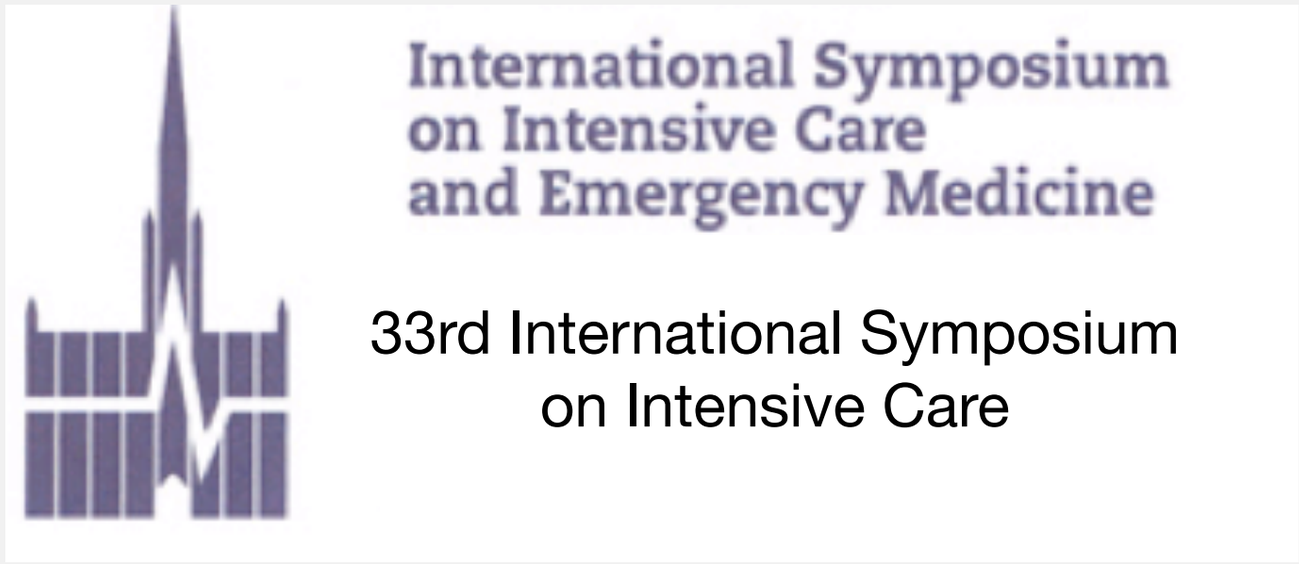
Best of Brussels - 2013

Part 1



Best of Brussels - 2013

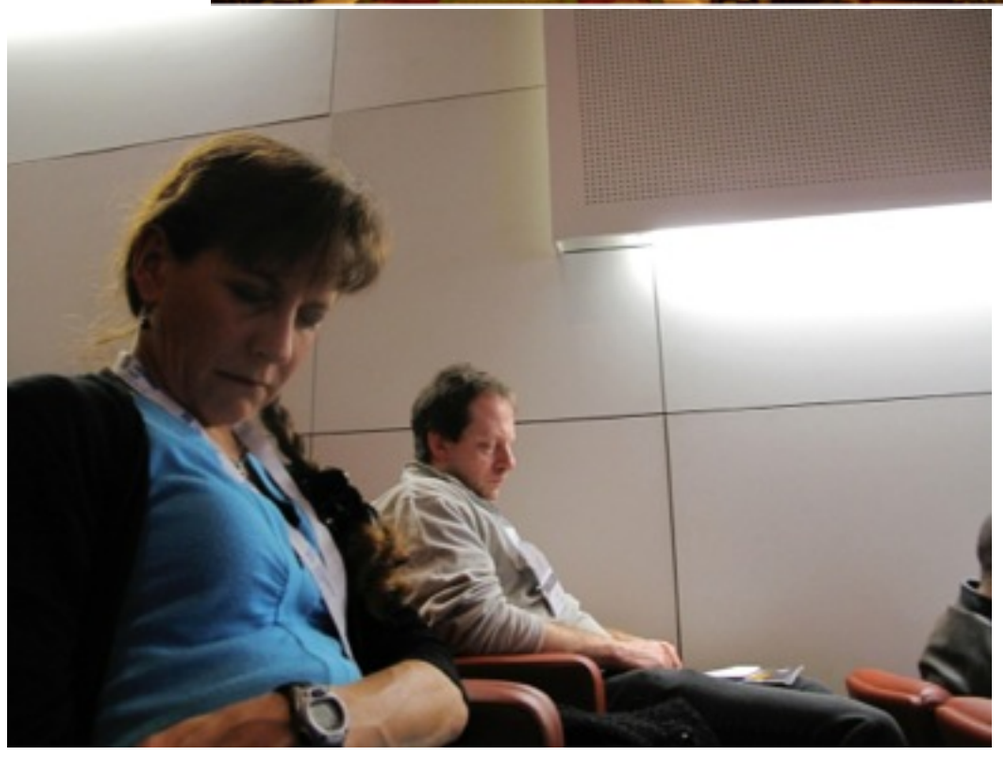
Part 1

- Surviving sepsis - Pro/Con
- CPR
- Glycocalyx
- Perioperative haemodynamic management
- Microvascular flow
- Detecting fluid responsiveness

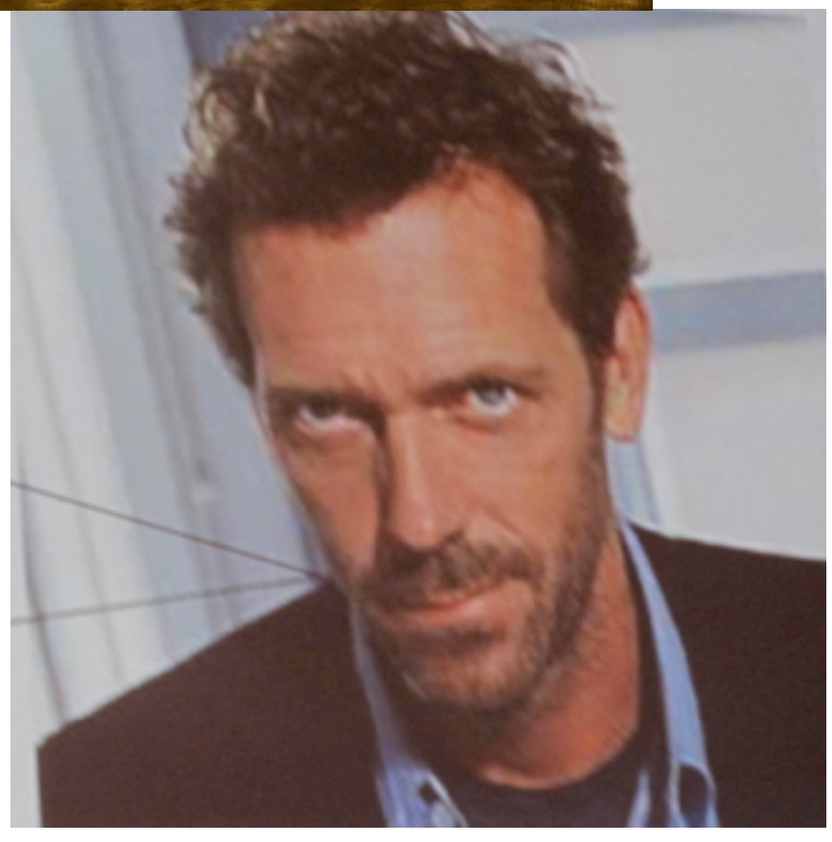
Part 2

- Diastolic dysfunction
- Thermodilution derived variables
- Infections
- Good medical websites
- Pancreatitis
- Obstetrics - PPH
- Obsterics - Amniotic fluid embolism

Why Brussels?



5990 +10?
enthusiastic participants



Leading medical experts

Surviving Sepsis 2012 - Pro Con

Surviving Sepsis 2012 - Pro

Myth:
Critical care **unique(ly bad)** - ACC/AHA guidelines strength identical

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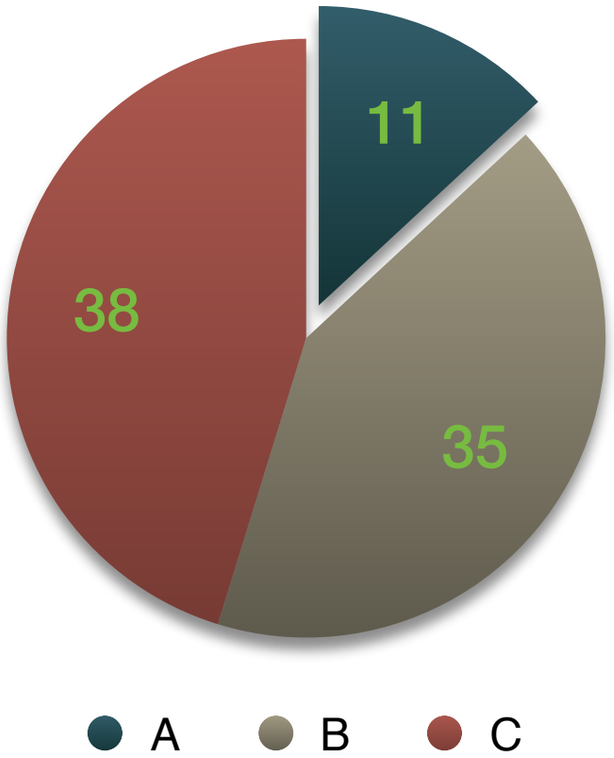
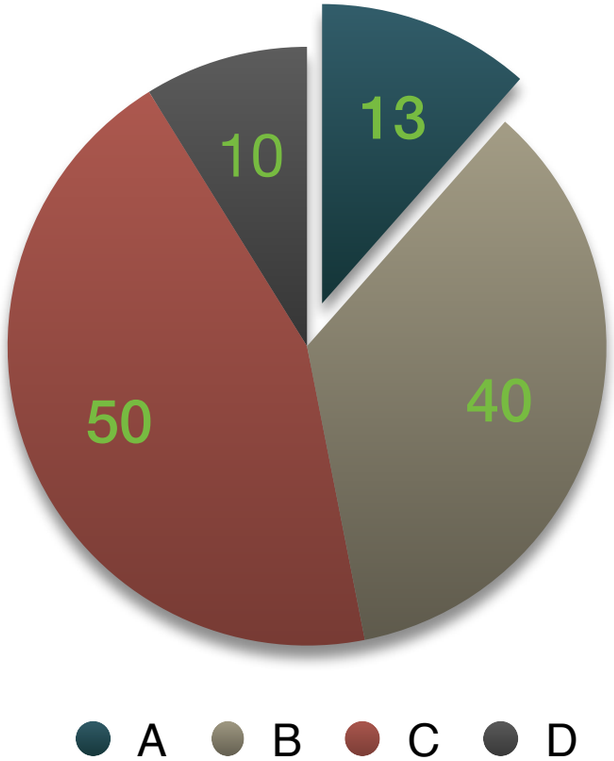
<u>Cardiology</u> guidelines only **11%** of the evidence is **strong**

Levels of evidence (%)



<u>Surviving Sepsis</u> guidelines only 13% of the evidence is **strong**

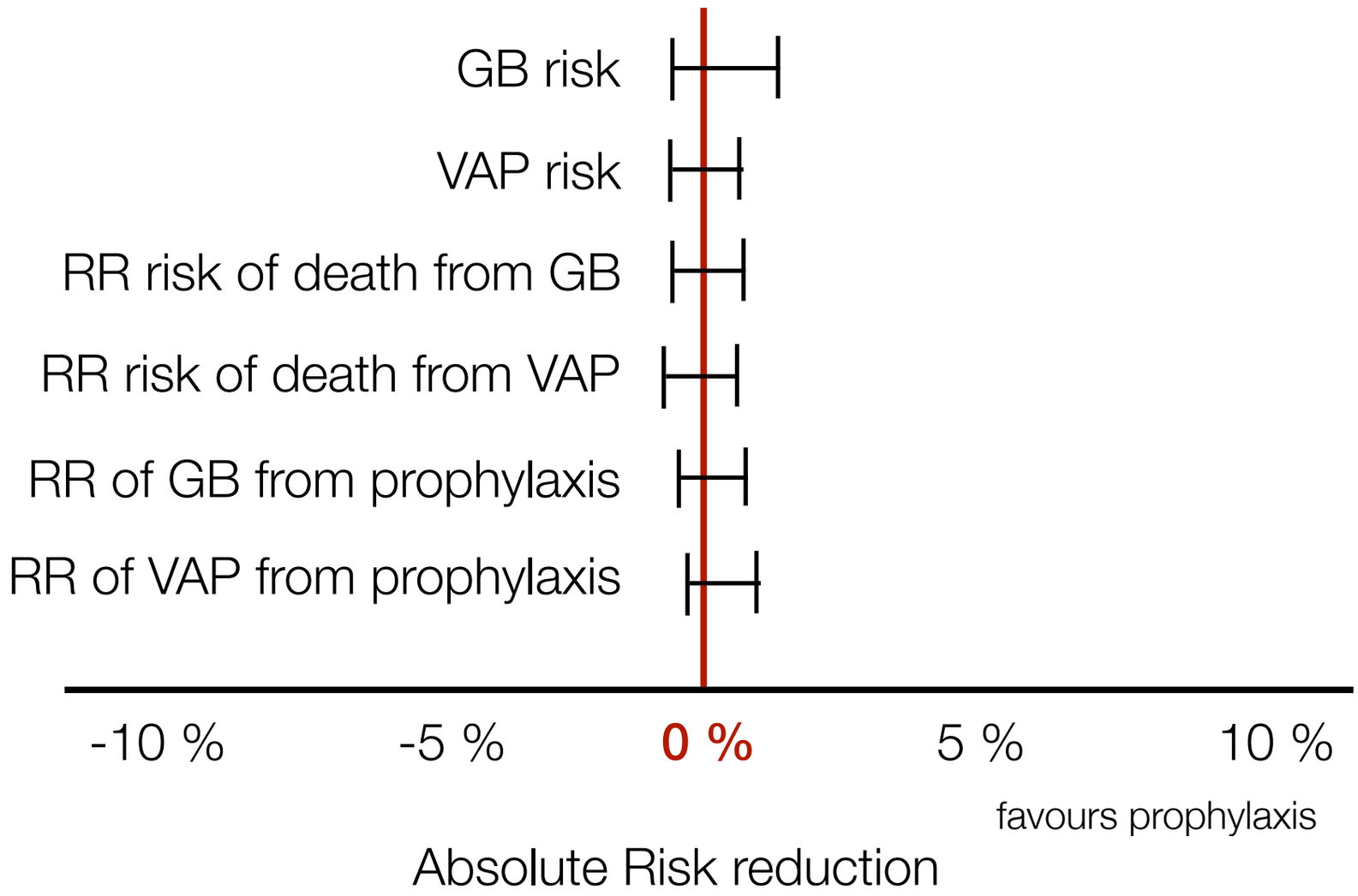
Levels of evidence (%)



Level of **evidence C: recommendation based on expert opinion**, case studies, or standards of care.

JAMA 2009:301 (8):831-841

Example - There is **no evidence** that acid suppression reduces **mortality** and there are known risks



Given the available evidence the decision to provide stress ulcer prophylaxis is one of general **equivalence**

Intensive Care Medicine (2006) 32:1151-1158

But the SSC authors know this

Meta-analysis show prophylaxis-induced reduction of GI bleed, which we consider significant despite absence of mortality benefit.

The benefit must be weighed against the effect of **increased** gastric pH on greater incidence of VAP and C. Difficile infection...

