TURIN, 20TH—21ST NOVEMBER 2008

GREAT INNOVATIONS IN CARDIOLOGY

4TH JOINT MEETING WITH MAYO CLINIC

4TH TURIN CARDIOVASCULAR NURSING CONVENTION

SESSION IV:

THE NEW CARDIAC INTENSIVE CARE UNIT—NO LONGER THE CCU?

R. Hubmayr (Rochester—MN—USA)

Recognition and management of severe sepsis in the cardiac patient

Recognition and Management of the Cardiac Patient with Sepsis

Rolf D Hubmayr, MD

Mayo Clinic College of Medicine

http://mayoresearch.mayo.edu/mayo/research/hubmayr/index.cfm

American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis

Systemic Inflammatory Response Syndrome: The systemic inflammatory response to a variety of severe clinical insults. The response is manifested by two or more of the following conditions:

- Temperature >38°C or <36°C
- Heart rate >90 beats/min
- Respiratory rate >20 breaths/min or $Paco_2$ <32 torr (<4.3 kPa)
- WBC >12,000 cells/mm^3, <4000 cells/mm^3, or >10% immature (band) forms

Sepsis: The systemic response to infection. This systemic response is manifested by two or more of the following conditions as a result of infection:

- Temperature >38°C or <36°C
- Heart rate >90 beats/min
- Respiratory rate >20 breaths/min or $Paco_2$ <32 torr (<4.3 kPa)
- WBC >12,000 cells/mm^3, <4000 cells/mm^3, or >10% immature (band) forms

Severe Sepsis: Sepsis associated with organ dysfunction, hypoperfusion, or hypotension. Hypoperfusion and perfusion abnormalities may include, but are not limited to lactic acidosis, oliguria, or an acute alteration in mental status

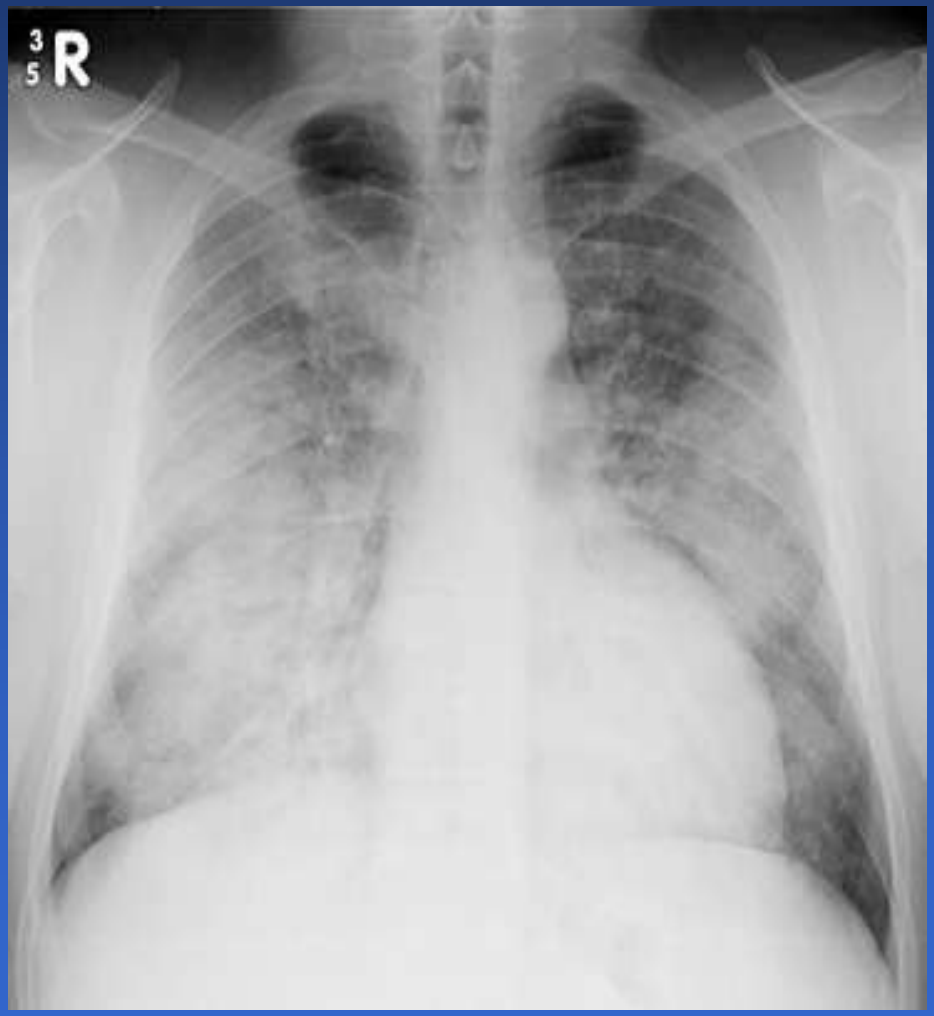
Septic Shock: Sepsis with hypotension, despite adequate fluid resuscitation, along with the presence of perfusion abnormalities that may include, but are not limited to, lactic acidosis, oliguria, or an acute alteration in mental status. Patients who are on inotropic or vasopressor agents may not be hypotensive at the time that perfusion abnormalities are measured

Hypotension: A systolic BP of <90 mm Hg or a reduction of >40 mm Hg from baseline in the absence of other causes for hypotension

Multiple Organ Dysfunction Syndrome: Presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention

CCM: 1992, 20:864

Does this patient have pneumonia or heart failure?



Optimal therapeutic approaches to ICU-acquired pneumonia

On Which Grounds Should Empiric Therapy for ICU-Acquired Pneumonia be Initiated

- Several observational studies have shown that immediate initiation of appropriate antibiotics is associated with a reduced mortality in patients suspected of pneumonia
- Excess mortality of inappropriate antibiotics is not reduced by correction of regimens when culture results are available 24-48 hours later
- Microbiological specimens must be obtained and antibiotics begun promptly if there is sufficient clinical suspicion of ICU-AP
- However, the benefits of such an approach requires discontinuation of antibiotics if culture results are negative and the patient has not deteriorated in the ensuing 48 to 72 hours

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

Initial resuscitation (first 6 hrs)

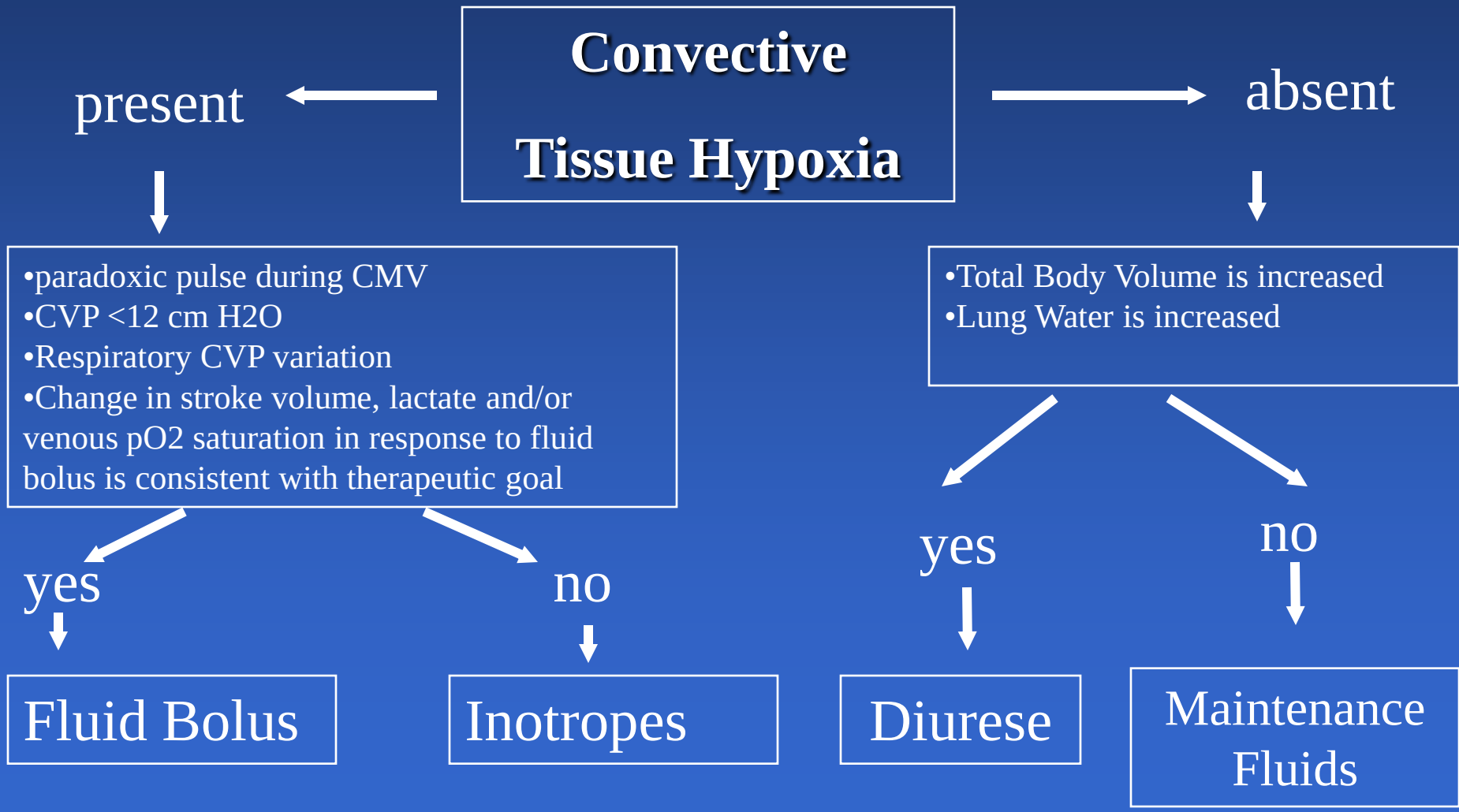
- Begin resuscitation immediately in patients with hypotension or elevated serum lactate >4 mmol/L; do not delay pending ICU admission (1C)
- Resuscitation goals (1C)
  CVP 8–12 mm Hg[a]
  Mean arterial pressure ≥ 65 mm Hg
  Urine output ≥0.5 mL·kg^{-1}·hr^{-1}
  Central venous (superior vena cava) oxygen saturation ≥70% or mixed venous ≥65%
  - If venous oxygen saturation target is not achieved (2C)
    Consider further fluid
    Transfuse packed red blood cells if required to hematocrit of ≥30% and/or
    Start dobutamine infusion, maximum 20 μg·kg^{-1}·min^{-1}

Crit Care Med 2008 Vol. 36, No. 1

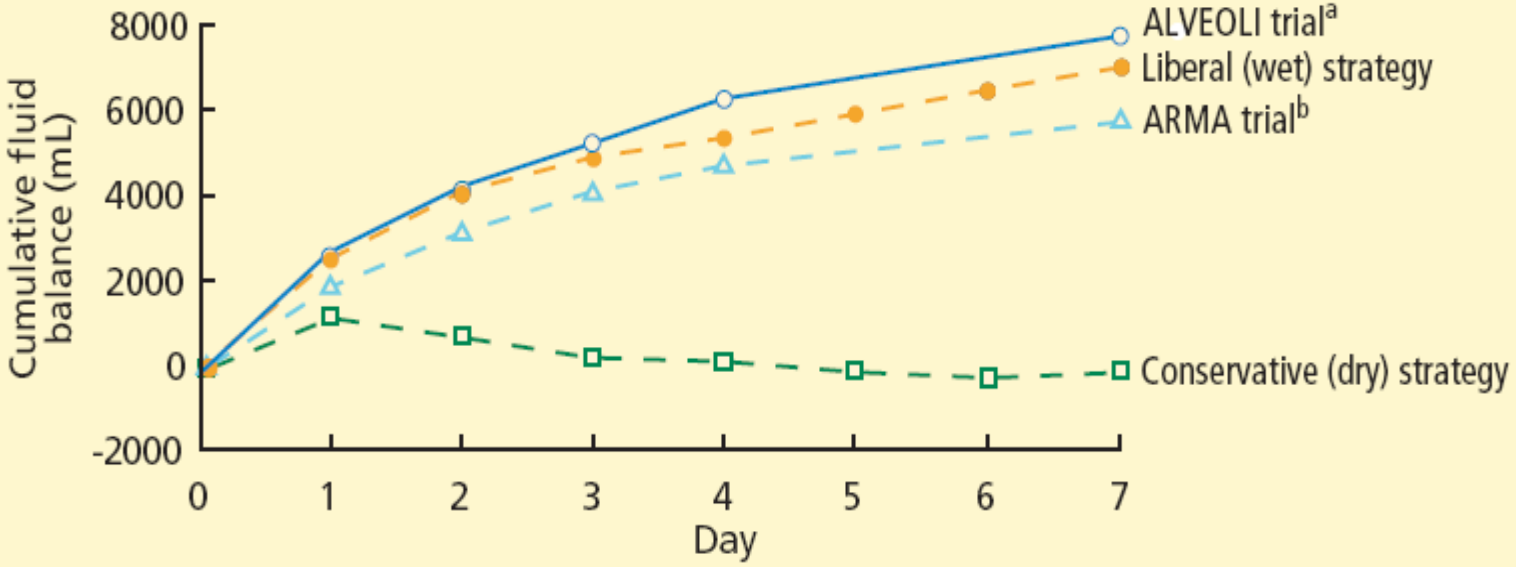
Rivers et al
Early Goal Directed Therapy in the Treatment of Sepsis and severe septic Shock
NEJM Vol 345, pg 1368, Nov 2001

