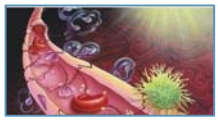
Sepsis & Beyond…Guidelines & Goal-Directed Therapy

Canadian Association of Critical Care Nurses
2014 Quebec City



Presented by:
Nicole Kupchik RN, MN, CCNS, CCRN, PCCN

Objectives

- Review the 2012 Surviving Sepsis Campaign Guidelines
- Discuss appropriate technology to assess fluid responsiveness
- Discuss the concepts of functional hemodynamics
- Review the evidence behind CVP monitoring
- Integrate a case scenario applying goal directed therapy

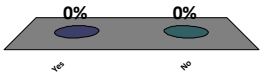
Case Presentation

- 54 year old male presents with shortness of breath & fevers for 3 days
- **Initial VS:** HR 108, RR 28, BP 106/54 (62), T 100.6 F (38.1 C), O2 sat 91% on RA
- **Does he meet SIRS criteria?**

Does he meet SIRS Criteria?

HR 108, RR 28, BP 106/54 (62), T 100.6 F (38.1 C), O_2 sat 91% on RA

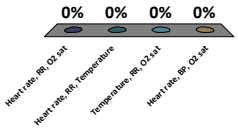
A. Yes
B. No



Which criteria qualify for SIRS?

HR 108, RR 28, BP 106/54 (62), T 100.6 F (38.1 C), O2 sat 91% on RA

A. Heart rate, RR, O2 sat
B. Heart rate, RR, Temperature
C. Temperature, RR, O2 sat
D. Heart rate, BP, O2 sat



Early Recognition is Key!!!

Systemic **I**nflammatory **R**esponse **S**yndrome
SIRS: 2 of the following:
- Temperature > 38°C or < 36°C
- Heart rate > 90 bpm
- RR > 20 bpm or $PaCO_2$ < 32 mm Hg or resp. fail
- WBC > 12 or < 4 or > 10% band forms

Step 1: "Does the patient have **SIRS**?"
Step 2: "Do you suspect an infection?"

Note: SIRS is also seen in sepsis, burns, trauma, surgery, autoimmune disorders, pancreatitis

Degrees of Sepsis

SIRS

HR > 90, RR > 20, Temp >38 or < 36, WBC > 12 K or < 4 K

Sepsis

SIRS + infection

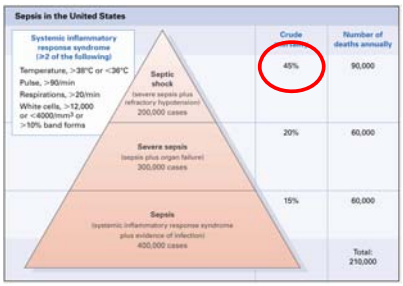
Severe Sepsis

Sepsis + Organ dysfunction

Septic Shock

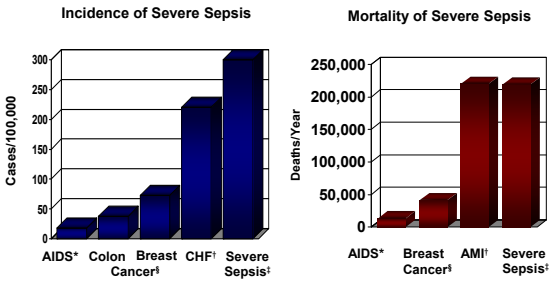
Severe Sepsis + either: SBP < 90, MAP < 65, lactate > 4 after fluids

Sepsis Outcomes



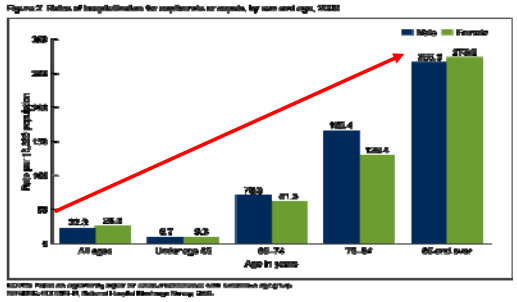
Wenzel 2002

Sepsis Compared to Other Diseases



†National Center for Health Statistics, 2001. §American Cancer Society, 2001. *American Heart Association. 2000. ‡Angus DC et al. *Crit Care Med.* 2001;29(7):1303-1310.

Highest risk?