Local assessment of risks/benefits can justify **different decisions** that are **not "wrong"**

Myth: Guidelines apply to all patients

- Treatment response **varies** by baseline risk and pathophysiologic mechanism
- Science for assessing individual benefit without performing subgroup analysis evolving
- **Doctors must do this at the bedside** - hard for guidelines

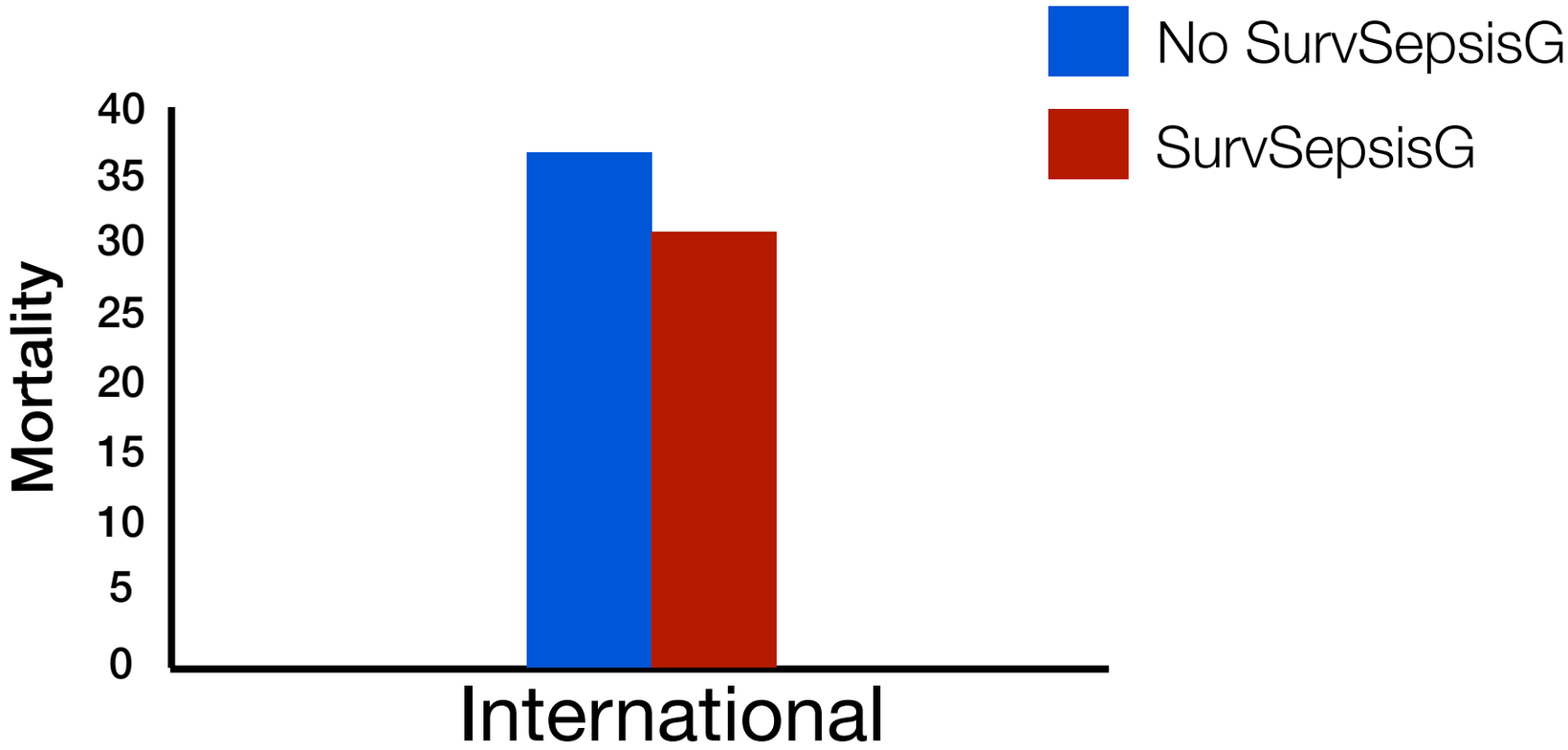
Kent et al Trials 2010, 11:85

Individualizing treatment - **Read the guideline not just the recommendation**

- We recommend that vasopressor therapy initially target a MAP of 65 mm Hg (1C)
- ...but the **optimal MAP should be individualized**....
- .... supplementing end points with assessment of regional and global perfusion, such as lactate, skin perfusion, mental status and urine output is important.

The most important question facing clinicians today...

Surviving Sepsis guidelines **reduces mortality**

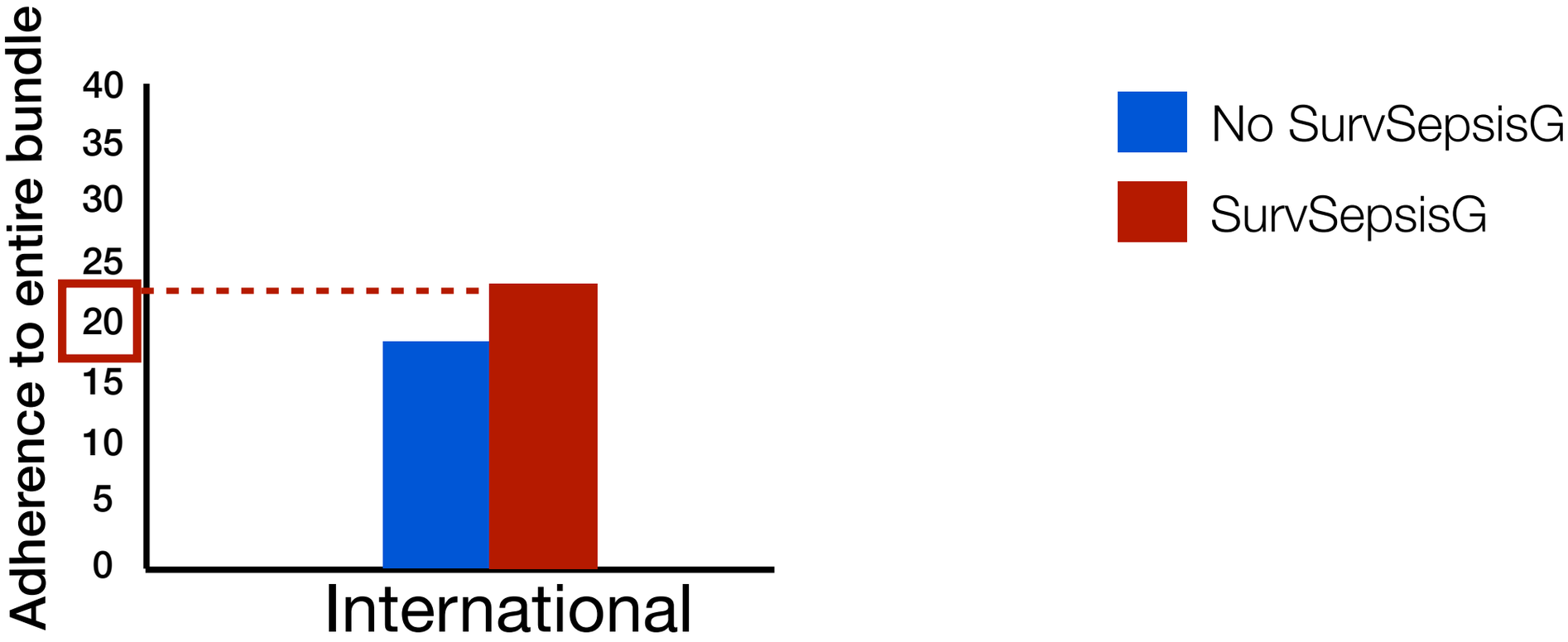


NNT=14

JAMA 2008;299(19) 2294-2303 CCM 2010; 38:367-374

Surviving sepsis guidelines reduce mortality but **why?**

Since **adherence** was <u>low</u>



JAMA 2008;299(19) 2294-2303 CCM 2010; 38:367-374

Surprising since most of the bundle **probably doesn't work**

Something else is going on

- Sepsis resuscitation bundle (first 6 hrs)
  - measure lactate ✓
  - blood cultures before antibiotics ✓
  - broad spectrum antibiotics ✓
  - fluids and vasopressors
  - CVP >=8 mmHg
  - ScvO2 >=70%

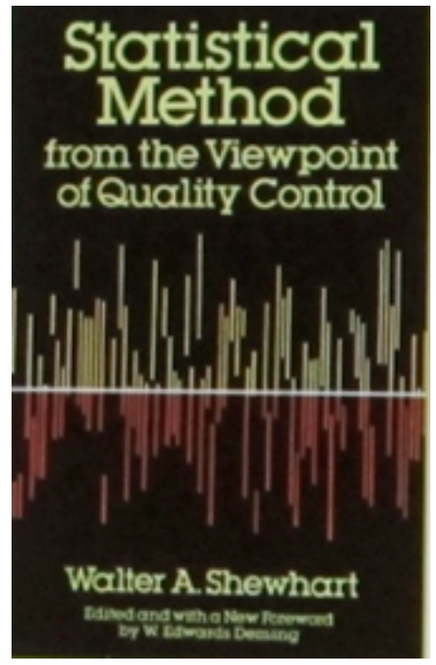
Single center trial being repeated

- Sepsis management bundle (first 24 hrs
  - low dose steroids ⊘
  - drotrecogin alfa (activated) ⊘
  - glucose control ⊘
  - plateau pressure control ✓

Is there value in **standardizing** and following guidelines when the **evidence is weak?**

But this is empiricism...the opposite of evidence based medicine!!!

- Elimination of variation in process is a key manufacturing process in quality control
- Many, but **not all**, believe this is true for medicine
- Changing your practice when the evidence is modest will depend on **whether you believe** standardization improves outcome



Surviving Sepsis 2012 - Con

Surviving Sepsis - Con

Initial resuscitation

- Protocolized, quantitative resuscitation of **sepsis**-induced hypoperfusion (=hypotension persisting after initial fluid challenge or lactate concentration >= 4 mmol/L)

Goals during first 6 hours:

- CVP 8-12 mmHg
- MAP >=65 mmHg
- Urine output >= 0.5 ml/kg/hr
- ScvO2 70% (grade 1C)

Surviving Sepsis - Con

The New England Journal of Medicine

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*

The patients in this study are **not representative** of septic shock patients seen **elsewhere**

Their hemodynamic profile is more of a **volume shock** than a vasoplegic shock

Their low ScvO2 (49%) suggests normal 02 extraction.....**uncommon** in cases of severe **sepsis**

Surviving Sepsis - Con


The New England Journal of Medicine

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Caution before applying the EGDT protocol to every patient with septic shock

The SSC haemodynamic resuscitation targets are methodologically and physiologically **questionable**

- CVP 8-12 mmHg .... why CVP? Why 8-12?
- MAP >= 65 mmHg
- SCVO2 70%

Surviving Sepsis - Con

CVP

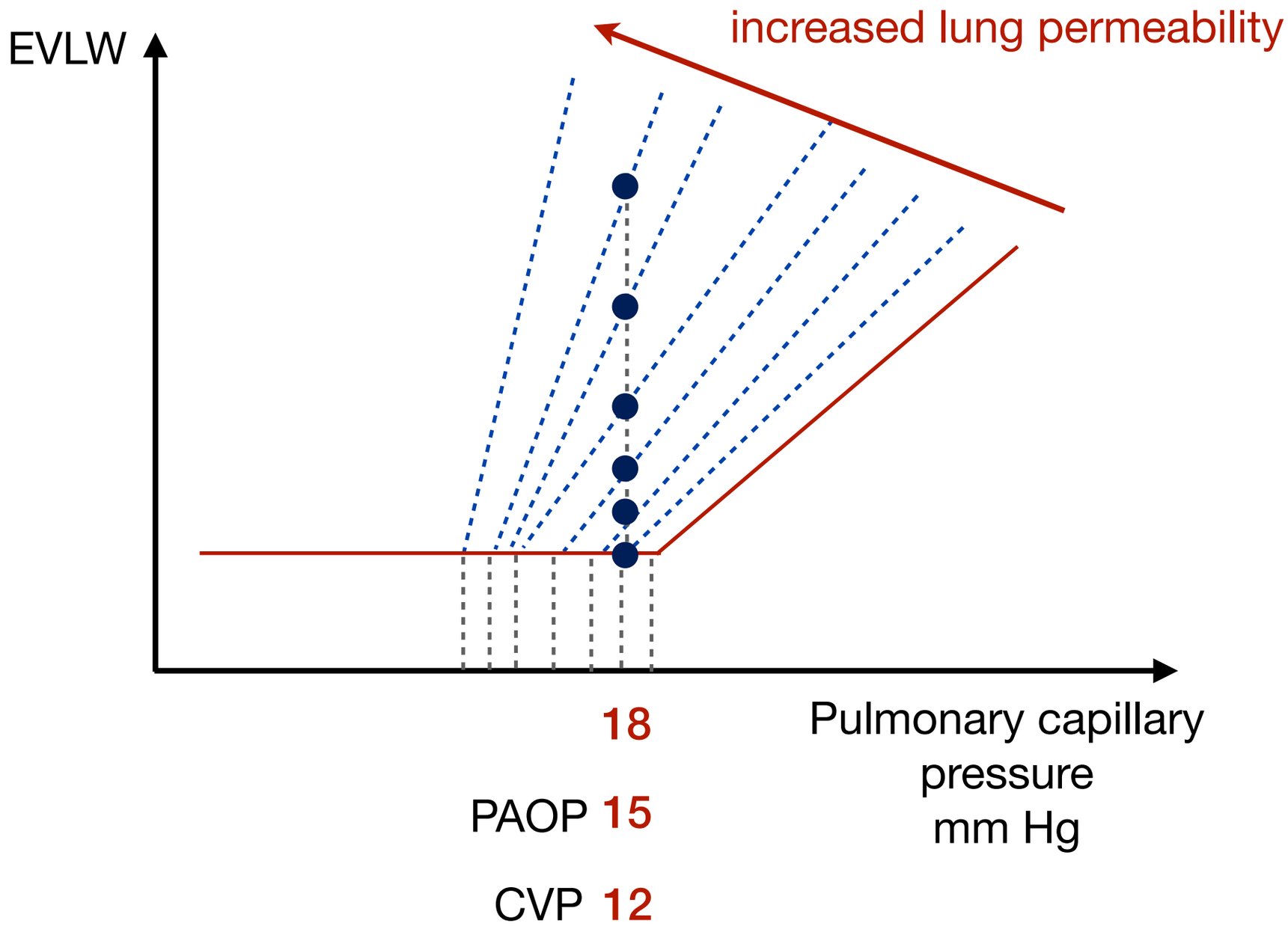
- not simple to measure:
  - “zero” level
  - Must be measured at end expiration
  - Which values if PEEP or intrinsic PEEP?

CVP = 12 mmHg (at end expiration) PEEPi = 12 mmHg (at end expiration) Airway pressure transmission = 60%

true CVP? 12? 0? 7?

true CVP= 12 - (12 x 0.6) = 7mmHg

Surviving Sepsis - Con



CVP : targeting 12-15 mmHg...a **high risk of lung oedema**

Surviving Sepsis - Con

CVP

- not so simple:
  - “zero” level
  - Must be measured at end expiration
  - Which values if PEEP or intrinsic PEEP?
  - CVP: inappropriate to assess volume status

Ex. in a COPD patient (high PEEPi) a CVP of 12 can be associated with profound hypovolaemia

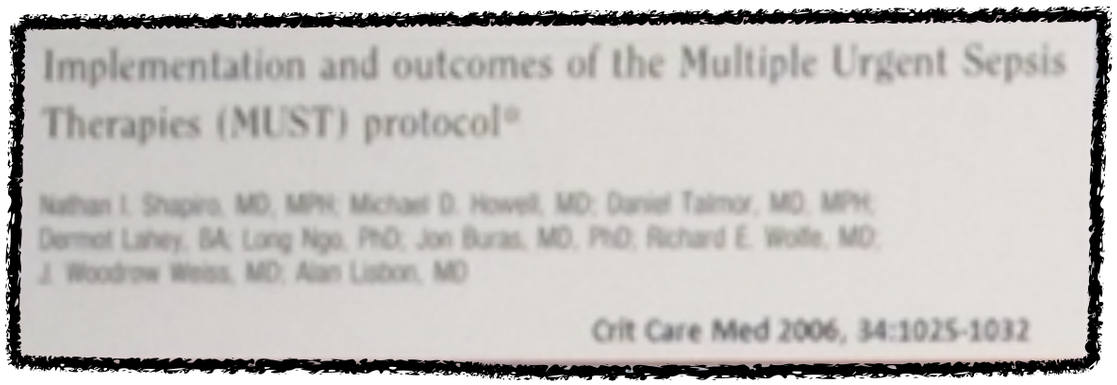
Lactate but **not** SCVO2 predict increase in oxygen consumption in fluid responders

	VO_2 Change ≥ 15% ($n = 14$)	
	Before Volume Expansion	After Volume Expansion
Mean arterial pressure (mean ± sd, mm Hg)	76	83
Cardiac index (L/min/m	2.7	3.7
VO	103	135
Lactate (mean ± sd, mmol/L)	5.5	3.6
Central venous oxygen saturation (mean ± sd, %)	70	71

