THE IMPACT OF SEPSIS ON CARDIAC ARREST

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An ounce of prevention...

Is worth a pound of cure
Outcomes are bad

Retrospective study for outcomes of in-hospital cardiac arrest over 49k adult ICU patients.
- Survival to discharge was 15.9%
- Survival to discharge for patients on pressors at time to arrest was 9.3% compared to 21.2% in those not requiring pressors.


Outcomes vary on type of arrest

Retrospective study designed to evaluate relationship between cause and outcome of in-hospital cardiac arrest. 1041 patients.
- PEA arrest in 41%, Vfib in 39%, and asystole in 20%.
- Cardiac origin in 63% or patients with 35% due to MI.
- Non-cardiac origin most commonly due to pulmonary failure at 15%.
- Cardiac origin survival 44% compared to non-cardiac 23%.

Resuscitation 83 (2012) 1206–1211
Poor outcomes in sepsis

Long-Term Outcomes in Critically Ill Septic Patients Who Survived Cardiopulmonary Resuscitation*

Pei-Wen Chao, MD1,2; Hsi Chu, MD3,4; Yung-Tai Chen, MD5,6; Yu-Ning Shih, MD7,8; Shu-Chen Kuo, MD3,4; Su-Yuan Li, MD, PhD9,10; Shuo-Ming Ou, MD3,4; Chia-Jen Shih, MD3,4,10

- Retrospective study designed to look at long-term survival rate of critical ill sepsis survivors following cardiopulmonary resuscitation. 272k Taiwanese patients.
- Only 7% sepsis patient who received CPR survived to discharge.
- Overall 1-, 20, and 5- year post-discharge survival rates following CPR were 28%, 23%, and 14% respectively.
- Sepsis survivors who received CPR had a greater risk of all-cause mortality after discharge (HR 1.38%; 95%, CI 1.34 - 1.46) although this mortality risk diminished at 2 years


Focus on 3 key areas

- Pre-Code sick patient
- Pre-Intubation
- Cardiopulmonary arrest
Pre-Code

- The tachycardic, hypotensive, febrile, anuric, lethargic patient ➔ biggest opportunity for impact.
  - Access
  - Fluids
  - Antibiotics
  - Multifactorial shock

Pre-Code: Obtaining access
Intraosseous (IO) administration

- Sites:
  - Proximal/distal tibia
  - Femur
  - Proximal humerus
  - Manubrium

- Safe to infuse pressors/inotropes, crystalloid, colloids, blood products, adenosine, heparin, lidocaine, atropine, paralytics.

- Likely obtain access via IO faster or more successful in critical situations than traditional IV or central access.
Intraosseous (IO) administration

- Intraosseous versus intravenous vascular access during out-of-hospital cardiac arrest: a randomized controlled trial.
  - Tibial IO had a higher 1st attempt success rate (91%) and faster time to access as compared to humeral IO (51%) and peripheral IV (43%).

- Is the intraosseous access route fast and efficacious compared to conventional central venous catheterization in adult patients under resuscitation in the emergency department? A prospective observational pilot study.
  - Tibial IO had higher 1st attempt success rate (90%) versus CVC (60%) and faster mean procedure time (2.3min vs 9.9min)

Pre-Code

Surviving Sepsis Campaign

International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

Surviving Sepsis Campaign

Updated Bundles in Response to New Evidence
Updated Surviving sepsis guidelines

- Guidelines evolved in 2015
  - “With publication of 3 trials that do not demonstrate superiority of required use of a central venous catheter (CVC) to monitor central venous pressure (CVP) and central venous oxygen saturation (ScvO2) in all patients with septic shock who have received timely antibiotics and fluid resuscitation…”

- Focus changed to 3 hour and 6 hour intervals.