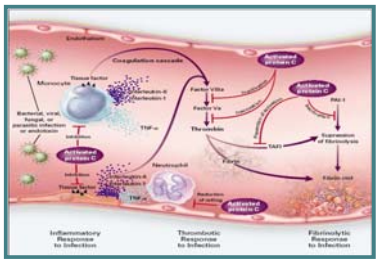
Advanced age puts the patient at highest risk. Why?

Can early detection & treatment make a difference?

- Over 6 million cases sepsis world-wide
- Over 30,000 cases of sepsis in Canada each year
- National average mortality of 30%
  - ***Sepsis is Canada's highest in-patient cause of mortality***
- 9,000 deaths per year
- What if the national mortality average dropped to 15%?
- Survival benefit: **4,500** lives per year!!!!

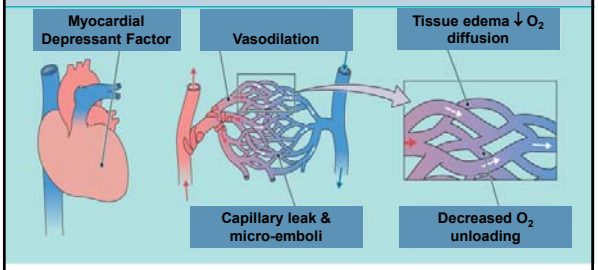
http://bcpsqc.ca/clinical-improvement/sepsis/

Pathogenesis of Sepsis…it's complicated!

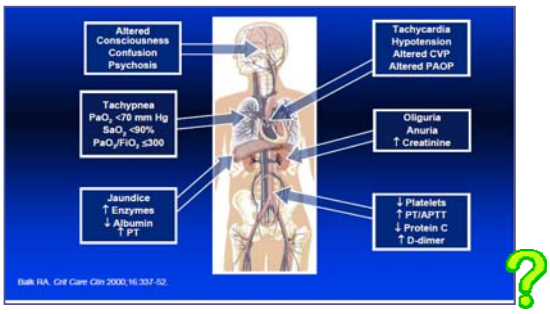


Bernard GR, Vincent J-L, Laterre P-F, et al. Efficacy and safety of recombinant human activated protein C for severe sepsis. *N Engl J Med.* 2001;344:699-709.

Tissue hypoxia of severe sepsis, caused by Cardiovascular Abnormalities

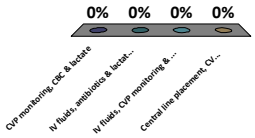


Severe Sepsis – Acute Organ Dysfunction



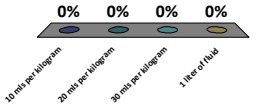
What are the priorities during the 1st hour of detection?

A. CVP monitoring, CBC & lactate
B. IV fluids, antibiotics & lactate level
C. IV fluids, CVP monitoring & central line placement
D. Central line placement, CVP monitoring & antibiotics



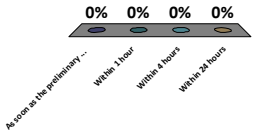
Initial fluid recommendations are:

A. 10 mls per kilogram
B. 20 mls per kilogram
C. 30 mls per kilogram
D. 1 liter of fluid



According to the SS guidelines, how quickly should we administer antibiotics?

A. As soon as the preliminary culture report is back
B. Within 1 hour
C. Within 4 hours
D. Within 24 hours



Next steps?

- **Initial VS:** HR 108, RR 28, BP 96/54 (62), T 100.6 F (38.1 C), O2 sat 91% on RA
- Start IVs, obtain CBC with differential, lactate level, chemistry panel, cultures
- Priorities in the first hour of recognition:

Fluids + Antibiotics + Labs & Source Control!!!

Case con't

- Start 30 ml/kg IV fluids
- Administer antibiotics
- Repeat Lactate level after fluids

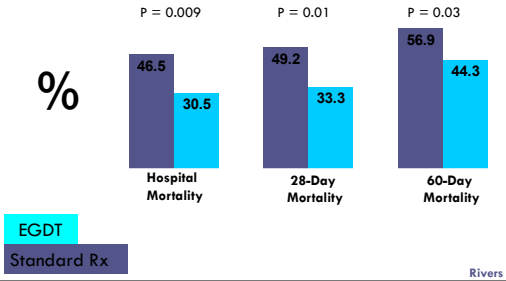
Lab results:
- WBC 25, neutrophils 14, lactate 4.5
- Na 146, K 3.9, glucose 110
- **ABG:**
- pH 7.31, $PaCO_2$ – 28, PaO_2 - 78, HCO_3 – 20, SaO_2 84%

Shock Index

- HR ÷ Systolic BP
- Normal Range: 0.5 to 0.7 in adults
- Shock Index ≥ 1.0 predictor of elevated lactate > 4 in septic patient
  - >0.8 elevated
- Used to assess hypovolemia in bleeding and infectious process since 1967
- Example: HR 108, SBP 96 in patient with fever & productive cough
- SI = 1.125 …get a lactate!!!

