p=0.008)</td>
</tr>
<tr>
<td>Mean white blood count (× 10^9/L)</td>
<td>7.5 (7.5)</td>
<td>8.0 (8.0)</td>
<td>-0.5 (p=0.008)</td>
</tr>
<tr>
<td>Mean haemoglobin (g/L)</td>
<td>130 (130)</td>
<td>140 (140)</td>
<td>-10 (p=0.008)</td>
</tr>
<tr>
<td>Mean PCV (%)</td>
<td>37 (37)</td>
<td>38 (38)</td>
<td>-1 (p=0.008)</td>
</tr>
</tbody>
</table>

Figure 2: Kaplan-Meier plot for probability of survival from random assignment to day 365, in the modified intention-to-treat analysis.

Kinetic profiles of different biomarkers of bacterial infection. Adapted from Lancet Infec Dis 2016 Jul; 16(7):819-27.
**PROCALCITONIN**

<table>
<thead>
<tr>
<th>FALSE HIGH PCT</th>
<th>FALSE LOW PCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>• major trauma</td>
<td>• Infection contained in a tissue compartment</td>
</tr>
<tr>
<td>• Surgery</td>
<td>• 24-48 hour lag time in infection onset to peak PCT release</td>
</tr>
<tr>
<td>• ARDS</td>
<td>• Burns</td>
</tr>
<tr>
<td>• Multiorgan failure</td>
<td>• Heat stroke</td>
</tr>
<tr>
<td>• Post-transplantation rejection</td>
<td>• ??? HIV</td>
</tr>
<tr>
<td>• Cardiogenic shock</td>
<td>• ??? Neurocritical care</td>
</tr>
</tbody>
</table>

**TAKE HOME**

• A collaborative approach to reducing antibiotic use is instrumental in reducing poor outcomes related to antibiotic use
• Antimicrobial stewardship has been shown to decrease mortality, length of stay and antibiotic utilization in the ICU
• Rapid diagnostics plays a significant role in decreasing antibiotic utilization in the ICU population IF used correctly
• There is increasing evidence that procalcitonin decreases mortality and improves antibiotic utilization in the ICU
• CAVEAT 1: Must be studied much more in special populations
• CAVEAT 2: Does not replace clinical judgement
• CAVEAT 3: Needs to be used appropriately and interpreted correctly
Nutrition Risk Scores in the Critically Ill Patient

Ashley DePriest, MS, RD, LD, CNSC
adepriestrd@gmail.com
No conflicts of interest to disclose

Objectives

• Describe the process of assessing nutrition risk in the critically ill.
• Identify those critically ill patients with the highest nutrition risk score.
• Describe expected outcomes with medical nutrition therapy for high nutrition risk patients vs low nutrition risk patients.

Previous Practices

• Early screening
• Prealbumin, albumin
• Anthropometrics (BMI?)
Effects of Nutrition Intervention

- Limited and conflicting data
- Obesity Paradox??

NUTRITION RISK!

“Two prospective nonrandomized studies show that patients at high nutrition risk are more likely to benefit from early EN with improved outcome (reduced nosocomial infection, total complications, and mortality) than patients at low nutrition risk.”

Obesity Paradox, Explained

- When considering nutrition risk and not just BMI, it all makes sense!
Assessing Nutrition Risk

How to use this information
• Still want early EN, when medically feasible
• Dosing may change based on a number of factors:
  – Severity score
  – Projected LOS
  – Prognosis

Low Nutrition Risk Score
• Have lower need for full feeding
• Must consider predicted LOS, prognosis for improvements
• Does not mean purposely withholding feeds
ARDS/ALI, Low Nutrition Risk

- Consider trophic feeds over the 1st week
- Again considering expected LOS, prognosis for improvement

High Nutrition Risk

- Patients require as close to full EN as soon as possible.
- Volume based, rather than hourly rate feeding has shown improvements in outcomes
- Goal is at least 80% of estimated needs
- Most ICUs are around 60-70%

Conclusion

- Feed SOMETHING early when the gut works
- Utilize nutrition professionals (RDs!) for nutrition assessments
  - Malnutrition
  - Nutrition Risk Scoring
- Higher risk = more aggressive
  - Volume based feeding?
- Lower risk = less aggressive
KETAMINE FOR ICU SEDATION
A solo pro and con debate
Prem Kandiah, MD
Assistant Professor
Neurocritical Care Fellowship Director.
Co-appt. 5E Surgical/Transplant Critical Care
Emory University Hospital
prem.kandiah@emoryhealthcare.org
No conflicts of interest to disclose

PRO DEBATE
Ketamine is a useful and safe adjunct for continuous sedation in the ICU

DESI RABLE FEATURES OF KETAMINE SEDATION
• Consistency with providing analgxo-sedation (A1 sedation)
• Good Hemodynamic profile - maintain BP
• Bronchodilation
• Minimal respiratory depression at lower doses
• Protective for Depression & anti-suicidal effect
• Anti-seizure, Anti-emetic & Anti-shivering effect
• Safe in head injury
• Tolerable psychotomimetic effects
KETAMINE ANALGO-SEDATION

Analytic postulated to be produced by:

- binding opioid receptors including mu (μ), delta (δ), and kappa (κ).
- upregulating muscarinic acetylcholine receptors in the central nervous system
- sodium channels and voltage sensitive calcium channels leading to local anesthetics and gabapentin-like effect

Seron E et al. Anesth Analg 2001
Krupitsky EM et al. Neuropsychopharmacology 2001
KETAMINE ANALGOSEDATION

- Provides an alternative to benzodiazepines with no effects of Gaba receptors
- Provides an alternative to Propofol with no effects on lipid metabolism and minimal hemodynamic problems
- Provides more analgesia when compared to Dexmedetomidine

FAVORABLE HEMODYNAMIC PROFILE

- Less hypotension when compared to Propofol
- Absence of bradycardia seen with Dexmedetomidine
- Increased cardiac output in healthy volunteers by 40-50% at blood concentrations of 40-320 ng/ml
- Postulated mechanisms for increased cardiac output:
  - Indirect mechanism by potentiation of catecholamines
  - Positive isotropic effect on human myocyte
BRONCHODILATION

• Mechanism of Bronchodilation:
  • Blocks the re-uptake of norepinephrine into presynaptic sympathetic neurons resulting in sympathomimetic bronchodilatation (ß2).
  • Exerts an anti-cholinergic effect on bronchial smooth muscles by inhibiting vagal outflow.
  • Multiple proposed immunomodulatory effects of ketamine.

KETAMINE IN STATUS ASMATICUS

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>No.</th>
<th>Age</th>
<th>Study Design</th>
<th>Dosage &amp; Routes</th>
<th>Duration</th>
<th>Markers of Improvement</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mathewson HS et al.</td>
<td>42</td>
<td>66</td>
<td>Case report</td>
<td>0.7 mg/kg IV</td>
<td>&lt;1 hour</td>
<td>Clinical, anxiety, muscle tone</td>
<td>Improved</td>
</tr>
<tr>
<td>Pabelick CM et al.</td>
<td>86</td>
<td>1104</td>
<td>Case report</td>
<td>0.5 mg/kg IV</td>
<td>&gt;1 hour</td>
<td>Respiratory, comfort</td>
<td>Improved</td>
</tr>
<tr>
<td>Hirota K et al.</td>
<td>76</td>
<td>266</td>
<td>Case report</td>
<td>0.7 mg/kg IV</td>
<td>&lt;2 hours</td>
<td>Respiratory, comfort</td>
<td>Improved</td>
</tr>
<tr>
<td>Goyal S et al.</td>
<td>17</td>
<td>154</td>
<td>Case report</td>
<td>0.7 mg/kg IV</td>
<td>&gt;2 hours</td>
<td>Respiratory, comfort</td>
<td>Improved</td>
</tr>
</tbody>
</table>

MINIMAL RESPIRATORY DEPRESSION

• Ketamine depresses ventilation but does not reduce the respiratory response to rising levels of carbon dioxide.
• Maintains functional residual capacity and minute ventilation in adults and children.
• Allows for spontaneous breathing trials without contributing to apnea from over sedation.
• Also provides the prospect of maintaining subanesthetic doses through and beyond extubation which minimizes interruption in pain control in especially special scneros.
• Facilitates comfort in addition to bronchodilatory properties in COPD patients who are being extubated to Non-invasive ventilation.
**Efficacy of Ketamine in Bipolar Depression: Systematic Review and Meta-analysis.**

**Authors:**
- PARSIAK, AJAY; MD, MS
- SINGH, BALWINDER; MD, MS
- KHOSH-CHASHM, DAWSON; MD,
- MASCARENHAS, SONIYA


**DOI:** 10.1097/PRA.0000000000000106

---

**From: Efficacy of Intravenous Ketamine for Treatment of Chronic Posttraumatic Stress DisorderA Randomized Clinical Trial (N=44)**


---

**PROTECTIVE FOR DEPRESSION, PTSD & SUICIDAL IDEATION**

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Pts</th>
<th>Mean</th>
<th>SD</th>
<th>Improvement</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>Case Control</td>
<td>50</td>
<td>20</td>
<td>5</td>
<td>30%</td>
<td>0.05</td>
</tr>
<tr>
<td>Study 2</td>
<td>Randomized</td>
<td>40</td>
<td>15</td>
<td>4</td>
<td>25%</td>
<td>0.02</td>
</tr>
<tr>
<td>Study 3</td>
<td>Open Label</td>
<td>30</td>
<td>25</td>
<td>3</td>
<td>40%</td>
<td>0.01</td>
</tr>
</tbody>
</table>

---

**From: The JAMA Network**

**Favorable Outcomes of Intravenous Ketamine for Treatment of Chronic Posttraumatic Stress Disorder: Randomized Clinical Trial (N=44)**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Improvement</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>30%</td>
<td>0.05</td>
</tr>
<tr>
<td>Depression</td>
<td>25%</td>
<td>0.02</td>
</tr>
<tr>
<td>Suicidal Ideation</td>
<td>40%</td>
<td>0.01</td>
</tr>
</tbody>
</table>

---

**From: The JAMA Network**

**Favorable Outcomes of Intravenous Ketamine for Treatment of Chronic Posttraumatic Stress Disorder: Randomized Clinical Trial (N=44)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Outcome</th>
<th>Improvement</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Anxiety</td>
<td>15%</td>
<td>0.15</td>
</tr>
<tr>
<td>Treatment</td>
<td>Depression</td>
<td>30%</td>
<td>0.05</td>
</tr>
<tr>
<td>Treatment</td>
<td>Suicidal Ideation</td>
<td>45%</td>
<td>0.01</td>
</tr>
</tbody>
</table>

---

**Page 68**
KETAMINE IN ALCOHOL WITHDRAWAL?

- One retrospective series of 23 patients given low dose Ketamine as an adjunct to alcohol withdrawal.
- The median change in BZD requirements at 12 and 24 hours post-ketamine initiation were ~40.0 and ~13.3 mg, respectively.
- The mean time to AWS resolution was 5.6 days. There
- One documented adverse reaction of oversedation, requiring dose reduction.

Table 1: Comparison of Post-operative ICP, ICP, MABP and ICP, CI and ICP, CI and ICP, follows and after trauma occurrence.

<table>
<thead>
<tr>
<th>Group</th>
<th>ICP</th>
<th>BP</th>
<th>MABP</th>
<th>CI</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>123</td>
<td>11</td>
<td>105</td>
<td>1.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Group 2</td>
<td>135</td>
<td>12</td>
<td>110</td>
<td>1.7</td>
<td>1.2</td>
</tr>
<tr>
<td>Group 3</td>
<td>123</td>
<td>13</td>
<td>105</td>
<td>1.5</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Wong A et. al. Annals of Pharmacotherapy 2015, Vol. 49(1) 14–19
**CON DEBATE**

Ketamine is a useful and safe adjunct for continuous sedation in the ICU

**UNDESIRABLE QUALITIES OF KETAMINE**

- Emergence Delirium
- Tachycardia
- Myocardial depression
- Intracranial Pressure Elevation
- Sialorrhea
- Laryngospasm
- Inadequate respiratory control

**EMERGENCE DELIRIUM**

- Domino et al. in 1965 described “strange feelings” in 1 in 3 subjects. Patients experienced feelings of floating in space or not being able to feel their bodies.
- Systematic review of 30 ketamine trials, the rate of hallucinations was 7.4% in patients who received the drug compared to 3.7% in controls.
- Rate of Nightmares was 2.4% in those who received ketamine compared to 0.8% in controls.
- 18.2% of patients who received ketamine had pleasant dreams compared to 9.7% of controls.

Domino EF. Taming the ketamine tiger. 1965. Anesthesiology 2010;113:678-84.
Patanwala AE. Journal of Intensive Care Medicine 2015
PSYCHOTOMIMETIC EFFECTS

• Lower doses (< 1 mg/kg by slow infusion) and plasma concentrations (<100 ng/mL) have been associated with schizophrenia-like and dissociative symptoms in healthy volunteers.

• Until a better understanding of how ketamine affects ICU delirium, caution and restraint should be employed with its use in the ICU.

• Patients with a history of psychosis or polysubstance use are at a greater risk of developing behaviors that mimic psychotic reactions.

CJ Morgan, Neuropsychopharmacology, 29 (2004), pp. 208–218
A Stefanovic, J Clin Psychopharmacol, 29 (2009), pp. 124–133

TACHYCARDIA AND TACHYARRHYTHMIA

• Predictably leads to tachycardia, which can be harmful in patients with stenotic heart lesions or coronary artery disease.

• In an animal model, ketamine increased myocardial oxygen consumption by up to 50%. It may also increase the arrhythmogenic potential of epinephrine.

• In multiple small trials, new onset atrial fibrillations was a commonly observed tachyarrhythmia in 2–7% of patients.

Patschke D Prakt Anaesth 1975;10:325-34.
Koehntop DE Anesthesiology 1977;46:83-93

DOES KETAMINE INCREASE ICP?

<table>
<thead>
<tr>
<th></th>
<th>Pre-Ketamine</th>
<th>Post-Ketamine</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICP (mmHg)</td>
<td>10</td>
<td>12</td>
<td>+2</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>70</td>
<td>75</td>
<td>+5</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>60</td>
<td>70</td>
<td>+10</td>
</tr>
</tbody>
</table>

**DOES KETAMINE INCREASE ICP ?**

- **Answer:** It can......especially in non-communicating hydrocephalus and possibly in severe communicating hydrocephalus.
- **Kaul et al. in 1984 reported ICP elevations with Ketamine use in hydrocephalic children.**

**OTHER ADVERSE EFFECT**

- **Salivation & Bronchitis -** very common. Implications with ET tube dislodgement, difficulty with tongue manipulation during reintubation, unknown contribution to VAP risk.
- **Laryngospasm -** Low incidence but has been reported during procedural sedation.
- **Inadequate respiratory control -** Predominantly a problem in patients with ventilator dyssynchrony and ARDS.
- **Ketamine Ulcerative Cystitis -** noted in recreational use. Requires further understanding.

**SUMMARY**

- **Ketamine certainly has desirable effect that will compliment our current limited armamentarium in sedation management.**
- **There remains many unknowns about the long term effects of Ketamine sedation which requires further investigation.**
- **Clinicians using Ketamine at this time for ICU sedation have to be very familiar with the limitations and adverse effects associated with it.**
Objectives

• Identify concerns of ICU providers when consultation of palliative care teams are considered

• Discuss strategies for successful integration of primary and subspecialty palliative care
When the “Dance” is Going Well:

- Sense of accomplishment
- Sense of progress
- Collaborative discussion
- Attainment of mutual goals

When the “Dance” is NOT going Well:

- Lack of clinical progress
- Patient/Family vs. Team in conflict
- Identified unresolved distress
  - Physical, spiritual, psychological or social
- OFTEN revolve around END OF LIFE ISSUES

Five Things Physicians and Patients Should Question

Don’t continue life support for patients at high risk for death or severely impaired functional recovery without offering patients and their families the alternative of care focused entirely on comfort.