Updated Surviving sepsis guidelines

SURVIVING SEPSIS CAMPAIGN BUNDLES

TO BE COMPLETED WITHIN 3 HOURS:
1) Measure lactate level
2) Obtain blood cultures prior to administration of antibiotics
3) Administer broad spectrum antibiotics
4) Administer 30 mL/kg crystalloid for hypotension or lactate ≥4 mmol/L

TO BE COMPLETED WITHIN 6 HOURS:
5) Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥85 mm Hg
6) In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥4 mmol/L (36 mg/dL):
   - Measure central venous pressure (CVP)*
   - Measure central venous oxygen saturation (ScvO2)*
7) Remeasure lactate if initial lactate was elevated*

*Targets for quantitative resuscitation included in the guidelines are CVP of ≥8 mm Hg, ScvO2 of ≥70%, and normalization of lactate.
Some Cliff’s Notes

- Administration of effective IV antimicrobials w/in the 1st hour (1B).
- Initial empiric antimicrobials should activity against all likely pathogens (1B).
- Cultures as clinically appropriate before antimicrobial therapy if there is no significant delay (>45m).
- Initial fluid challenge 30ml/kg for hypotension of lactic acidosis. More may be needed!!!
Pre-Code

- Shock can be multifactorial.
  - Hypovolemic or distributive

- Or even cardiogenic...
  - Sepsis-induced cardiomyopathy

- Surviving Sepsis Campaign recommend a trial of dobutamine (up to 20mcg/kg/min) can be administered in the presence of myocardial dysfunction or ongoing signs of hypotension despite adequate resuscitation and adequate MAP

Pre-Code

- SSC recommend norepinephrine as 1st choice vasopressor (1B) and epinephrine as next line vasopressors (2B).

- Phenylephrine is not recommended for treatment of septic shock unless (1C):
  - Norepinephrine associated with serious arrhythmias
  - Cardiac output is high and MAP persistently low
  - Or as salvage therapy
Intubation

- Intubation is a very key time during sepsis resuscitation. The use of positive pressure ventilation can raise intra-thoracic pressure:
  - causing reduced venous return
  - decreased filling pressures
  - decreased cardiac output leading to PEA arrest

- Hemodynamically unstable or pressors requirement prior to intubation is the biggest factor associated with death and complications.¹

- Make sure patient is as intravascular replete as possible prior to intubation. Keep fluids available.

¹Schwartz et al. Anesthesiology1995;82:367
What meds to use?

- There are lots of options for RSI:
  - Propofol
  - Benzodiazepines
  - Barbiturates
  - Etomidate
  - Ketamine

- You want to minimize potential for hypotension as much as possible.

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What meds to use?

- Ketamine
  - Dissociative anesthetic agent similar to PCP.
  - Provided analgesia along with amnestic/sedative effects.
  - Preserves respiratory drive.
  - Also stimulates catecholamine receptors causing sympathetic stimulation!!!
What meds to use?

- **Ketamine**
  - While good for hypotensive patient, sympathetic stimulation can be problematic in patients with cardiac ischemia.
  - Despite a recent meta-analysis demonstrating no adverse effects\(^1\), there remains theoretical concern that ketamine can raise ICP. This effect seems mitigated by use of fentanyl\(^2\).


What meds to use?

- **Etomidate**
  - Sedative-hypnotic.
  - Does not provide analgesia and is often paired with opioid analgesic.
  - Also has favorable hemodynamic profile\(^1,2\).
  - There is some concern that etomidate causes adrenocortical suppression. Single dose etomidate does cause decreased serum cortisol\(^3\) and a higher rate of adrenal insuff compared to ketamine\(^4\). Etomidate use does not increase mortality though\(^5,6\).