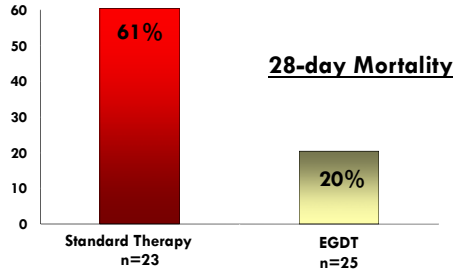
West, Journal of Emergency Medicine 2013

EGDT Improves Mortality



Rivers NEJM 2001

"Cryptic"* Septic Shock



Lactate > 4 mmol/L, SBP >100

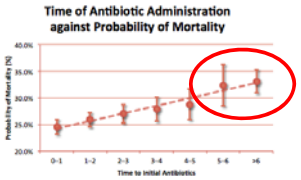
Donnino, 2003

Time matters

- Each 1-hr delay in ICU physician seeing the patient:
  - 2.1% increased risk of hospital death
- Each hour delay in abx administration:
  - 7.6% decrease in survival

Engoren 2005

Mortality increases with delay in first antibiotic administration!!!



- Retrospective review of prospective data
- N = 17,990
- Severe sepsis & septic shock
- In-hospital mortality was 29.7% as a whole
- Linear increase for each hour antibiotics were delayed

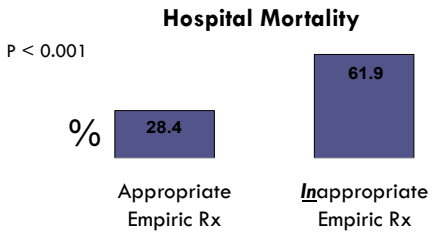
Ferrer et al (2014) Critical Care Medicine; 42(8)

Antibiotics

- "We recommend that intravenous antibiotic therapy be started as early as possible and ***within the first hour*** of recognition of septic shock (1B) and severe sepsis without septic shock (1C)".

(Best Practice versus Stand of Care)

Choosing the Correct Antibiotics



Prospective Cohort Study

Ibrahim Chest 2000

Antibiotics…

The Right Antibiotic, Right Now!!!

- Order sets
- Available in the ED?
- EMS?
- Acute care & critical care areas?

Other thoughts on Antibiotics…

- MIC – Minimum Inhibitory Concentration
- Minimum concentration an antibiotic will inhibit growth

Example:

- Vancomycin dosing & levels
  - 1.5 & 2 grams vs. 1 gram
  - Trough goal 15 – 20 mcg/ml
- Pip/Tazo (Zosyn) – every 6 - 8 hours over 4 hours
- General antibiotic recommendations: www.globalrph.com

Procalcitonin

- Rises with bacterial infections **(not viral!!!)**
- Precursor to calcitonin (responsible for calcium homeostasis)
- Normal level is < 10 pg/ml (< 0.5 ng/ml)
- 0.5 – 2 ng/ml "grey zone"; repeat level in 6 – 24 hrs
- > 10 ng/ml associated with severe sepsis/shock
- Half life of 25 – 30 hours
- Discontinue/taper antibiotics

- 2 meta-analysis CAP
- 6 days antibiotics (trmt group) vs. 10 days (control)

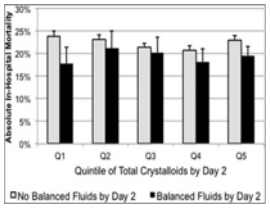
IV Fluids

TABLE 6. Recommendations: Hemodynamic Support and Adjunctive Therapy

G. Fluid Therapy of Severe Sepsis

1. Crystalloids as the initial fluid of choice in the resuscitation of severe sepsis and septic shock (grade 1B).
2. Against the use of hydroxyethyl starches for fluid resuscitation of severe sepsis and septic shock (grade 1B).
3. Albumin in the fluid resuscitation of severe sepsis and septic shock when patients require substantial amounts of crystalloids (grade 2C).
4. Initial fluid challenge in patients with sepsis-induced tissue hypoperfusion with suspicion of hypovolemia to achieve a minimum of 30mL/kg of crystalloids (a portion of this may be albumin equivalent). More rapid administration and greater amounts of fluid may be needed in some patients (grade 1C).
5. Fluid challenge technique be applied wherein fluid administration is continued as long as there is hemodynamic improvement either based on dynamic (eg, change in pulse pressure, stroke volume variation) or static (eg, arterial pressure, heart rate) variables (UG).