Patients and their families often value the avoidance of prolonged dependence on life support. However, many of these patients receive aggressive life-sustaining therapies, in part due to clinicians’ failures to elicit patients’ wishes and goals, and to provide patient-centered recommendations. Routinely engaging high-risk patients and their surrogates in concise end-of-life discussions about the option of Forgoing life-sustaining therapies may promote patients’ and families’ values, improve the quality of dying and reduce family distress and burnout. Care among patients perceive the outcome (life-sustaining therapy, instead palliative care) often inactivity with ongoing disease-focused therapy may be beneficial.

Released January 26, 2014
Team Decision Tree

Patient Likely to Die

Add more consultants?

Yes

No

Should we call Palliative Care? Why? Why Not?

Models for Structuring An ICU-Palliative Care Initiative

Consultative Model

Integrative Model

The Changing Role of Palliative Care in the ICU

Rebecca A. Aslakson, MD, PhD, J. Randall Curtis, MD, MPH, and Judith E. Nelson, MD, JD

Crit Care Med 2014 November ; 42(11): 2418–2428
Key Challenges to Palliative Care Integration

- Timing
- Level of response
- Concern about duplicity
- Concern about "added value"
- Concern about PC will overstep the limits of discussion
- Concerns PC will overstep the limits of discussion

Possible Benefits

- Another set of eyes and ears to assess:
  - Perception of effectiveness?
  - Are key needs met?
  - Communication gaps
- What’s Needed to Dance together Well? Palliative Care-Critical Care
  - Collaborative discussion
  - Willingness to try something new
  - Willingness to allow missteps and try it again
Avoiding Intubation
The role of non-invasive ventilation and high-flow oxygen systems

William Bender MD, MPH
Assistant Professor
Division of Pulmonary, Allergy, Critical Care and Sleep
Emory University School of Medicine
william.bender@emory.edu

I have no financial disclosures

Objectives
• Review the basic principles and physiology of non-invasive ventilation and high flow oxygen systems
• Understand the role both NIV and HF oxygen systems can play in managing acute respiratory failure
• Explore the evidence surrounding the question of utilizing HF oxygen systems instead of NIV with acute respiratory failure
Non-Invasive Ventilation

• The application of positive pressure support to the upper airway via a sealed face-mask or other interface without the need for intubation
  – Continuous positive airway pressure
  – Bi-level modes
• Can be delivered by specifically designed devices to full-service ICU ventilators

Non-Invasive Ventilation

• Associated with a number of benefits
  – Relative decrease in technical difficulty
  – Minimal, if any, use of sedation
  – Avoids complications associated with intubation
  – Decreased morbidity and mortality
  – Decreased cost
High Flow Nasal Cannula

- Initially developed in neonatal medicine
  - Introduced as an alternative to CPAP to treat neonatal distress syndrome
- Recently and increasingly adapted to deliver oxygenated gas to adults
- Systems exist with the ability to deliver adequately heated and humidified gas at flows up to 60L/min


High Flow Nasal Cannula

- Physiological Effects
  - Wash out of anatomical dead space
    - Thoracoabdominal synchrony is better with HFNC
    - Breathing frequency is lower while PaCO₂ and V̇ remain constant
    - Ṁ is lower – less dead space
  - PEEP effect
    - Airway pressure is increased
    - Closed mouth → 1cm H₂O for every 10L/min
    - Adequate to increase lung volume and recruit alveoli

Parke RL, McGuinness SP. Pressures delivered by nasal high-flow oxygen during all phases of the respiratory cycle. Respir Care 2013;58:1621-1624.
High Flow Nasal Cannula

- **Physiological Effects**
  - Consistent FiO₂ delivery
  - Inspiratory flow (VT) varies breath by breath
  - FiO₂ delivery is not consistent with low flow systems
  - **Ritchie et al.**

- **Humidification**
  - Inhaling dry/cold oxygen provokes upper airway dryness potentially impairing mucociliary functions
  - Associations with discomfort, mucosal dryness, aspiration and gastric distention

- **HFNC** reduces discomfort through consistent provision of humidity

Non-Invasive Ventilation Evidence

- **Acute exacerbations of COPD**
  - Plant et al
  - 236 patients - 118 received standard therapy alone and 118 received additional NIV
  - The use of NIV significantly reduced the need for intubation
  - 27% failure in the standard group versus 15% in the NIV group
  - In-hospital mortality was also reduced in the NIV group as was a more rapid improvement in pH, improvement in respiratory rate and duration of breathlessness


Non-Invasive Ventilation Evidence

- **Acute exacerbations of COPD**

Non-Invasive Ventilation Evidence

• Acute exacerbations of COPD

<table>
<thead>
<tr>
<th>Study</th>
<th>Mode of Ventilation</th>
<th>Primary Endpoint</th>
<th>Total</th>
<th>Failure</th>
<th>Mortality</th>
<th>t</th>
<th>Upper Limit of 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>NIV</td>
<td>Mortality</td>
<td>32</td>
<td>12</td>
<td>0</td>
<td>1</td>
<td>0.51</td>
</tr>
<tr>
<td>B</td>
<td>NIV</td>
<td>Mortality</td>
<td>48</td>
<td>16</td>
<td>2</td>
<td>2</td>
<td>0.61</td>
</tr>
<tr>
<td>C</td>
<td>NIV</td>
<td>Mortality</td>
<td>80</td>
<td>24</td>
<td>6</td>
<td>3</td>
<td>0.71</td>
</tr>
<tr>
<td>D</td>
<td>NIV</td>
<td>Mortality</td>
<td>120</td>
<td>36</td>
<td>12</td>
<td>4</td>
<td>0.81</td>
</tr>
</tbody>
</table>

Non-Invasive Ventilation Evidence

• Cardiogenic Pulmonary Edema

<table>
<thead>
<tr>
<th>Study</th>
<th>Ventilation Method</th>
<th>Primary Endpoint</th>
<th>Total</th>
<th>Failure</th>
<th>Mortality</th>
<th>t</th>
<th>Upper Limit of 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>NIV</td>
<td>Mortality</td>
<td>62</td>
<td>12</td>
<td>2</td>
<td>1</td>
<td>0.51</td>
</tr>
<tr>
<td>F</td>
<td>NIV</td>
<td>Mortality</td>
<td>93</td>
<td>18</td>
<td>4</td>
<td>2</td>
<td>0.61</td>
</tr>
<tr>
<td>G</td>
<td>NIV</td>
<td>Mortality</td>
<td>144</td>
<td>36</td>
<td>8</td>
<td>3</td>
<td>0.71</td>
</tr>
<tr>
<td>H</td>
<td>NIV</td>
<td>Mortality</td>
<td>216</td>
<td>54</td>
<td>12</td>
<td>4</td>
<td>0.81</td>
</tr>
</tbody>
</table>

Non-Invasive Ventilation Evidence

• Cardiogenic Pulmonary Edema

<table>
<thead>
<tr>
<th>Study</th>
<th>Ventilation Method</th>
<th>Primary Endpoint</th>
<th>Total</th>
<th>Failure</th>
<th>Mortality</th>
<th>t</th>
<th>Upper Limit of 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>NIV</td>
<td>Mortality</td>
<td>78</td>
<td>15</td>
<td>3</td>
<td>1</td>
<td>0.51</td>
</tr>
<tr>
<td>J</td>
<td>NIV</td>
<td>Mortality</td>
<td>117</td>
<td>23</td>
<td>5</td>
<td>2</td>
<td>0.61</td>
</tr>
<tr>
<td>K</td>
<td>NIV</td>
<td>Mortality</td>
<td>174</td>
<td>34</td>
<td>8</td>
<td>3</td>
<td>0.71</td>
</tr>
<tr>
<td>L</td>
<td>NIV</td>
<td>Mortality</td>
<td>252</td>
<td>46</td>
<td>12</td>
<td>4</td>
<td>0.81</td>
</tr>
</tbody>
</table>
Non-Invasive Ventilation Evidence

- Beneficial effects of NIV not as clear with acute hypoxemic respiratory failure
  - Possibly more likely to fail
  - May worsen outcomes by delaying intubation in those who have failed
  - Can result in an adverse work load on nurses and respiratory therapists

- Parke et al, post-operative cardiac surgery patients with mild to moderate acute hypoxemic respiratory failure
  - HFNC patients less likely to need escalation to NIV and had fewer desaturations than those treated with a standard high flow face mask

- Roca et al, retrospective analysis of lung transplant patients
  - HFNC at the time of admission to the ICU was associated with a decreased risk of intubation

High Flow Nasal Cannula Evidence

- Acute Hypoxemic Respiratory Failure
  - Parke et al
  - Post-operative cardiac surgery patients with mild to moderate acute hypoxemic respiratory failure
  - HFNC patients less likely to need escalation to NIV and had fewer desaturations than those treated with a standard high flow face mask
  - Roca et al
  - Retrospective analysis of lung transplant patients
  - HFNC at the time of admission to the ICU was associated with a decreased risk of intubation
High Flow Nasal Cannula Evidence

• Acute Hypoxemic Respiratory Failure
  – Maggiore et al.
    - Compared HFNO (50 L/min) to oxygen supplied via a Venturi mask, with FiO2 adjusted in both groups in the postextubation setting
    - Both groups had mild oxygenation defects and respiratory distress
      - HFNO achieved:
        - Better oxygenation
        - Lower respiratory rate
        - Improved comfort related to the interface and dryness
        - Lower intubation rate
    - Inclusion of room air with the Venturi mask led to an underestimation of the PaO2/FiO2


High Flow Nasal Cannula Evidence

• Acute Hypoxemic Respiratory Failure
  – FLORALI Trial
    - 310 ICU patients with acute hypoxemic respiratory failure (PaO2 ≤ 300)
    - Examined the rate of endotracheal intubation among three groups
      - High flow oxygen at 50L/min via large bore nasal cannula
      - Standard oxygen therapy
      - Non-invasive ventilation
    - Excluded patients with a history of chronic respiratory disease

High Flow Nasal Cannula Evidence

• Acute Hypoxemic Respiratory Failure
  — FLORALI Trial
    • High-flow oxygen also had a significantly increased number of ventilator free days as well as a reduced 90-day mortality compared with standard oxygen therapy (P=0.046) or NIV (P=0.006)
    • High-flow oxygen was associated with less respiratory discomfort and a reduction in dyspnea as well


• Acute Hypoxemic Respiratory Failure
  — FLORALI Trial
    • The study was underpowered
    • A negative trial – the primary outcome did not differ significantly between groups
    • Patients randomized to the NIV arm actually received NIV for only 8 h/day on the first 2 consecutive days and then received HFNO for the remaining 16 h/day
    • Greater septic shock population in the NIV group

• Prevention of Reintubation
  — Hernandez et al
    • Multicenter randomized clinical trial examining critically ill patients ready for planned extubation with at least 1 high-risk factor for reintubation
      — Age greater than 65 years
      — Acute Physiology and Chronic Health Evaluation II score higher than 12 points on day of extubation
      — BMI greater than 30
      — Inadequate secretions management
      — Difficult or prolonged weaning
      — More than 1 comorbidity
      — Heart failure as primary indication for mechanical ventilation
      — Moderate to severe chronic obstructive pulmonary disease
      — Airway patency problems
    — Prophylactic mechanical ventilation

High Flow Nasal Cannula Evidence

• Prevention of Reintubation
  – Hernandez et al
  • Patients randomized to 24 hours of NIV or HFNC after extubation
  • HFNC was noninferior to NIV for preventing postextubation respiratory failure
    – Incidence of 26.9% versus 39.8%
  • HFNC was noninferior to NIV for preventing reintubation
    – Incidence of 22.8% versus 19.1%
  • Median post-randomization ICU LOS was lower in the HFNC group compared to the NIV group by ~1 day
  • Adverse events were significantly greater in the NIV group although poorly characterized

Summary

• Non-invasive ventilation and high flow oxygen systems both offer robust physiological profiles to assist with the respiratory management of patients
• The use of non-invasive ventilation in COPD exacerbations and cardiogenic pulmonary edema should continue to be utilized given its strong evidence base
• High flow oxygen systems should increasingly be considered for use in the setting of acute hypoxemic respiratory failure as well as in the postextubation setting

Questions?
Post Intensive Care Syndrome

Alex Truong, M.D., M.P.H.
alex.d.truong@emory.edu

No conflicts of interest to disclose

Patient

• 61yo CrossFit athlete with hx of BPH and OA presenting with weakness, cough, sputum production and fever of 101F
• 7.46/40/49/27.6 on BiPAP with 60% supplemental oxygen
• Intubated
• 7.32/57/76/28.6 no AC
22/470/70%/10cmH2O

02/17/2015
ICU course

- Intubated for 9 days
- Sedated on propofol, haldol, and seroquel for almost two weeks.
- Receive 8 PT sessions during hospitalization
  - 7 of which occurred in the ICU
  - First session 6 days after admission
- Bronched 02/17/2015 and 02/23/2015
- Extubated 02/26/2015
- Discharged 03/09/2015

At home...

- Lost >20lbs of muscle
- Could not get up from seated position or manage stairs easily
- Was dependent on 2LNC
- Could not get back to the gym
- Depressed and anxious
- Nightmares

IS THIS NORMAL?
ARDS Interventions

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Benefit</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-volume ventilation</td>
<td>Improves mortality</td>
<td>Potential for derecruitment</td>
</tr>
<tr>
<td></td>
<td>Reduces systemic inflammation</td>
<td>Higher needs for sedation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hemodynamic instability</td>
</tr>
<tr>
<td>Prone positioning</td>
<td>Improves oxygenation</td>
<td>Pressure ulcers</td>
</tr>
<tr>
<td></td>
<td>May improve mortality</td>
<td>ETI dislodgement</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nursing issues</td>
</tr>
<tr>
<td>Paralysis</td>
<td>Improves oxygenation</td>
<td>Risk for ICUAW</td>
</tr>
<tr>
<td></td>
<td>May improve mortality</td>
<td>Higher needs for sedation</td>
</tr>
<tr>
<td>HFOV</td>
<td>Improves oxygenation</td>
<td>Pneumothorax</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ETI dislodgement</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Higher needs for sedation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cardiovascular instability</td>
</tr>
<tr>
<td>Conservative fluid</td>
<td>Improves lung mechanics</td>
<td>Renal failure</td>
</tr>
<tr>
<td>management</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Improves oxygenation</td>
<td>ICUAW</td>
</tr>
<tr>
<td></td>
<td>May improve mortality</td>
<td>Infection risk</td>
</tr>
<tr>
<td>ECMO</td>
<td>May improve mortality</td>
<td>Hemorrhage</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Need for specialty units</td>
</tr>
</tbody>
</table>

Improved ARDS Mortality

And After Discharge?
Significant disability

- 40% of patients with prolonged ICU stays needed assistance with some of the ADLs for at least a year

Common complaints

- Taste-loss
- Poor appetite
- Hair loss
- Nail rigidity
- Puritis
- Sexual dysfunction
- Fatigue and generalized weakness
- Chronic pain

Problems on Follow-up

- Neuromuscular weakness
- Neurocognitive impairment
  - Long and short term memory loss (up to 40% of patient)
- PTSD
  - Mood changes
  - Nightmares
  - Flashbacks
- Anxiety
- Depression
  - Avoiding company and social isolation
Neuromuscular weakness

- 1/3 of patients with ARDS had muscle weakness at hospital discharge
- Greater strength at discharge was associated with improved 5yr survival

Cognitive Impairment

- Cognitive impairment occurred in patients of all ages and across ICU etiologies, though higher in patients with ARDS
  - 70-100% at hospital discharge
  - 46-80% at 1yr
  - 20-47% at 2yrs
  - 20% at 5yrs

Cognitive Impairment

- Unclear if related to critical illness, treatment, or comorbid conditions
  - Not associated w/ severity of illness or age
  - One study found an association with short periods of hypoxia
  - Cohort studies suggest association between onset/duration of delirium and long-term cognitive impairment
What can help?