	Standard Rx	Goal Directed Rx	Relative risk	Probability
In-hospital mortality	46.5%	30.5%	0.38 - 0.87	0.009
28 day Mortality	49.2%	33%	0.39 – 0.87	0.01
60 day Mortality	56.9%	43.3%	0.46 – 0.96	0.03

A guide to fluid management in the critically ill patient



The ARDS Network FACTT Trial

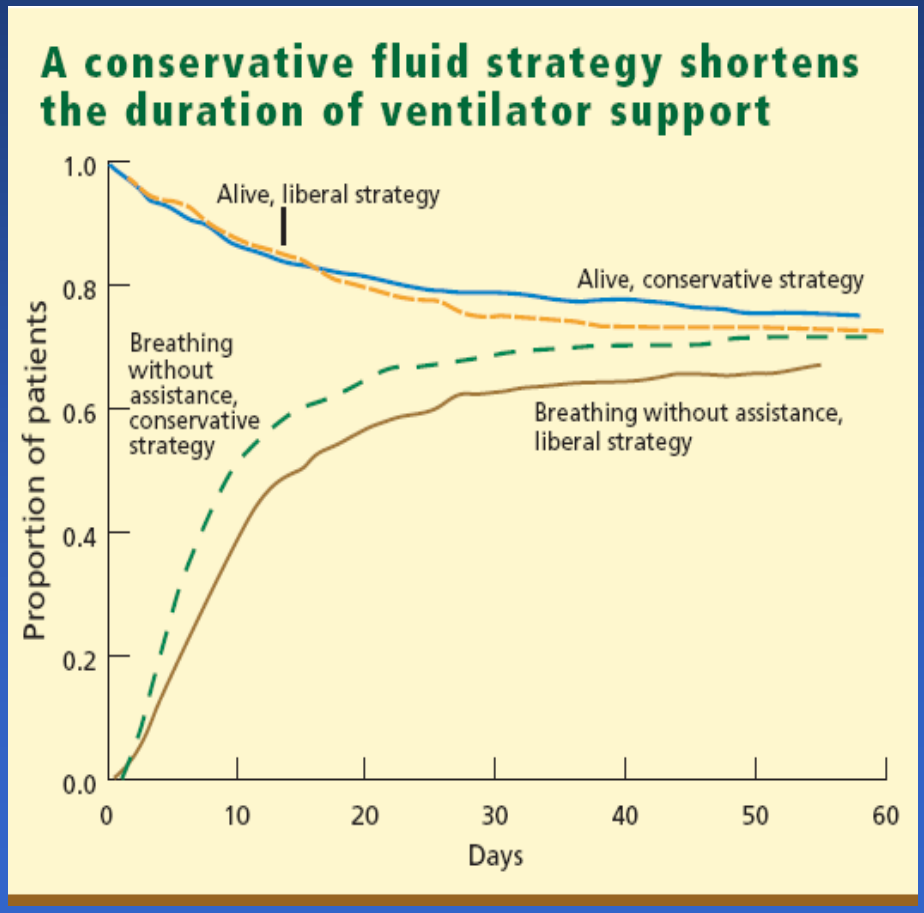


[a]ALVEOLI trial: Assessment of Low Tidal Volume and Elevated End-expiratory Volume to Obviate Lung Injury (N Engl J Med 2004; 351:327–336).

[b]ARMA trial: Prospective, Randomized, Multi-Center Trial of 12 mL/kg/ Tidal Volume Positive Pressure Ventilation for Treatment of Acute Lung Injury and Acute Respiratory Distress Syndrome (N Engl J Med 2000; 342:1301–1308).

N Engl J Med 2006;354:2564-75.

The ARDS Network FACTT Trial

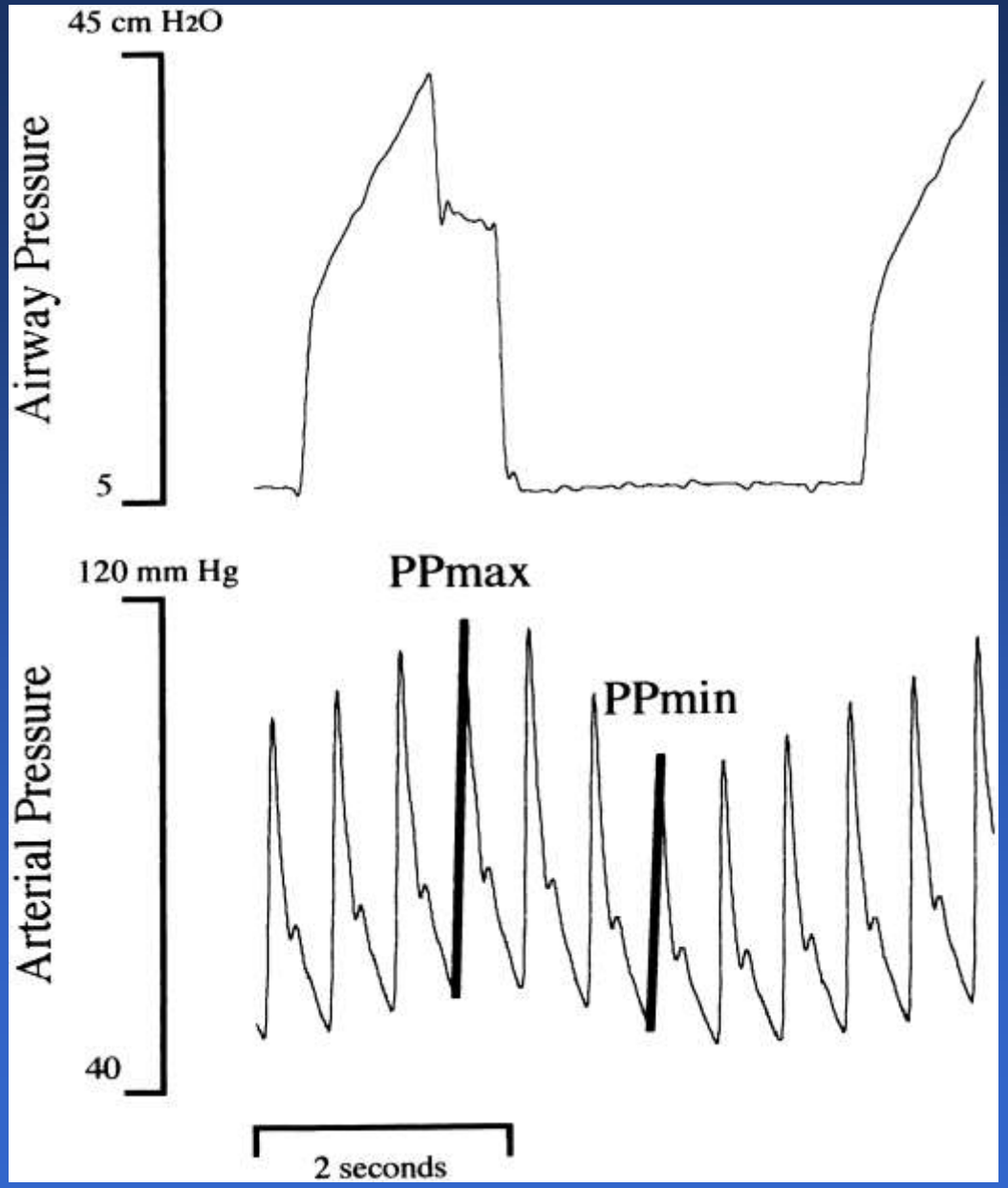


Renal and metabolic function. At day 7, the conservative-strategy group had a significantly higher blood urea nitrogen level (33.62 vs 28.44 mg/dL; P = .009). No significant differences were seen between the groups in creatinine levels at day 7 and day 28.

N Engl J Med 2006;354:2564-75.

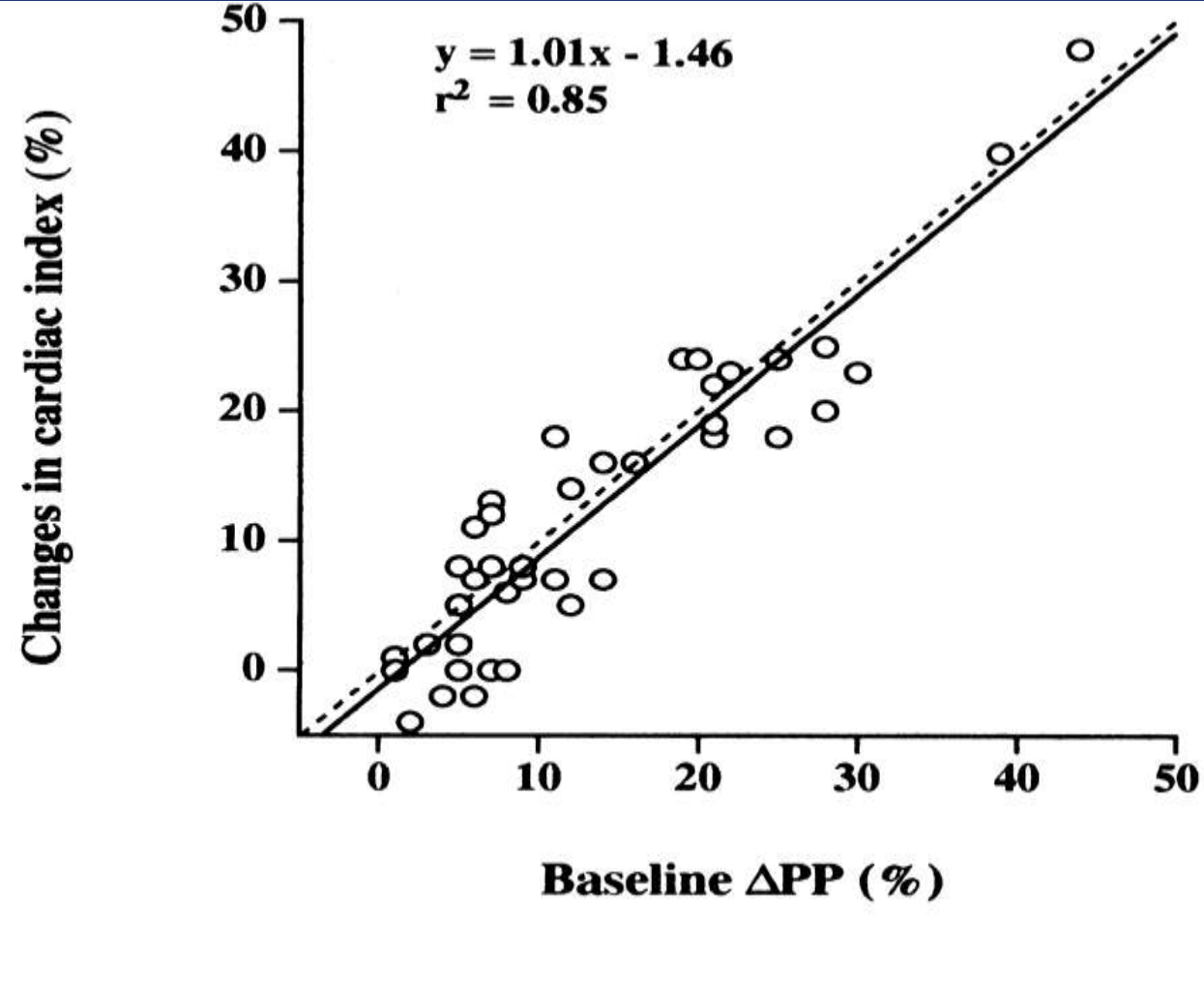
Heart-Lung Interactions in Mechanically Ventilated Patients