Does the type of fluid matter?
Lactated Ringers vs. Normal Saline



- Retrospective
- N = 53,448

Balanced fluids (LR):

- More likely to receive mechanical ventilation, invasive monitoring, colloids, steroids & larger crystalloid resuscitation
- However, was associated with lower mortality
- 19.6% vs. 22.8% (CI 0.78 – 0.94)
- No higher incidence of AKI
- No higher incidence of increased ICU or hosp LOS

Raghunathan et al (2014) Critical Care Medicine

Case #1 con't

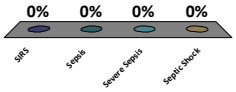
- Blood cultures drawn, 30 mL/kg IV fluids complete, antibiotics
- Repeat lactate 4.5

Repeat VS:

- HR 104 (ST)
- BP 88/42 (48)
- RR 36
- T 39
- O2 sat 86% on 3 L NC; increased to 50% mask

How would you classify this patient?

A. SIRS
B. Sepsis
C. Severe Sepsis
D. Septic Shock



Lactate?

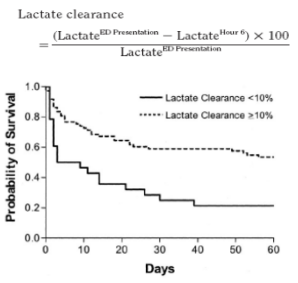
- In sepsis, lactate should be viewed as a marker of tissue perfusion
- Lactate has some prognostic utility
  - Sustained (>6 h) elevated lactate portends increased mortality
  - Mortality increases as lactate levels increase

0 – 2.5 mmol/L	4.9% mortality
2.5 – 4.0 mmol/L	9.0%
> 4.0 mmol/L	28.4%

Nguyen Crit Care Med 2004
Shapiro Ann Emerg Med 2005

Lactate Clearance

- 111 severe sepsis pts.
- Survivors
  - 38.1% clearance
- Non-survivors
  - 12.0%
  - $P = 0.005$
  - Only significant variable in logistic regression model



Nguyen 2004

Case #1 con't

HR 104 (ST), BP 88/42 (48), RR 36, T 39, O2 sat 86% on 3 L NC

- Other recommendations?
- Increased to 100% NRB
- Fluids – additional 1 L
- Re-check the lactate!!!
- Repeat VS after fluids:
- HR 102, BP 92/48 (62), RR 32, T 38.6, O2 sats 91%
- Feels like he is struggling to breath

ABG Results:

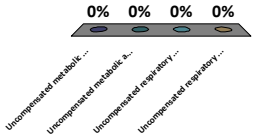
- On 100% NRB mask & becoming more somnolent

- pH 7.20
- PaCO2 68
- PaO2 89
- HCO3 28
- O2 sat 90%

- What is your interpretation of this ABG?

pH 7.20, $PaCO_2$ 68, PaO_2 89, HCO_3 28, O_2 sat 90%

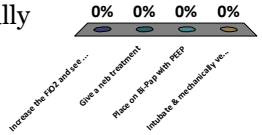
A. Uncompensated metabolic acidosis
B. Uncompensated metabolic alkalosis
C. Uncompensated respiratory acidosis
D. Uncompensated respiratory alkalosis



Recommendations?

pH 7.20, $PaCO_2$ 68, PaO_2 89, HCO_3 28, O_2 sat 90%

A. Increase the FiO2 and see how he responds
B. Give a neb treatment
C. Place on Bi-Pap with PEEP
D. Intubate & mechanically ventilate



Next steps...

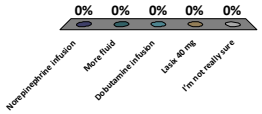
- Intubated and mechanically ventilated on 8 cc/kg, rate 16, +5 PEEP
- Continue in-line nebulizers
- Chest x-ray post intubation

- Post-intubation VS:
- HR 112, BP 90/46 (60), RR 18, T 38.9, O2 sats 94%
- Labs?
  - ABG, Lactate, WBC

What does the patient need?