Outpatient Rehab Programs

- Trended towards improved physical function
- SF-36 Physical Function score trended towards improvement at 8wks and 6 months
- PTSD rates were lower at 8wks but not 6 months
- No changes in anxiety and depression
- *Home-based rehab programs showed no effect

Potential Benefits of Clinics

- Screen for illness
- Access to appropriate health services
- Access to community support
- Feedback and the potential for ICU quality improvements

Crit Care 2011;15:R142
Crit Care Med 2003;31:2456-2461
Post-ICU Clinic

- PRaCTICaL Study
  - RCT of intensive care physical therapy follow-up program to improve long term outcomes in 286 patients.
  - Any ICU patient >18yo and expected to survive their hospitalization
  - RN lead, manual based, self directed, physical rehab program
  - Seen in clinic at 3 months and 9 months after d/c
  - Critical care consultants available and referrals to specialists made

BMJ 2009;339:b3723

PRaCTICaL Results

- Primary outcome was health related quality of life (HRQoL) scores at 12 months
  - No difference noted
- Secondary outcomes included HRQoL at 6 months, incidence of PTSD, anxiety and depression
  - No difference noted
- 17.1% loss to follow-up
- 10-13% mortality
- 37-40% return to work
- Mean cost of $9127 vs. $6161

BMJ 2009;339:b3723

Clinic Intervention

Critical Care 2012, 16:88c
Clinic Intervention

- Patients >16yo who spent >96hrs in the ICU
- Primary outcome was psychological distress in men and women at 14 months after discharge

Results

<table>
<thead>
<tr>
<th>Measure</th>
<th>Follow-up</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTSD</td>
<td>3 months</td>
<td>0.49</td>
</tr>
<tr>
<td>Anxiety</td>
<td>2-3 months</td>
<td>0.26</td>
</tr>
<tr>
<td>Depression</td>
<td>6 months</td>
<td>0.95</td>
</tr>
<tr>
<td>Emotional distress</td>
<td>12 months</td>
<td>0.76</td>
</tr>
</tbody>
</table>

Women may be more susceptible to PTSD, anxiety and depression after critical illness, but may be better helped with post-ICU clinics

Pooled Analysis of Post-ICU Clinics

- Effect on HRQoL
  - No effect up to 12 months follow-up
- Effect on anxiety
  - No effect at 2-3, 6, and 12 months
- Effect on depression
  - No effect at 2-3, 6, and 12 months
- Effect on PTSD
  - Favoring effect at 3-6 months [RR 0.49, (0.26-0.95), p=0.03]
Pooled Analysis of Post-ICU Clinics

- Effect on physical function
  - No effect at 1yr
- Effect on cognition
  - No difference at 2 months
- Effect on return to work
  - No effect at 6 and 12 months

Limitations of current trials

- Heterogeneous interventions
- Heterogeneous follow up
- Dependence on exhausting questionnaires
- Poor study design

Back to the patient...

- Weaned off oxygen after 6 months
- Gained weight
- Regained 80% of strength after 2yrs
- Nightmares stopped after 4-6 months
- Anxiety only improved with addition of SSRI
Questions

• Are we asking the right questions or looking at the right outcomes?
  – Recidivism?
  – Duration of mental illness as oppose to incidence?
• Are we targeting the right patient population?
• Are we timing the interventions appropriately?
• Does the initial pathology matter?
Roundtable Discussion:

Dr. Micah Fisher – Moderator
Panel: W. Jaber, M. Fisher, J Javidfar

Current approach to massive and sub-massive PE
7:30 - 8:00  CONTINENTAL BREAKFAST

8:00 - 8:10  WELCOME AND INTRODUCTION – M. Fisher

8:10 - 9:20  FIRST MORNING SESSION
  • Choosing the Right Hemodynamic Platform: ABG, SV to PAC – B. McLean
  • Steroids for community acquired pneumonia – O. Ioachimescu
  • Update on fluid choices for resuscitation – M. Connor
  • Introducing precision in AKI prevention in the surgical ICU – A. Bihorac

9:20 - 9:30  FIRST MORNING BREAK

9:30 - 10:50  SECOND MORNING SESSION
  • Year in Review - Medical Critical Care – M. Luthra
  • Year in Review - Surgical & Burn Critical Care – R. Williams
  • Year in Review - Neurological Critical Care – J. Ratcliff

10:50 - 11:00  SECOND MORNING BREAK

11:00 - 12:00  DAY 2 PLENARY LECTURE
  ABCDEF – W. Ely

12:00 - 1:00  LUNCH

1:00 - 2:00  BREAKOUT SESSION #1
  • Basics of mechanical ventilation/advanced mechanical ventilation – Bray, Esper
  • ICU Ultrasonography – Mehta, Green, Hunt
  • Mechanical circulatory support and ECMO - Raikhelkar
  • Hemodynamic Monitoring – McLean, Still, O’Buck, Fisher
  • CRRT – Connor, Bihorac
  • TTM - Webb
  • Delirium - Ely

2:00 - 2:10  FIRST AFTERNOON BREAK

2:10 - 3:10  BREAKOUT SESSION #2

3:10 - 3:20  SECOND AFTERNOON BREAK

3:20 - 4:20  BREAKOUT SESSION #3

4:20 - 4:30  Wrap-up and raffle drawing – J. Han
Making a Choice: Minimal to Maximal Hemodynamic Platform

Barbara McLean, MN, RN, CCNS-BC, NP-BC, CCRN, FCCM
Division of Critical Care
Grady Health System
Atlanta, GA
bamclean@mindspring.com

Developing a hemodynamic platform: when the shoe fits....

• Outline your approach to the evaluation of critical patients beginning with the most available, least invasive, most reliable methods possible
• Progress to a higher level when necessary or when the picture does not improve despite therapeutic interventions that you think should have helped

Monitoring Measures

MACRO
• Stroke volume beat to beat average over one minute: Arterial, Pulsatile, Aortic volume, Thoracic Volume
• Echocardiogram
• Bioreactance
• Arterial blood pressure
• Pulmonary artery
• Intracranial arterial
• Central Displacement (PA/SV)
• Temperature change over one minute: PA catheter

MICRO
• SvO2, ScvO2
• indicators of metabolic acidosis
  • lactate
  • Base deficit
  • Anion gap
  • P(a-v)CO2

The endpoint of all monitoring is to evaluate adequate arterial volume and tissue perfusion indicators.
CVP/PaOP: predicting volume load

What do they mean?
• Useful in application of Starling’s Law
• Poor estimate of LVEDV (i.e., preload)
• Not a good correlation with volume-responsiveness
• Reflects relationship of veno-volume and compliance
• Profoundly affected by pulmonary dynamics
• Overpredicts volume when compliance changes

Read more about it

LV based Stroke Volume
measuring ventricular effectiveness

What does it mean?
• Evaluating the ejection properties of the left ventricle as influenced by
  – Preload: load to ventricle before ejection (volume/compliance)
  – Afterload: load resisting after ejection (tension development)
  – Contractility: inherent sliding property of myofibrils
• Multiple methodologies: non shown superior to another
  – Cost
  – Familiarity
  – Minimally invasive vs non-invasive

Stroke Volume (SV) and Stroke Volume Index: This is what we resuscitate

• Stroke Volume
  – Volume of blood that is ejected during systole
  – SV = end diastolic volume (EDV) – end systolic volume (ESV)
    – Normal: 60 to 100 ml/beat
    – Max SV: 120 to 200 ml/beat, depending on size, heredity, and
• Stroke Volume Index
  – Stroke index is defined as the amount of blood ejected per beat indexed to BSA
    – Normal: 25 to 35 ml/m²

Most important function
• Delivery of oxygen to tissues (left heart dynamics)
• Delivery of carbon dioxide to alveoli (right heart dynamics)
• Achieved by maximizing function of both ventricles
Continuous stroke volume monitoring is the gold standard to monitor the response to a fluid challenge (and to inotropic and vasopressor support).

We MUST measure SV.....

<table>
<thead>
<tr>
<th></th>
<th>Uses</th>
<th>Ease of use</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doppler – USCOM</td>
<td>Anywhere</td>
<td>Good</td>
<td>Good</td>
</tr>
<tr>
<td>Doppler (EDM)</td>
<td>OR, ICU</td>
<td>Good</td>
<td>Good</td>
</tr>
<tr>
<td>ECON</td>
<td>OR, ICU</td>
<td>Good</td>
<td>Fair</td>
</tr>
<tr>
<td>Bioimpedance</td>
<td>Anywhere</td>
<td>Good</td>
<td>Fair</td>
</tr>
<tr>
<td>Pulse contour (FloTrac, LiddCo, PICCO)</td>
<td>OR, ICU</td>
<td>minimal invasive</td>
<td>Fair</td>
</tr>
<tr>
<td>NICO</td>
<td>OR, ICU</td>
<td>Difficult</td>
<td>Fair</td>
</tr>
<tr>
<td>PAC</td>
<td>OR, ICU</td>
<td>invasive</td>
<td>Good</td>
</tr>
<tr>
<td>Bioreactance</td>
<td>OR, ICU</td>
<td>Good</td>
<td>Good</td>
</tr>
<tr>
<td>Peripheral pulsative analysis</td>
<td>anywhere</td>
<td>Good</td>
<td>Good</td>
</tr>
</tbody>
</table>

Fluid Challenge

- Fluid into the veins
  - Venous overload
  - Extravasation into extravascular compartment
  - Mobilized to arterial circulation

Stroke Volume monitoring is the only way to assure arterial volume loading.
Fluid Challenge: Have to have a method to measure stroke volume

Fluid Challenge: Aim is to improve SV (and hence CO) by increasing preload (testing the inotropic activity)

Frank-Starling mechanism

Passive leg-raising

What does it mean?
Increase in RV filling induced by passive leg raising does not depend on respiratory changes

A marker for fluid responsiveness in spontaneously breathing patients
- Leg raising will "bolus" the patient without actually giving sustainable volume
  - Needs to be measured in real time with stroke volume response!
    - Esophageal doppler
    - Echocardiogram
    - Arterial based stroke volume
    - Pulsatile stroke volume
    - Stroke volume variation
    - Thoracic volume shifts

Read more about it

Spontaneously breathing patients

Figure 1 The passive leg-raising test consists of measuring the hemodynamic effects of a leg elevation up to 45°

A simple way to perform the postural maneuver is to transfer the patient from the semirecumbent position to the passive leg-raising position by using the automatic motion of the bed.
Is the arterial volume adequate to maintain tissue oxygenation?

Lactate

What does it mean?

- LA levels represent balance between production and clearance
- Increased production (anaerobic glycolysis)
  - Tissue hypoperfusion
  - Tissue dysoxia
  - Tissue dymetabolism
- Reduced metabolism
  - Hepatic and Renal
- May be altered in critical illness
  - Increased glycolytic flux
  - Impaired pyruvate utilization
  - Absence of frank O2 deprivation
- Clearance trend over time
- Best predictor of anaerobiosis and hyperlactic acidemia is critical $P_{O_2}$ of 27 mmHg

BaseExcess or Deficit

What does it mean?

Buffer/Base: A substance that can bind or release $H^+$ ions in solution, thus keeping the pH of the solution relatively constant despite addition of large amounts of acid or base.

- Calculated to reflect anions and cation relationship
- Positive value, excess base, less $H^+$, metabolic acidosis
- Negative value, excess acid, less base, metabolic alkalosis
- Metabolic component of acid-base status
- $PCO_2$ independent
**Anion Gap (AG):**

What does it mean?
- The calculated difference between the positively charged (cations) and negatively charged (anions) electrolytes in the body:
  - AG = Na⁺ less (Cl⁻ + HCO₃⁻)
  - Normal AG = 12 ± 2 (10 – 14)
- Effected by concentration of the excess unmeasured anion (H⁺ metabolic acid) in the serum
- Metabolic acidosis evaluator
- Anion gap must always be calculated to decipher more accurately the complex acid-base disorders in critically ill patients.

**Metabolic acidosis**

- Characterized by fall in plasma HCO₃⁻ & fall in pH & a more negative base deficit
- Causes:

<table>
<thead>
<tr>
<th>Normal Anion Gap</th>
<th>Increased Anion Gap</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Loss of HCO₃⁻</td>
<td>1. Metabolic disorders: Lactic acidosis, DKA, Alcoholic ketoacidosis</td>
</tr>
<tr>
<td>Diarrhoea, CA inhibitors, Listeriosis/maldonancy, Proximal RTA</td>
<td>2. Failure to excrete H⁺</td>
</tr>
<tr>
<td>2. Failure to excrete H⁺</td>
<td>2. Addition of exogenous acids: Salicylate/methanol poisoning</td>
</tr>
<tr>
<td>Distal RTA</td>
<td>3. Addition H⁺</td>
</tr>
<tr>
<td>3. Add H⁺ NH₄Cl infusion</td>
<td>3. Failure to excrete acid: Acute/chronic renal failure</td>
</tr>
</tbody>
</table>

**P (v-a) CO₂**

- Reflects the difference between cellular production (venous) and residual CO₂ after lung clearance (arterial)
- Hypoperfusion initially decreases blood flow but not oxidative phosphorylation
  - Tissue partial carbon dioxide tension (PCO₂) reflects both local metabolism and regional blood flow
  - Normal venous PCO₂: 40-50 mmHg
  - Normal arterial PCO₂: 35-45 mmHg
  - Venous–Arterial should be less than 8 mmHg
- Correlate with respiratory rate to fully evaluate cellular production and ventilation work
**PO₂ and PCO₂ in Blood**

Central venous oxyhemoglobin
- Reflects Regional oxygen utilization (upper extremities and cerebral use)
- Depends on DaO₂, oxyhemoglobin dissociation, oxygen demand and mitochondrial function
- Target > 70%

**ScvO₂**

What does it mean?
- Central venous oxyhemoglobin
- Reflects Regional oxygen utilization (upper extremities and cerebral use)
- Depends on DaO₂, oxyhemoglobin dissociation, oxygen demand and mitochondrial function
- Target > 70%

What is the role of the pulmonary artery catheter in the ICU?
- Who knows?
  - Everyone should have one?
  - Nobody should have one?
  - We should use them, but only use the information they provide if it confirms what we already think!!!!
The PAC is a Right Heart Catheter: Never was a left heart catheter

- Important information required to assess adequacy of right ventricular function
  - continuous cardiac output measurements
  - Allows for right heart “volumetric” data
    - RVEDV, RVEF, and RVSV
    - RVSW and RVSWI
  - continuous $S_O_2$ measurements
  - Global oxygen utilization
  - Pulmonary pressures (RV afterload sensitive)

Continuous Cardiac Output

- Newer generation catheter
  - Uses continuous cardiac output measurements without need for bolusing
  - Allows for right heart “volumetric” data
    - RVEDV, RVEF, and RVSV
    - RVSW and RVSWI
  - Also provides continuous $S_O_2$ measurements
    - Reflects the mixing of all venous return volumes including coronary sinus

Read more about it

PvO2 and SvO2

- $S_O_2$ changes rapidly when $DO_2$ altered
- May allow for rapid interventions as patients’ condition changes
- PvO2 below 28 torr and SvO2 below 50% imply severe $O_2$ deficits and must be corrected if survival expected
Continuous $S_vO_2$ Monitoring

- Incorporated into PA catheter
- $S_vO_2$ changes rapidly when DO$_2$ altered
- May allow for rapid interventions as patients' condition changes

Hemodynamic Assessment Parameters

- Static/Venous
  - CVP/PAOP
  - Right Ventricular Function
    - RVEF
    - RVADV
  - PA pressures
- Dynamic/Arterial
  - SV
  - SVV
  - PPV
  - SPV
  - IVC collapse
  - PLR
  - Echo
  - US
- Tissue/Capillary
  - SVo2
  - ScVO2
  - BD
  - AG
  - Lactate
  - $P(v-a)CO_2$

A suggested platform

- Validate arterial volume: choose volume resuscitation or isotope
  - Volume challenge effect on Stroke Volume (index, variability)
  - DPP to Stroke Volume: Frank Starling (index, variability)
  - Arterial or LV based monitoring
- Validate effectiveness of stroke volume manipulation AT THE CELLULAR LEVEL
  - Lactic acid and base deficit
  - Anion gap
  - RV-aSV$_O_2$
- Validate the increasing load on the right heart
  - Pulmonary artery measurements when right heart function is challenged
  - PA pressures reflect RV work
  - RVET/RVEDV reflects true volumerelationships
- Validate the increasing $MV_O2$ in myocardial compromised state
  - $SVO_2$
Read More About It

(Glucocorticoid) Steroids for Community Acquired Pneumonia

Octavian C. Ioachimescu, MD, PhD
Associate Professor of Medicine
Emory University &
Atlanta VA Medical Center
oioachi@emory.edu

Academic Freedom Saves Lives

Disclosures

• Recent research support: Astrazeneca, Pearl Therapeutics and Department of Veterans Affairs

• I served as the Local Site Investigator (LSI) for the Veterans Affairs Cooperative Study CSP-574 (ESCAPE), which investigated the role of Corticosteroids in CAP. Its results and publication are pending, and I will not mention any results of this study, as this is under embargo until publication.