$$dPP = \frac{(Ppmax - Ppmin)}{avg(Ppmax, min)}$$



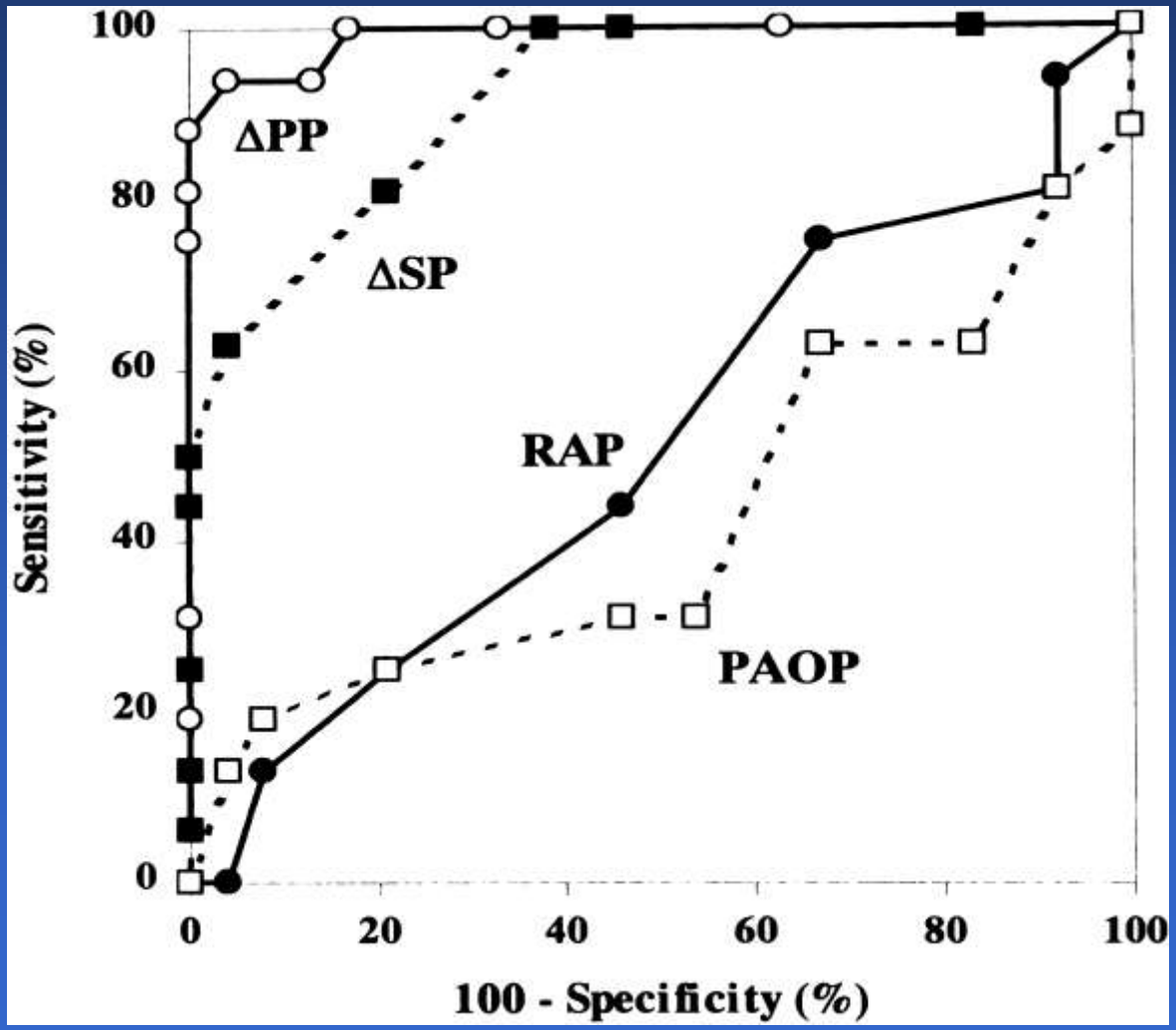
F Michard et al._Am. J. Respir. Crit. Care Med. 2000 162: 134-138.

Paradox Pulse in Mechanically Ventilated Patients with septic Shock



F Michard et al._Am. J. Respir. Crit. Care Med. 2000 162: 134-138.

Predictive Value of Different Methods used to Assess Fluid Status

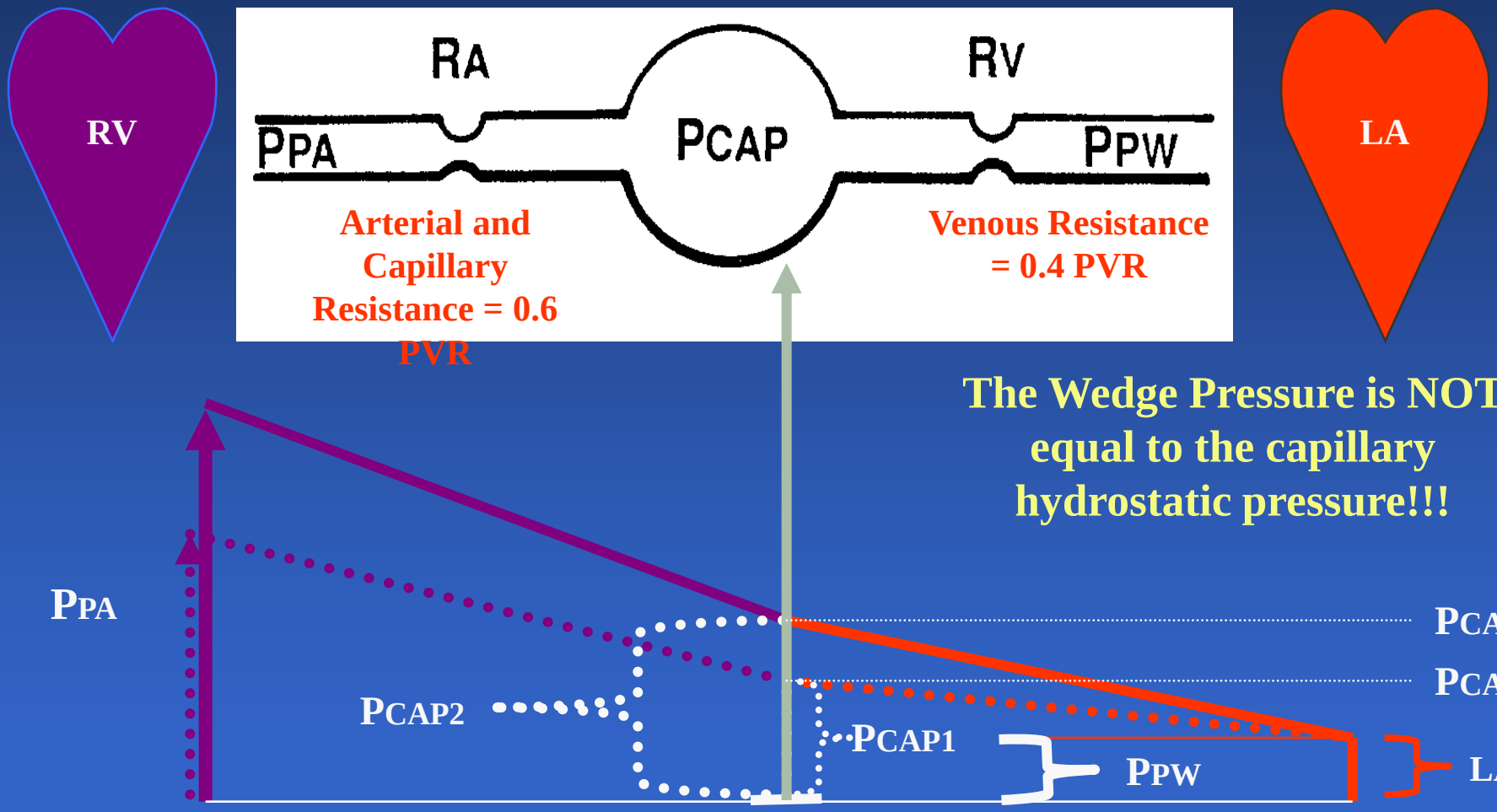


F Michard et al._Am. J. Respir. Crit. Care Med. 2000 162: 134-138.

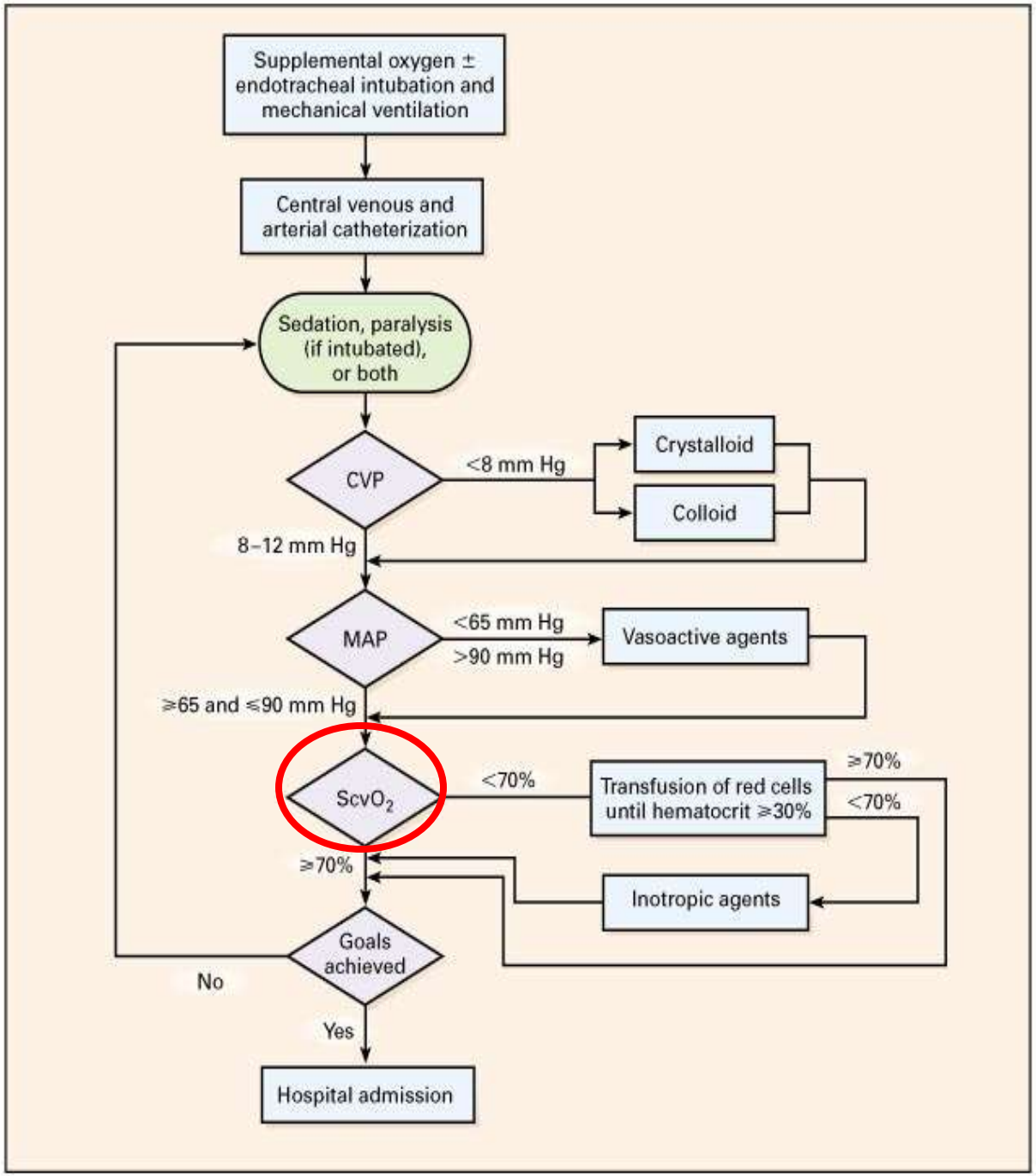
Arterial Pressure Monitoring

Current Opinion in Critical Care 2006, 12:219–227

There is Nothing Magical about a Wedge of 18

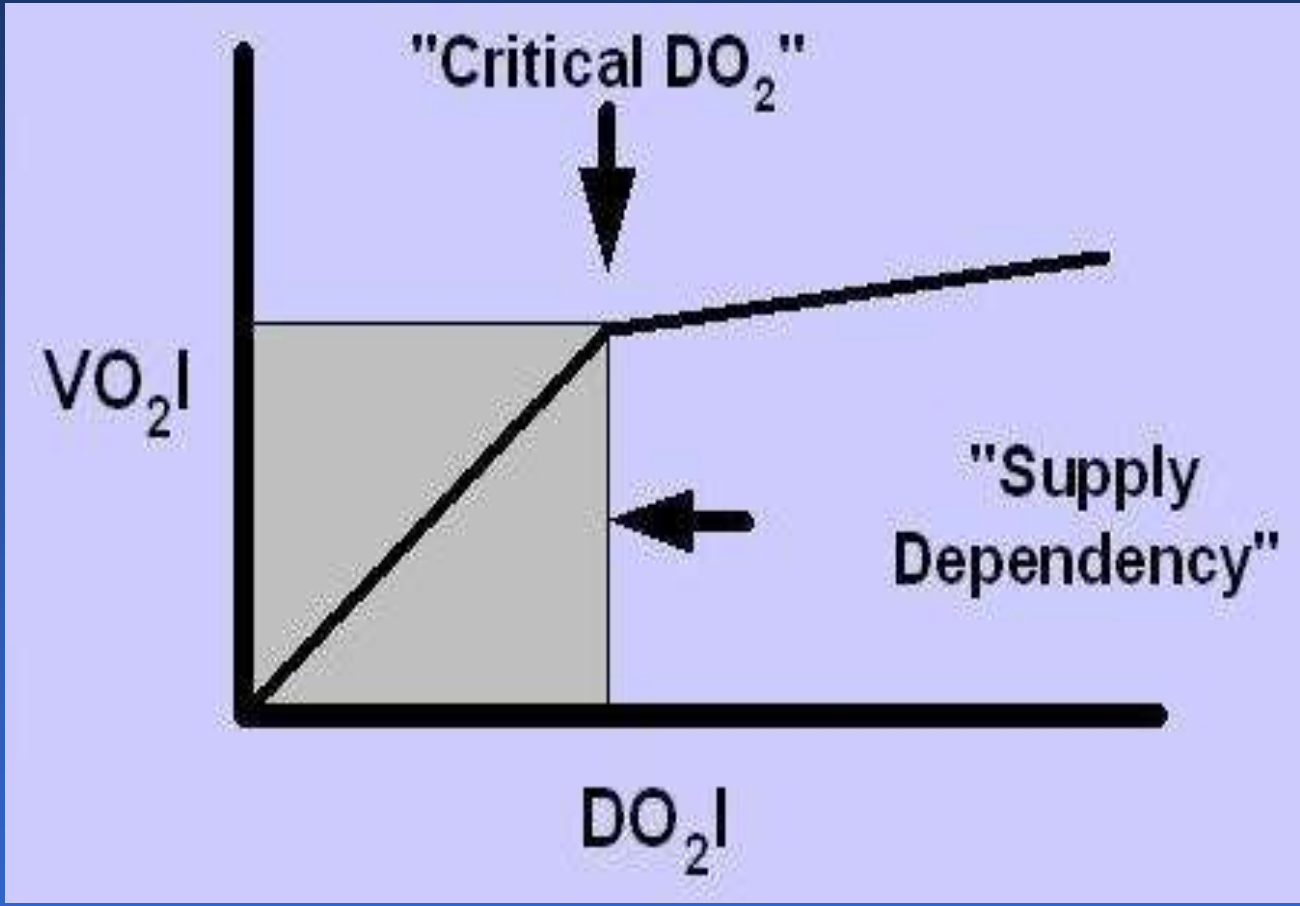


Rivers et al Early Goal Directed Therapy in the Treatment of Sepsis and severe septic Shock NEJM Vol 345, pg 1368, Nov 2001