Significant benefits obtained from fluids in spite of SCVO2 of 70%

CCM June 2013 • Volume 41 • Number 6

Surviving Sepsis - Con

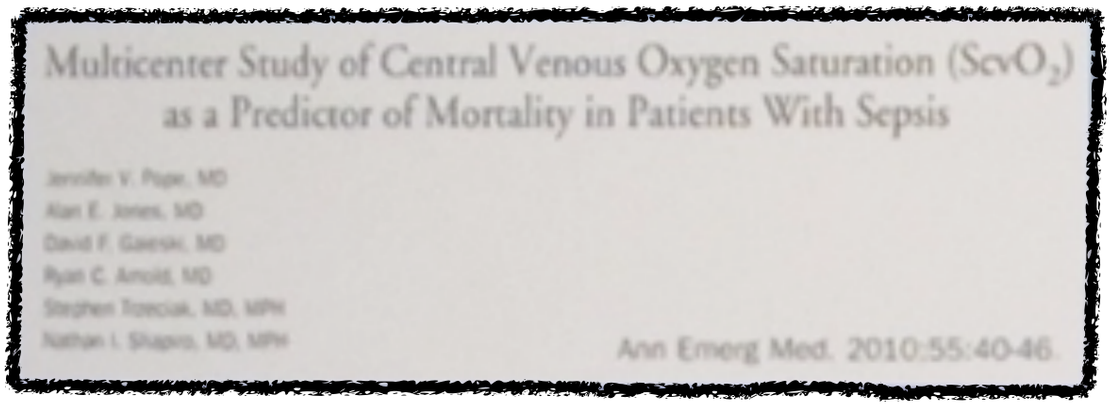


Implementation and outcomes of the Multiple Urgent Sepsis Therapies (MUST) protocol*

Nathan I. Shapiro, MD, MPH; Michael D. Howell, MD; Daniel Talmor, MD, MPH; Dermot Lahey, BA; Long Ngo, PhD; Jon Buras, MD, PhD; Richard E. Wolfe, MD; J. Woodrow Weiss, MD; Alan Lisbon, MD

Crit Care Med 2006, 34:1025-1032

Initial SCVO2 - 72%

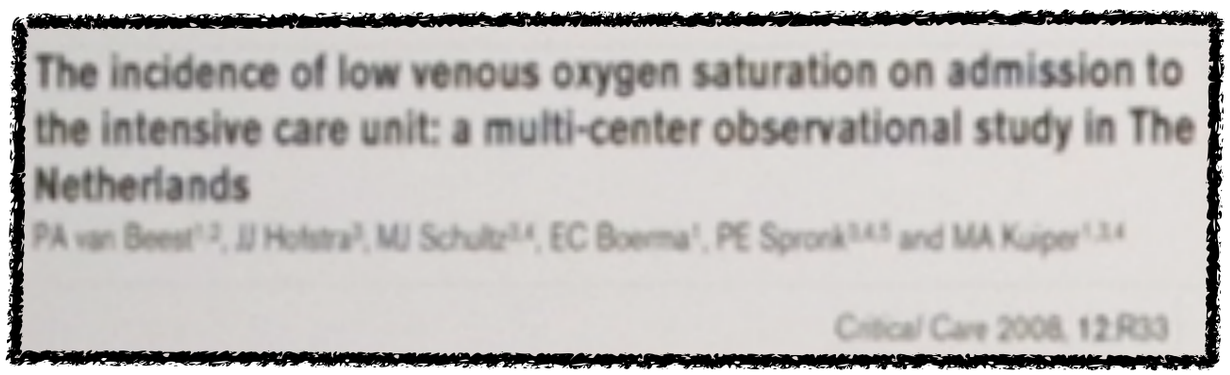


Multicenter Study of Central Venous Oxygen Saturation ($ScvO_2$) as a Predictor of Mortality in Patients With Sepsis

Jennifer V. Pope, MD
Alan E. Jones, MD
David F. Gaieski, MD
Ryan C. Arnold, MD
Stephen Trzeciak, MD, MPH
Nathan I. Shapiro, MD, MPH

Ann Emerg Med. 2010;55:40-46.

Initial SCVO2 - 73%

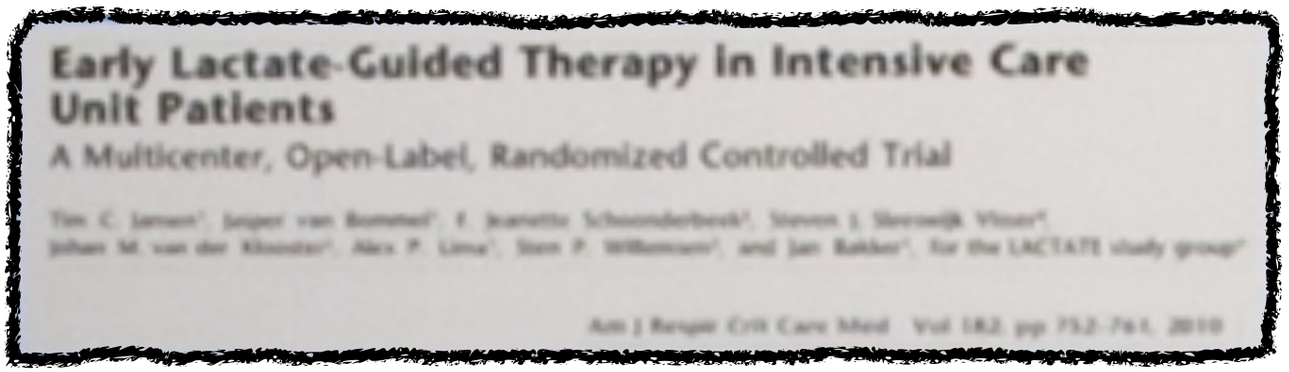


The incidence of low venous oxygen saturation on admission to the intensive care unit: a multi-center observational study in The Netherlands

PA van Beest[1,2], JJ Holstra[3], MJ Schultz[3,4], EC Boerma[1], PE Spronk[3,4,5] and MA Kuiper[1,3,4]

Critical Care 2008, 12:R33

Initial SCVO2 - 74%



Early Lactate-Guided Therapy in Intensive Care Unit Patients

A Multicenter, Open-Label, Randomized Controlled Trial

Tim C. Jansen[1], Jasper van Bommel[2], F. Jeanette Schoonderbeek[1], Steven J. Sleeswijk Visser[1], Johan M. van der Klooster[1], Alex P. Lima[1], Sten P. Willemsen[1], and Jan Bakker[1], for the LACTATE study group*

Am J Respir Crit Care Med Vol 182, pp 752–761, 2010

Initial SCVO2 - 73%

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

"A trial of dobutamine infusion up to 20 mcg/kg/min be added to vasopressor in the presence of:

a) myocardial dysfunction suggested by elevated filling pressure and **low cardiac output**

b) or signs of hypoperfusion despite **adequate volume** and **MAP**"

Which filling pressure?

What is a low cardiac output?

What is a adequate volume?

What is a adequate MAP?

Dobutamine administration without any echocardiographic assessment of cardiac function.....**unbelievable in 2013!!!**

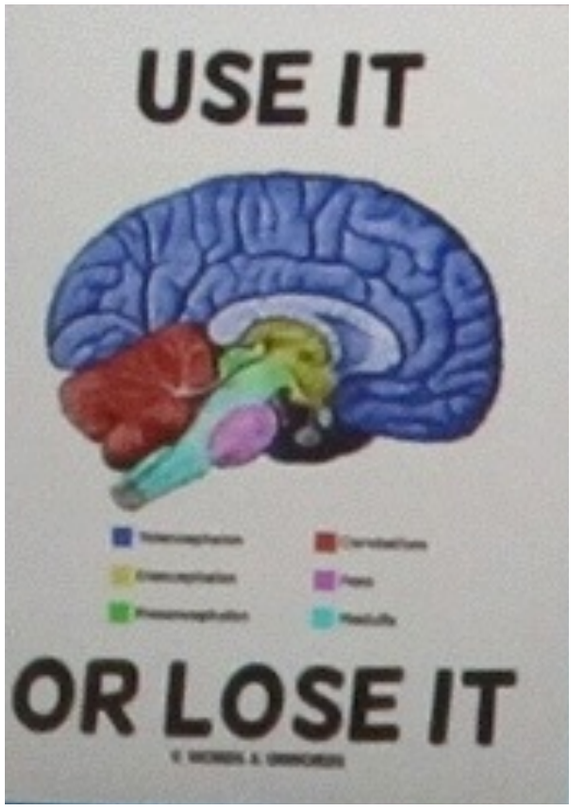
Surviving Sepsis - Con

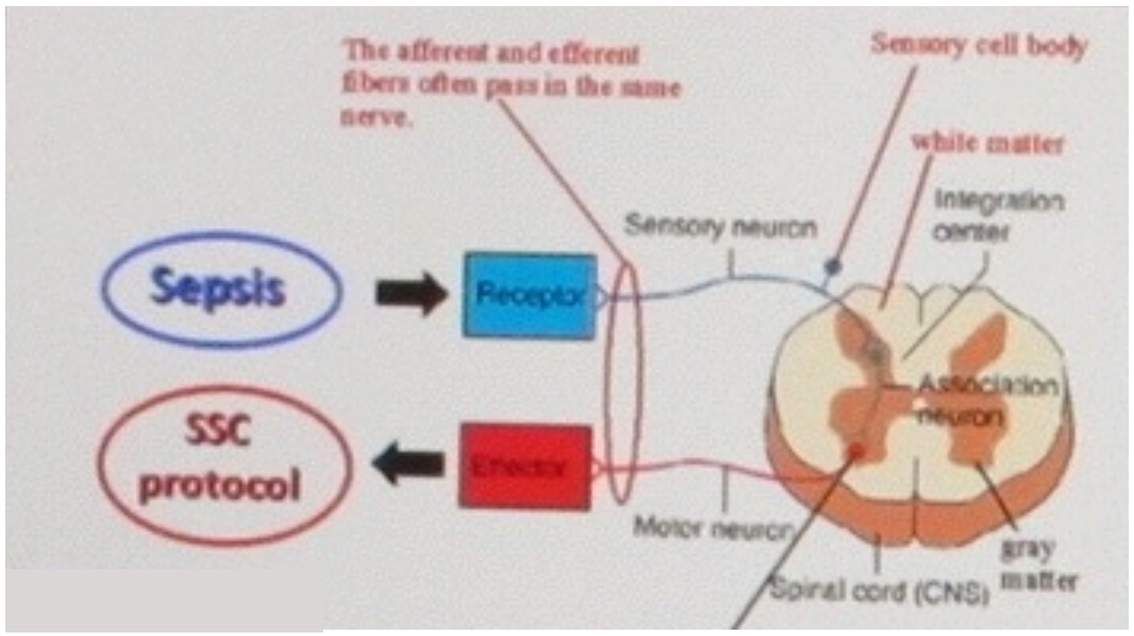
The initial hemodynamic resuscitation of septic patients according to Surviving Sepsis Campaign guidelines - **does one size fit all?**

No!!.... **One size** does **not fit all**

Let's individualize treatment

Let's **use our brain** ...rather than our spinal cords





CPR

In-hospital CPR

<16% in-hospital survival rates

despite awareness, education, monitoring, drugs, equipment, cardiac arrest teams

Pretty much **unchanged since 1960s**

N Engl J Med 1996;334:1578-82

But help is on the way !

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

CARDIOPULMONARY RESUSCITATION ON TELEVISION

Miracles and Misinformation

TV CPR- 77% success!

N Engl J Med 1996;334:1578-82

Better still

Baywatch CPR- **100% success**!

Maybe our arrest teams need different attire?

DNAR orders

Outreach teams are becoming the hospital's surrogate dying team

Almost **1/3rd** of all calls have limitations of treatment

CCM 2012; 40(1):98-103

Why do patients arrest in hospital?

Up to **80%** of all so-called “arrests”are **preceded by at least 8 hours** of slow deterioration in vital signs

Schein et al Chest 1990;98:1388

Chain of events

Sick patient

↓

Nurse observes but can't act

↓

Trainee doctors act but not trained

↓

Specialist trained - but not in acute medicine

↓

Eventual multiorgan failure/cardiac arrest and admitted to ITU

Vital sign documentation

- Sporadic
- Inaccurate
- Inconsistent
- Variable
- Especially the **most important -**
  - **Respiratory rate**

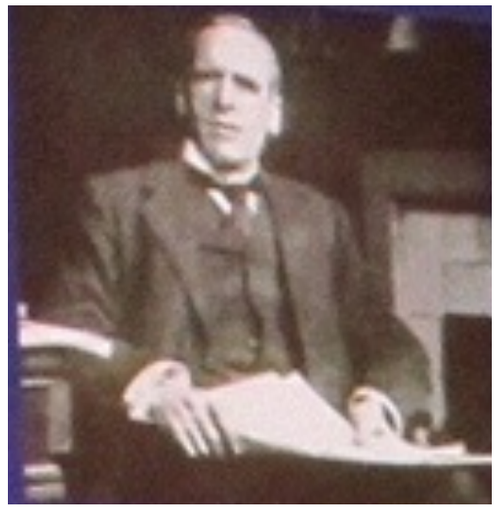
Resuscitation 2009;80:35

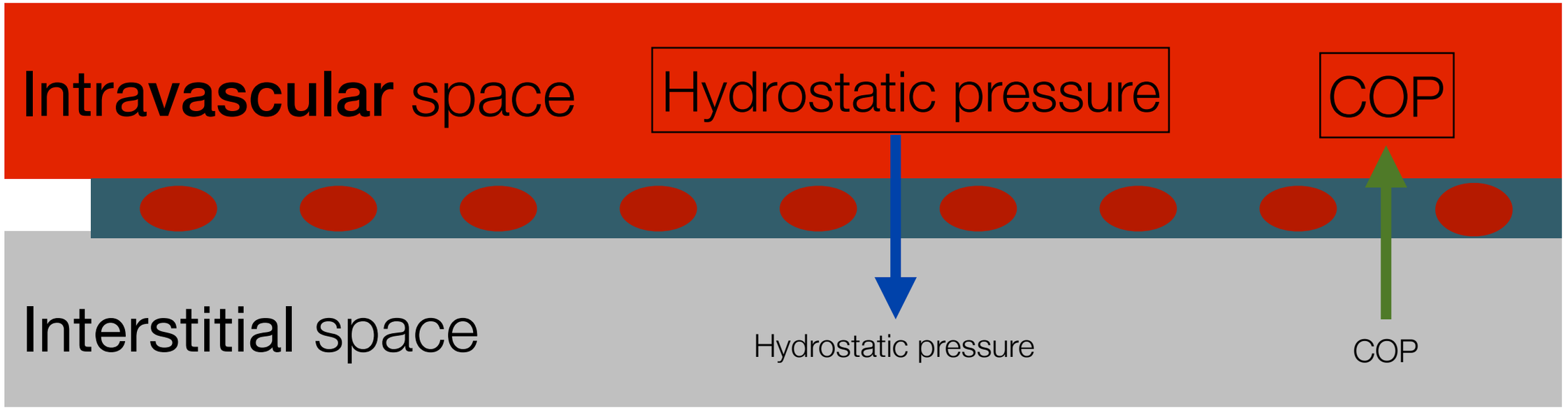
Lancet 2005;365:2097

Glycocalyx

Single vascular barrier

Ernest Starling: 1866-1927





Microvascular fluid exchange and the revised Starling principle

But.....