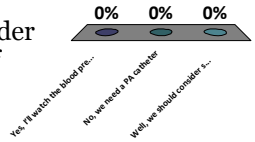
HR 112, BP 90/46 (60), RR 18, T 38.9, O2 sats 94%

A. Norepinephrine infusion
B. More fluid
C. Dobutamine infusion
D. Lasix 40 mg
E. I'm not really sure



Do any of the current methods of VS predict fluid responsiveness?

A. Yes, I'll watch the blood pressure and heart rate, it's adequate
B. No, we need a PA catheter
C. Well, we should consider some other method of assessing fluid responsiveness



Case con't

- Insert ScvO2 catheter & measure CVP (Surviving Sepsis Guidelines, 2012)
- Anything else?
  - Arterial line & assess contractility measures & pulse pressure or stroke volume variation
- ScvO2 catheter is placed
- What are the goals for a septic patient?
  - CVP: 8 - 12 mm Hg
  - ScvO2 (>70%)
  - What can you measure if the provider didn't insert the continuous ScvO2 cath?
    - Central line – obtain intermittent venous oxygen values from the distal port

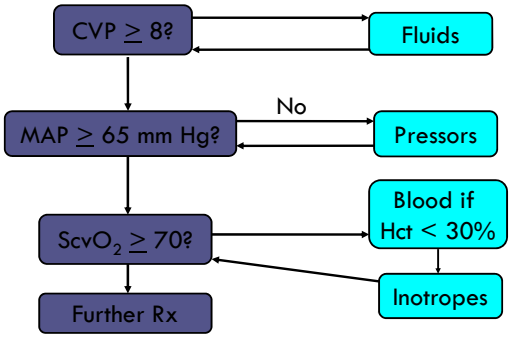
6 Hour sepsis bundle

Early detection – 1st hour	Critical Care

• Obtain serum lactate
• Cultures & targeted antibiotics
• Monitor for other signs of hypoperfusion:
  ▫ MAP < 65 mmHg
  ▫ Lactate > 4 mmol/L
  ▫ UOP < 0.5 ml/kg/hr
• Initial fluid Bolus of **30 ml/kg**
• **Antibiotics**
	• Start vasopressors if MAP < 65 despite fluids
	  ▫ Norepinephrine
	  ▫ Vasopressin 0.03 units/min
	• CVP 8 – 12 mmHg
	• ScvO2 > 70%
	  ▫ Inotropes
	  ▫ PRBCs if Hgb < 7

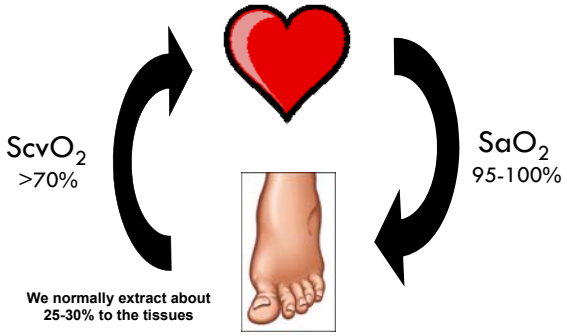
Surviving Sepsis Guidelines 2012

The Core EGDT Protocol



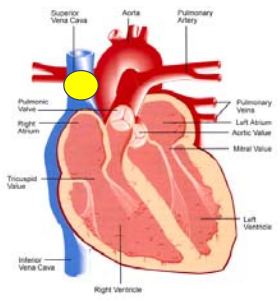
Rivers NEJM 2001

Easy way to interpret $ScvO_2$:



We normally extract about 25-30% to the tissues

$ScvO_2$



- Draw from distal tip of TLC/PICC (thorax)
- Send to lab in ABG syringe
- Mixed venous
- Surrogate mixed venous
- Runs about 5 – 8% higher than true mixed venous
- ***Goal >70%***

If $ScvO_2$ is low, first ask yourself if it is a delivery problem!