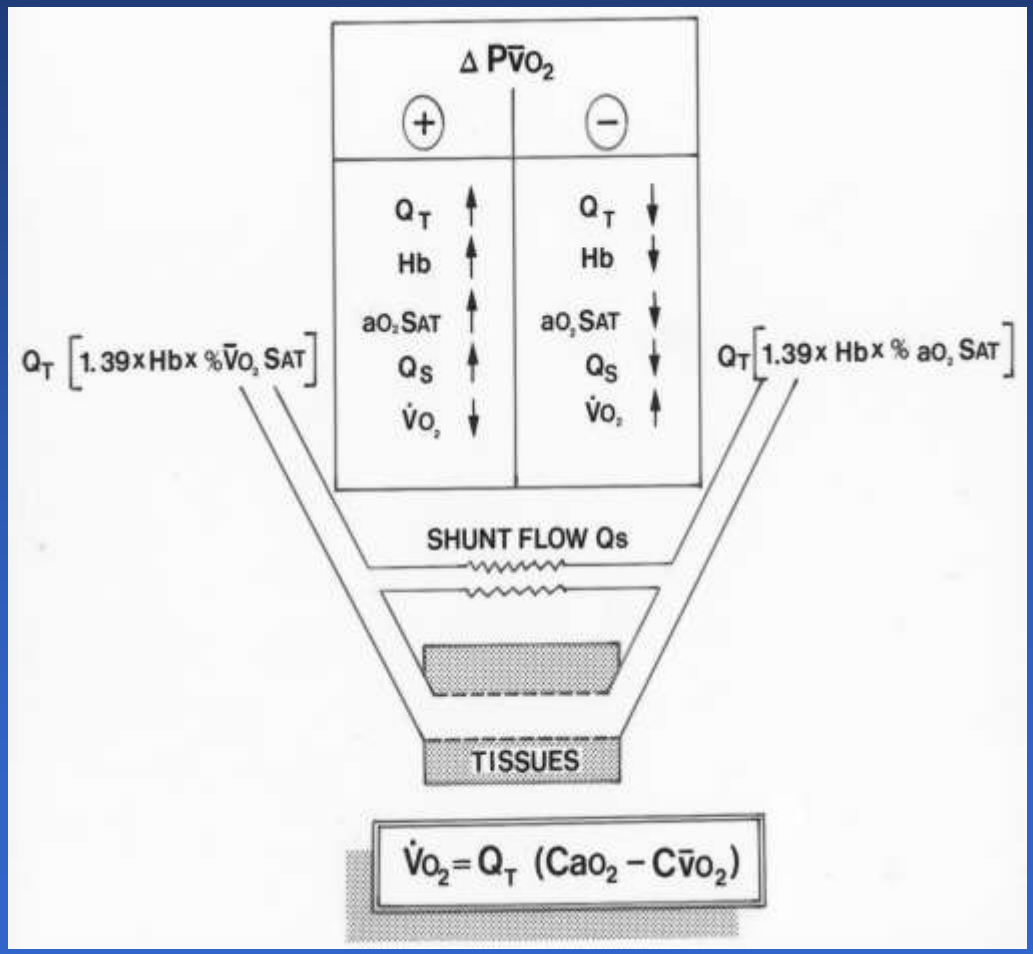
Supply Dependence of O2 Consumption

Metabolic Rate

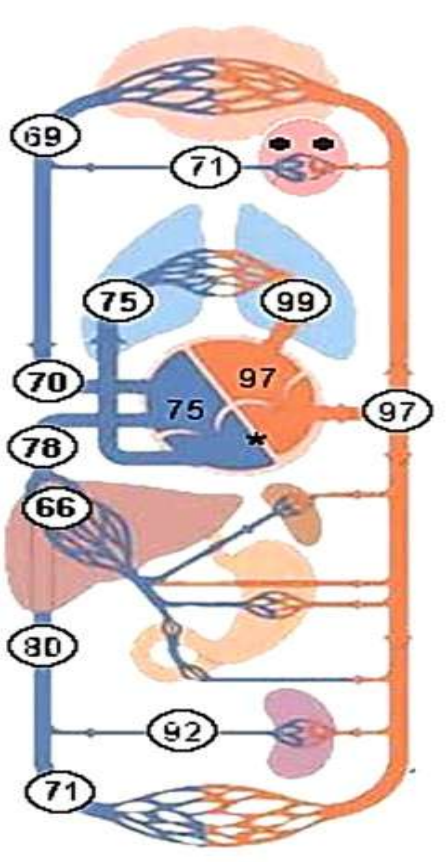


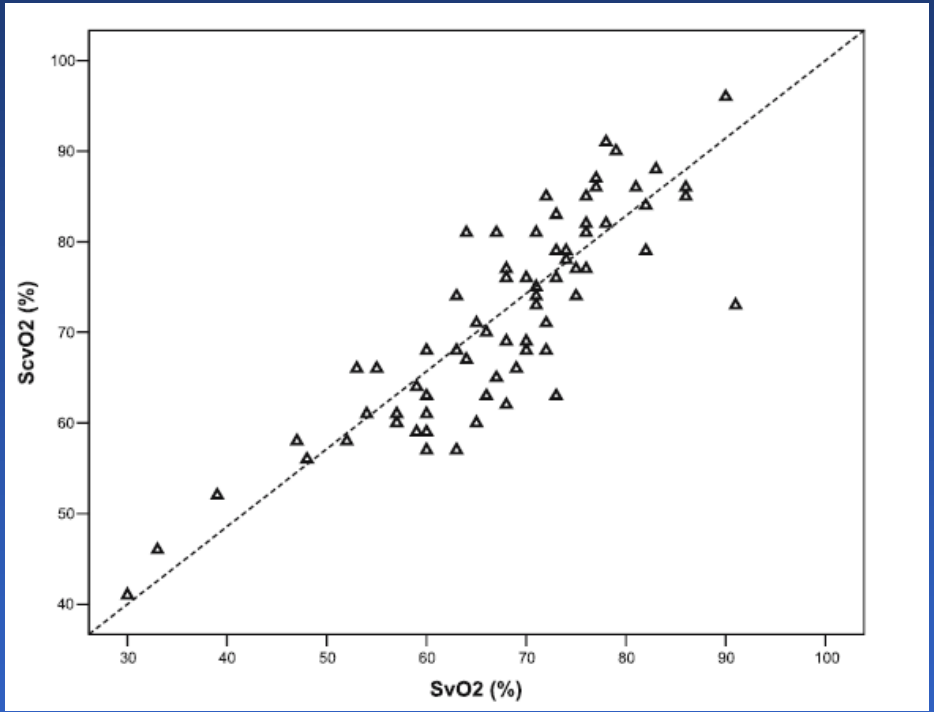
Cardiac Output, Arterial O2 Content

The Determinants of the Mixed Venous O_2 Tension



Where should venous O2 saturation be monitored?





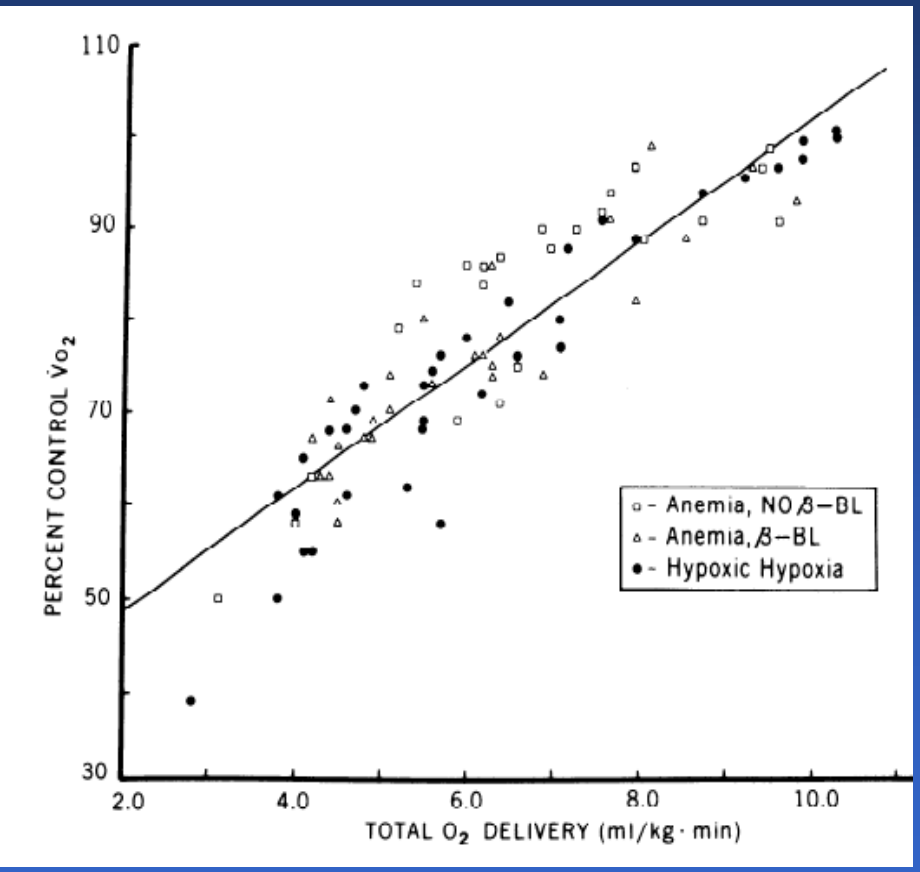
Intensive Care Med (2006) 32:1336–1343
DOI 10.1007/s00134-006-0270-y

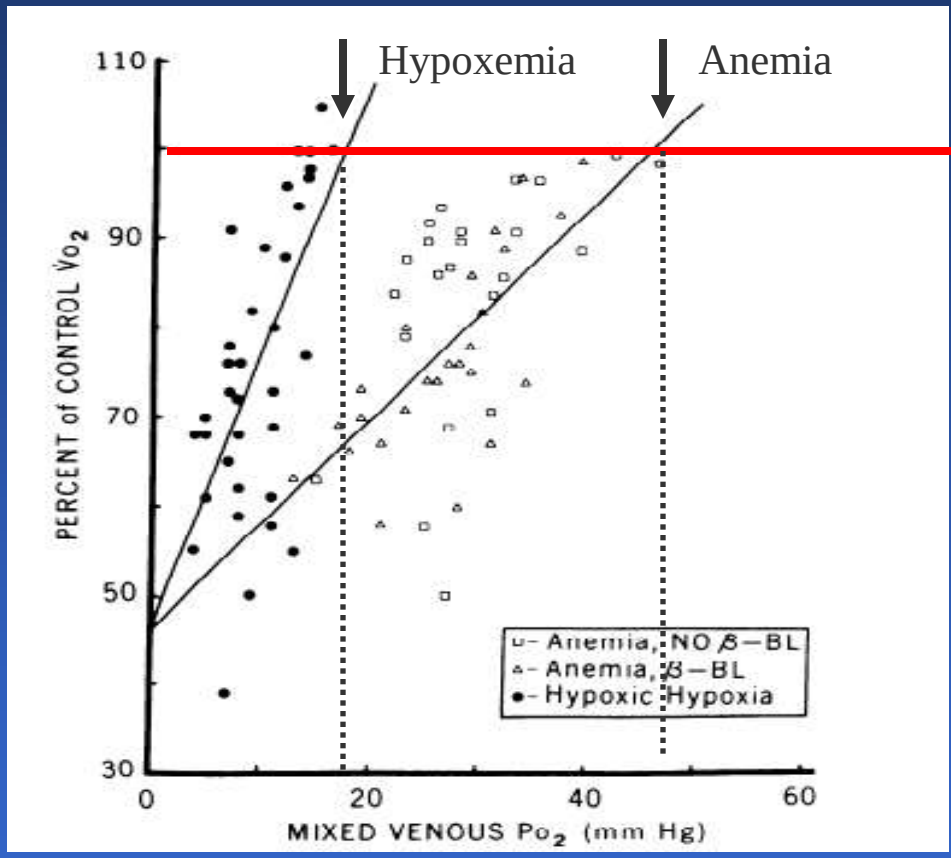
Searching for non-invasive markers of tissue hypoxia

Juan Carlos Puyana[1] and Michael R Pinsky[2]