CAP: GC Rx RCTs

Cortisone, an active principle of the adrenal glands, was isolated by Kendall and Reichstein in the late 1940s. In 1949, at the First Clinical ACTH Conference, Honeck “electricly” the meeting with the first report on the effects of cortisone in rheumatoid arthritis [22].


Components of Pneumonia

- Pathogens invade the sterile lower respir. tract
  1. Activation of the innate immune response
  2. Local and systemic inflammation

Present Treatment

- Directed predominantly at:
  ✓ Eradicating the etiologic agent(s)
Pathogens – Antibiotic Rx

**Antibiotics alone are insufficient**

1. 1940-50s introduction: reduction in *acute* mortality
2. In 24 hours: causative bacteria are largely eradicated from tracheal secretions and blood
3. Deaths occur after eradication of bacteria
4. 1950-2010: No additional reduction in *acute* mortality
5. For many patients, death is only delayed

---

What leads to excess mortality?

---

Dysregulated Syst. Inflammation

- In pneumonia of varied etiology:
  - *Bacterial, Viral, Fungal*
- Central pathogenetic process for morbidity and mortality:
  - Short-term [hospital] and
  - Long-term [post-hospitalization]
- **Persistent elevation** in circulation of inflammatory and hemostasis mediators
Systemic Inflammation: HSP admission

Higher IC levels are associated with:
- presence of bilateral pneumonia
- bacteremia
- higher Pneumonia Severity Index (PSI)
- higher APACHE II and MODS scores
- higher risk for treatment failure
- higher risk for ARF (MV) and ARDS
- higher hospital and long-term mortality
- worsen long-term function

Plasma levels at ICU admission [N= 375]

- Systemic inflammation
  - ▲ C-reactive protein, IL-6, IL-8, and matrix metalloproteinase (MMP)1-8
  - Activation of coagulation system
    - ▲ D-dimer, PT, APTT
    - ▼ anticoagulants: protein C and antithrombin
  - Endothelial cell activation
    - ▲ soluble E-selectin, soluble intercellular adhesion molecule-1, and angiopoietin-2 levels
  - Disturbed vascular integrity
    - ▼ angiopeotin-1 [maturation and stability]

Systemic Inflammation: CRP over time

Failure to decrease CRP levels by:
- Day 2 to 4 1,3 and 7 4 is associated with increased ICU 4 or 30 days mortality 1,3
- Day 3 5,6 and 7 6 is independently associated with a higher risk of any treatment failure 5,6

Rate of reduction (slow vs. rapid) is associated with increased mortality

- Severe CAP admitted to ICU (n=191)
  - ▼ CRP reduction preceded ▼ SOFA score
  - Similar CRP at admission
  - Rapid responders
    - D5 CRP < 0.4 of D1 CRP
    - ICU Mort: 4.8%
  - Slow responders
    - D5 CRP > 0.4 of D1 CRP
    - ICU Mort: 17.3%
  - Non responders
    - D7 CRP > 0.8 of D1 CRP
    - ICU Mort: 36.4%

---

**Systemic Inflammation: GenIMS**

- Subjects hospitalized with CAP (n=1890)
  - Abnormal vital signs (SIRS)
    - Fever: 0.8%
    - Tachycardia: 8.7%
    - Tachypnea: 2.3%
- Subjects discharged alive (Analysis cohort) (n=1799): 5%
- Alive at 1 year (n=1402), Dead (n=307) 16.2%

---

**Hospital Admission → 30-90 D Outcome**

- Methods: This is a cohort study of 188 subjects hospitalized with CAP through the emergency departments of 12 US academic and community hospitals.
- D-dimer

---

**References**

Clinical Criteria

- Clinical criteria for systemic inflammation
  - Fever
  - Leukocytosis
  - Tachypnea
  - Tachycardia

Traditional pathophysiological model of pneumonia

Clinical criteria for “Syst. Inflammatory Response Syndrome”

Duration of biologically significant (damaging to the host) systemic inflammation

Clinical ≠ Biological Resolution

Inflammatory cytokine elevation persisted for weeks after resolution of clinical signs of inflammation (SIRS), irrespective of initial severity.

Argument: are they important for lung repair or damaging to the host?


Inflammatory Markers at Hospital Discharge Predict Subsequent Mortality After Pneumonia and Sepsis

Hospital discharge IL-6

AJRCM 2008; 177: 1242-7.

Hospital discharge D-dimer

PloS ONE 2011; 6: 847
Causes of Death over 1 Year

- 60% without pre-existing CV disease

<table>
<thead>
<tr>
<th>Causes of Death over 1 Year</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>92 (31)</td>
</tr>
<tr>
<td>Infection</td>
<td>32 (11)</td>
</tr>
<tr>
<td>Cancer</td>
<td>73 (25)</td>
</tr>
<tr>
<td>Chronic lower respiratory disease</td>
<td>47 (16)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>19 (6)</td>
</tr>
<tr>
<td>Others</td>
<td>33 (11)</td>
</tr>
</tbody>
</table>

1. Cardiovascular causes of death include atherosclerotic cardiovascular disease, acute myocardial infarction, chronic ischemic heart disease, congestive heart failure, and cerebrovascular accident.
2. Infectious causes of death include pneumonia, influenza, and sepsis.


COMMUNITY-ACQUIRED PNEUMONIA

How the updated pathophysiological model may impact the design of GC Rx protocol

- Within the new pathophysiological model, the duration of glucocorticoid treatment directed at achieving clinical resolution should be deemed inadequate.
- A longer duration of glucocorticoid treatment—similar to those for ARDS and Pneumocystis jirovecii pneumonia—would maximize the improvement in morbidity and mortality during and after hospitalization.
GC Rx RCTs over time: 1970-2016

Daily Dose* Duration Effect On Inflammation

Dictated by faulty laboratory model
Directed to clinical resolution
Directed to biological resolution

Systemic Inflammation
Day

1 3 5 7 9 11 13 15 17 19 21

* Methylprednisolone equivalent

Pneumocystis Jiroveci Pneum.

Adjunctive corticosteroids for Pneumocystis jiroveci pneumonia in patients with HIV infection (Review)

The Cochrane Library 2015, Issue 4
CSP #574 Treatment Protocol

<table>
<thead>
<tr>
<th>Day 0</th>
<th>Days 0-7</th>
<th>Days 8-14</th>
<th>Days 15-17</th>
<th>Days 18-20</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>40</td>
<td>20</td>
<td>12</td>
<td>4</td>
</tr>
</tbody>
</table>

**Methylprednisolone (mg/day)**

**Secondary prevention:**
- Infusion (in ICU) to avoid glycemic variability
- Infection surveillance for early identification of NI
- Tapering over 6 days to avoid rebound

Academic Freedom Saves Lives

Prolonged Glucocorticoid Treatment in Patients Hospitalized with Community-acquired Pneumonia

Literature Update
February 2017

Experimental Pneumonia

- GC Rx vs. placebo = significant
  - ▼ circulating and pulmonary IC levels 1-6
  - ▼ histopathological severity score 2,4,6,7
  - ▼ pulmonary bacterial burden 2,6
- Large study – mice *E. coli* pneumonia
  - ▼ risk of death following challenge with both low or high organisms load 1
- Others reported improved outcome
  - ▼ in severe and not mild pneumonia 5,7

References:
1. Intensive Care Med 2007;33:616-77
2. Eur Respir J 2008;31:1527-32
5. Intensive Care Med 2012;38:2063-71
Randomized Trial (N=13)
- CAP – Not severe
  - 7 RCTs (N= 1627)
- CAP - Severe
  - 6 RCTs (N= 390)

Randomized Trials (N=13)
- Results positive for outcome: primary, secondary, none

Duration of Treatment
- 1-7 days (1 had tapering)
- Directed to ≈ clinical resolution
Investigational Medication

- Hydrocortisone 6
- Prednisolone 4
- Methylprednisolone 2
- Dexamethasone 1

<table>
<thead>
<tr>
<th>Name</th>
<th>Hydrocortisone</th>
<th>Prednisolone</th>
<th>Methylprednisolone</th>
<th>Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blum 2015</td>
<td>6</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meijvis 2011</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fernandez 2011</td>
<td>10</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Snijders 2010</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mikami 2007</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mc Hardy 1972</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wagner 1956</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Torres 2015</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nafae 2015</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salby 2011</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>El-Ghamrawy 2006</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confalonieri 2007</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mark 1993</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CAP- GC Rx - Meta-analyses

Corticosteroid Therapy for Patients Hospitalized With Community-Acquired Pneumonia
A Systematic Review and Meta-analysis

Estimation of absolute effect = from the median absolute effect of control groups of included studies
**CAP - not severe: Mortality**

- RR = 1.00 (CI, 0.79 - 1.26); I² = 0%

**CAP – Severe: Mortality**

- RR = 0.39 (CI, 0.20 - 0.77); I² = 0%

**CAP – Severe: Mortality**

- 8 RCTs, RR = 0.46 (CI, 0.28 - 0.77) p = 0.003, I² = 0%
Progression to Mechanical Ventilation

- RR = 0.45 (CI, 0.26 - 0.79); I² = 0%
- Moderate evidence = small No. of events (46)

Moderate evidence = small No. of events (46)

Ann Intern Med. 2015;163:519-528

Progression to ARDS

- Overall vs. pts with severe CAP

Ann Intern Med. 2015;163:519-528

Duration of Hospitalization

- Mean difference, 1.00 day (CI, 1.79 - 0.21); I² = 0%
- High certainty
Complications: Hyperglycemia

- RR, 1.49 (CI, 1.01 - 2.19); I² = 6%
- High certainty

<table>
<thead>
<tr>
<th>Study</th>
<th>Glucocorticoids</th>
<th>Control</th>
<th>Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blum 2015</td>
<td>Hospital</td>
<td>Taper</td>
<td>2.36 (1.30 - 4.30)</td>
</tr>
<tr>
<td>Robinson 2015</td>
<td>Oral</td>
<td>Taper</td>
<td>3.57 (1.92 - 6.64)</td>
</tr>
<tr>
<td>Blanchard 2016</td>
<td>Hospital</td>
<td>Taper</td>
<td>3.54 (1.90 - 6.59)</td>
</tr>
<tr>
<td>Nathan 2016</td>
<td>Hospital</td>
<td>Taper</td>
<td>3.74 (2.14 - 6.52)</td>
</tr>
<tr>
<td>Engemann 2016</td>
<td>Hospital</td>
<td>Taper</td>
<td>3.06 (2.04 - 4.58)</td>
</tr>
<tr>
<td>Total (6 studies)</td>
<td>2.43 (1.36 - 4.38)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Random effects (I²)</td>
<td>6%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Prolonged Glucocorticoid Treatment in Patients Hospitalized with Community-acquired Pneumonia: What to do?

- Hospital Admission
  - Consider Prednisone, 40 mg oral daily for 7d, taper over 6 days [risk/benefit]
  - CRP and D-dimer - Monitor CRP daily
  - Assess ASCVD risk factors > optimize Rx

- Hospital DC
  - CRP, D-dimer - instructions on AI – ASA

- Outpatient
  - RTO in 2-4 weeks > hsCRP, D-dimer - consider Coronary Ca+ scan
  - RTO Q 3 months

1. Blum 2015: Prednisone, 50 mg oral daily for 7d
Does aspirin use prevent acute coronary syndrome in patients with pneumonia: multicenter prospective randomized trial
Fahrettin Ozg, Sule Gu, Mehmet G. Kay, Mehmet Yagc, Ionat Bulut.

Table 1: Baseline characteristics of the study patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group A (n=100)</th>
<th>Group B (n=100)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64.2 ± 14.3</td>
<td>65.5 ± 14.8</td>
<td>0.52</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.2 ± 4.3</td>
<td>26.7 ± 4.8</td>
<td>0.20</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>50/50</td>
<td>50/50</td>
<td>1.00</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>70 pneumonia</td>
<td>70 pneumonia</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Figure 1: Oral treatment for risk prediction

Risk reduction: 8%
Fluid Management in Critically Ill: Choosing Fluids for Acute Resuscitation

2017 Southeastern Critical Care Summit

Michael J. Connor, Jr., MD
Assistant Professor of Medicine – Critical Care Medicine & Nephrology
Emory University School of Medicine
michael.connor@emory.edu @criticalbeansmd

Disclosures
Prior Member: ASN AKI Advisory Group

Prior Advisory Board:
- CR Bard, Inc
- Baxter, Inc - Acute Kidney Injury + CRRT (non-compensated)

Prior member of Clinical Events Adjudication Committee for clinical trials in AKI performed by Cytopherx, Inc & AbbVie, Inc

Co-PI on NIH grant submission to research IAH & AKI

Wife (Emory faculty physician): no conflicts of interest

Objectives

Describe the differences in isotonic crystalloids

Describe studies comparing isotonic crystalloids for acute fluid resuscitation

Understand need to individualize fluid selection
Case

57 yo F with h/o HTN & HLD presents to the ED with altered mental status. Found to have Temp 39.2C, HR 117, SBP 72/35, sats 88% on RA. Coarse crackles in B bases and pyuria noted. CXR with B basilar infiltrates R > L. CR ~ 2 secs, warm throughout with bounding pulses.

Labs reveal: WBC 18.3, Hgb 13, creat 1.7, BUN 27, and lactic acid 5.7.

Question #1

What is the next step in management of this patient’s hemodynamic status?

A. start norepinephrine infusion & titrate to goal MAP > 70
B. give 3L bolus 0.9% NaCl
C. give 1L bolus 5% albumin
D. give plamsalyte-A 30 ml/kg bolus
E. insert central venous line

Phases of Fluid Management

ADQI 12th Consensus Conference. 2013. Available at: www.adqi.org

IV fluids are the most common drug used in the ICU!