Affected by 3 physiologic parameters:

The Pump
CO/CI
LVSWI
SV/SVI

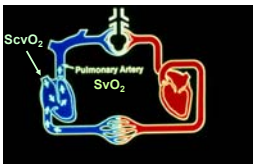
The Hgb
Affinity for oxygen

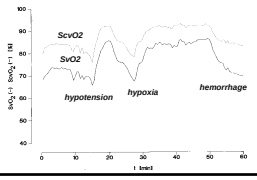
The Lungs
O_2/CO_2 exchange

Central Venous Oxygen Saturation ($ScvO_2$)

A surrogate for mixed venous

- $ScvO_2$ correlates with SvO_2 in shock states
  - Superior vena cava, r = 0.86
  - Right atrium, r = 0.95
  - Difference < 5%
  - More equal at lower saturations (<50%)
- Feasible in the early settings
- Trends more important



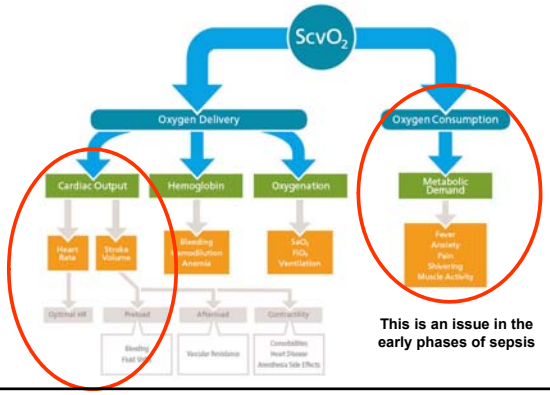


(Reinhart, Chest, 1996)
(Ladakis, Respiration , 2001)

SVO_2: 60-75% $ScvO_2$: >70%

Balance of O_2 delivery & consumption

DECREASED O_2 DELIVERY (DO_2)	INCREASED O_2 CONSUMPTION (VO_2)
• ↓Hemoglobin	• Increased work of breathing
• ↓Cardiac output	• Shivering
• ↓SaO_2	• Fever
	• Infection
	• Agitation
	• Nursing care



This is an issue in the early phases of sepsis

Case con't

- After additional IV fluids were administered, the VS were:
  - HR 98
  - BP 98/48 (54)
  - Temp 38.4 C
  - RR 22 (vent rate is 16), O2 sat 94%
  - CVP 10 mmHg
  - ScvO2 59%
  - Lactate 4.0

Are you satisfied with the current hemodynamic state?

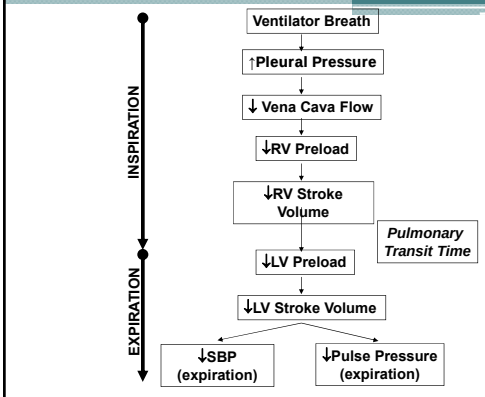
Will any of the measures predict fluid responsiveness?

Case Continued…

- An arterial line is placed
- Measure the pulse pressure (PPV) or stroke volume variation (SVV)
- Normal is 10-13%
  - Closed chest
  - Ventilated
  - Regular rhythm

This patient's SVV is 28% & Cardiac index is 2.0 L/min (low)

Recommendations?



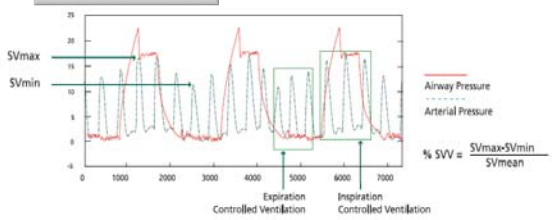
Used with permission of E. Bridges, University of Washington

Stroke Volume Variation Optimization

Guiding Fluid Therapy in Controlled Ventilated Patients

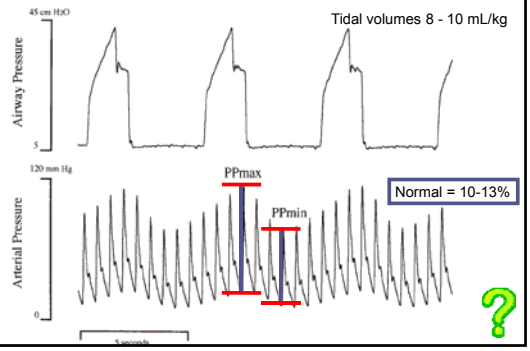
By monitoring SVV, it can be determined whether a patient is fluid responsive before fluid is given.