Critical Care 2007, 11:116 (doi:10.1186/cc5691)

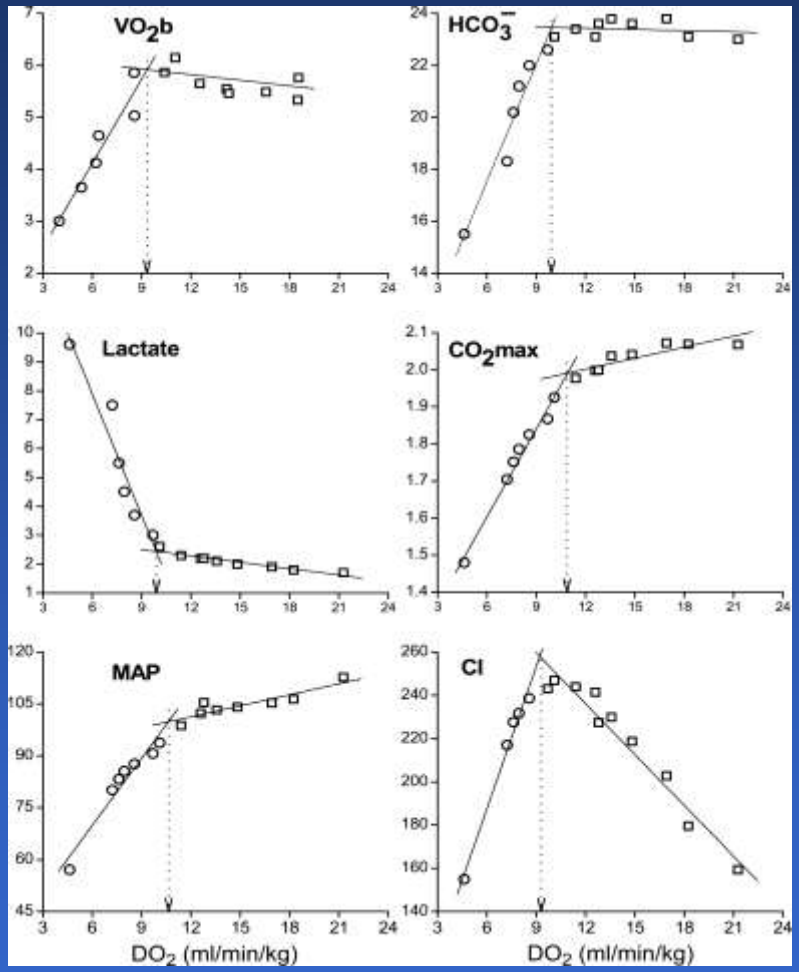
Is there a single venous O_2 saturation threshold indicative of tissue hypoxia ?

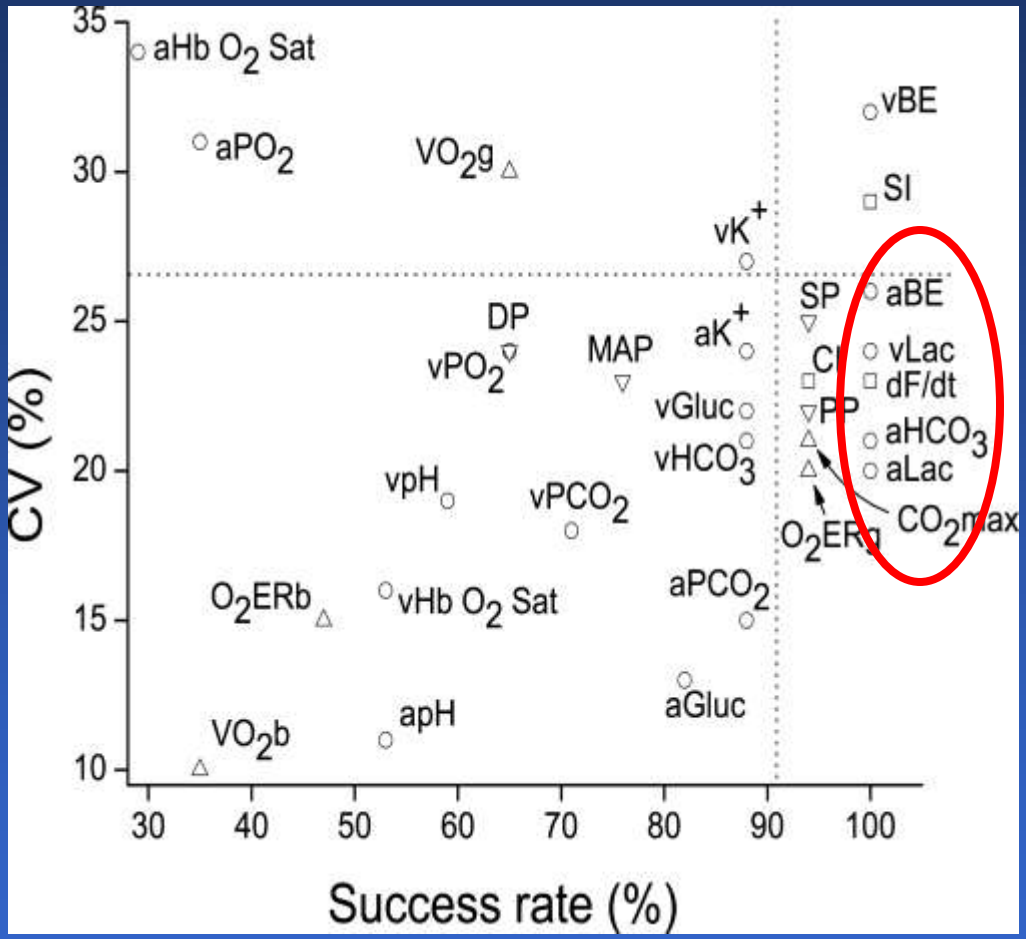




CAIN, STEPHEN M. *Oxygen delivery and uptake in dogs during anemic and hypoxic hypoxia*. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 42(2): 228–234, 1977. – Three

Surrogate Markers of D_{CRIT} during Anemic Hypoxia

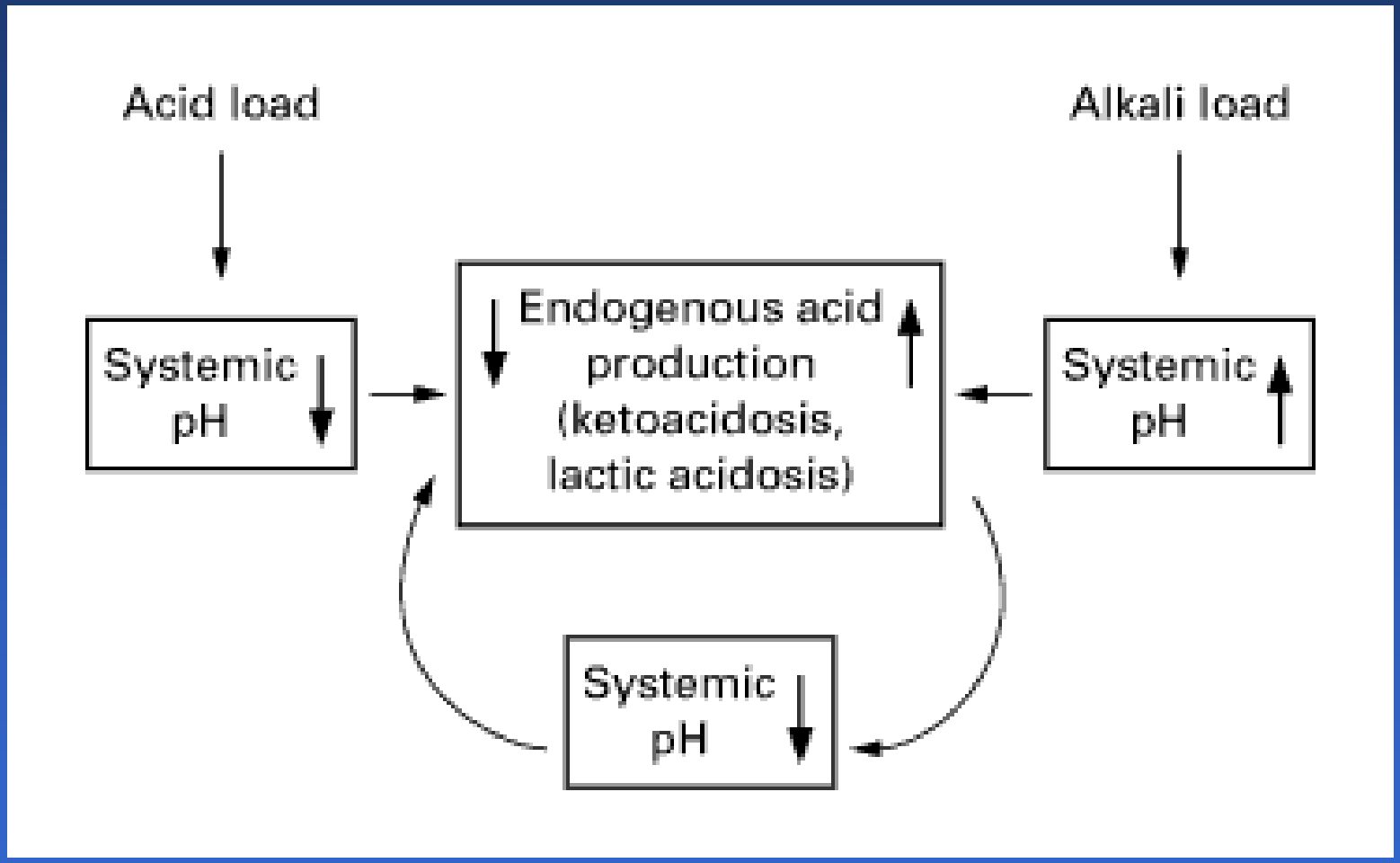




Torres Filho, I. P. et al. Am J Physiol Heart Circ Physiol 288: H1071-H1079 2005;
doi:10.1152/ajpheart.00884.2004

AJP - Heart and Circulatory Physiology

Negative Feedback Control of Endogenous Acid Production



Hood & Tannen. NEJM 339: 819, 1998

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

Initial resuscitation (first 6 hrs)

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- Resuscitation goals (1C)
  CVP 8–12 mm Hg[a]
  Mean arterial pressure ≥ 65 mm Hg
  Urine output ≥0.5 mL·kg^{-1}·hr^{-1}
  Central venous (superior vena cava) oxygen saturation ≥70% or mixed venous ≥65%
- ○ If venous oxygen saturation target is not achieved (2C)
  Consider further fluid
  Transfuse packed red blood cells if required to hematocrit of ≥30% and/or
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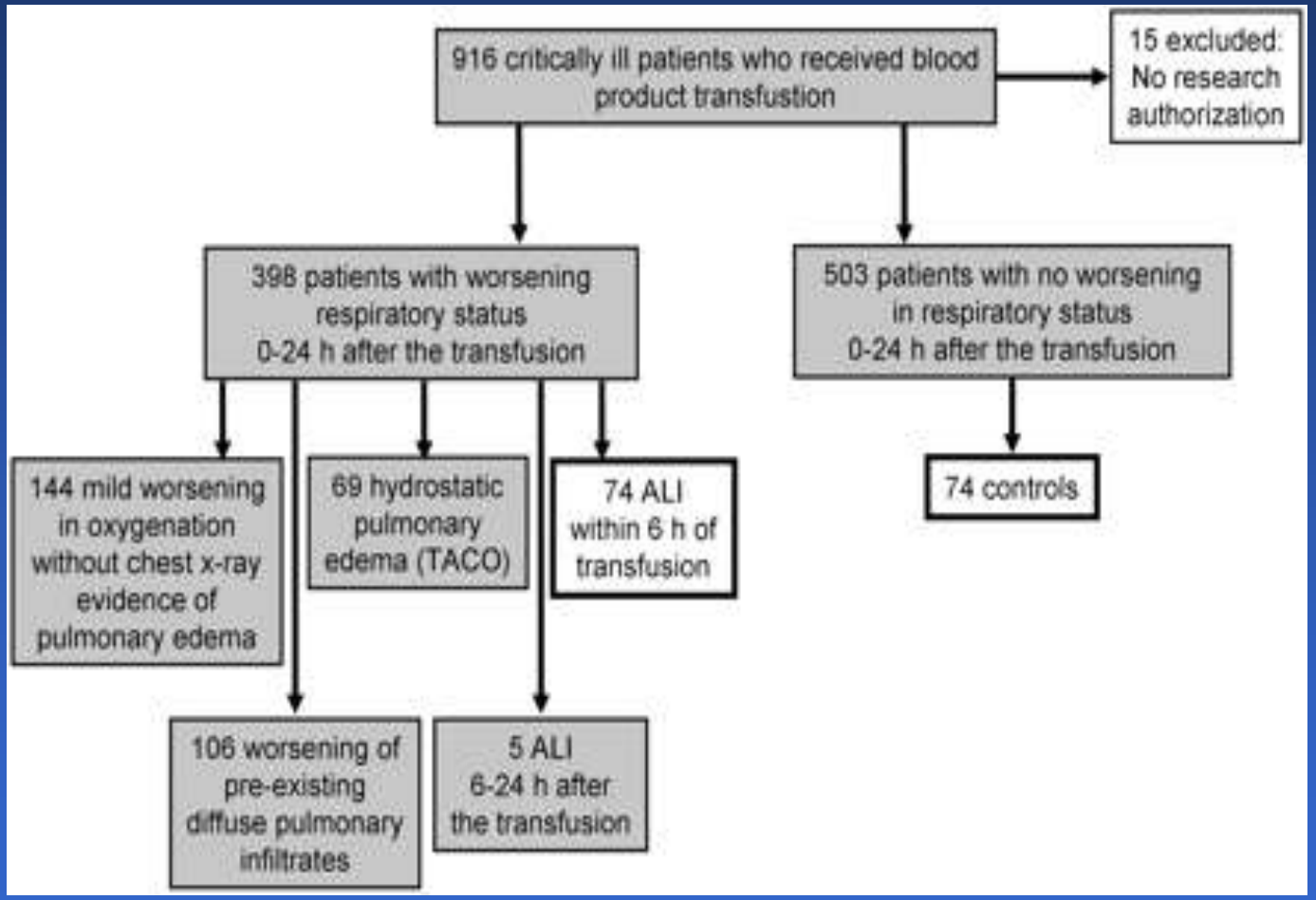
Transfusion related Risk for ALI