**Intravenous Fluid = Drug**

- Proper/correct Fluid
- Dose – amount
- Timing of administration – rate, frequency

<table>
<thead>
<tr>
<th>EHC IV Fluid Purchases</th>
<th>FY 2013</th>
<th>FY 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9% NS (1L bag)</td>
<td>212,856</td>
<td>211,186</td>
</tr>
<tr>
<td>LR (1L bag)</td>
<td>76,888</td>
<td>85,782</td>
</tr>
<tr>
<td>PlasmaLyte (1L bag)</td>
<td>8,884</td>
<td>17,598</td>
</tr>
</tbody>
</table>

**Intravenous Fluids – 2 Uses**

**Volume Resuscitation – bolus**

- Isotonic crystalloids or colloids
- Rapid administration to correct *symptomatic* volume depletion
- **Limited & discreet**

**“Maintenance” Fluids**

- Isotonic or hypotonic crystalloids
- Targeted fluids in *high risk patients* – high ongoing and/or predictable losses
- Too often: indiscriminate & too much

---

**Colloids vs Crystalloids**

Isotonic crystalloids vs colloids (albumin, gelatin) = No demonstrable difference in mortality

- **SAFE Trial** – saline vs albumin
- **CRISTAL** – colloid vs crystalloid for all resuscitation fluids throughout ICU
- **ALBIOS** – albumin + crystalloid vs crystalloid to keep alb > 3.0 for 28 days

Hydroxyethyl Starches (HES) = *nephrotoxic*
3 Cases

48 yo male with severe septic shock in ED (BP 64/33)

<table>
<thead>
<tr>
<th>Ionic Conc (mEq/L)</th>
<th>Normal</th>
<th>Sodium</th>
<th>Lactated Ringers</th>
<th>Plasmalyte A</th>
<th>Hartmann's Solution</th>
<th>Plasmalyte 148 Normosol-R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>154</td>
<td>150</td>
<td>130</td>
<td>140</td>
<td>130</td>
<td>140</td>
</tr>
<tr>
<td>Potassium</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Chloride</td>
<td>154</td>
<td>100</td>
<td>98</td>
<td>111</td>
<td>98</td>
<td>98</td>
</tr>
<tr>
<td>Magnesium</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Calcium</td>
<td>150</td>
<td>26</td>
<td>29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactate</td>
<td>23</td>
<td>23</td>
<td>23</td>
<td>23</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>Glucuronate</td>
<td>27</td>
<td>27</td>
<td>27</td>
<td>27</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td>Osmolarity</td>
<td>308</td>
<td>300+</td>
<td>273</td>
<td>294</td>
<td>276</td>
<td>294</td>
</tr>
<tr>
<td>pH</td>
<td>5.4</td>
<td>8.06</td>
<td>6.5</td>
<td>7.4</td>
<td>6</td>
<td>5.5</td>
</tr>
</tbody>
</table>

2L bolus 0.9% NaCl vs Hartmann’s in Healthy Volunteers
2L bolus 0.9% NaCl vs Hartmann’s in Healthy Volunteers


<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Hartmann’s solution</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to first micturition (min)</td>
<td>18±(15-30)</td>
<td>8 (6-14)</td>
<td>0.00</td>
</tr>
<tr>
<td>Number of voidations over 6 h</td>
<td>3 (2-5)</td>
<td>1 (0-4)</td>
<td>0.61</td>
</tr>
<tr>
<td>Post-voided urine volume over 6 h (ml)</td>
<td>255 (215-318)</td>
<td>166 (113-228)</td>
<td>0.04</td>
</tr>
<tr>
<td>Voided volume of urinary output over 6 h (ml)</td>
<td>71 (54-118)</td>
<td>13 (7-215)</td>
<td>0.09</td>
</tr>
<tr>
<td>Urine osmolarity (mOsm/kg)</td>
<td>232 (219-254)</td>
<td>168 (148-172)</td>
<td>0.01</td>
</tr>
<tr>
<td>Total post-voided urinary output pressure over 6 h (mnHg)</td>
<td>34 (24-47)</td>
<td>22 (14-40)</td>
<td>0.18</td>
</tr>
<tr>
<td>Osmolarity of post-voided urine (mOsm/kg)</td>
<td>461 (461-575)</td>
<td>461 (371-485)</td>
<td>0.36</td>
</tr>
<tr>
<td>Osmolarity of arterial urine (mOsm/kg)</td>
<td>475 (458-486)</td>
<td>423 (332-440)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

2L bolus 0.9% NaCl vs Plasmalyte 148 in Healthy Volunteers


<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Plasma-Lyte 148</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to first micturition (min)</td>
<td>18±(15-30)</td>
<td>8 (6-14)</td>
<td>0.00</td>
</tr>
<tr>
<td>Number of voidations over 6 h</td>
<td>3 (2-5)</td>
<td>1 (0-4)</td>
<td>0.61</td>
</tr>
<tr>
<td>Post-voided urine volume over 6 h (ml)</td>
<td>255 (215-318)</td>
<td>166 (113-228)</td>
<td>0.04</td>
</tr>
<tr>
<td>Voided volume of urinary output over 6 h (ml)</td>
<td>71 (54-118)</td>
<td>13 (7-215)</td>
<td>0.09</td>
</tr>
<tr>
<td>Urine osmolarity (mOsm/kg)</td>
<td>232 (219-254)</td>
<td>168 (148-172)</td>
<td>0.01</td>
</tr>
<tr>
<td>Total post-voided urinary output pressure over 6 h (mnHg)</td>
<td>34 (24-47)</td>
<td>22 (14-40)</td>
<td>0.18</td>
</tr>
<tr>
<td>Osmolarity of post-voided urine (mOsm/kg)</td>
<td>461 (461-575)</td>
<td>461 (371-485)</td>
<td>0.36</td>
</tr>
<tr>
<td>Osmolarity of arterial urine (mOsm/kg)</td>
<td>475 (458-486)</td>
<td>423 (332-440)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

2L bolus 0.9% NaCl vs Plasmalyte 148 in Healthy Volunteers


- Plasma-Lyte 148
- 0.9% Saline
Normal Saline vs Balanced Crystalloids

Retrospective database analysis of major open abdominal surgery (2005-2009)

- Exclusive balanced crystalloid (Plasmalyte) versus exclusive 0.9% (normal) saline on day of surgery

High Chloride vs Balanced Crystalloids in ICU

<table>
<thead>
<tr>
<th>RIFLE Class</th>
<th>Risk (AKIN 1)</th>
<th>Injury (AKIN 2)</th>
<th>Failure (AKIN 3)</th>
<th>Injury &amp; Failure (AKIN 2 + 3)</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Period (n=760)</td>
<td>71 (9.0%)</td>
<td>48 (6.3%)</td>
<td>57 (7.4%)</td>
<td>105 (14%)</td>
<td>15%</td>
</tr>
<tr>
<td>Intervention Period (n=773)</td>
<td>57 (7.4%)</td>
<td>23 (3.0%)</td>
<td>42 (5.4%)</td>
<td>65 (8.4%)</td>
<td>13%</td>
</tr>
<tr>
<td>P Value</td>
<td>0.16</td>
<td>0.002</td>
<td>0.4</td>
<td>&lt;0.001</td>
<td>0.44</td>
</tr>
</tbody>
</table>

Meta-analysis: High- vs Low-Chloride Fluids in Periop & Critical Illness Fluid Resuscitation
Meta-analysis: High- vs Low-Chloride Fluids in Periop & Critical Illness Fluid Resuscitation


Balanced Crystalloid in Sepsis

Prospective, blinded, cluster-randomized, double crossover study in 4 tertiary ICUs in New Zealand (3 = mixed med/surg, 1 = cardiothoracic/vasc surg) comparing balanced crystalloid (Plasmalyte-148) & 0.9% NaCl in critically ill patients

Inclusion: All ICU patients receiving crystalloid therapy
Exclusion: ESRD, AKI requiring RRT expected to require RRT within 6 hrs. Those admitted to ICU for palliative care or organ donation consideration
Primary Outcome: development of RIFLE stage I or greater AKI based ONLY on serum creatinine criteria

SPLIT Trial: Methods
ICUs assigned to use blinded study fluid (Fluid A or Fluid B) exclusively for alternating 7 week periods for a total of 28 weeks.

- Patients continued with their originally assigned fluid if they remained in the ICU over 1 or more crossover point

Treating clinician determined rate, frequency, total volume of fluid administration

- Open label solutions available if there was a clear indication for a given solution (i.e. severe hypochloremia)
- No other restrictions on type/volume of other solutions used (i.e. colloid, blood products)

SPLIT Trial: Results

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Balanced Crystalloid</th>
<th>0.9% NaCl</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AKI</td>
<td>152/1067 (9.6%)</td>
<td>94/1025 (9.2%)</td>
<td>1.04 (0.80-1.36)</td>
<td>0.77</td>
</tr>
<tr>
<td>RRT Use</td>
<td>38/1152 (3.3%)</td>
<td>38/1110 (3.4%)</td>
<td>0.96 (0.62-1.50)</td>
<td>0.91</td>
</tr>
<tr>
<td>In Hospital Mortality</td>
<td>87/1152 (7.6%)</td>
<td>95/1110 (8.6%)</td>
<td>0.88 (0.67-1.17)</td>
<td>0.40</td>
</tr>
</tbody>
</table>
SPLIT Trial: Results

<table>
<thead>
<tr>
<th>Balanced Crystalloid</th>
<th>0.9% NaCl</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU days (mean)</td>
<td>1.50</td>
<td>1.47</td>
<td>1.02 (0.94-1.11)</td>
</tr>
<tr>
<td>Mech vent use</td>
<td>790/1152 (68.6%)</td>
<td>751/1110 (67.7%)</td>
<td>1.01 (0.96-1.07)</td>
</tr>
<tr>
<td>Mech vent hrs (mean)</td>
<td>15.32</td>
<td>14.24</td>
<td>1.05 (0.91-1.21)</td>
</tr>
</tbody>
</table>

SPLIT Trial: Results

eTable 3

| Volume of fluid administered (mL) & proportion of patients receiving fluid–mean ± SD; no. / total no. (%) |
|---------------------------------|-----------------------------------------------------------------|
|                                | Balanced Crystalloid | 0.9% NaCl |
| Day 0                          | 1711±1389            | 1694±1292 |
| Total (90 days)                | 2655±3052            | 2594±2120 |

SPLIT Trial: Conclusions & Limitations

**Authors:** In this cluster randomized, double-crossover trial, there was no significant difference in the primary outcome of incidence of AKI or failure within 90 days after enrollment in a heterogenous population of ICU patients who received a buffered [balanced] crystalloid or saline for crystalloid fluid therapy.

**Limitations:**
- Low exposure to intravenous fluids in general
- No discussion of serum chloride levels
- Low severity of illness with low expected (and realized) AKI incidence
- No report of renal biomarkers

**My conclusion:** In this well designed and implemented trial without subject cross over, there appears to be no demonstrable risk to 0.9% saline when used in small quantities to critically ill patients at low risk for AKI as would be expected for a drug with low to moderate toxicity used in small quantities. However, on the basis of this trial, I can make no conclusions regarding the safety of 0.9% NaCl when used in large quantities in high-risk patients.
Conclusion: IV Solutions

**IV Fluids = medication**
- Proper fluid, dose, and amount
- Tailor therapy for each patient

Hyperchloremic solutions [i.e. (ab)normal 0.9% saline] appear to have detrimental effects on somatic & renal function (in large quantities)
- More volume retention & peripheral edema
- Less vigorous UOP response to bolus
- Increase severity of AKI/ARF and more dialysis needs
- Lower MAP & increased mortality?

Balanced crystalloids (LR, Plasmalyte, Hartmann's solution) should be considered for large volume resuscitations (shock, DKA, volume depletion, etc)

---

Questions?

**ICU truisms:**

Save the kidneys to save the patient
Pee to be free of the ICU

Contact me anytime at:

michael.connor@emory.edu @criticalbeansmd
Introducing precision in AKI prevention in surgical ICU

Azra Bihorac
Precision and Intelligent Systems in Medicine Partnership
University of Florida
http://www.prisma-p.org

Disclosure

• Current support: Center for Sepsis and Critical Illness P50 GM-111152 and R01 GM-110240 from the National Institute of General Medical Sciences
• Biases
  Woman
  Intensivist
  Data Scientist

Subtle

Invisible

Huber, Hobson & Bihorac, Ann Vasc Surg 2015
Vaught, Caraguel-Bawiet & Bihorac, BJOG 2015
Costly

Cardiovascular death
Competing risk model

Challenge

- Acute kidney injury is complex syndrome that is often (un)avoidable by-product of health care delivery
- It is untraceable in real-time
- The metrics is based on antiquated highly imprecise ICD codes
- Prevention depends on the timely and accurate identification of patients at risk
80 years old white male scheduled for elective Whipple surgery with HTN, Atrial fibrillation (on BB and ACEI), eGFR 60, admission sCr slightly above baseline at 1.09.

Intraoperative occasional hypotension, couple of doses of neo during induction. EBL ~ 500 ml, 2 units pRBC, 3 L crystalloids. Preop prophylactic vancomycin one dose.

<table>
<thead>
<tr>
<th>Sepsis-10%</th>
<th>AKI-30%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Interventions</strong></td>
<td><strong>Cover</strong></td>
</tr>
<tr>
<td>Preoperative optimization of renal function</td>
<td>No</td>
</tr>
<tr>
<td>Biomarker guided guidelines implementation</td>
<td>RCT</td>
</tr>
<tr>
<td>Ischemic preconditioning</td>
<td>RCT</td>
</tr>
<tr>
<td>Off-Pump Cardiac surgery</td>
<td>Benefit in RCT and meta-analysis</td>
</tr>
<tr>
<td>Hemodynamic optimization in OR / postoperative</td>
<td>Benefit in RCT and meta-analysis</td>
</tr>
<tr>
<td>N-Acetylcysteine</td>
<td>No</td>
</tr>
<tr>
<td>Intrasp Diuretics</td>
<td>No</td>
</tr>
<tr>
<td>Intrasp Mannitol</td>
<td>No</td>
</tr>
<tr>
<td>Atrial natriuretic peptide</td>
<td>No</td>
</tr>
<tr>
<td>Fenoldopam</td>
<td>No</td>
</tr>
</tbody>
</table>


**Bundle it UP**

- **Sepsis Bundle**
  - At Risk 20%
    - Risk stratify using MEWS score
    - Biomarkers
    - Initiate Standardized Care Bundle at early sepsis stage
    - First 12-24 hours critical

- **AKI Bundle**
  - At Risk 50%
    - Risk stratify using risk stratification tools
    - Biomarkers
    - Initiate Standardized Care Bundle for High Risk patients
    - First 24-48 hours critical
From injury to recovery
Acute Kidney Disease

Chawla LS et al, ADQI 16, Nat Rev Nephrol. 2017

Standardized Clinical Assessment
And Management Plan for AKI

• "Sound practice"
• Synthesis of current medical knowledge and best clinical judgment
• Recommendations on medical management are structured as decision trees, providing guidance for decision making.

EHR based AKI Risk

<table>
<thead>
<tr>
<th>Elements</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SUSCEPTIBILITY/RESILIENCE</strong></td>
<td>Maximum 8</td>
</tr>
<tr>
<td>Baseline renal function</td>
<td></td>
</tr>
<tr>
<td>a. Chronic kidney disease</td>
<td>2</td>
</tr>
<tr>
<td>b. Estimated GFR on admission &lt;60</td>
<td>2</td>
</tr>
<tr>
<td>c. AKI stage</td>
<td>2</td>
</tr>
<tr>
<td>Urine output &lt; 0.5 ml/kg/hr for 3 consecutive hours in spite of fluid</td>
<td>2</td>
</tr>
<tr>
<td><strong>EXPOSURES</strong></td>
<td>Maximum 9</td>
</tr>
<tr>
<td>Sepsis</td>
<td>2</td>
</tr>
<tr>
<td>Hypotension within 24 hours prior to admission</td>
<td>2</td>
</tr>
<tr>
<td>a. Any MAP &lt; 50 or need for vasopressors at ICU admission</td>
<td>2</td>
</tr>
<tr>
<td>Hemorrhagic shock on admission (&gt; 6 pRBC)</td>
<td>2</td>
</tr>
<tr>
<td>Respiratory failure with hypoxia within 24 hours prior to admission</td>
<td>2</td>
</tr>
<tr>
<td>a. Intubated on admission or P/F ratio &lt; 200</td>
<td>2</td>
</tr>
<tr>
<td>Nephrotoxic Drugs and contrast</td>
<td></td>
</tr>
</tbody>
</table>
**AKI Risk Stratification**

Assess the Stress

If clinical risk score ≥ 3 order Urinary TIMP2*IGFBP7 test

**Treatment algorithm**

- TIMP2*IGFBP7 < 0.3 LOW RISK
  - Proceed with usual care, low risk for AKI. Other issues are priority.