How SVV is calculated:



Michard F. Volume Management Using Dynamic Parameters. Chest. 2005; 128:1902-1903 (modified)

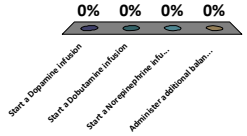
Pulse pressure variation



Recommendations?

This patient's SVV is 28% & Cardiac index is 2.0 L/min (low)

A. Start a Dopamine infusion
B. Start a Dobutamine infusion
C. Start a Norepinephrine infusion
D. Administer additional balanced fluid

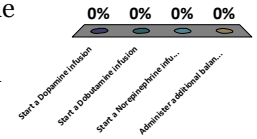


Case con't

- **Additional 1L IV fluids given**
- Next steps?
  - HR 92, BP 96/48 (64)
  - SVV18%
  - CVP 12 mmHg
  - ScvO2 64%
  - Cardiac index 2.4 L/min
  - Repeat lactate 3.2
  - **Recommendations?**

Recommendations? HR 92, BP 96/48 (64) SVV18%, CVP 12 mmHg, ScvO2 64%, Cardiac index 2.4 L/min, Repeat lactate 3.2

A. Start a Dopamine infusion
B. Start a Dobutamine infusion
C. Start a Norepinephrine infusion
D. Administer additional balanced fluid



Case con't

- **Additional 1L IV fluid given**
- Next steps?
  - HR 92, BP 96/48 (64)
  - SVV18%
  - CVP 12 mmHg
  - ScvO2 64%
  - Cardiac index 2.4 L/min
  - Repeat lactate 3.2

Case continued…

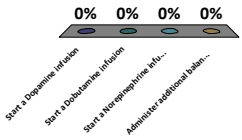
- Additional IV fluids given (5 L total)
- Repeat lactate level 1.6
- HR 94, BP 88/46 (52), RR 15 (Vented 16), O2 sats 96%
- Stroke volume variation 8%
- CVP 10 mmHg
- ScvO2 64%, Cardiac index 2.5 L/min

- Recommendations?

Recommendation? Repeat lactate level 1.6

HR 94, BP 88/46 (52), RR 15 (Vented 16), O_2 sats 96%
Stroke volume variation 8%, CVP 10 mmHg
$ScvO_2$ 64%, Cardiac index 2.5 L/min

A. Start a Dopamine infusion
B. Start a Dobutamine infusion
C. Start a Norepinephrine infusion
D. Administer additional balanced fluid

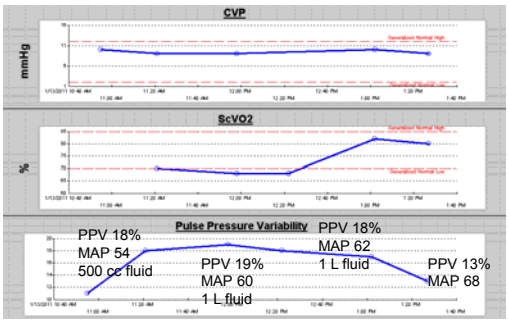


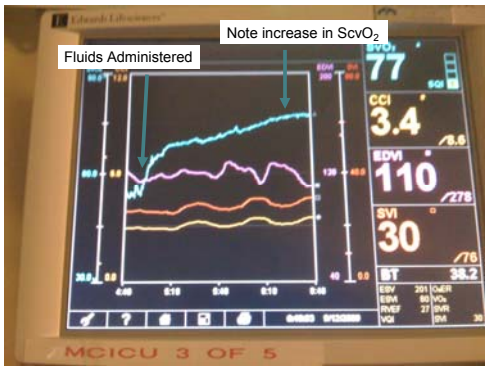
SSG 2012 Recommendations:

- Norepinehrine infusion
  - 1st line vasopressor
- Vasopression 0.3 units/min (do not titrate)
  - 2nd line vasopressor
- ****Dopamine no longer recommended****

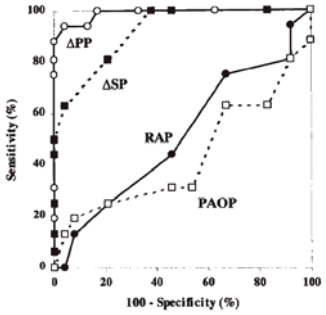
- What about an Inotrope?
- Dobutamine?