Ognjen Gajic[1,4], Am J Respir Crit Care Med Vol 176. pp 886–891, 2007

Transfusion related Risk Factors in ALI

Variable	Unadjusted* OR (95% CI)	Unadjusted* P Value	Adjusted† OR (95% CI)	Adjusted† P Value
Any high plasma volume components (FFP or platelets)	2.55 (1.27–5.11)	0.009	2.78 (1.21–6.38)	0.016
Number of units	1.09 (0.99–1.20)	0.081	1.11 (0.99–1.25)	0.086
Number of units from female donors	1.30 (1.03–1.66)	0.029	1.51 (1.08–2.12)	0.016
Amount of plasma from male donors, L	1.55 (0.79–3.06)	0.202	1.60 (0.76–3.37)	0.215
Amount of plasma from female donors, L	3.23 (1.17–8.91)	0.024	5.09 (1.37–18.85)	0.015
Amount of plasma from female donors with at least one pregnancy, L	4.41 (1.00–19.55)	0.050	9.48 (1.38–65.35)	0.022
Number of pregnancies among donors	1.11 (1.00–1.22)	0.047	1.19 (1.05–1.34)	0.007
Number of HLA class I+ units	1.81 (0.97–3.38)	0.061	1.70 (0.94–3.09)	0.098
Number of HLA class II+ units	1.93 (0.88–4.28)	0.103	3.08 (1.15–8.25)	0.025
Number of GIF+ units	4.19 (1.22–14.32)	0.023	4.85 (1.32–17.86)	0.018
Mean LysoPC 16:0** (per 10-mol/L increase)	1.16 (1.04–1.30)	0.011	1.16 (1.02–1.32)	0.022
Mean LysoPC 18:0** (per 10-mol/L increase)	1.58 (1.10–2.26)	0.013	1.61 (1.08–2.38)	0.018

Definition of abbreviations: CI = confidence interval; FFP = fresh-frozen plasma; LysoPC = lysophosphatidylcholine; OR = odds ratio.

For continuous variables, ORs were calculated per unit of measurement: for each additional unit transfused, for each additional liter of plasma (1 L of plasma corresponds to a usual dose of about 4 units of FFP), for each 10-μmol/L increase in LysoPC).

* Unadjusted for baseline APACHE III score, sepsis, and chronic alcohol abuse.

† Adjusted for baseline APACHE III score, sepsis, and chronic alcohol abuse.

** 16:0 and 18:0 refer to palmitic and stearic acid, respectively.

Ognjen Gajic[1,4], Am J Respir Crit Care Med Vol 176. pp 886–891, 2007

Transfusion Risk: Key Points

1. Transfusion associated Respiratory Impairment is common
2. The majority of cases are TACO
3. The incidence TRALI is approximately1:3000 units transfused and afflicts approximately 1 in 500 patients
4. The risk is greatest for units containing female plasma
5. Efforts to reduce unnecessary transfusions lower the incidents of hospital acquired ALI

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

Vasopressors

- Maintain MAP ≥65 mm Hg (1C)
- Norepinephrine and dopamine centrally administered are the initial vasopressors of choice (1C)
  - Epinephrine, phenylephrine, or vasopressin should not be administered as the initial vasopressor in septic shock (2C). Vasopressin 0.03 units/min may be subsequently added to norepinephrine with anticipation of an effect equivalent to norepinephrine alone
  - Use epinephrine as the first alternative agent in septic shock when blood pressure is poorly responsive to norepinephrine or dopamine (2B).
- Do not use low-dose dopamine for renal protection (1A)
- In patients requiring vasopressors, insert an arterial catheter as soon as practical (1D)

Inotropic therapy

- Use dobutamine in patients with myocardial dysfunction as supported by elevated cardiac filling pressures and low cardiac output (1C)
- Do not increase cardiac index to predetermined supranormal levels (1B)

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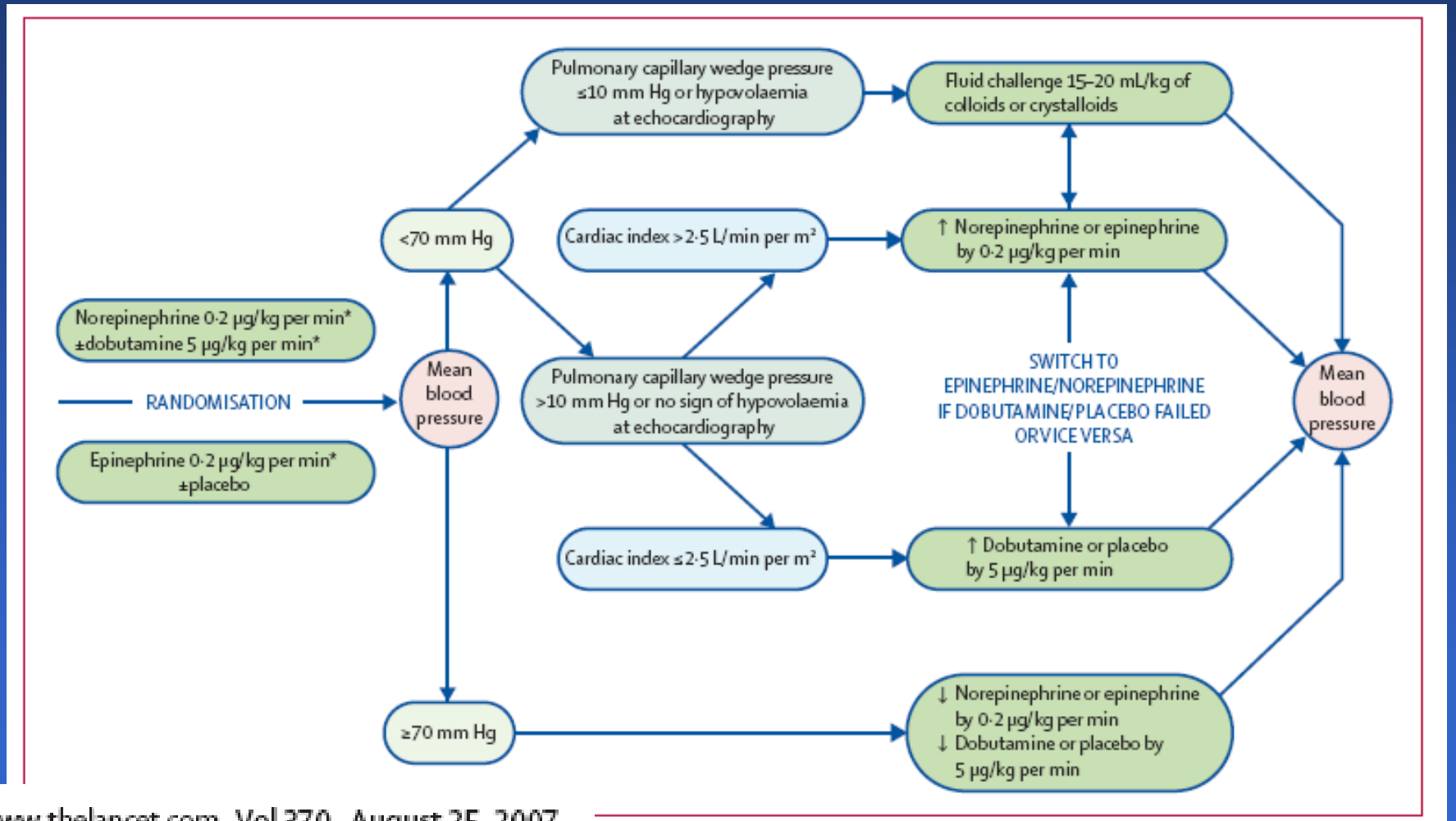
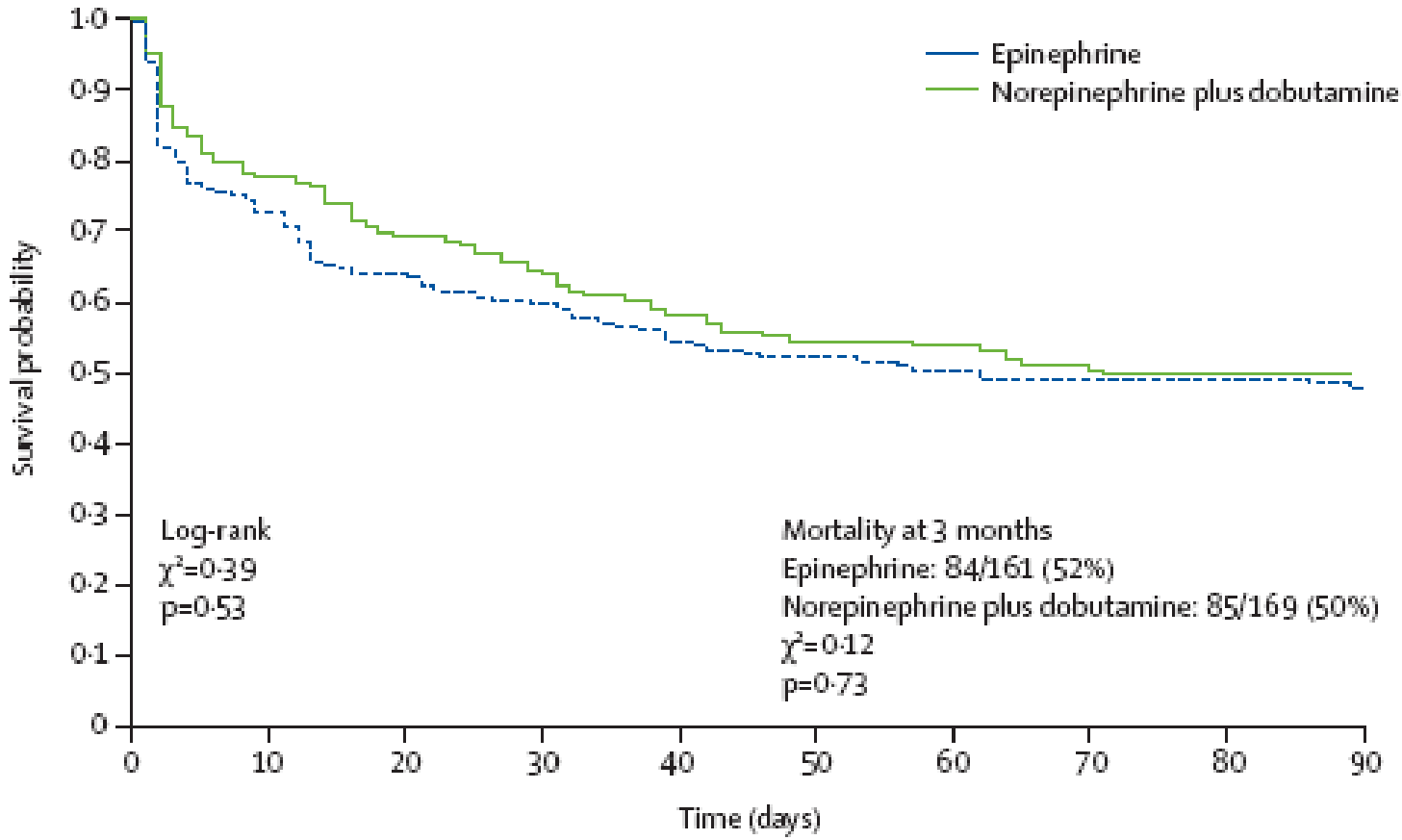
Norepinephrine plus dobutamine versus epinephrine alone for management of septic shock: a randomised trial

*Djillali Annane, Philippe Vignon, Alain Renault, Pierre-Edouard Bollaert, Claire Charpentier, Claude Martin, Gilles Troché, Jean-Damien Ricard, Gérard Nitenberg, Laurent Papazian, Elie Azoulay, Eric Bellissant, for the CATS Study Group**