- 0.3 < TIMP2*IGFBP7 < 2 HIGH RISK
  - Start ABCDE, reassess in 12 hrs

- TIMP2*IGFBP7 > 2 CRITICALLY HIGH RISK
  - Start CPR, reassess in 12 hrs

**Cause of AKI**

- Urinary Exam
- Renal Ultrasound
- Renal Doppler
- Specialized Immunochemical tests

**Prevention**

- Assess UOP and sCr
- Blood pressure optimized
- Circulation and fluid optimized
- Drugs adjusted
- Evaluate again!

**Reassessment**

- Dynamic GFR
- Urine output
- Urinary biomarker
- Fluid balance
- Recovery of organ failure
Rapidly Resolved AKI in ICU

High Clinical Risk

- 70 yo after complex spine surgery with history of CKD (baseline 1.1), just admitted to ICU with admission sCr 1.3.
  - Exposures: intubated, hypotension and large resuscitation in OR
  - No cuff leak on BEST
  - Total score 4
- 80 yo with history of CKD after vascular surgery, just admitted to ICU with admission sCr slightly above baseline (1) at 1.3, oliguria for 3 hours
  - Exposures: hypotension and nephrotoxic drugs
  - Total score 7

High Clinical Risk

- 77 yo male with no CKD, just admitted to ICU for intraabdominal severe sepsis
  - Exposures: intubated, hypotension, contrast, severe sepsis, sCr 1.35
  - Total score 10
  - T2T 3.16
  - TTE guided fluid
  - War on Drugs with ID - Vancomycin changed

Tubular stress Intervention 12 hrs
Rapidly Resolved AKI 48 hours
Persistent AKI
High Clinical Risk

- 77 yo male with no CKD, just admitted to ICU for intraabdominal severe sepsis
  - Exposures: Intubated, hypotension, contrast, severe sepsis, sCr 1.35
  - Total score 10
  - T2I7 3.16
  - War on Drugs with ID - Vancomycin changed
  - Progressed to stage 3, no RRT, partial recovery

- 64 yo M with no known CKD, baseline sCr 0.96. Just admitted to ICU for sepsis after abdominal surgery.
  - Exposures: Intubated, sepsis, sCr 1.45.
  - Total score 8
  - T2I7 3.58
  - TTE guided fluid, early nephrology consult, echogenic kidneys and thin cortex.
  - Held contrast
  - Progressed to stage 2 and recovered in two days

Very High Biomarker Risk
T2I7>2

- 8% of all patients, clinical risk 3-13
- At the time of test
  - AKI stage 1 - 62%
  - CKD 38%
- 87% of patients progressed to Stage 2 or 3, no RRT
- Complete recovery at discharge 37%
Key to success

- Easy clinical risk stratification tool
- Automated ordering process
- Standardized set of interventions
- Champion team

What do we do?

- Critical Care and Kidney Health
- Big Data, Deep learning
- Context-Aware Intelligent Systems
- High Performance Cloud Computing
- Human-Machine Interaction
- Medical Informatics and predictive analytics

Kidney Love
@azrabihorac

Azra Bihorac, MD, MS, FASM, FCCM
R. Glenn Davis Associate Professor of Medicine, Surgery and Anesthesiology
http://www.prisma-p.org/lab-director/
www.prisma-p.org
www.mysurgeryrisk.com
www.GatoRisk.com

KidneyLove
@PrismaPartnership
@PrismaP

PrismaPartnership
Preventive and Intelligent Systems in Medicine Partnership
www.prisma-p.org
www.azrabihorac.org
www.bihorac.com

Year in Review: Medical Critical Care

Munish Luthra, MD
Assistant Professor, Dept. of Medicine
Emory University SOM
Munish.Luthra@emory.edu
May 5, 2017

Disclosures
Financial: None
Intellectual: None

Objectives
1) Review most relevant medical critical care literature within the last year
2) Critique the quality of the research
3) Interpret if the research is applicable in real life clinical practice
Methodology

• Reviewed Core Clinical Journals for articles published since May 2016- April 2017

• Solicited input from colleagues and trainees

Background & Objective

• Adjunctive hydrocortisone therapy is suggested by the Surviving Sepsis Campaign only in refractory septic shock

• The efficacy of hydrocortisone in patients with severe sepsis without shock remains controversial

• To determine whether hydrocortisone therapy in patients with sepsis prevents development of septic shock
Design

- Double-blind, RCT
- Study performed in 34 ICUs in Germany
- Included 380 patients with severe sepsis not in septic shock

Methodology

- Patients were randomly allocated 1:1 either to receive:
  1. A continuous infusion of 200 mg of hydrocortisone for 5 days followed by dose tapering until day 11 (n = 190) or
  2. Receive placebo (n = 190)
- Main exclusion criteria was septic shock
- Baseline characteristics were similar

Outcomes

- **Primary**: Development of septic shock within 14 days
- **Secondary**:
  - Time until septic shock
  - Mortality in the ICU or hospital
  - Survival up to 180 days
  - Development of secondary infections
  - Hyperglycemia (Blood glucose >150 mg/dL) & delirium
Results

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Placebo Arm</th>
<th>Hydrocortisone Arm</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septic Shock</td>
<td>12.5%</td>
<td>12.9%</td>
<td>0.90</td>
</tr>
<tr>
<td>90-day Mortality</td>
<td>8.5%</td>
<td>8.6%</td>
<td>0.90</td>
</tr>
<tr>
<td>30-day Mortality</td>
<td>4.0%</td>
<td>4.0%</td>
<td>0.90</td>
</tr>
<tr>
<td>Secondary Infections</td>
<td>16.5%</td>
<td>15.5%</td>
<td>0.20</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>6.4%</td>
<td>6.4%</td>
<td>0.90</td>
</tr>
<tr>
<td>Multiple Infections</td>
<td>24.9%</td>
<td>20.7%</td>
<td>0.003</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>8.6%</td>
<td>8.9%</td>
<td>0.90</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>24.9%</td>
<td>22.5%</td>
<td>0.005</td>
</tr>
</tbody>
</table>

At 14 days, hydrocortisone had no beneficial effect on the development of septic shock versus placebo.

Critique

- Multicenter study, appropriate blinding of medications, and similar baseline characteristics
- The observed rate of septic shock in the placebo group (23%) was lower than 40% presumed, reducing sensitivity for this outcome
- Secondary analyses not corrected for multiple comparisons, (e.g., benefit of steroids on delirium) possibly due to chance

Conclusion

- In patients with severe sepsis, hydrocortisone therapy does not reduce progression to septic shock at 14 days
- Hydrocortisone failed to improve short- or intermediate-term mortality
- A 10% absolute increase in hyperglycemia and an absolute 13% reduction in delirium was noted
- When to use steroids in sepsis and septic shock?
Background

• Norepinephrine (NE) is currently recommended as the first-line vasopressor in septic shock

• Small clinical studies suggest vasopressin maintains GFR and improve creatinine clearance compared with NE

• It has been proposed that the combination of vasopressin and corticosteroids may improve survival in septic shock

Design

• A factorial (2×2), double-blind, RCT, February 2013 – May 2015

• 18 ICUs in the United Kingdom, with 421 patients

• Patients with septic shock requiring vasopressors despite fluid resuscitation within 6 hours after the onset of shock
Methodology

• Patients were randomly allocated 1:1:1:1 to:
  1. Vasopressin (titrated up to 0.06 U/min) and hydrocortisone (n = 101),
  2. Vasopressin and placebo (n = 104),
  3. Norepinephrine (0-12mcg/min) and hydrocortisone (n = 101), or
  4. Norepinephrine and placebo (n = 103).

• MAP target: 65-75 mm of Hg

Critical Care Summit
Emory Division of Pulmonary, Allergy & Critical Care Medicine

Method

• Primary outcome: AKIN-3 kidney failure–free days during the 28-day period

AKIN-3 kidney failure:
Any one criteria:
  1. Creatinine >3 times baseline
  2. Creatinine > 4 mg/dL
  3. Urine output <0.3 ml/kg/hr for 24 hours
  4. Anuria for 12 hours
  5. Initiation of dialysis

• Secondary Outcomes:
Rates of renal replacement therapy, mortality, and serious adverse events
Results

- Patients treated with vasopressin did better in terms of both lower creatinine and higher urine output over first 7 days.

- Compared to NE, vasopressin caused a reduction in dialysis requirement (25% vs 35%, OR -0.40; CI- 0.20-0.73), reduced creatinine levels and higher urine output.

- There was no difference in the primary endpoint (days free of AKIN-3 renal failure) among groups.

- No difference in mortality and complication rates.

- No impact on patient outcomes with use of stress dose steroids.
Critique

- Well conducted study, clinical staff and researchers were blinded
- The baseline characteristics were well matched for APACHE II score, co-morbidities, median fluid volume received
- Negative primary outcome reflects imprecision in the AKIN-3 definition (Composite outcome)!
- Timing of initiation of renal replacement therapy were not controlled

Conclusion

- Vasopressin reduces the need for renal replacement therapy, and is associated with lower creatinine and improved UOP.
- Vasopressin does not reduce AKIN-3 kidney failure rates, and had no effect on mortality.
- What is best first-line vasopressor for septic shock?
- Is vasopressin renoprotective and clinically effective in reducing AKI?
**Background**

- Early severity assessment and risk stratification for CAP is challenging because of overt clinical signs at presentation.
- Biomarkers can aid clinicians in guiding ICU admission decisions, treatment and outcomes.
- Procalcitonin has shown to decrease antibiotic prescription in CAP, VAP, and COPD exacerbations.

**Design**

- Prospective, multicenter cohort study, 1770 patients.
- Adults hospitalized with CAP in the CDC’s Etiology of Pneumonia in the Community (EPIC) study cohort.
- PCT levels at admission were compared between patients who required IRVS and those who did not.
- Logistic regression models were used to assess the association of PCT concentration and the risk of IRVS.

**Methodology**

- **Primary outcome**: PCT concentration and risk of IRVS for septic shock within 72 h of hospital presentation.
- **Secondary outcome**: To assess whether PCT had a statistically significant additive contribution to each of the pneumonia severity scores for predicting IRVS.
- Pneumonia severity scores used were PSI, ATS minor criteria and SMART-COP.
Results

• PCT strongly associated with risk of IRVS within 72 hours of admission (Primary outcome)

• PCT < 0.05 ng/mL: 4% risk of IRVS.
• >10 ng/mL, risk for IRVS of 22%.
• IRVS risk plateaued at PCT concentrations > 10 ng/mL

• Between 0.05 ng/mL and 10 ng/mL, PCT concentration had an approximate linear association with IRVS risk

• Each 1 ng/mL increase in PCT corresponds to a 1% to 2% absolute increase in IRVS risk

• The addition of PCT to each of the pneumonia severity score models (PSI, ATS, SMART-COP) increased the area under the ROC curve
Critical Care Summit
Emory Division of Pulmonary, Allergy & Critical Care Medicine

Critical Care Summit
Emory Division of Pulmonary, Allergy & Critical Care Medicine

Critical Care Summit
Emory Division of Pulmonary, Allergy & Critical Care Medicine

Low-risk (< 3 criteria):
- PCT < 0.05 ng/mL corresponded to a 2.4% IRVS risk.
- PCT concentration of 10 ng/mL corresponded to a 12.0% risk.

High risk (>3 criteria):
- PCT < 0.05 ng/mL was associated with a 13.2% IRVS risk.
- PCT concentration of 10 ng/mL corresponded to a 36.2% risk.

Critique

- Time to retrieve the PCT levels was not standardized
- Median PCT levels (~0.15 ng/ml) and IRVS rate were low
- 2/3 patients had unknown cause of pneumonia and that virus were the cause of CAP two-fold than bacteria (23% vs. 11%)
Conclusion

• Serum PCT concentrations were strongly associated with the risk of IRVS during the following 72 h

• Incorporation of PCT with clinical scoring systems is likely to improve identification of patients with CAP needing intensive care

• The accuracy of PCT alone for IRVS is not strong enough to base clinical decisions

Background

• Sepsis-3 task force recommends the use of the qSOFA criteria to identify patients at high risk of mortality from sepsis

• qSOFA has not been prospectively validated in some settings, and their added value in the emergency department remains unknown

• To prospectively validate the qSOFA as a predictor of mortality in patients a risk of sepsis and compare it with previous SIRS criteria
Design

• Prospective cohort study

• 30 ED’s in France, Spain, Belgium and Switzerland, May-June, 2016

• All patients with suspected infection over 4 week period admitted to ED had measurement of SIRS, qSOFA and SOFA scores

Methodology

• Primary outcome: In-hospital mortality

• Secondary outcome:
  o Admission to ICU
  o length of ICU stay of more than 72 hours
  o composite of death or ICU stay of more than 72 hours
The AUCROC curves for qSOFA is 0.80; SOFA: 0.77; SIRS: 0.65; and severe sepsis: 0.65.

**Table 1: Diagnostic Performance for the Prediction of In-Hospital Death**

<table>
<thead>
<tr>
<th>Predictor of Death</th>
<th>qSOFA</th>
<th>SOFA</th>
<th>SIRS</th>
<th>Severe Sepsis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (95% CI)</td>
<td>75 (59-84)</td>
<td>73 (55-82)</td>
<td>75 (67-83)</td>
<td>97 (80-100)</td>
</tr>
<tr>
<td>Specificity (95% CI)</td>
<td>75 (59-84)</td>
<td>76 (67-85)</td>
<td>27 (20-35)</td>
<td>82 (68-86)</td>
</tr>
<tr>
<td>Positive Predictive Value (95% CI)</td>
<td>24 (18-30)</td>
<td>18 (14-22)</td>
<td>13 (10-18)</td>
<td>20 (14-27)</td>
</tr>
<tr>
<td>Negative Predictive Value (95% CI)</td>
<td>57 (55-72)</td>
<td>97 (85-98)</td>
<td>98 (95-99)</td>
<td>94 (90-96)</td>
</tr>
<tr>
<td>AUROC (95% CI)</td>
<td>0.80 (0.74-0.85)</td>
<td>0.77 (0.71-0.82)</td>
<td>0.67 (0.60-0.74)</td>
<td>0.60 (0.53-0.67)</td>
</tr>
</tbody>
</table>

**Result**

- Overall, in-hospital mortality of the cohort was 8%.

- Patients with qSOFA scores less than 2, the mortality rate was 3% vs 24% for qSOFA > 2.

- The highest AUROCs were for the qSOFA score 0.80 and the SOFA score 0.77 compared with 0.65 for SIRS and 0.65 for severe sepsis ($P < .001$, compared with qSOFA).
Results

• The hazard ratio of qSOFA score for in-hospital mortality was 6.2 as compared with 3.5 for severe sepsis.

• Results were similar for predicting ICU admission and long ICU stay (≥72 hours) with qSOFA.

• Interestingly, adding lactate level measurement to qSOFA did not improve its prognostic value.

Critique

• Study did not follow up discharged patients and only focused on in-hospital mortality.

• Data was incomplete on 14% of patients, limiting the conclusions’ strength.

• Experts could not have been blinded to the value of the components of the scores (Bias?).

Conclusion

• A prospective validation study focused on ED patients to support the new recommendations of Sepsis-3.

• qSOFA a better predictor of in-hospital mortality than SIRS and severe sepsis for patients at risk of sepsis in ED.

• Does qSOFA scores help providers intervene earlier and modify outcomes in patients who present with sepsis??
Honorable Mention

• Prognostic Accuracy of the SOFA Score, SIRS Criteria, and qSOFA Score for In-Hospital Mortality Among Adults With Suspected Infection Admitted to the Intensive Care Unit. JAMA. 2017;317(3):290-300.

  Eamon P. Raith, MBBS, MACCP; Andrew Udy, PhD, FCICM; Michael Bailey, PhD, et al. for the Australian and New Zealand Intensive Care Society (ANZICS) Centre for Outcomes and Resource Evaluation (CORE)


  Kathryn M. Rowan, Ph.D., Derek C. Angus, M.D., M.P.H., Michael Bailey, Ph.D., Anice E. Bendixen, M.D., Rebecca Bellomo, M.D., Kathryn C. Cerra, M.D., Timothy J. Coats, M.D., Francis Fiks, Ph.D., Michael C. Reade, Donald M. Yealy, M.D., et al.