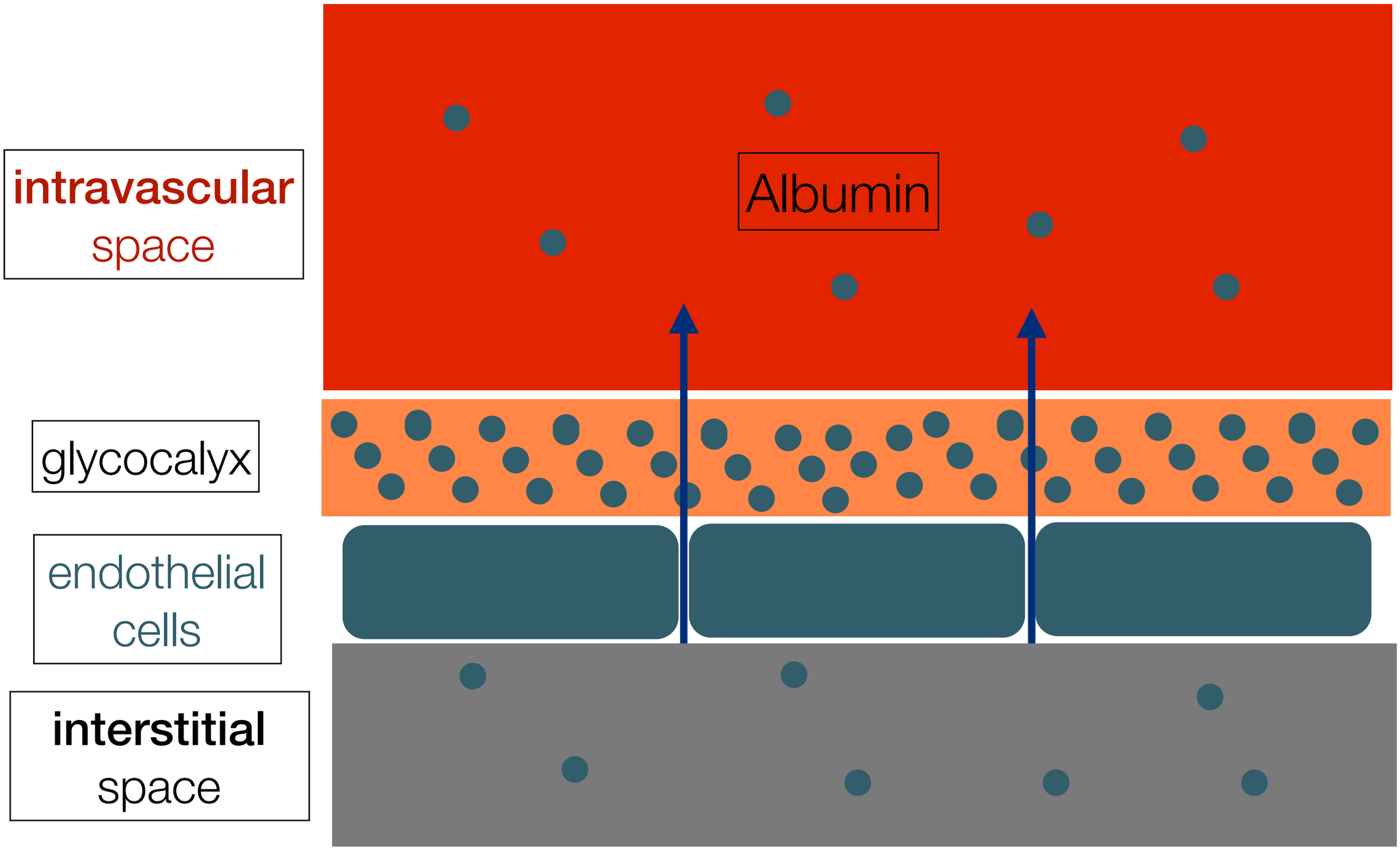
- **lymph** flow produced is **orders of magnitude smaller** then predicted

- In experiments, even when the COP inside and outside of the vessel were **equal**, there was **still effective COP drawing fluid in !**

- The endothelial **glycocalyx** binds plasma proteins and has a **high internal oncotic pressure** generating the **effective oncotic gradient** within a very small space.

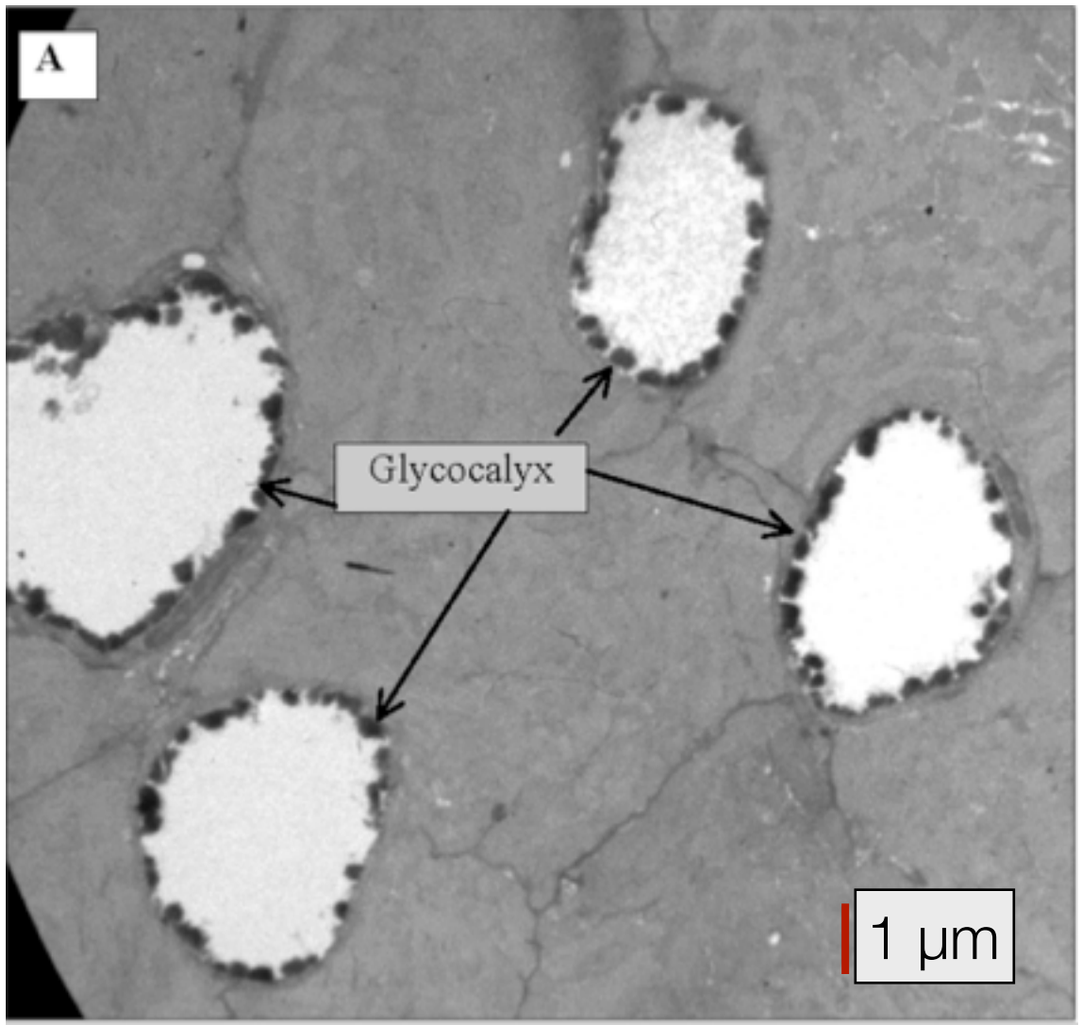
Cardiovascular Research (2010) 87, 198–210