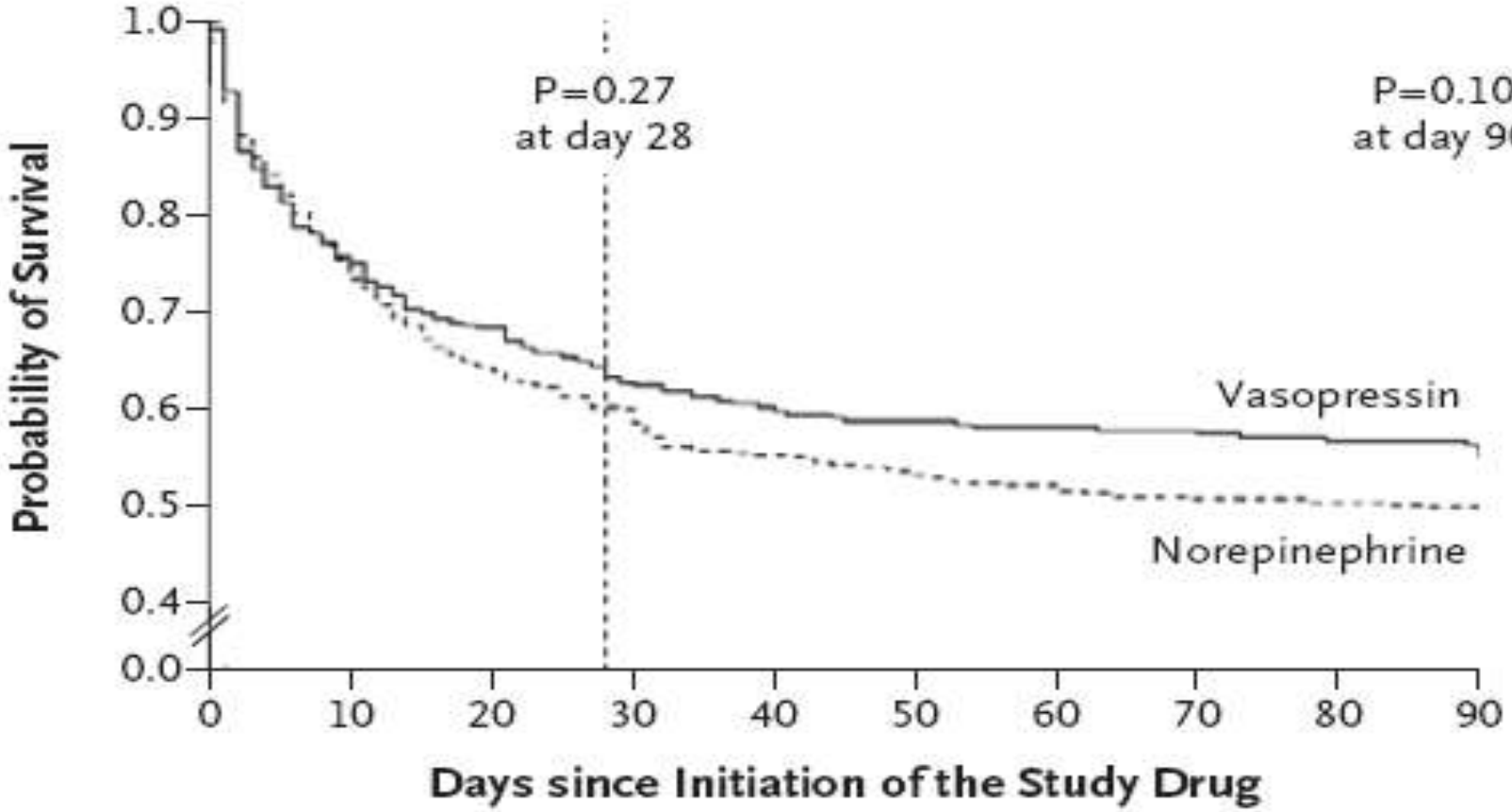
Norepinephrine plus dobutamine versus epinephrine alone for management of septic shock: a randomised trial



Number at risk

Epinephrine	161	117	102	96	88	84	81	79	79	74
Norepinephrine plus dobutamine	169	131	117	108	98	92	91	85	84	84

Vasopressin versus Norepinephrine Infusion in Patients with Septic Shock



No. at Risk

Vasopressin	397	301	272	249	240	234	232	230	226	220
Norepinephrine	382	289	247	230	212	205	200	194	193	191

N Engl J Med 2008;358:877-87.

Sanjay Subramanian
Murat Yilmaz
Ahmer Rehman
Rolf D. Hubmayr
Bekele Afessa
Ognjen Gajic

Intensive Care Med
DOI 10.1007/s00134-007-0862-1

Liberal vs. conservative vasopressor use to maintain mean arterial blood pressure during resuscitation of septic shock: an observational study

		Conservative vasopressor therapy ($n = 49$)	Liberal vasopressor therapy ($n = 46$)	Significance (p)
Fluid resuscitation and tissue perfusion	Fluid received in 6 h (l)	3.31 (1.6–4.8)	5.5 (4.1–8.6)	< 0.01
	CVP at 6 h, mm Hg, $n = 69$	6 (2–9)	8 (6–12)	< 0.01
	$ScvO_2$ at 6 h, %, $n = 45$	65 (56–74)	67 (58–77)	0.45
	Adequate global perfusion, n (%) perfusion, n (%)	28 (57)	35 (76)	0.04
	Serum lactate (mmol/l)	2.2 (1.2–3.5)	3.4 (1.8–4.9)	0.02
Vasopressor use	AUC of untreated hypotension (< 65) mm Hg×h, median (IQR)	26.96 (39.51–14.33)	3.812 (8.88–0.55)	< 0.01
	Duration of untreated hypotension, minutes, median (IQR)	153 (106–244)	38 (23–60)	< 0.01
	Type of pressor			
	Dopamine	4	7	0.28
	Phenylephrine	7	7	0.89
	Norepinephrine	22	33	< 0.01
	Vasopressin	13	28	< 0.01
Other interventions	Adequate antibiotic therapy, n (%)	36 (73)	32 (69)	0.17
	Dobutamine, n (%)	4 (8)	8 (17)	0.17
	RBC transfusion, n (%)	14 (29)	14 (30)	0.84
	Mechanical ventilation at the onset of septic shock, n (%)	9 (18)	27 (59)	< 0.01
	Mechanical ventilation any, n (%)	24 (48)	36 (78)	< 0.01
	Steroids for relative adrenal insufficiency, n (%)	8 (16)	18 (39)	0.03
	Activated protein C, n (%)	11 (23)	16 (35)	0.18

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Liberal vs. conservative vasopressor use to maintain mean arterial blood pressure during resuscitation of septic shock: an observational study

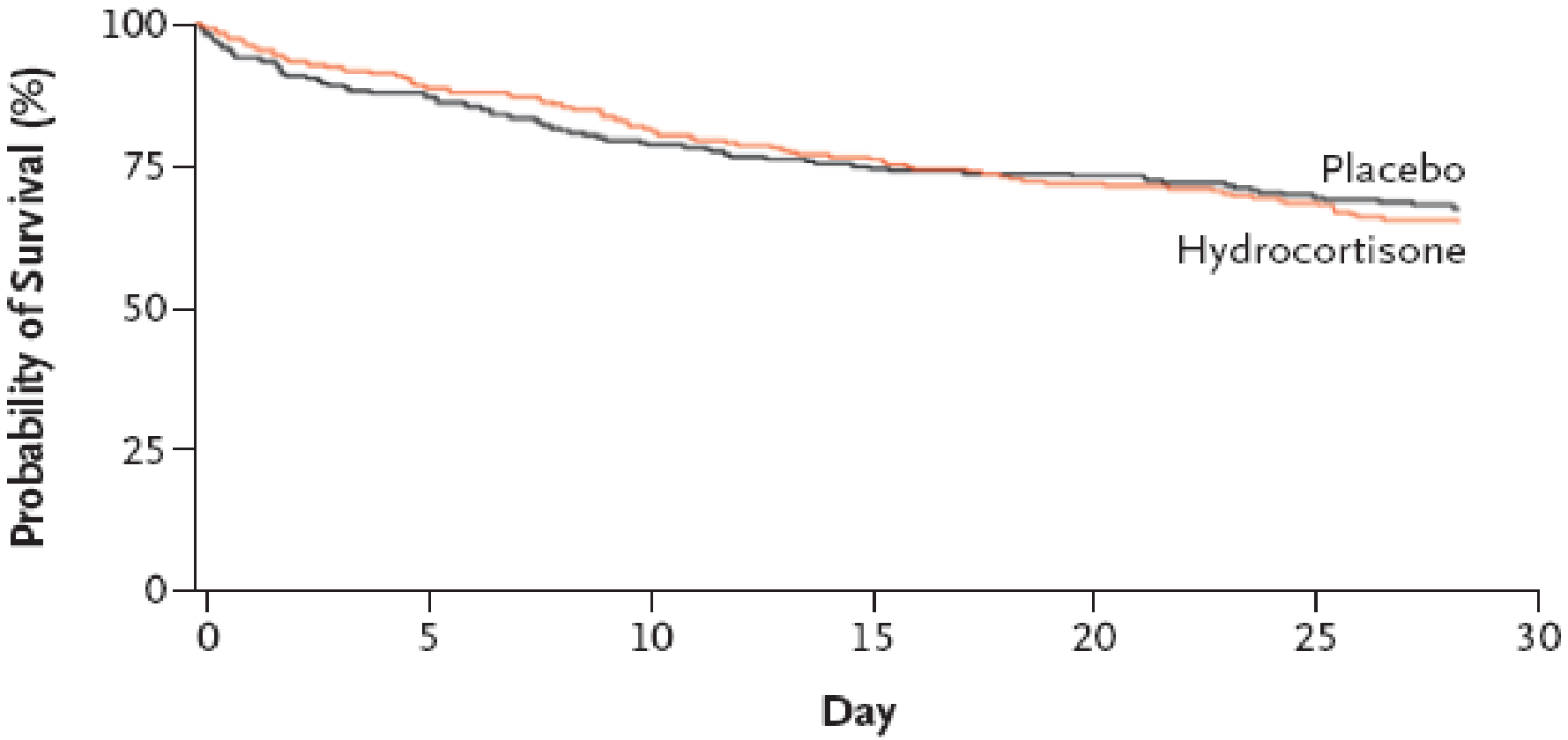
	Conservative vasopressor therapy ($n = 49$)	Liberal vasopressor therapy ($n = 46$)	Significance (p)
SOFA at 24 h, median (IQR)	8 (4–11)	10 (6–13)	0.04
Non-cardiovascular SOFA at 24 h, median (IQR)[a]	6 (4–8)	7 (4–10)	0.06
Change in SOFA at 24 h, median (IQR)	−1 (−2 to 2)	+1 (−1 3 to 3)	0.05
Progression of organ failures (SOFA worsening at 24 h), n (%)	18 (37)	27 (59)	0.03
Change in non-cardiovascular SOFA at 24 h, median (IQR)[a]	0 (−3 to 0)	0 (0–2)	< 0.01
Progression of organ failures (non-cardiovascular SOFA worsening at 24 h), n (%)[a]	10 (20)	21 (46)	< 0.01
Change in creatinine (mg/dl), median (IQR)	−0.1(0 to −0.4)	−0.2 (0.02 to −0.4)	0.59
Hospital mortality, n (%)	15 (30)	16 (34)	0.66
ICU LOS, days, median (IQR)	2.73 (5.23–1.56)	4.14 (6.67–2.08)	0.09

N Engl J Med 2008;358:111-24. JANUARY 10, 2008 VOL. 358 NO. 2

Hydrocortisone Therapy for Patients with Septic Shock

Charles L. Sprung, M.D., Djillali Annane, M.D., Ph.D., Didier Keh, M.D., Rui Moreno, M.D., Ph.D., Mervyn Singer, M.D., F.R.C.P., Klaus Freivogel, Ph.D., Yoram G. Weiss, M.D., Julie Benbenishty, R.N., Armin Kalenka, M.D., Helmuth Forst, M.D., Ph.D., Pierre-Francois Laterre, M.D., Konrad Reinhart, M.D., Brian H. Cuthbertson, M.D., Didier Payen, M.D., Ph.D., and Josef Briegel, M.D., Ph.D., for the CORTICUS Study Group*

C All Patients



N Engl J Med 2005;353:1332-41.