Paralytics

- Depolarizing agent (Succinylcholine):
  - Rapid onset RSI med
  - Contraindications include malignant hyperthermia, rhabdomyolysis, hyperkalemia with EKG changes, or ACh receptor upregulation (denervation injury/disease, crush, burn)

- Non-depolarizing agent
  - Rocuronium or vecuronium (requires priming dose)
  - Longer duration of action
  - Reversal agent - sugammadex

Slow down

- Assuming you have the opportunity:
  - Obtain reliable access
  - Ensure adequate volume resuscitation
  - Early, empiric antimicrobials
  - Tailor anesthetics (onset of action may be increased)
  - Initiate pressors prior to intubation and initially target a slightly higher MAP
During code

- Specific considerations during sepsis:
  - Hypoglycemia: particularly in liver disease as liver has less capacity to convert glycogen to glucose.
  - Hyperkalemia: particularly in renal failure and exacerbated by acidosis.

During code

- Bicarb therapy to buffer acidemia
  - Controversy as far back as 1962 where researchers reported a case of refractory Vfib until acidosis was corrected by bicarb

Pro-Bicarb

  - Retrospective study investigating bicarb use and out-of-hospital cardiac arrest.
  - Bicarb use assoc with rate or ROSC (33.5% vs 25.7%) and hospital discharge (5.3% vs 3%).

  - Study investigating lidocaine and epinephrine on out-of-hospital arrest demonstrated some questionable benefit in patients receiving bicarb infusions.

  - Prospective randomized, double-blind investigation of 874 prehospital cardiac arrests.
  - Overall survival was 13.9.
  - No statistical difference in survival comparing patients who received bicarb (7.4%) vs placebo (6.7%).
  - There was a trend towards improved survival in prolonged (>15m) arrests (32.8% vs 15.4%; P = 0.007).

Con-Bicarb

- Despite theoretical benefit, there are a variety of adverse effects of bicarb use:
  - Bicarb infusion can reduce aortic and coronary perfusion pressure (pig).\(^1\)
  - Bicarb infusion can produce hypernatremia.
  - Bicarb infusion can shift oxyhemoglobin saturation curve and inhibit oxygen release.
  - Bicarb infusion increases production of CO2 which can freely diffuse from serum and exacerbate intracellular acidosis (dog).\(^2\)

- What does the literature say?

Con-Bicarb

Figure 23-5
Factors that shift the oxyhemoglobin dissociation curve.

<table>
<thead>
<tr>
<th>Study</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Resuscitation. 1989; 17 suppl:S161–S172; S199-S206</td>
<td>Mortality worse with bicarb use</td>
</tr>
<tr>
<td>Chest. 1990;97:413–419.</td>
<td>No improvement in mortality</td>
</tr>
<tr>
<td>Resuscitation. 1995;29:89–95.</td>
<td>No improvement in mortality</td>
</tr>
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Bicarb?

- No clear indication for routine bicarb use:
  - AHA recommendation “routine administration of sodium bicarbonate is not recommended in cardiac arrest”
  - Focus should remain on adequate compressions and ventilation.

- There may be benefit in specific populations:
  - Acidotic <7.10\textsuperscript{1,2} or prolonged cardiac arrest
  - Hyperkalemia
  - TCA overdose

\textsuperscript{1}JAMA 1991 Dec 18;266(23):3286.; \textsuperscript{2}Science. 1985;227:754–756.

During code

- Epinephrine + Vasopressin + Steroids\textsuperscript{1}
  - Randomized, double-blind, placebo-controlled, parallel group trial.
  - 268 patients with prehospital cardiac arrest received either VSE or epinephrine for the first 5 cycles of CPR.
  - VSE group had higher probability of ROSC or 20 minutes or longer (83.9\% vs 65.9\%, \( P = 0.005 \))
  - VSE group had higher survival to hospital discharge (13.9\% vs 5.1\%, \( P = 0.02 \))

\textsuperscript{1}JAMA. 2013 Jul;310(3):270-9.
Review

- Outcomes particularly bad for PEA and sepsis related cardiac arrests.
- Prompt treatment of sepsis with fluids, antibiotics, and pressors.
- Slow down and stabilize before intubation if possible. Tailor anesthetic and paralytic to the situation.
- Pay close attention to sepsis associated conditions during cardiac arrest – hypoglycemia and hyperkalemia.
- Bicarb use remains controversial.