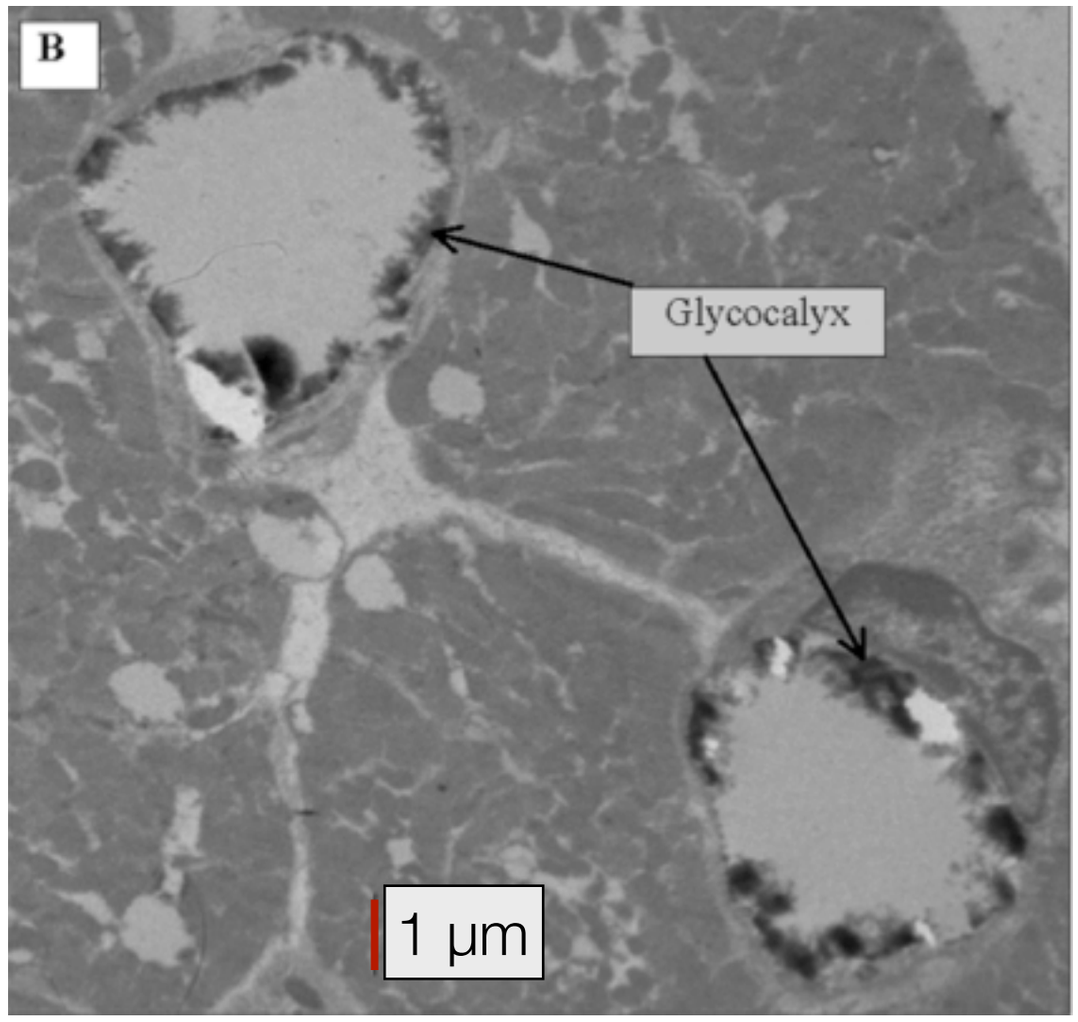
Double vascular barrier



Rehm et al Anesthesiology 2004;100:1211

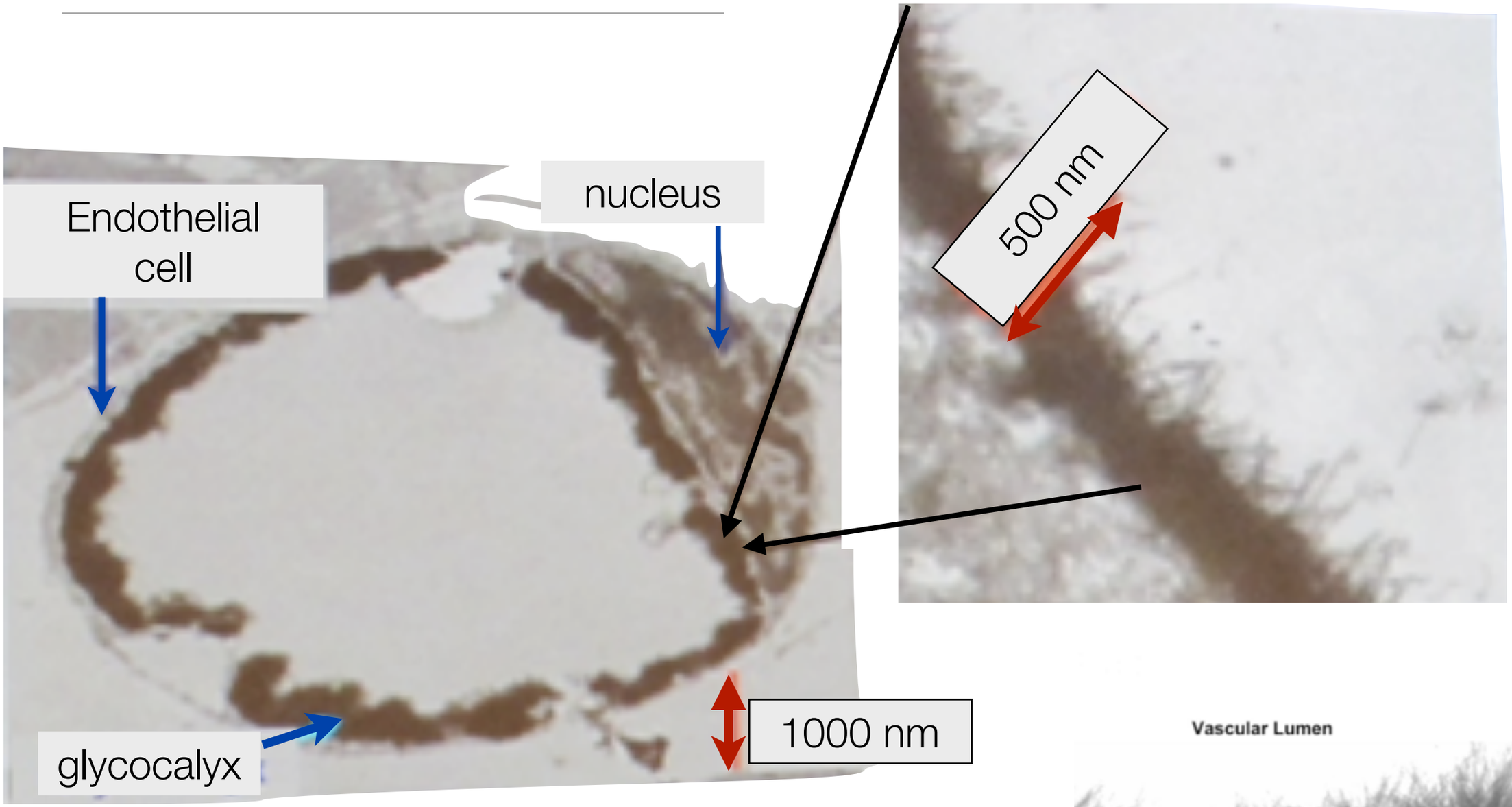
Glycocalyx - electron microscopy

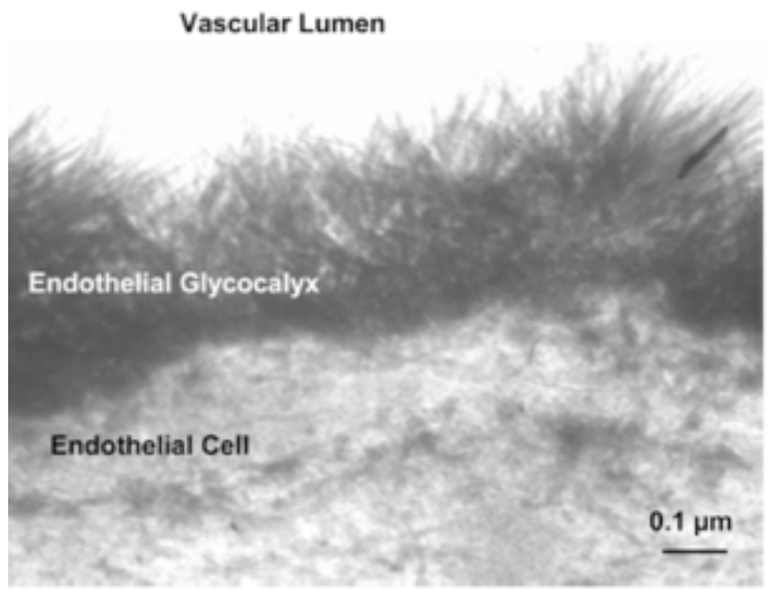




Rehm et al Anesthesiology 2004;100:1211

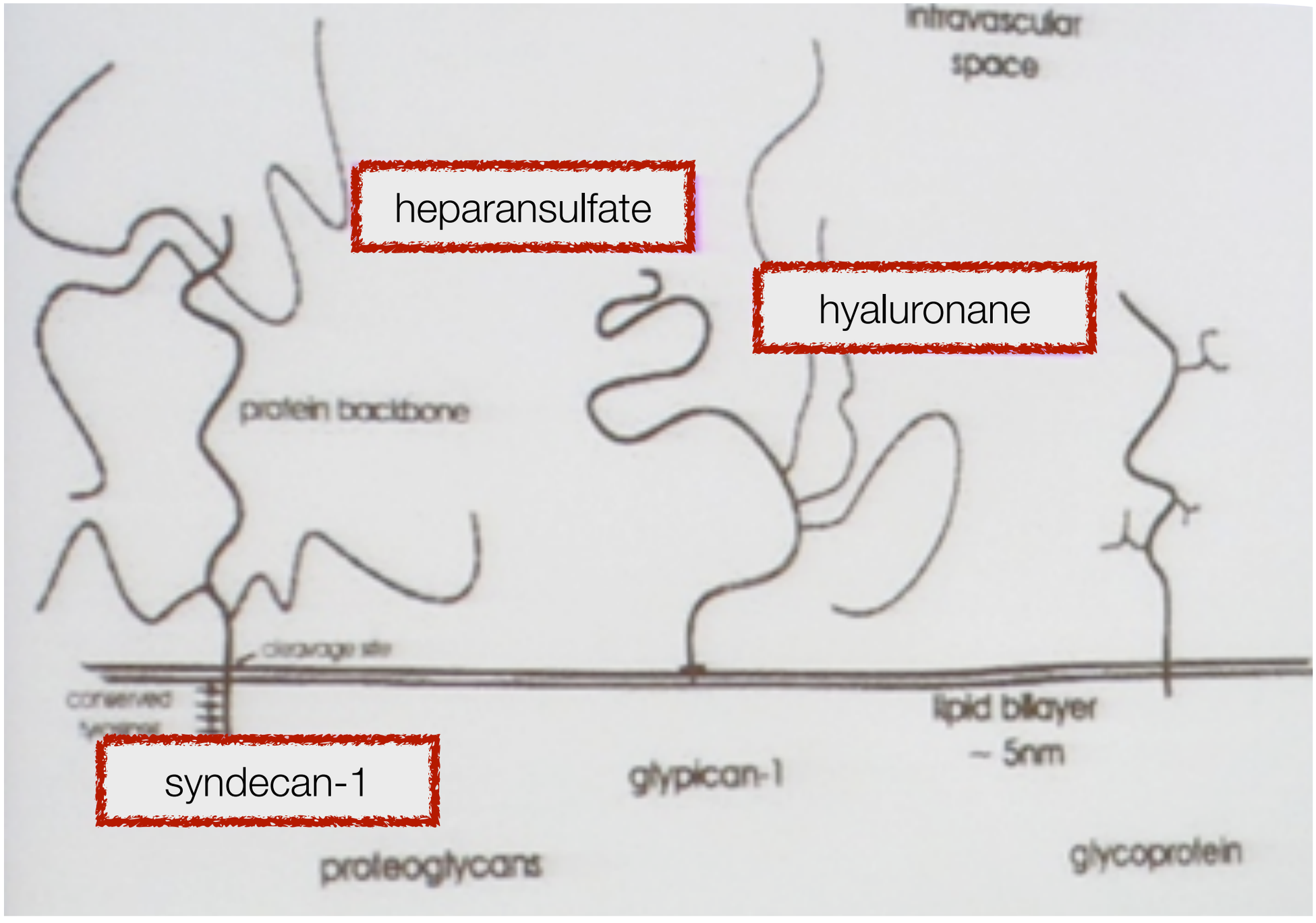
Electron microscopy - glycocalyx





Rehm et al Anesthesiology 2004;100:1211

Glycocalyx - components



Pries et al Eur J Physiol; 440:653-666, 2000

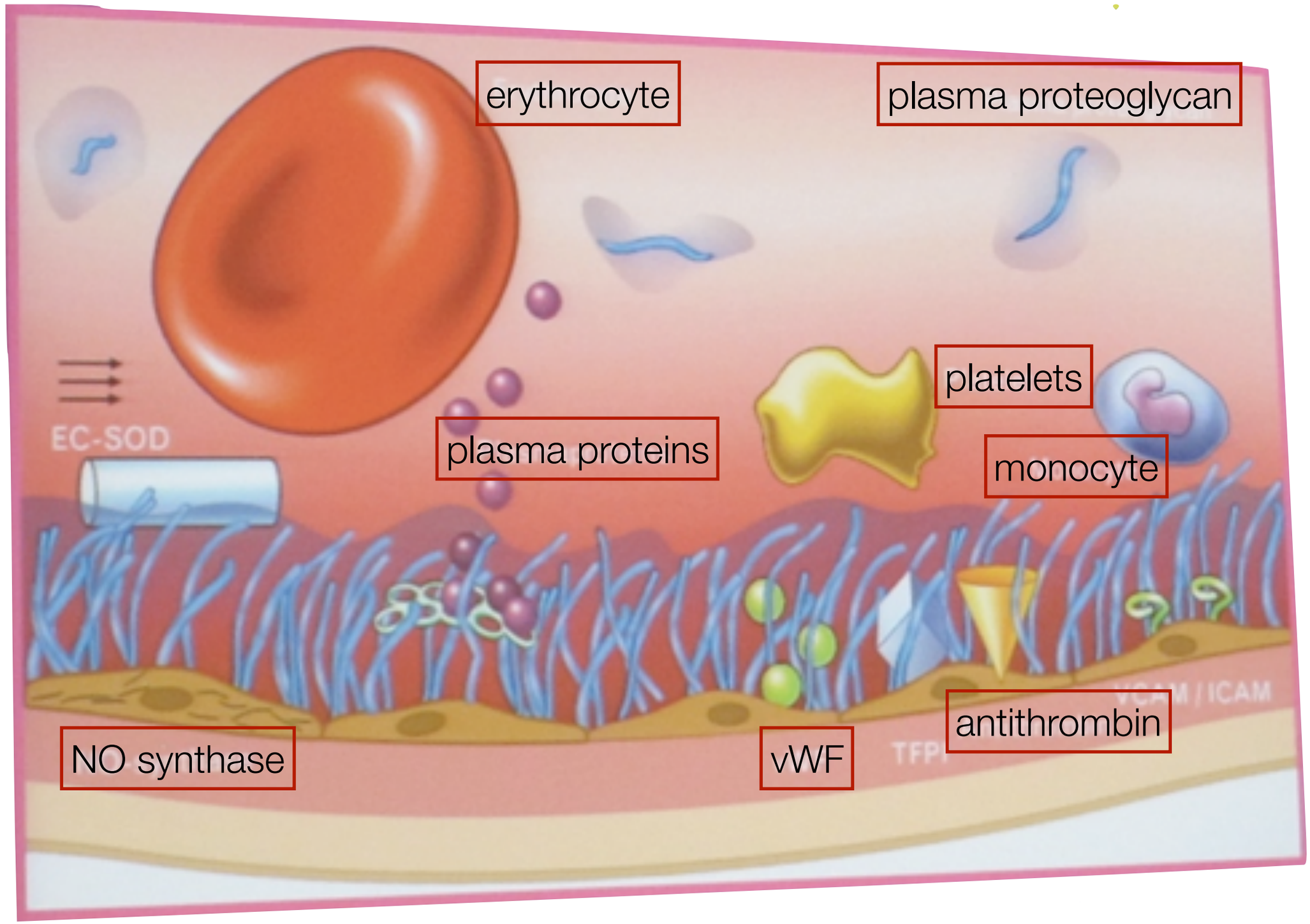
Glycocalyx

The colloid oncotic **competence of the glycocalyx** determines fluid filtration

Jacob et al Anesthesiology 2006, 104:1223-1231

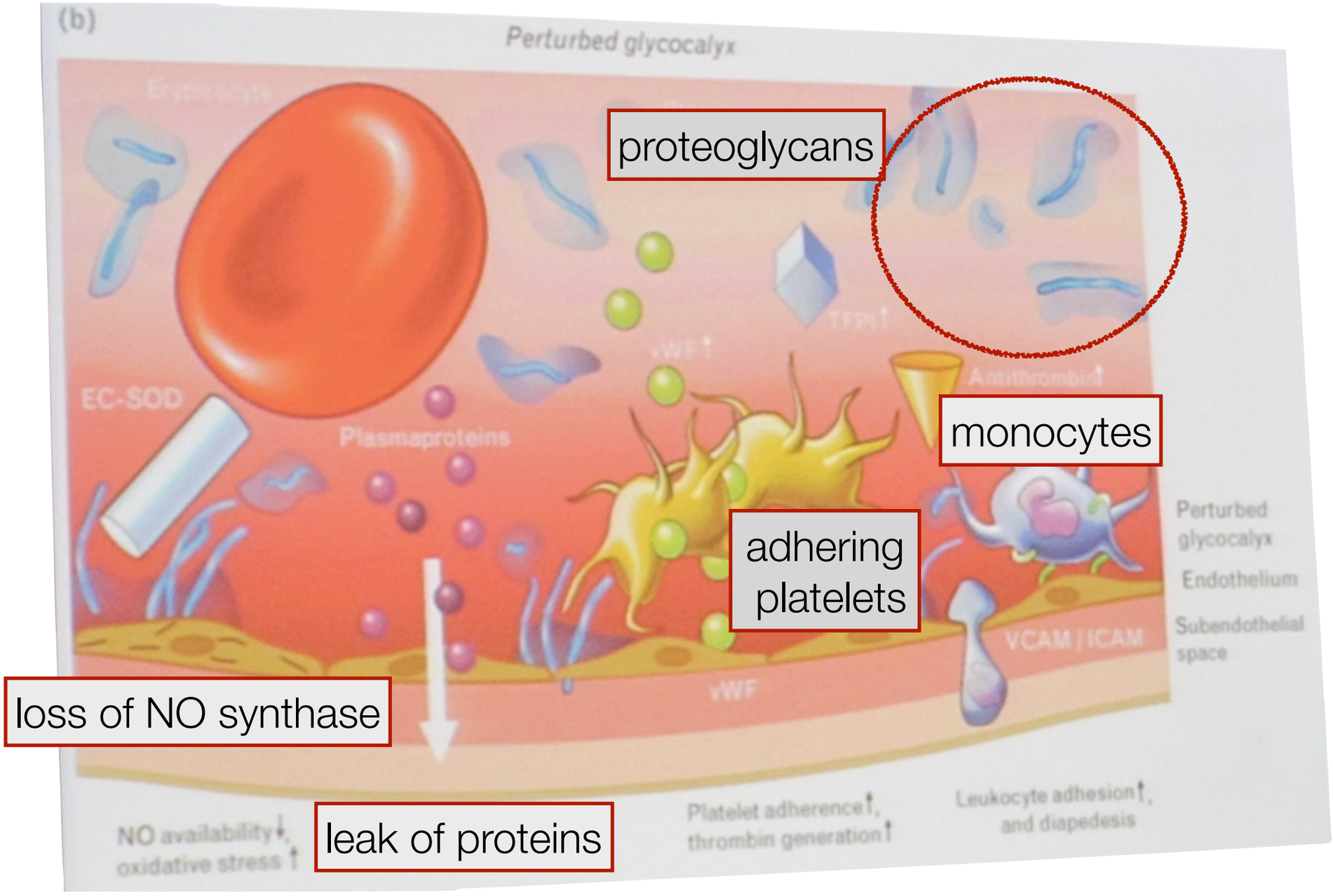
Jacob et al Cardiovasc Res 2007, 73:1235-1242

Healthy endothelial glycocalyx



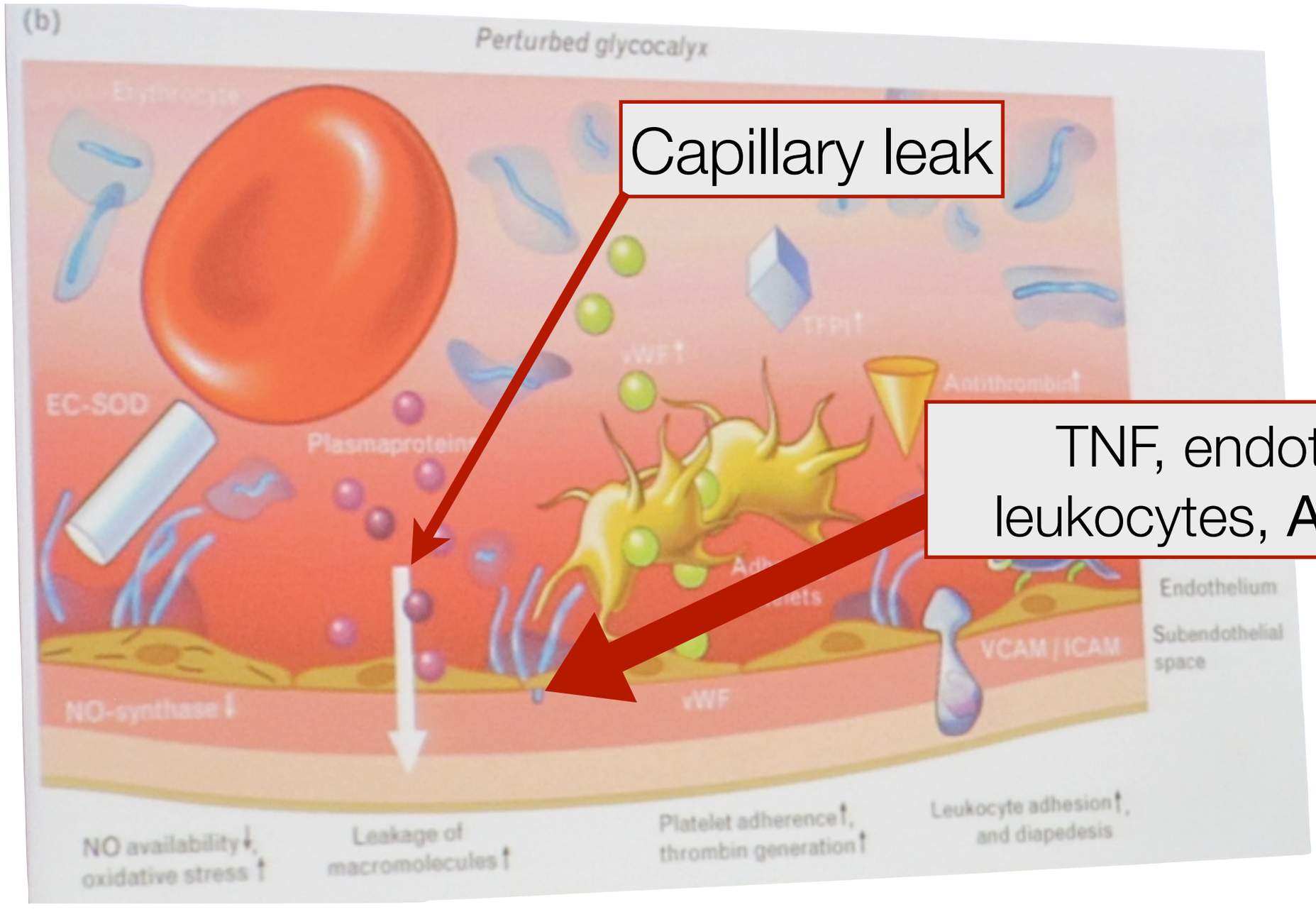
Nieuwdorp et al Curr Opin Lipidol 2005; 16:507

Destruction of the glycocalyx



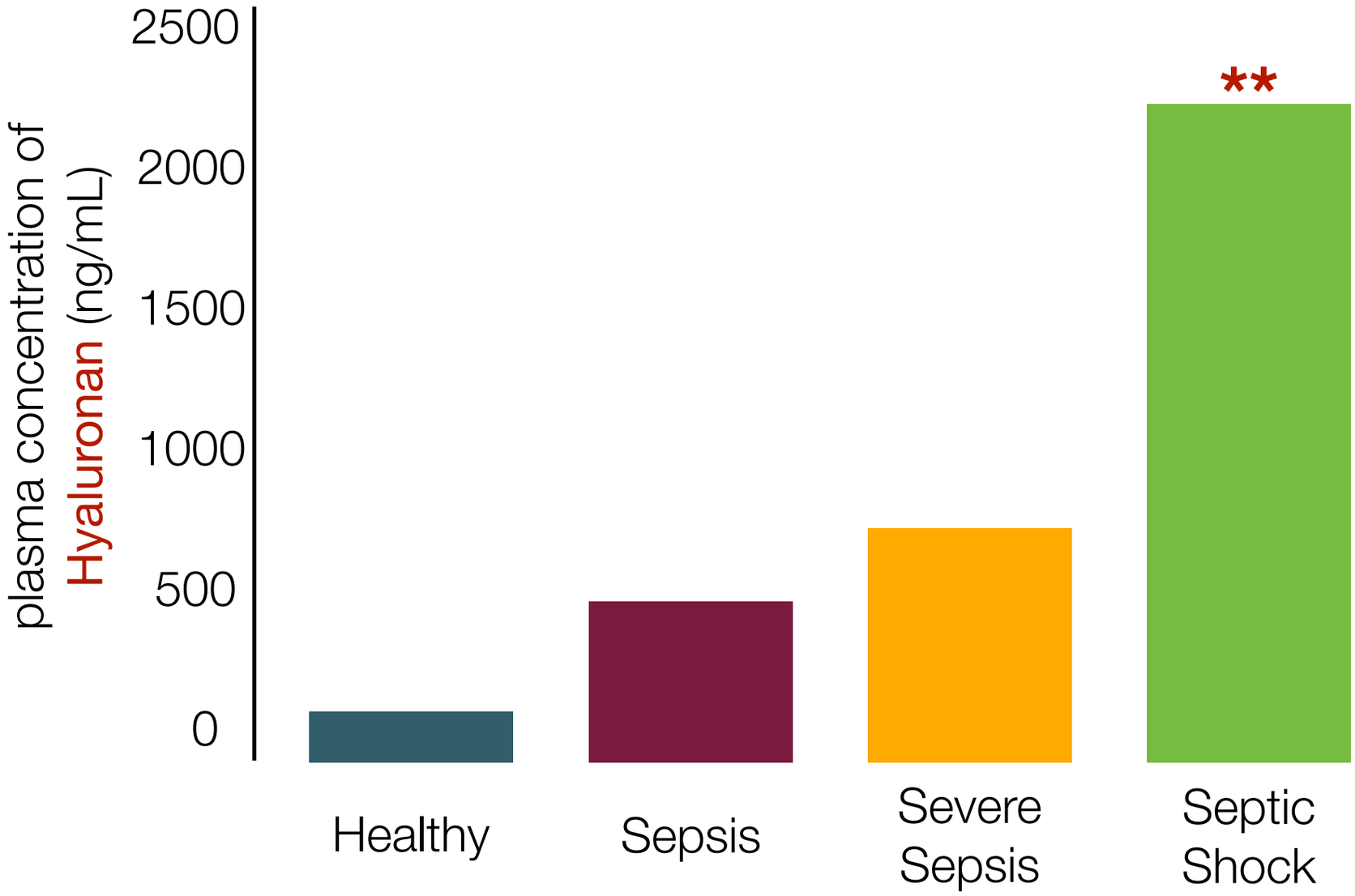
Nieuwdorp et al Curr Opin Lipidol 2005; 16:507