  Stéphane Gaudry, M.D., David Hajage, M.D., Fréderique Schortgen, M.D., Laurent Martin-Lefèvre, M.D., Bertrand Pons, M.D., Éric Boulé, M.D., Alexandra Boyer, M.D., Guillaume Chever, M.D., Nicolas Lantink, M.D., Ph.D., Didier Dreyfus, M.D., et al.


Year in Review of Surgical and Burn Critical Care

Rachael Williams, MHS, MD
Assistant Professor of Surgery
Emory University School of Medicine
Grady Burn Unit

Disclosures

Consultant for Integra with departmental and Emory Conflict of Interest Committee approval

Outline

- Frailty
- Resuscitation
- Nutrition
- ECMO
- Infections and Sepsis
Frailty

Trauma: Frailty

Preinjury physical frailty and cognitive impairment among geriatric trauma patients determine postinjury functional recovery and survival

Cathy A. Maxwell, PhD, RN, Lorraine C. Mira, PhD, RN, Kanshik Mahkour, MD, Mary S. Bratrick, PhD, Anna Minnick, PhD, RN, Addison May, MD, and Richard S. Miller, MD
Nashville, Tennessee

• Prevalence of frailty among community dwelling older adults is ≤10%

• Prevalence of frailty among geriatric trauma patients ranges from 44% to 78%
• Barthel Index score was the most important predictor of morality at 6 months and 1 year.
• Patients never returned to baseline frailty scores.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Unadjusted</th>
<th></th>
<th>Adjusted*</th>
<th></th>
<th></th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.07</td>
<td>0.003</td>
<td>1.07</td>
<td>0.005</td>
<td>1.03-1.33</td>
<td></td>
</tr>
<tr>
<td>Injury severity</td>
<td>1.65</td>
<td>0.047</td>
<td>1.65</td>
<td>0.005</td>
<td>1.38-2.23</td>
<td></td>
</tr>
<tr>
<td>Comorbidity index</td>
<td>1.64</td>
<td>0.284</td>
<td>1.64</td>
<td>0.292</td>
<td>0.97-2.69</td>
<td></td>
</tr>
<tr>
<td>Cognitive (mini-mental state)</td>
<td>1.69</td>
<td>0.055</td>
<td>1.69</td>
<td>0.059</td>
<td>1.09-2.53</td>
<td></td>
</tr>
<tr>
<td>Frailty (preinjury Barthel index score)</td>
<td>1.51</td>
<td>0.001</td>
<td>1.38</td>
<td>0.005</td>
<td>1.24-1.57</td>
<td></td>
</tr>
</tbody>
</table>

Burns: Frailty

Frailty Score on Admission Predicts Outcomes in Elderly Burn Injury

Kathleen S. Romanowski, MD, Meza Baner, RN, C, Tim L. Pani, MD, FACS, FCCM, David G. Grendahl, MD, FACS, Sonam Sun, MD, FACS

Burns: Frailty

• High admission frailty score
  - Increased risk of discharge to skilled nursing facility (OR=2.5)
  - Increased risk of mortality (OR= 1.67)
EGS: Frailty

Emergency general surgery specific frailty index: A validation study

Tahereh Groufj Jokar, MD, Karen Bresheen, MD, Peter Shaw, MD, MPH,
Nasim Kalamkar, MD, Anah Al-Hadeer, MD, Herbi Al-Falih, MD, Mady Fain, MD,
Martha Jane Mohler, PhD, MPH, and Bellal Jouven, MD, Tadros, Arora

---

**EMERGENCY GENERAL SURGERY SPECIFIC FRAILTY INDEX**

**Co-Morbidities**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Yes (1)</th>
<th>No (0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dementia</td>
<td>Mild (0.25)</td>
<td>Moderate (0.5)</td>
</tr>
</tbody>
</table>

**Daily Activities**

<table>
<thead>
<tr>
<th>Activity</th>
<th>Yes (1)</th>
<th>No (0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need help with grooming</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Help managing money</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Need help with housework</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Need help with shopping</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Help with bathing</td>
<td>Wheelchair (1)</td>
<td>Walker (0.75)</td>
</tr>
</tbody>
</table>

**Health Attitude**

<table>
<thead>
<tr>
<th>Feeling</th>
<th>Most of time (1)</th>
<th>Sometime (0.5)</th>
<th>Rarely (0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feel less useful</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feel sad</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feel effort to do everything</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feel lonely</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feel sexually active</td>
<td>Yes (0)</td>
<td>No (1)</td>
<td></td>
</tr>
</tbody>
</table>

**Nutrition**

<table>
<thead>
<tr>
<th>Albumin</th>
<th>&lt;3 mg/dl (1)</th>
<th>&gt;5mg/dl (0)</th>
</tr>
</thead>
</table>
EGS: Frailty

- The 15-variable validated EGSFI is a simple and reliable bedside tool to determine the frailty status of patients undergoing EGS.

- Preinjury frailty is an independent predictor of postinjury functional status, postoperative complications, and mortality.

Summary

- Knowing the frailty status of your patient is an important indicator of disposition, functionality, and mortality.
Resuscitation

Trauma: Massive Transfusion

The Massive Transfusion Score as a decision aid for resuscitation: Learning when to turn the massive transfusion protocol on and off

Richard A. Callam, MD, MB/BChir; Michael W. Cripps, MD, Mary F. Nation, RN, MPA; Amanda S. Courey, Bryan R.R. Robinson, MD, and Mitchell J. Cohen, MD, San Francisco, California

Trauma: Revised MTS

| SBP, mm Hg | <90 |
| HR, bpm   |  |
| Positive FAST finding |  |
| Penetrating mechanism |  |
| Hb, mmol/L |  |
| INR | >1.5 |
| Hgb, g/dL | <11 |
| Temperature, °C | <35.5 |
For each positive trigger at 6 hours, patients were more likely to need subsequent transfusion in Hours 7 to 12 (odds ratio [OR], 2.74; 95% CI, 1.65–4.55; p < 0.001).

**Trauma: Revised MTS**

- Calculate the revised MTS 6 hours after ED presentation.
- Predicts who needs ongoing MTP in hours 7-12.
- If the score is 0 then patients are unlikely to require any further blood products.
- If the score is not 0 then risk of 24 hour mortality was high (OR death at 24 hours, 4.6; 95% CI, 2.3–9.3).

**Burns: Albumin**

Albumin in Burn Shock Resuscitation: A Meta-Analysis of Controlled Clinical Studies

Roberta J. Naknick, PhD,* David G. Gurnahalp, MD, FACS;†
Malvin K. Wilkes, PhD*
Burns: Albumin

- Fluid in excess of the predicted volume was accompanied by increased odds of
  - Pneumonia (OR = 1.92)
  - Bloodstream infections (OR = 2.33)
  - ARDS (OR = 1.55)
  - MODS (OR = 1.49)
  - Death (OR = 1.74)
Burns: Albumin

- Albumin infusion was associated with
  - reduced mortality (OR = 0.34 with a 95% confidence interval of 0.19 to 0.58 (P < .001).
  - decreased occurrence of compartment syndrome (OR = 0.19; 95% confidence interval, 0.07–0.50; P < .001).

SCC: Volume Responsiveness

Ultrasound assessment of volume responsiveness in critically ill surgical patients: Two measurements are better than one

Summary

- The revised MTS score (calculated 6 hours after a patient presents to the ER) serves as an adjunct in deciding when to stop massive transfusion protocol.
- Albumin can improve outcomes in burn shock resuscitation.
- Forget about the IVC. A combination of left ventricle outflow measurement and internal jugular vein variation gives the clinician an indication of volume responsiveness.
SCC: Nutrition

Parenteral and enteral nutrition in surgical critical care: Plasma metabolomics demonstrates divergent effects on nitrogen, fatty-acid, ribonucleotide, and oxidative metabolism

TABLE 1. Demographic and Clinical Characteristics for Subjects Started on Nutrition Therapy at a Level I Trauma Hospital, and Healthy Volunteers

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Enteral (n = 10)</th>
<th>Parenteral (n = 10)</th>
<th>Volunteer (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>42.5 (31–56)</td>
<td>39 (25–52)</td>
<td>36 (30–47)</td>
</tr>
<tr>
<td>Female sex</td>
<td>4 (40)</td>
<td>4 (40)</td>
<td>5 (50)</td>
</tr>
<tr>
<td>BMI</td>
<td>27 (21–32)</td>
<td>22 (21–31)</td>
<td>26 (25–27)</td>
</tr>
<tr>
<td>Admission base deficit</td>
<td>5.8 (3.8–7.4)</td>
<td>8.2 (4.8–10.8)</td>
<td></td>
</tr>
<tr>
<td>Hospital day that nutrition was started</td>
<td>2.5 (2–4)</td>
<td>7 (5–9)</td>
<td></td>
</tr>
</tbody>
</table>
Parenteral Nutrition

- Increased Amino Acids
- Decreased Urea Cycle metabolites
- Decreased essential omega fatty acids

Summary

- Parenteral nutrients are used less effectively than enteral nutrients.

Burns: Vitamin D

Low Vitamin D Level on Admission for Burn Injury Is Associated With Increased Length of Stay

Institute of Medicine, K.S. Skelton, M.D., R.N., C.N.C.,† Robson Goffy, M.D., R.N.; Larry Jones, M.D.;‡ Claire V. Murphy, Pharm.D., BCPS, FCCM
Burns: Vitamin D

- Patients with low vitamin D levels had
  - longer length of stays and ICU days
  - trend toward increased complications such as sepsis, UTI, pneumonia, CV collapse and graft loss.

- Survival rate was very high in both groups:
  low group, 96.4%, and normal group, 96.9%.

Summary

- Low vitamin D levels are associated with increased morbidity in the burn patient population. There may be a role for supplementation.
ECMO

Trauma: ECMO

Extracorporeal membrane oxygenation after traumatic injury

Sarwat R. Ahmad, MD, Jay Menaker, MD, Joseph Kiefer, MA, Jones O’Connor, MD, Thomas M. Sekula, MD, and Deborah M. Sola, MD, MPH, Baltimore, Maryland

<table>
<thead>
<tr>
<th></th>
<th>Survivors</th>
<th>Non-survivors</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanism of injury, n (%)</td>
<td>12 (71)</td>
<td>10 (86)</td>
<td>0.26</td>
</tr>
<tr>
<td>Nonpenetrating</td>
<td>5 (29)</td>
<td>3 (14)</td>
<td></td>
</tr>
<tr>
<td>Penetrating</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISS</td>
<td>25 (18–32)</td>
<td>41 (26–59)</td>
<td>0.03</td>
</tr>
<tr>
<td>ISS &lt;40, n (%)</td>
<td>14 (85)</td>
<td>10 (65)</td>
<td></td>
</tr>
<tr>
<td>ISS &gt;40, n (%)</td>
<td>3 (18)</td>
<td>12 (55)</td>
<td></td>
</tr>
<tr>
<td>Indication for ECMO, n</td>
<td>12 (71)</td>
<td>10 (45)</td>
<td>0.19</td>
</tr>
<tr>
<td>ARDS</td>
<td>5 (29)</td>
<td>12 (55)</td>
<td></td>
</tr>
<tr>
<td>Non-ARDS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of systemic anticoagulation, n (%)</td>
<td>16 (94)</td>
<td>12 (55)</td>
<td>0.01</td>
</tr>
<tr>
<td>Time from admission to ECMO, d</td>
<td>7 (1–49)</td>
<td>3.5 (2–5)</td>
<td>1.00</td>
</tr>
<tr>
<td>ECMO duration (IQR), d</td>
<td>13 (6–16)</td>
<td>5.5 (2–14)</td>
<td>0.09</td>
</tr>
<tr>
<td>ECMO-related complications (patients, %)</td>
<td>9 (53)</td>
<td>7 (32)</td>
<td>0.21</td>
</tr>
<tr>
<td>Hospital length of stay (IQR), d</td>
<td>41.1 (23–79.9)</td>
<td>10.7 (5.4–25.9)</td>
<td>0.000</td>
</tr>
</tbody>
</table>
Trauma: ECMO

- Neither mechanism of injury nor indication for ECMO was associated with mortality.
- Ninety-four percent of the survivors were anticoagulated with heparin versus 55% of nonsurvivors (p = 0.01).
- ISS was higher in non-survivors.

Burns: ECMO

A National Perspective on ECMO Utilization in Patients with Burn Injury

Laraa B. Noumey, MD, Maura M. Malek, RN, BSN, Marian V. Cruz, MD, Jason H. Chin, MD, and Jeffrey W. Shepp, MD

Burns: ECMO

- Demographics
  - ECMO-treated cohort
    - Mean age 32.3±22.7 years
    - 69.4% male
    - 59.0% Caucasian
    - 80% flame burns
    - 26.7% inhalation injury
Summary

- The use of venovenous ECMO for acute lung injury after trauma should be considered in special patient populations.

- ECMO is a viable option for supporting critically injured burn patients.

Infections and Sepsis
SCC: Intra-Abdominal Infection

The Surgical Infection Society Revised Guidelines on the Management of Intra-Abdominal Infection


SCC: Recommendations

• Routinely use a source control procedure unless there is clear evidence that a non-interventional approach is associated with a good clinical outcome (Grade 1-A).

• Initiate empiric antimicrobial therapy within one hour once a diagnosis of IAI is made in patients presenting with sepsis or septic shock (Grade 2-B).

SCC: Community Acquired

• Low risk:
  – Narrower-spectrum against Enterobacteriaceae, aerobic streptococci and obligate anaerobes.
  – Don’t cover pseudomonas, enterococcus, or fungus.
  – Cefotaxime or ceftriaxone plus metronidazole or ertapenem (Grade 1-A).
SCC: Community Acquired

- High risk:
  - Broader spectrum
  - Use piperacillin-tazobactam, doripenem, imipenem-cilastatin, meropenem, or cefepime plus metronidazole (Grade 2-A).
  - Do not use antifungal agents routinely for empiric therapy of higher-risk patients (Grade 1-B).

SCC: Hospital Acquired

- Use the broader-spectrum agents recommended for higher-risk patients with CA-IAI.
- Consider addition of other empiric agents based on the patient’s risk for an infection from Enterococcus spp., MRSA, resistant gram-negative bacilli, and Candida spp. (Grade 2-B).
- Consult local epidemiologic data and antibiograms for assistance in selecting empiric antimicrobial therapy in patients considered at risk for infection with resistant gram-negative pathogens (Grade 2-B).

SCC: Fungus

- Use an echinocandin (anidulafungin, caspofungin, or micafungin) for empiric therapy of severely ill patients at risk for infection with Candida spp. (Grade 1-B).
- Consider use of fluconazole for antifungal therapy of less severely ill patients at risk for infection with Candida spp. (Grade 2-B).
- Consider use of an echinocandin or voriconazole for empiric therapy of patients at risk for infection with a fluconazole-resistant strain of Candida (Grade 2-B).
SCC: Scenarios

- Do not use antibiotic agents to prevent infection in patients with severe or necrotizing pancreatitis (Grade 1-B).
- Limit antimicrobial therapy to no more than 24 hours in patients with traumatic bowel perforations operated on within 12 hours (Grade 1-A), gastroduodenal perforations operated on within 24 hours (Grade 1-C), acute or gangrenous appendicitis in the absence of perforation (Grade 1-A), acute or gangrenous cholecystitis in the absence of perforation (Grade 1-A), and ischemic non-perforated bowel (Grade 1-C).

SCC: Duration

- Limit antimicrobial therapy to four days (96 h) in patients who have had adequate source control (Grade 1-A).
- Consider limiting antimicrobial therapy to 5–7 days in patients with established IAI in whom a definitive source control procedure is not performed (Grade 2A).