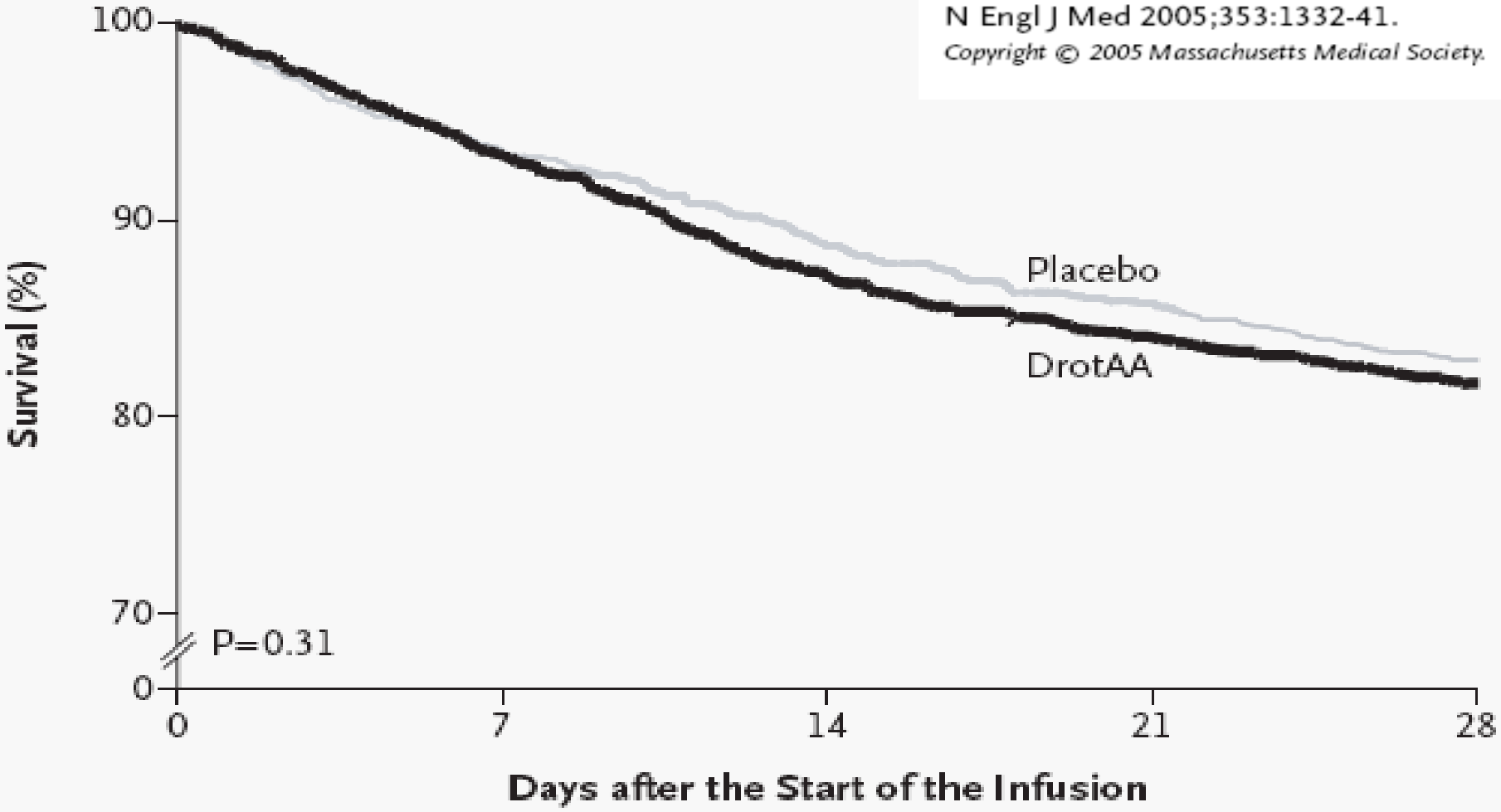


Figure 2. Kaplan–Meier Estimates of Survival among 1316 Patients with Severe Sepsis in the Drotrecogin Alfa (Activated) (DrotAA) Group and 1297 Patients in the Placebo Group.

There was no significant difference between the treatment groups in survival at 28 days (P=0.31 by the log-rank test).

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008

Sedation, analgesia, and neuromuscular blockade in sepsis

- Use sedation protocols with a sedation goal for critically ill mechanically ventilated patients (1B)
- Use either intermittent bolus sedation or continuous infusion sedation to predetermined end points (sedation scales), with daily interruption/lightening to produce awakening. Re-titrate if necessary (1B)
- Avoid neuromuscular blockers where possible. Monitor depth of block with train-of-four when using continuous infusions (1B)

Glucose control

- Use intravenous insulin to control hyperglycemia in patients with severe sepsis following stabilization in the ICU (1B)
- Aim to keep blood glucose <150 mg/dL (8.3 mmol/L) using a validated protocol for insulin dose adjustment (2C)
- Provide a glucose calorie source and monitor blood glucose values every 1–2 hrs (4 hrs when stable) in patients receiving intravenous insulin (1C)
- Interpret with caution low glucose levels obtained with point of care testing, as these techniques may overestimate arterial blood or plasma glucose values (1B)

Renal replacement

- Intermittent hemodialysis and CVVH are considered equivalent (2B)
- CVVH offers easier management in hemodynamically unstable patients (2D)

Bicarbonate therapy

- Do not use bicarbonate therapy for the purpose of improving hemodynamics or reducing vasopressor requirements when treating hypoperfusion-induced lactic acidemia with pH ≥7.15 (1B)

Deep vein thrombosis prophylaxis

- Use either low-dose UFH or LMWH, unless contraindicated (1A)
- Use a mechanical prophylactic device, such as compression stockings or an intermittent compression device, when heparin is contraindicated (1A)
- Use a combination of pharmacologic and mechanical therapy for patients who are at very high risk for deep vein thrombosis (2C)
- In patients at very high risk, LMWH should be used rather than UFH (2C)

Stress ulcer prophylaxis

- Provide stress ulcer prophylaxis using H2 blocker (1A) or proton pump inhibitor (1B). Benefits of prevention of upper gastrointestinal bleed must be weighed against the potential for development of ventilator-acquired pneumonia

Consideration for limitation of support

- Discuss advance care planning with patients and families. Describe likely outcomes and set realistic expectations (1D)

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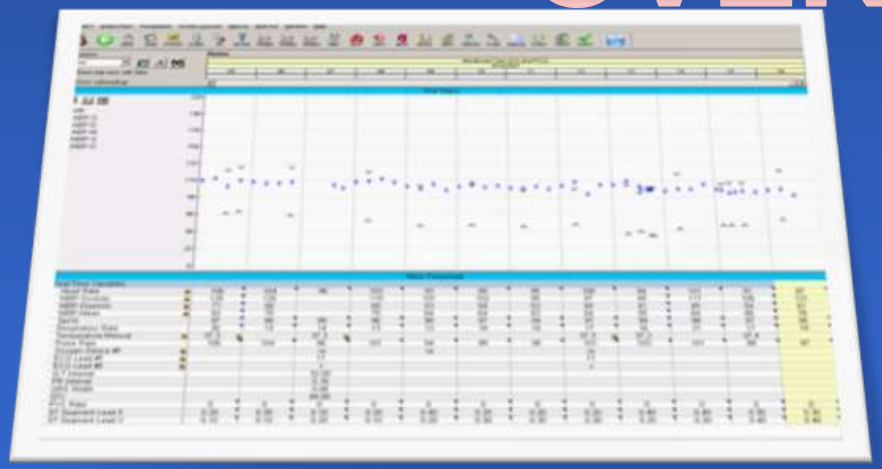
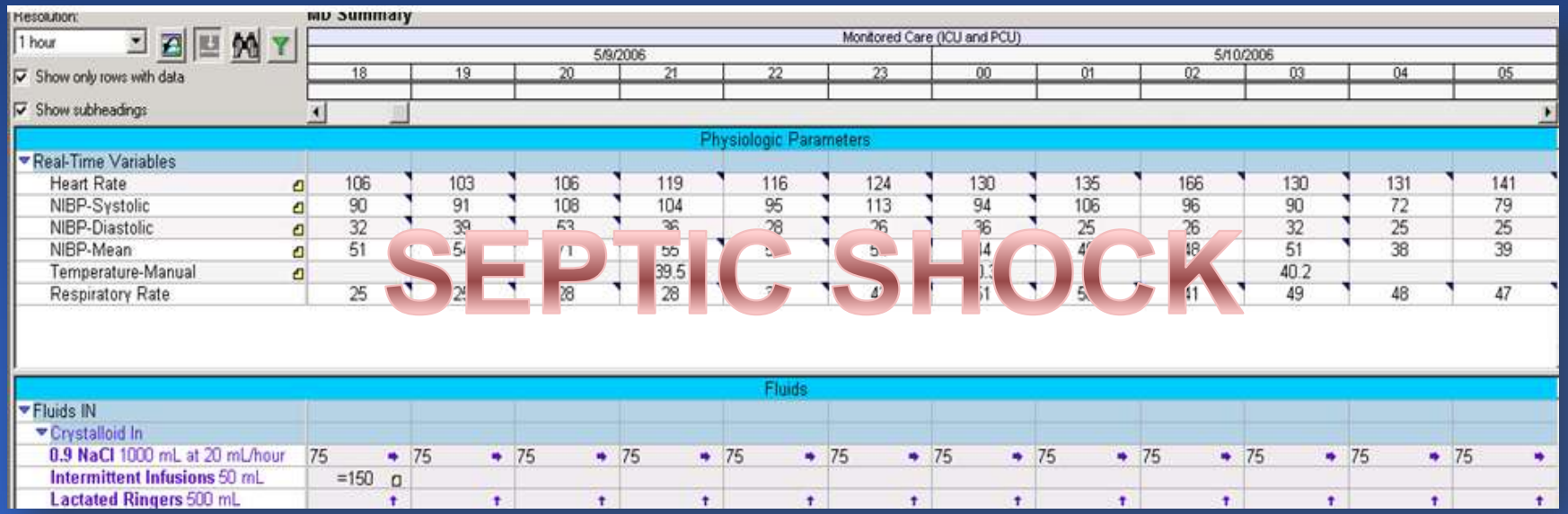
Medical informatics in ICU

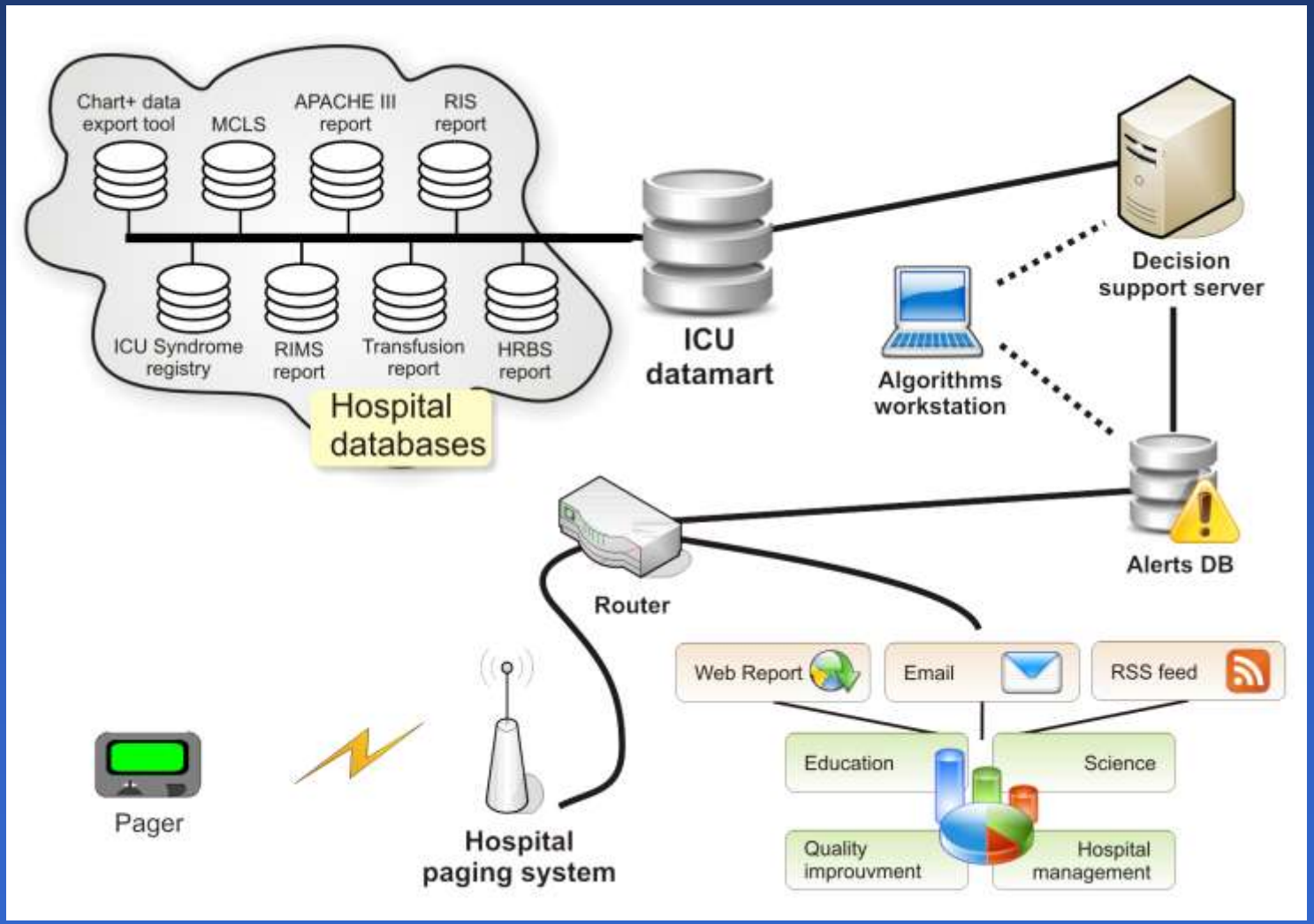
INFORMATION OVERLOAD



ICU SYNDROMES: PATTERN RECOGNITION



ICU Data Mart: Informatics infrastructure



Severe sepsis/septic shock sniffer

Infection

Blood culture order (within 12 hours)

AND

The systemic inflammatory

Two of the following

Respiratory rate > 25	***OR***	**WBC > 12000**	***OR***	**t < 36.0 Cº**
Heart rate > 100	***OR***	**WBC < 4000**	***OR***	**t > 38.6 Cº**

AND

Hypotension or organ hypoperfusion

Mean Arterial Blood Pressure < 65	***OR***	**Lactate > 2.5**
Metabolic acidosis: base < - 5	***OR***	**Anion gap > 12**

American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis.


WATCH
FOR
ICE