Sepsis-destruction of glycocalyx



Nieuwdorp et al Curr Opin Lipidol 2005; 16:507

Glycocalyx in sepsis



Increased shedding of glycocalyx in plasma with increasing severity of illness...a **prognostic factor**

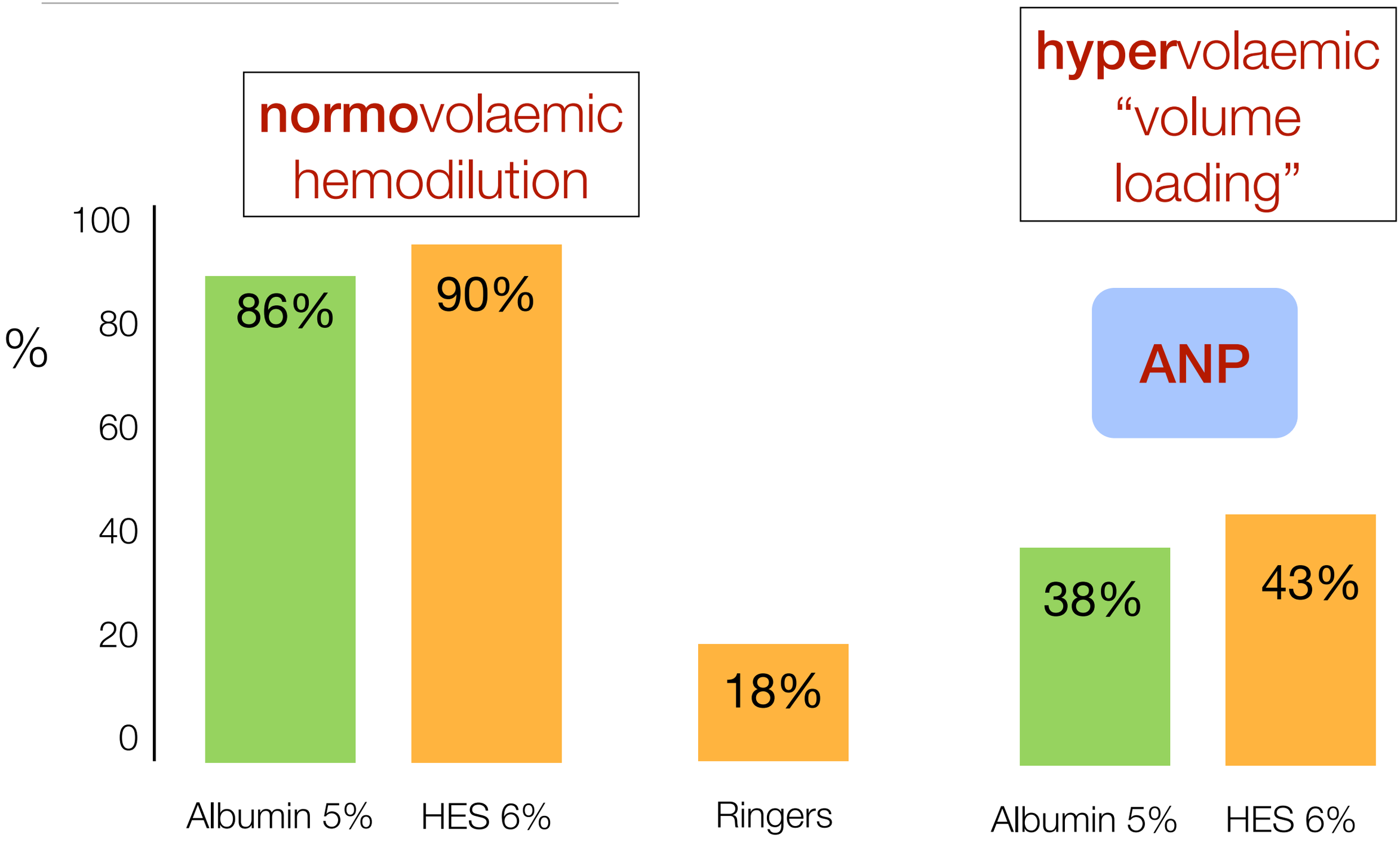
Kohler et al Infection 39:117-118; 2011

The **shedding** of **glycocalyx** is a **prognostic** factor for the outcome of sepsis.

Hyaluronan appears to **predict the survival** of septic shock and ITU length of stay in survivors.

Kohler et al Infection 39:117-118; 2011

Glycocalyx - volume of colloids effects are “context sensitive”



Alterations of the glycocalyx reduces the volume effects of colloids

Jacob et al Lancet 2007 16;369:1984-6

Atrial Natriuretic Peptide (ANP)

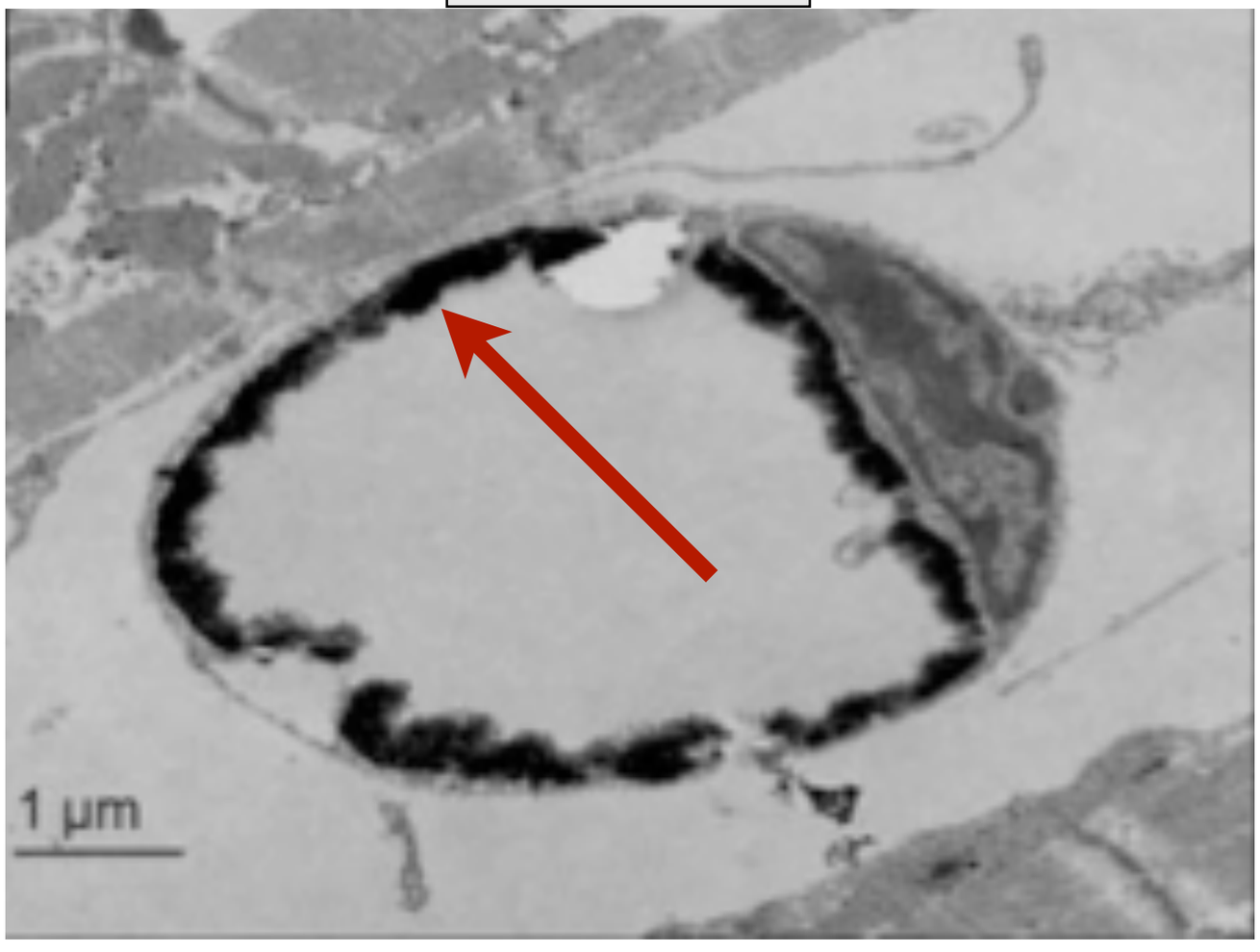
a cardiac hormone released by acute volume loading, plays a key role in blood volume regulation

Isbister (1997) Trans Sci; 18:409-423

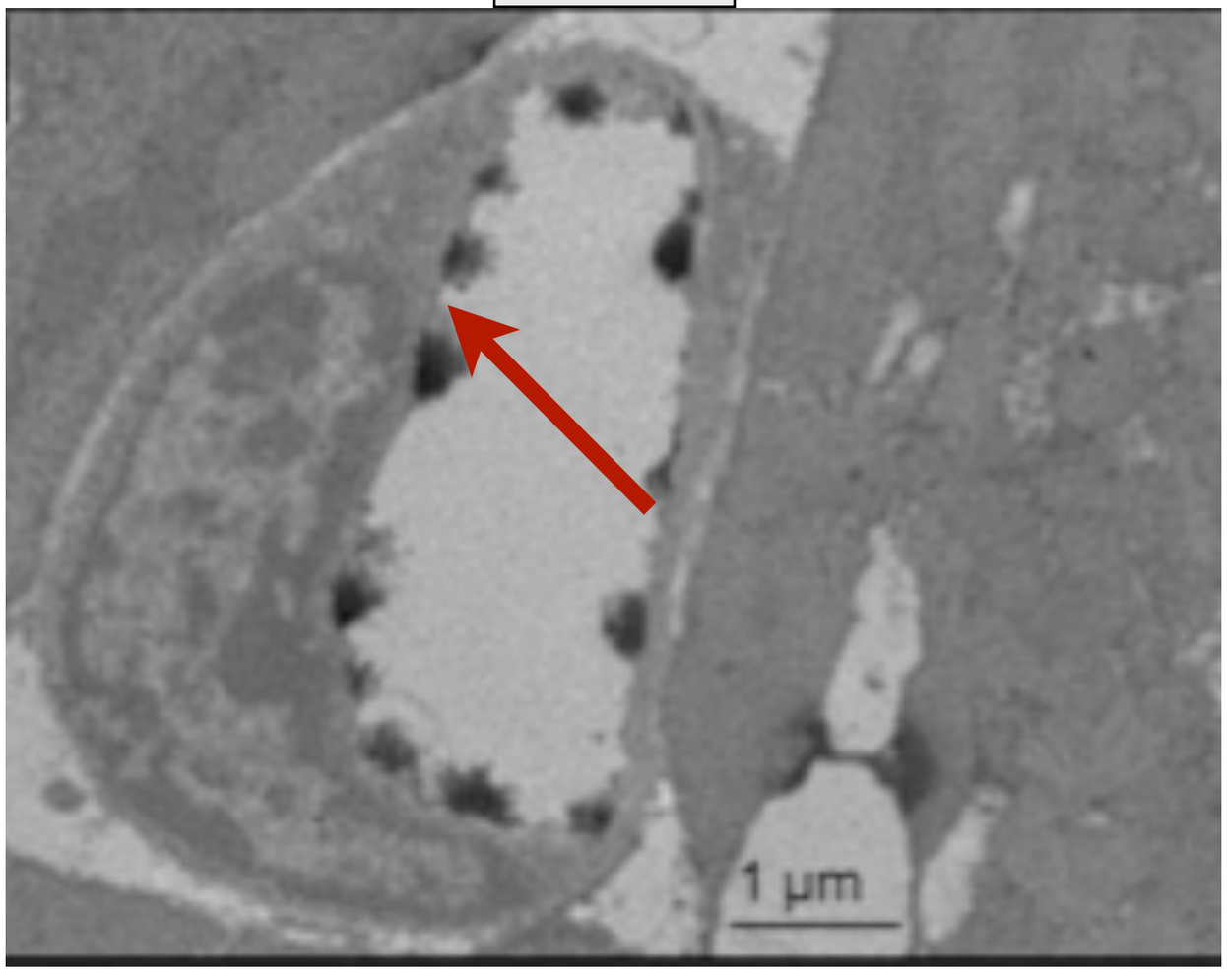
Tucker (1996) Am J Physiol; 271:R591

ANP “strips off” the glycocalyx

Control



ANP



Am J Physiol Heart Circ Physiol 289: H1993–H1999, 2005

Glycocalyx - summary

Large structure with **important functions**

- Vascular barrier function
- Thrombocyte and leucocyte adhesion (“teflon”)
- Inflammation

Jacob et al Anesthesiology 2006, 104:1223-1231

Jacob et al Cardiovasc Res 2007, 73:1235-1242

Summary

- Balanced infusions should be preferred
- Glycocalyx determine volume effects of infusions
- Healthy vascular barrier: volume effect of iso-oncotic colloids is 5 times, of hyperoncotic albumin 10 times higher than isotonic crystalloids (ANH)
- Affected vascular barrier: volume effect of iso-oncotic colloids is 2 times higher than isotonic crystalloids (ANH)

The Albumin molecule

- Single polypeptide chain
  - 585 amino acids
- Negatively charged
- Non-glycosylated

Distribution

- 360 gm total
  - 33% intravascular
  - 67% extravascular

Attributes

- Transport properties
- Anti-oxidant
- Anti-coagulant
- Protects microcirculation
- Anti-inflammatory

JL Vincent Best practice & research Clinical Anesthesiology 23(2009) 183-184

iv. fluids

Main Differences

Colloid osmotic force:

Colloid --- Crystalloid

Electrolyte composition

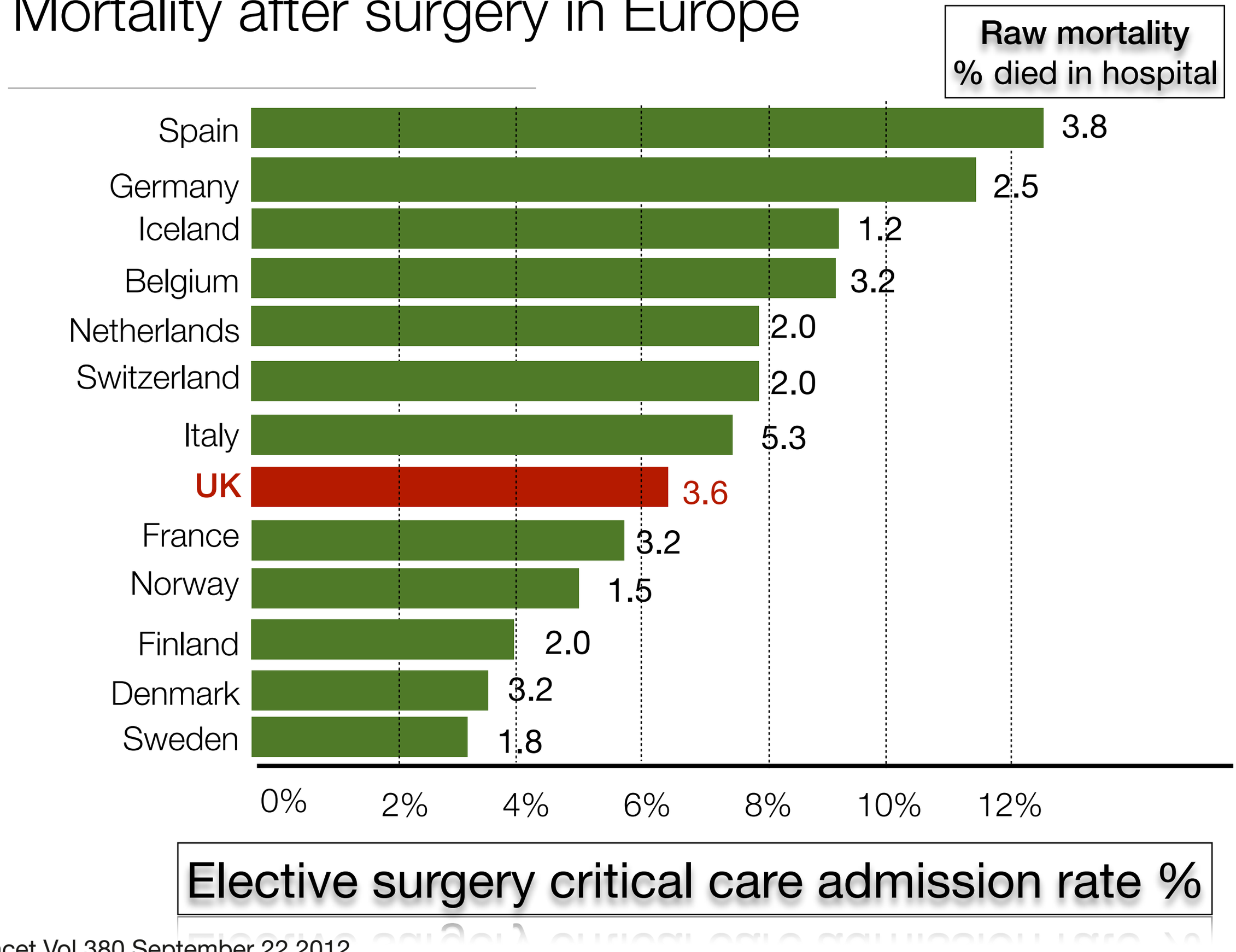
Saline based --- Chloride adapted

Purpose: Replacement of

Fluids (urine, perspiratio) --- Volume (blood, plasma)

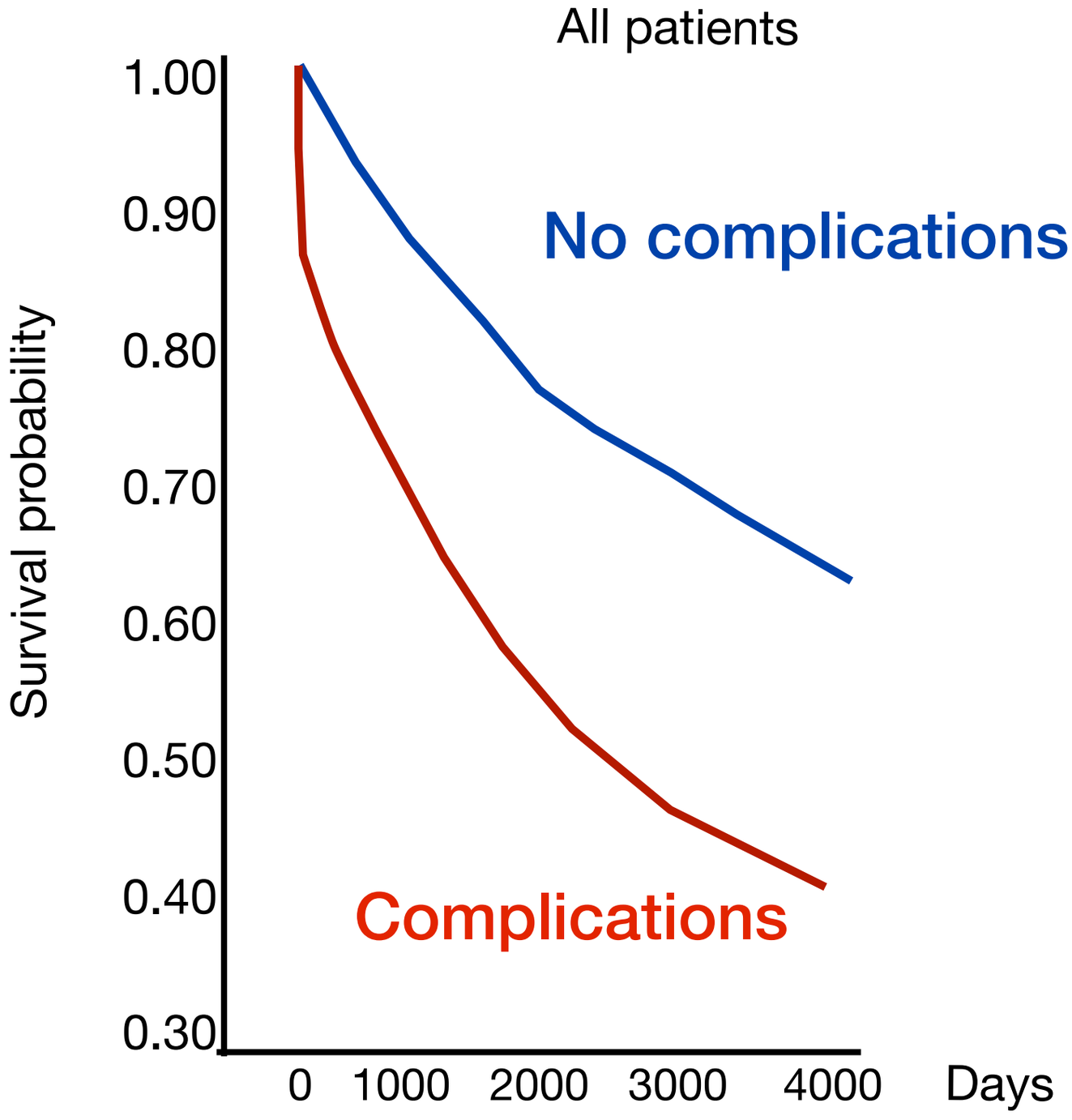
Perioperative haemodynamic management

Mortality after surgery in Europe

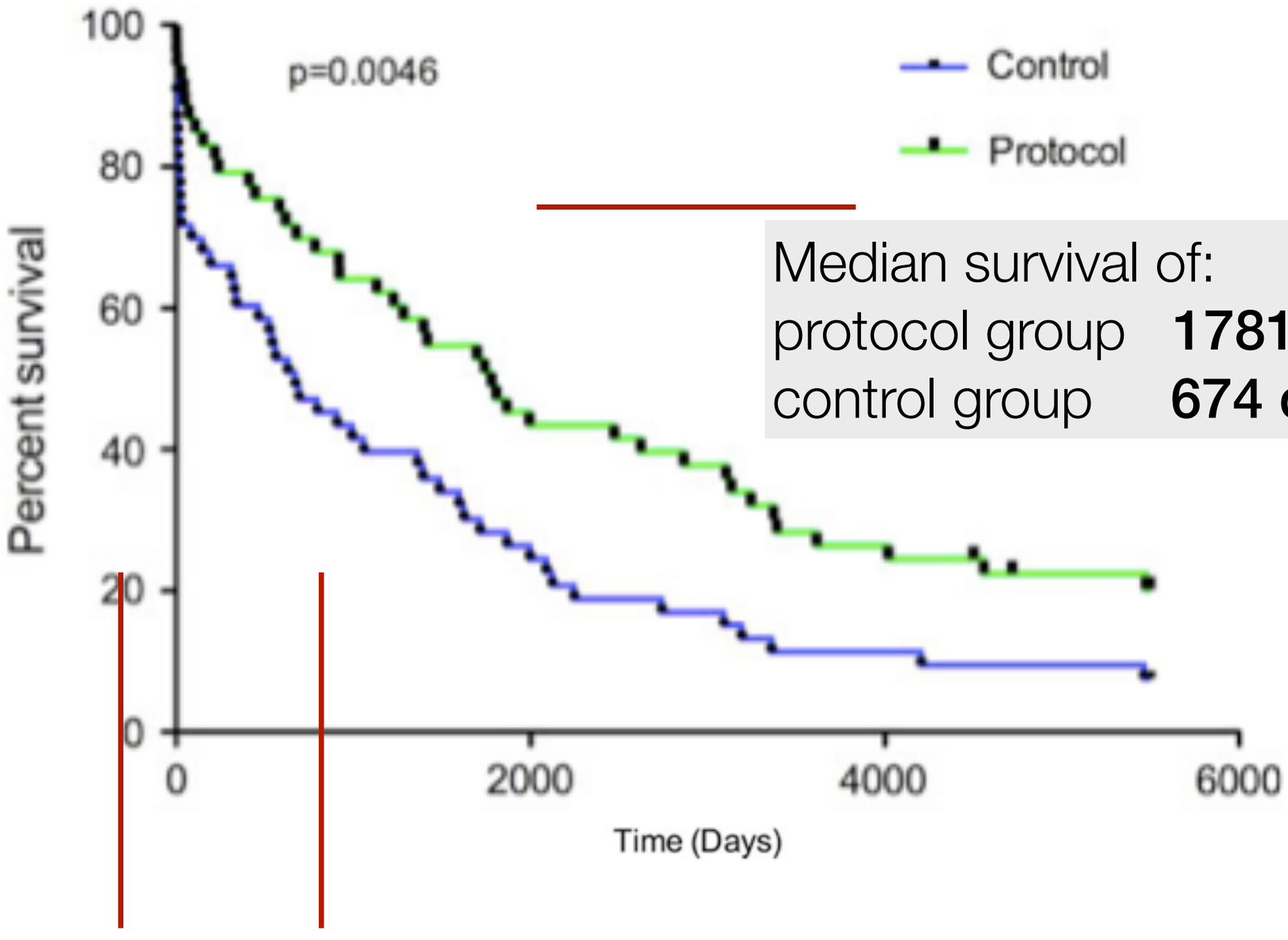


Lancet Vol 380 September 22,2012

Determinants of long term survival after major surgery and the adverse effects of postoperative complications



Goal-directed therapy in high risk surgical patients a **15 year** follow up study



Median survival of:
protocol group **1781 days**
control group **674 days**

Intensive Care Med (2010) 36:1327–1332

Summary

- Post operative complications are common and have long lasting effects
- We must look at ways of reducing the complication burden for these patients (goal directed therapy)
- But most studies showing a **positive** result of **goal directed therapy** have been small **(remember beta blocker studies!)**

Consensus for better perioperative haemodynamic management

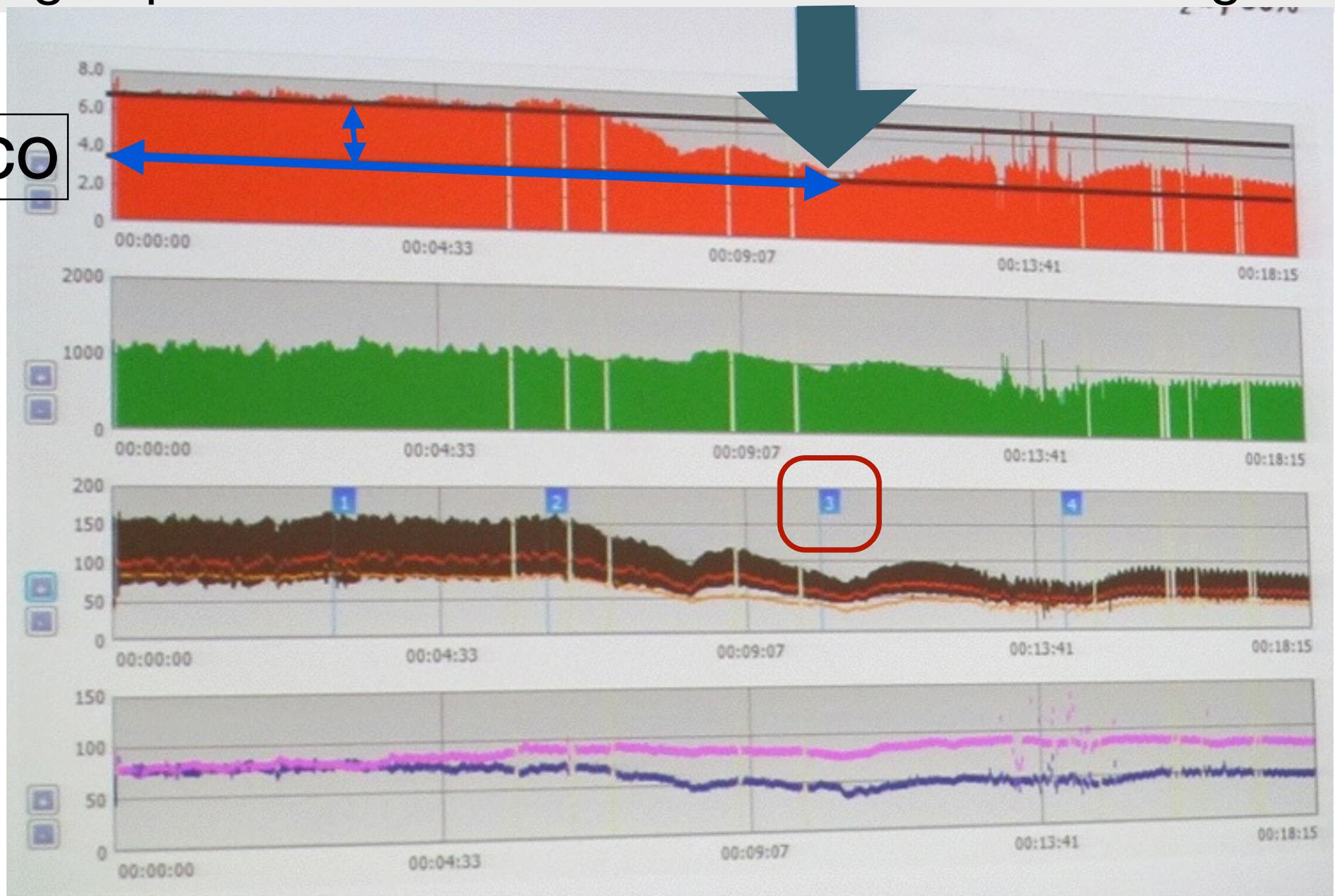
- In elective high risk patients, we ideally need to know the **cardiac output** and oxygen delivery **pre-induction** if we are to optimize them
- Can we do this **non-invasively?**

Consensus for better perioperative haemodynamic management

- During induction of anaesthesia in high risk patients, the fall in BP is due to a fall in preload as a result of increased venous capacitance
- It is not due to a fall in SVR...but due to **venodilation**
- ?? This is best treated with prophylactic fluids or venoconstrictors
- Phenylephrine infusion (1-2 mg/hr) commenced **pre-induction** maintains BP

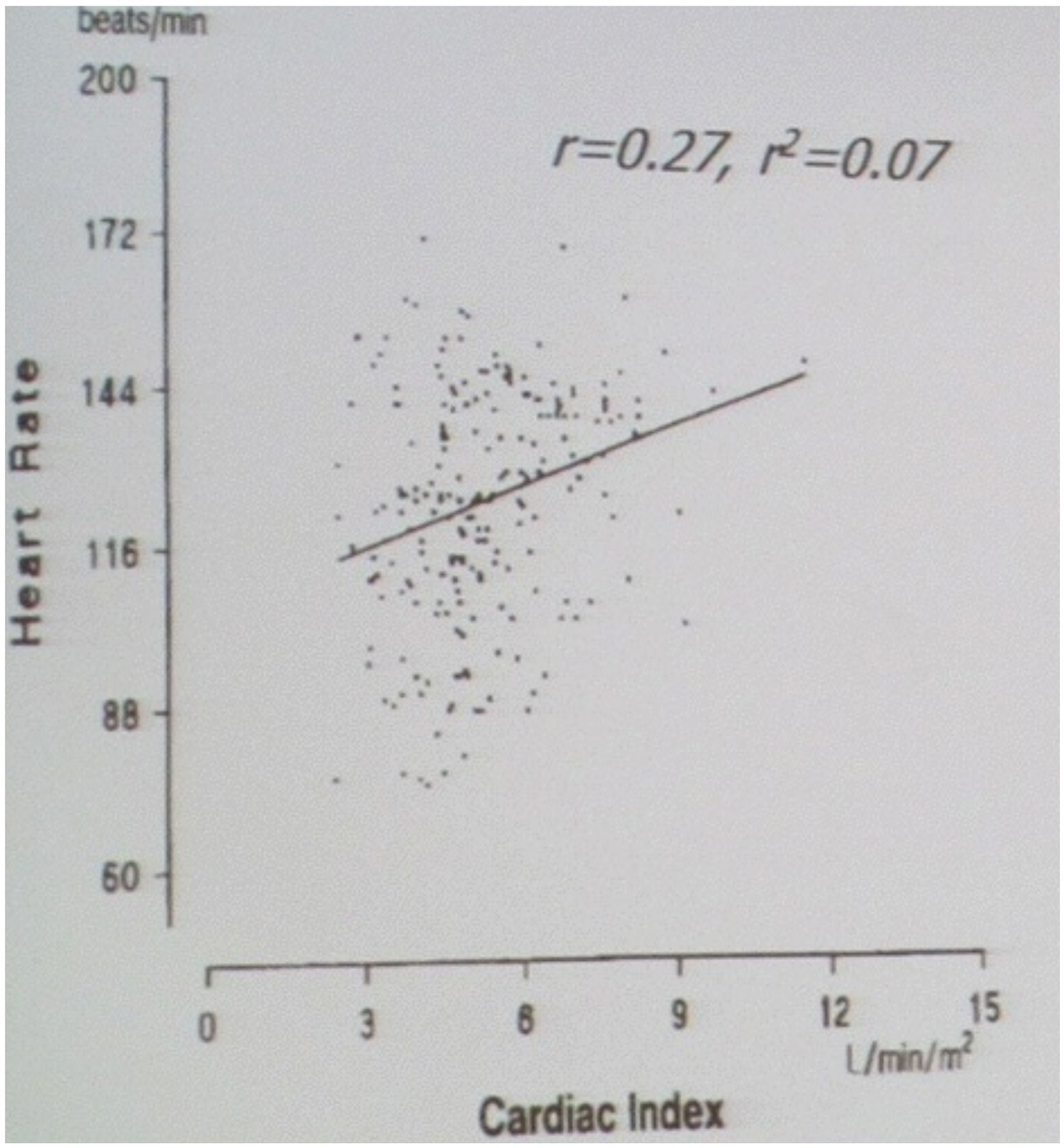
Induction sequence-Mr C for a Triple AAA