Note changes when volume given





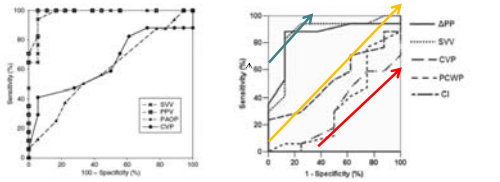
Michard et. al Am J Resp Crit Care Med, 2000



The ability of each parameter to predict fluid responsiveness

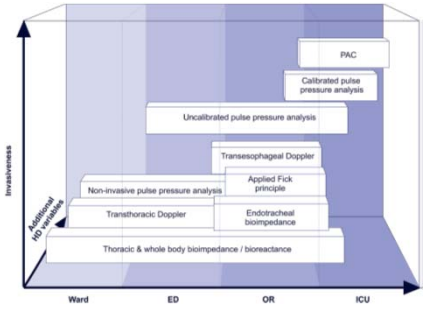
Preload Responsiveness: SVV

Study	Patients	Volume	Tidal Volume ml/Kg	R^2	Def. of Responder	Sensitivity	Specificity
Michard[2]	Sepsis	500 ml	8 to 12	0.85	ΔCO≥15%	94	96
Berkenstadt, et al.[1]	Neuro Surgery	100 ml	10	0.53	ΔSV≥5%	79	98
Reuter, et al.[3]	Cardiac	10 x BMI	10	0.64	ΔSV≥5%	79	85



Areas under the ROC curves for predicting SVI changes >= 5 % Biasis
BJA 2008; Cannesson Anesth Anal 2009

The Best Technology? It Depends!



Alhashemi et al CC 2011 **Integrative concept for the use of cardiac output monitoring devices.**
ED: emergency department; HD: hemodynamic; ICU: intensive care unit; OR: operating room; PAC: pulmonary artery catheter.

Stroke Volume Optimization

A Key Strategy for Reducing Postoperative Complications

Changes in SV can predict whether fluid administration will affect cardiac output.

Methods:

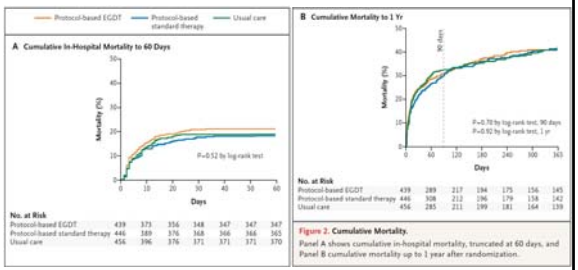
- **Fluid Challenge:** observing changes in SV and CO after the administration of a small volume of fluid will indicate whether additional fluid will increase cardiac performance.
- **Passive Leg Raises (PLR):** raising the legs acts as a self fluid challenge.

25. Source: Monnet X, Rienzo M, Osman D, et al. "Passive leg raising predicts fluid responsiveness in the critically ill." Crit Care Med 2006 Vol.34, No. 5.

ProCESS Trial

- **Pro**tocol-Based **C**are for **E**arly **S**eptic **S**hock
- 3 groups
  - Protocol-Based Early Goal Directed Therapy (EGDT)
  - Protocol-Based Standard Therapy
  - Usual Care
- Protocol-Based had higher use of central lines, fluids, blood transfusion & vasopressors
- ARISE (Australia)
- ProMISe (UK)

ProCESS Trial results



General Critical Care Guidelines

- Establish goals of care
- Hemodynamic goals & end points of resuscitation
- Normalize the lactate
- ARDS: Low TV/PEEP
- Plateau Pressure < 30
- Prone if P/F Ratio < 100
- Conservative Fluid Management if develop ARDS

General Critical Care Guidelines con't

- Keep glucose < 180
- Oral decontamination CHG (intubated)
- DVT Prophylaxis
- Stress Ulcer Prophylaxis
- PO/enteral feedings within 48 hours
- Delirium detection & prevention
- Early mobilization

What does the future hold?

What hasn't worked?

Future studies?

- Biomarkers?
- Does one size fit all?
  - Ethnicity
  - Type of sepsis
  - Phase of sepsis
- What role does EMS play?

In conclusion…

- Identify patients early and provide aggressive therapy in the first few hours
- Establish end-points of resuscitation
- Choose appropriate monitoring for the patient status
- CVP is not reliable method of predicting fluid responsiveness
- Consider formalized programs / approaches for sepsis identification & management throughout the hospital