Summary

- Intra-abdominal infection is the second most common cause of infectious mortality in the ICU.
- Start antibiotics early, obtain source control, remember principles of stewardship.
Burns: Sepsis

MR-proADM: A New Biomarker for Early Diagnosis of Sepsis in Burned Patients

Jochen Gilke, MD,* Haufried Ostermann, MD,* Adrian Dragu, PhD,† and Sarnia Sabirzai, PhD*

Burns: Adrenomedullin

- MRpro-ADM peptide released from endothelial and myocardial cells.
- Decreases endothelial permeability.
- Down regulates proinflammatory cytokines such as tumor necrosis factor-α, interleukin-1β, and interleukin.
- Bactericidal activity that is enhanced by its regulation and modulation of the complement system.
Burns: Sepsis

- MR-proADM levels demonstrated an increase one day earlier compared to what has been demonstrated in the critical care setting and in septic shock.

Summary

- MR-proADM may be a suitable marker for the early identification of sepsis in patient with burn injuries.
Acknowledgements

• Dr. Greene and Dr. Coopersmith
• Dr. Ingram and Dr. Hodge

Questions?
Overview

• 5 of the most *important* studies from 2016-2017

• Each addressed a pressing clinical question in treatment of:
  – ICH
  – IVH
  – Refractory Status Epilepticus
  – TBI

• AIS treatment dominated 2015-2016
• 408 TBI subjects with refractory ICP

• Randomized to decompressive craniectomy or medical management

• At randomization approx 50% had either no motor response, or had extensor posturing
Fire and Ice?

Hypothermia for Neuroprotection in Convulsive Status Epilepticus

- 270 patients in Convulsive SE requiring mechanical ventilation
- Randomized to 32-34°C for 24hrs + standard therapy vs standard therapy alone
- Block randomized on age (65 years) and duration of seizure (60 min)
- 11 French ICUs
It's just plumbing…

It's just plumbing…

Clot Busting

THE LANCET
Thrombolytic removal of intraventricular haemorrhage in treatment of severe stroke: results of the randomised, multicentre, multiregion, placebo-controlled CLEAR III trial

- 500 subjects with IVH entering the British
  - Randomised to tPA vs placebo (saline)
  - 1 mg tPA q 8hrs (max 12 doses); CT head q 24 hrs
  - 73 sites, 8 countries

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Treatment (n=139)</th>
<th>Control (n=139)</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome: GOS score of 5 at day 90</td>
<td>67 (49)</td>
<td>56 (39)</td>
<td>1.22 (0.75-1.99)</td>
<td>0.43</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total severe duration (days)</td>
<td>79 (76)</td>
<td>90 (90)</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>Interquartile range</td>
<td>33-180</td>
<td>43-153</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refractory status explained from day 1 to day 2</td>
<td>15 (11)</td>
<td>26 (22)</td>
<td>3.01 (1.21-7.39)</td>
<td>0.01</td>
</tr>
<tr>
<td>Refractory status explained on day 1</td>
<td>63 (46)</td>
<td>10 (8)</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>Intracranial pressure explained</td>
<td>22 (17)</td>
<td>36 (27)</td>
<td>3.14 (1.97-4.96)</td>
<td>0.05</td>
</tr>
<tr>
<td>Length of ICU stay (days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>5</td>
<td>7</td>
<td>0.44</td>
<td></td>
</tr>
<tr>
<td>Interquartile range</td>
<td>5-14</td>
<td>3-16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
<td>21</td>
<td>19</td>
<td>0.90</td>
<td></td>
</tr>
<tr>
<td>Interquartile range</td>
<td>10-88</td>
<td>10-40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death in ICU — no. (%)</td>
<td>13 (9)</td>
<td>13 (12)</td>
<td>0.53 (0.30-0.92)</td>
<td>0.04</td>
</tr>
<tr>
<td>Death in hospital, including in ICU — no. (%)</td>
<td>17 (12)</td>
<td>20 (15)</td>
<td>0.51 (0.30-0.88)</td>
<td>0.03</td>
</tr>
<tr>
<td>Death between randomisation and 90 days after discharge — no. (%)</td>
<td>18 (13)</td>
<td>20 (15)</td>
<td>0.54 (0.31-0.93)</td>
<td>0.07</td>
</tr>
</tbody>
</table>
Stop the bleeding...
Platelet transfusion versus standard care after acute stroke due to spontaneous cerebral haemorrhage associated with antiplatelet therapy (PATCH): a randomised, open-label, phase 3 trial

- 190 patients with supratentorial ICH, on antiplatelet therapy for > 7 day before ictus

- Randomized to standard care vs standard care with platelet transfusion within 90 min of diagnostic imaging and 6 hrs from ictus

- 97 randomized to platelets, 4 not treated; 93 randomized to standard care, 2 received platelets

- 41 enrolling sites
It’s just physics…

+ 1000 subjects with ICH (volume < 60ml)
+ Randomized to SBP 110 – 139 vs SBP 140 – 179mmHg using nicardipine
+ Treatment must be administered within 4.5 hours from ictus
+ 110 sites, 6 countries

**Intensive Blood-Pressure Lowering in Patients with Acute Cerebral Hemorrhage**

- 1000 subjects with ICH (volume < 60ml)
- Randomized to SBP 110 – 139 vs SBP 140 – 179mmHg using nicardipine
- Treatment must be administered within 4.5 hours from ictus
- 110 sites, 6 countries
### Summary

The great tragedy of Science – the slaying of a beautiful hypothesis by an ugly fact.

-TH Huxley
A New Frontier in Critical Care: Saving the Injured Brain

E. Wesley Ely, MD, MPH
Professor of Medicine and Critical Care
Vanderbilt University, Nashville, TN
VA TN Valley Health Care System GRECC

Disclosures: Physician-Scientist
- Honoraria from Abbott, Pfizer, Orion for CME Activities
- NIH and VA U.S. Federal Funding

“Medicine is more than a profession…It is not an occupation for those to whom career is more precious than humanity or for those who value comfort and serenity above service to others.”

Abraham Joshua Heschel
1964 AMA Convention
The Picture of Dementia Following ICU Care

Global Cognitive Scores by Age
Confirmed: Delirium Risk Factor for Long-Term Cognitive Problems after ICU Stay

- 1,101 survivors of critical illness, 37% with delirium
- Studied only survivors and used self-report
- Multivariable analysis with adjustment for gender, admission dx, severity of illness (both APACHE IV and cumulative SOFA)
- Delirium independent predictor of mild (O.R. 2.41, C.I. 1.57-3.69) and severe (3.1, 1.1-8.74) LTCI 1 year

Wolters AE, Crit Care 2014;18:R125

Cognitive Outcomes: Identical Cognitive Testing & Threshold*

<table>
<thead>
<tr>
<th>Prevalence of cognitive impairment</th>
<th>6 Months</th>
<th>12 Months</th>
<th>P-Value (6 vs 12 mo.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDEN/OMEGA – ARDS (2008-2012)</td>
<td>36%</td>
<td>25%</td>
<td>0.001</td>
</tr>
<tr>
<td>N=173</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAILS – SEPSIS-ARDS (2010-2014)</td>
<td>37%</td>
<td>29%</td>
<td>0.367</td>
</tr>
<tr>
<td>N=172</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*1 cognitive test score <2 standard deviations (SD) below population norm or at least 2 test scores <1.5 SD below norm

Needham D (ALTOS) AJRCCM 2013;188:567-76
Are Anesthesia and Surgery Implicated in POCD?

- Famous cohorts have advocated cognitive decline post-surgery (e.g. CAGB & Pump-Head) \(^1\)
- Trials have refuted that the cognitive decline had to do with bypass itself (OCTOPUS) \(^2\)
- And now others have posited that the term POCD is a fallacy \(^3\)–\(^5\)

\(^1\) Newman M, NEJM 2001;344:395-402 (n=261)
\(^2\) Van Dijk D, JAMA 2002;287:1405-12 (n=281)
\(^3\) Avidan M, Anesthesiol 2009;111:964-70 (n=575)
\(^4\) Avidan M, Anesthesiol 2010;113:1246-8
\(^5\) Avidan M, Anesthesiol 2016;124:255-8
Are Anesthesia and Surgery Implicated in POCD?

- Duration of anesthesia and repeat operations assoc with POCD at 1 week (n=1218) after major non-cardiac surgery (ISPOCD1)
- RCT (N=47) showed that general anesthesia was assoc with worse MMSE (26.5 to 26, P<0.001) decline at 3 days postop after major surgery
- General anesthesia may increase risk of POCD, meta-analysis of 21 studies (OR 1.34, 0.93-1.95). Mean study size N=100

Mason SE. J Alz Dis 2010; 22:97-79

No dose response curve between insult and outcome

- Outcomes are similar in
  - Percutaneous procedures requiring sedation and invasive surgery requiring general anesthesia
  - Regional/neuraxial and general anesthesia
  - Depths of anesthesia
- Degree of surgery/anesthesia insult does not correlate with outcomes


ANNALS OF SURGERY
A Weekly Review of Surgical Science and Practice Since 1899

Surgery and Anesthesia Exposure Is Not a Risk Factor for Cognitive Impairment After Major Noncardiac Surgery and Critical Illness

Christopher C. Malek, MD, Shray A. Madjid, MD, MPH, James C. Jackson, MD, FACP, Robert M. Fullerton, MD, MPH, Anil F. Kulkarni, MD, FACC, and Richard S. Driscoll, MD, FACS.
INSIGHT-ICU Study
Illuminating Neuropsychological dysfunction and Systemic Inflammatory mechanisms Gleaned after Hospitalization in Trauma ICU Study

LTCl is Not Well-Defined after Primary Brain Injury

Articles on ICU Delirium
### Unrecognized Delirium

<table>
<thead>
<tr>
<th>Study</th>
<th>Setting</th>
<th>Provider</th>
<th>Miss Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Francis et al. 1990</td>
<td>Medical</td>
<td>Physicians</td>
<td>84%</td>
</tr>
<tr>
<td>Elie et al. 2000</td>
<td>Emergency</td>
<td>Physician</td>
<td>65%</td>
</tr>
<tr>
<td>Inouye et al. 2001</td>
<td>Med-Surg</td>
<td>Nurses</td>
<td>81%</td>
</tr>
<tr>
<td>Han et al. 2009</td>
<td>Emergency</td>
<td>Physician</td>
<td>76%</td>
</tr>
<tr>
<td>Van Eijk et al. 2009</td>
<td>ICU</td>
<td>Physician</td>
<td>81%</td>
</tr>
<tr>
<td>Spronk et al. 2009</td>
<td>ICU</td>
<td>Phys/Nurses</td>
<td>79%</td>
</tr>
<tr>
<td>Grossmann et al. 2014</td>
<td>Emergency</td>
<td>Nurses</td>
<td>73%</td>
</tr>
<tr>
<td>Rice et al. 2014</td>
<td>Med-Surg</td>
<td>Nurses</td>
<td>77%</td>
</tr>
</tbody>
</table>

### MIND-USA

Modifying the Impact of ICU-Associated Neurological Dysfunction

### When Delirium strikes, don’t forget about Dr. DRE

- **Disease remediation**
  - Sepsis, COPD, CHF

- **Drug Removal**
  - SATs and stopping benzodiazepines/narcotics

- **Environment**
  - Immobilization, sleep and day/night, hearing aids, glasses, noise
Tools are useless if things aren’t organized towards sticky, stable, sustainable systems...
SAT + SBT = 4 day shorter ICU/hosp LOS

Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial


ABC Trial: One-Year Survival

NNT=7

ABC approach (n=167)
Control (n=168)

p=0.01

ABC Trial: One-Year Survival

NNT=7

ABC approach (n=167)
Control (n=168)

p=0.01


Sedation Interruption in SLEAP

Mehta S, JAMA 2012;308:1985-92
From Canadian Authors of SLEEP…

n=712 and 3,620 patient-days

“We found that nearly all patients were managed with continuous-infusion opioids and sedatives. We also found that actual practice was different from what we expected because the available clinical tools – such as protocols and assessment scales – were not necessarily applied at the bedside.”

Burry LD, Can J Anesth May 2014 epub
Data collected 2008-2009

Benzodiazepine Use in Trials *

<table>
<thead>
<tr>
<th>Study</th>
<th>Control</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kress NEJM 2000</td>
<td>90 mg/day</td>
<td>53 mg/day</td>
</tr>
<tr>
<td>Girard ABC Lancet 2007</td>
<td>84 mg/day</td>
<td>54 mg/day</td>
</tr>
<tr>
<td>Mehta SLEEP JAMA 2012</td>
<td>82 mg/day</td>
<td>102 mg/day</td>
</tr>
<tr>
<td>OSCILLATE NEJM 2013</td>
<td>141 mg/day</td>
<td>199 mg/day</td>
</tr>
</tbody>
</table>

* All values converted and expressed as mean midazolam dose per patient, median for ABC study were 8 mg and 5 mg, respectively

In any process, reducing variability in that process inevitably leads to greater efficiency and lower cost.

W. Edwards Deming
1900-1993
More disarray = more help from protocols
Likewise
Less disarray = less margin for improvement

Feeling “Sideways”

Teamwork – Brady’s Patriots
ICU PAD Guidelines
ABCDEF Bundle Checklist*
• A – Assess, Prevent and Manage Pain
• B – Both SATs and SBTs
• C – Choice of Sedation
• D – Delirium: Assess, Prevent and Manage
• E – Early Mobility and Exercise
• F – Family Engagement and Empowerment
*www.icudelirium.org
*www.iculiberation.org
Scientific Foundation for ICU Liberation and the ABCDEF Bundle...

B: Both SATs and SBTs

C: Choice of Sedation and Analgesia
7. Strøm T. Lancet. 2010;375:475-80
9. Reade M JAMA 2016;315:1460-1468
10. Su X. Lancet 2016; epub ahead of print

D: Delirium

E: Early Mobility
17. Puthucheary Z. JAMA. 2013;310:1591-1600
Scientific Foundation for ICU Liberation and the ABCDEF Bundle...

F: Family Engagement
20. Schneiderman L. JAMA. 2003;290:1166-72

PICS: Post-Intensive Care Syndrome
25. Ehlenbach W. JAMA. 2010;303:763-70

ABCDEF Bundle Objectives

- Optimize pain management.
- Break the cycle of deep sedation and prolonged mechanical ventilation.
- Reduce the incidence, duration of ICU delirium.
- Improve short, long-term ICU patient outcomes.
- Reduce health care costs!

Morandi et al. Curr Opin Crit Care 2011;17:43-9
Zaal et al. ICM 2013;39:481-88
Colombo et al. Minerva Anest 2012;78:1026-33

Liberation from...

- Public Health Problem
- Iatrogenic ignorance
- Acquisition of new injury (neck-up & neck-down)

How? By self-sacrifice, commitment, devotion to the truth of service to others, truth of these new data, and generation of a new way...
Survival and Delirium/Coma Improved after Implementing PAD Guidelines via ABCDEF Bundle in >6,000 patients

Mortality Improvement  Delirium and Coma Freedom

NOTE: Adjusted for age, APACHE III, and mechanical ventilation
7 California Hospitals, Interprofessional QI Implementation project

Page 204
A Doctor’s (ICU Team’s) Touch…
Verghese TED Talk

https://www.ted.com/talks/abraham_verghese_a_doctor_s_touch#t-937949
Start at 15:50 minutes (watch 2.5 min)

Liberated…?

Liberated...
Liberated... texting while on vent

Liberated... ventilated patient and nurse “talking”
Author’s note: “At its heart, this story is not at all about any specific belief system, but rather about making the ICU a place where EOL wishes and resolutions are respected by the ICU team and achieved by the patient and family.”

Swimming Pool in the ICU:
Ely WSJ Op-Ed on June 17, 2016
Ely WSJ, ICM 2016 Sep;42:1502-3
Breakout Session Notes:

Mechanical Ventilation
ICU Ultrasonography
Mechanical Circulatory Support / ECMO
Hemodynamic Monitoring
Continuous Renal Replacement Therapy
Targeted Temperature Management
Delirium and Post-ICU Cognitive Dysfunction