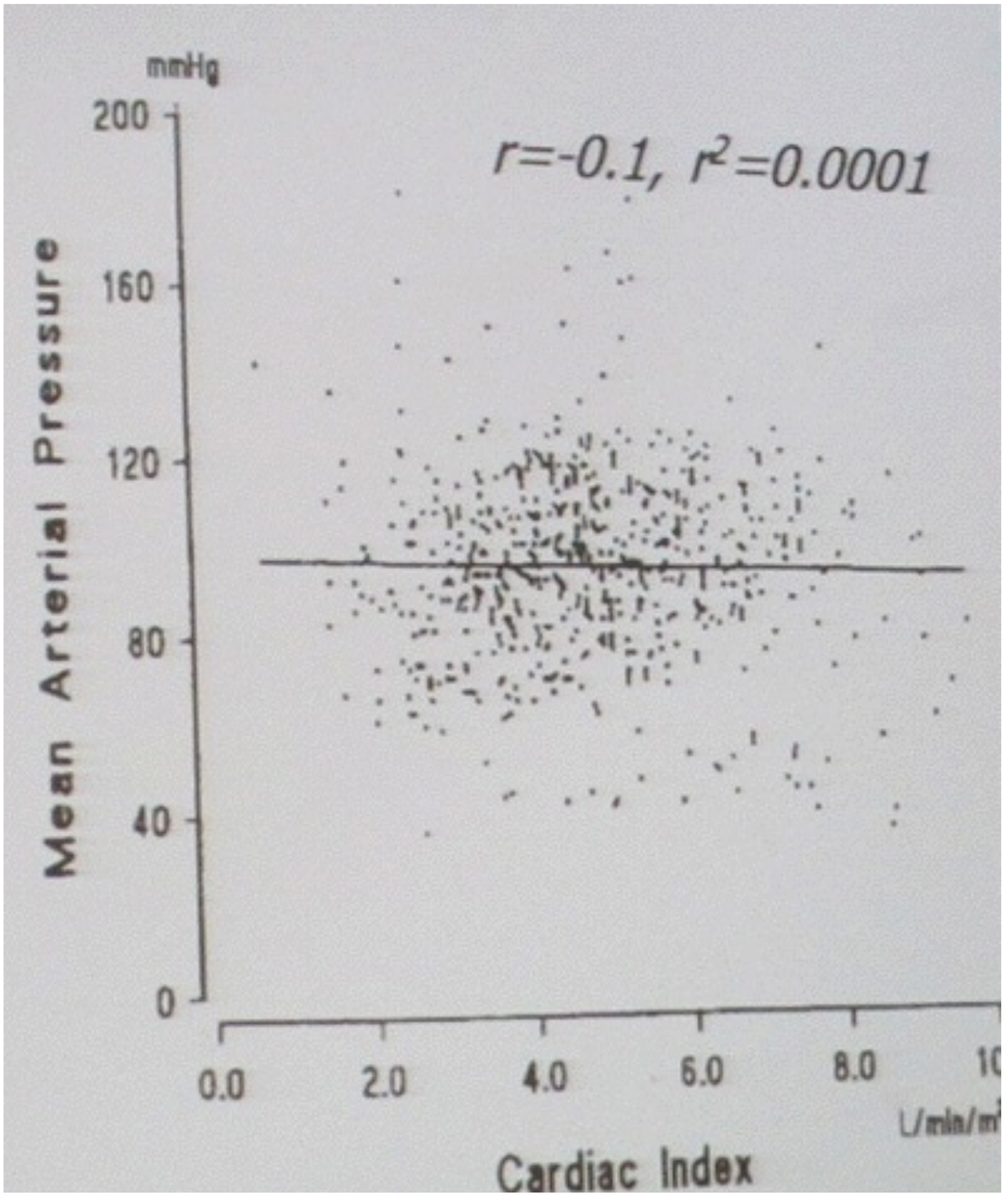
Monitoring at point 3 would have underestimated starting CO by 50%



Problem of using the **best evidenced** monitor (**oesophageal doppler**) is that you will be **blind** at **induction** and in **recovery** (when patient “third spaces” and the **crystalloid dissipates**).

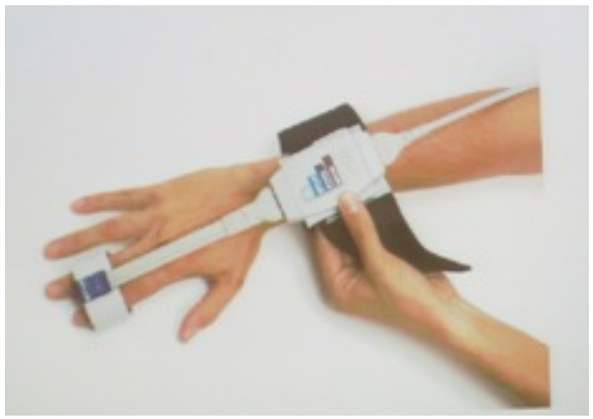
Why not use heart rate or blood pressure?



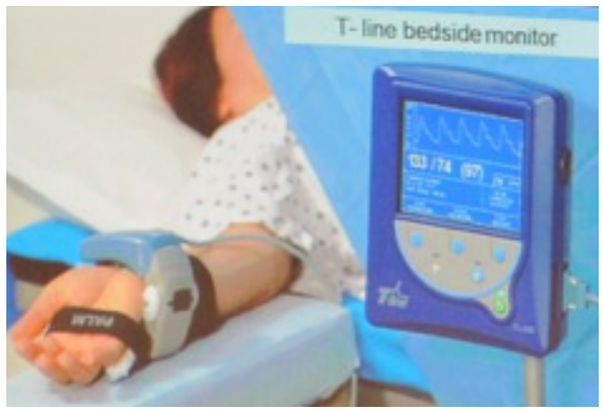


Shoemaker et al CCM 1993;21:218-222

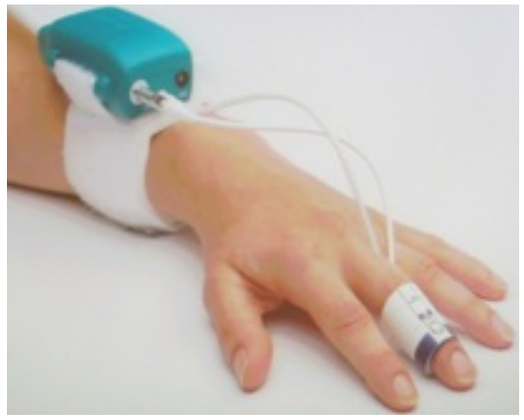
Non invasive cardiac output monitors



CNAP

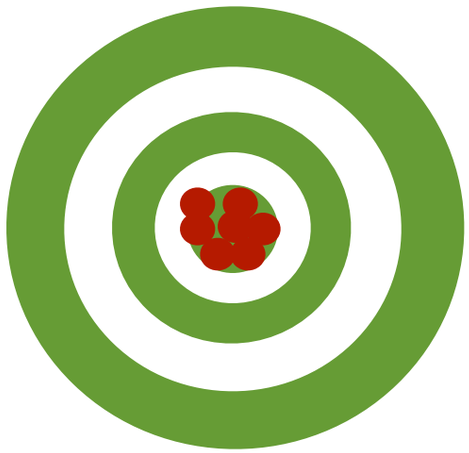


T line



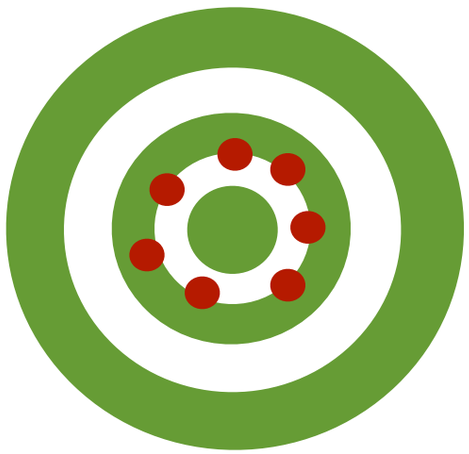
Nexfin

Accuracy and precision

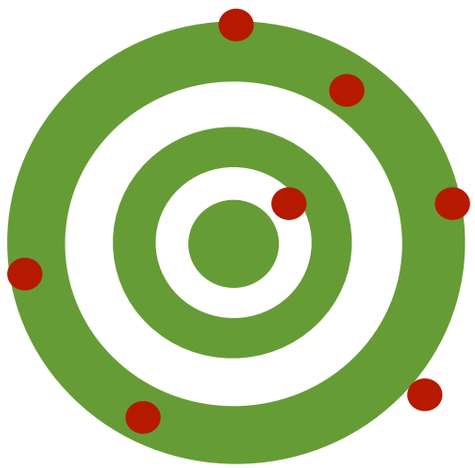


Accurate
Precise

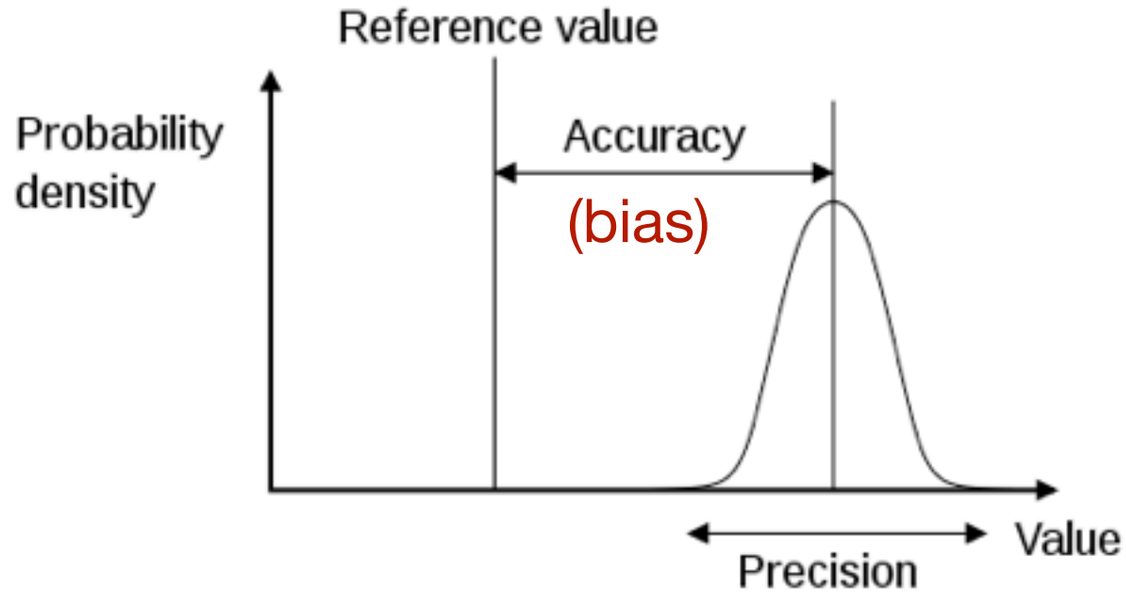
Not Accurate
Precise



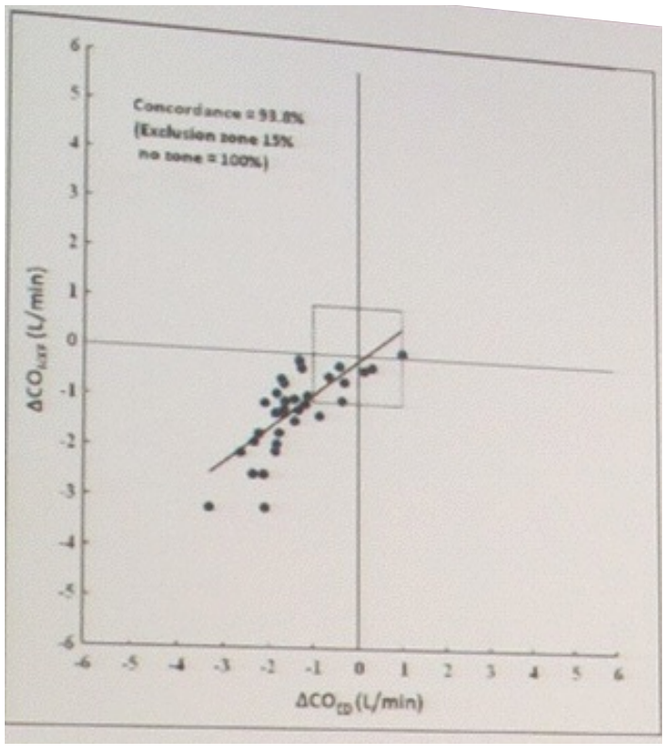
Accurate
Not Precise

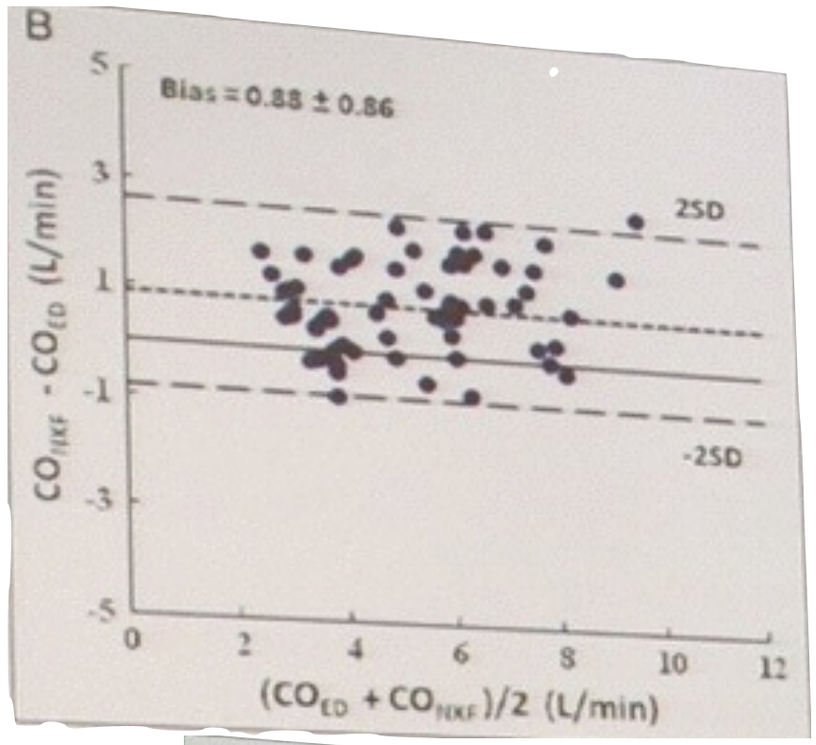


Not Accurate
Not Precise



Non invasive (Nexfin) v oesophageal doppler cardiac output monitors





Poor agreement
Septic shock
Noradrenaline

Good agreement
ASA 1/2
Periop patients

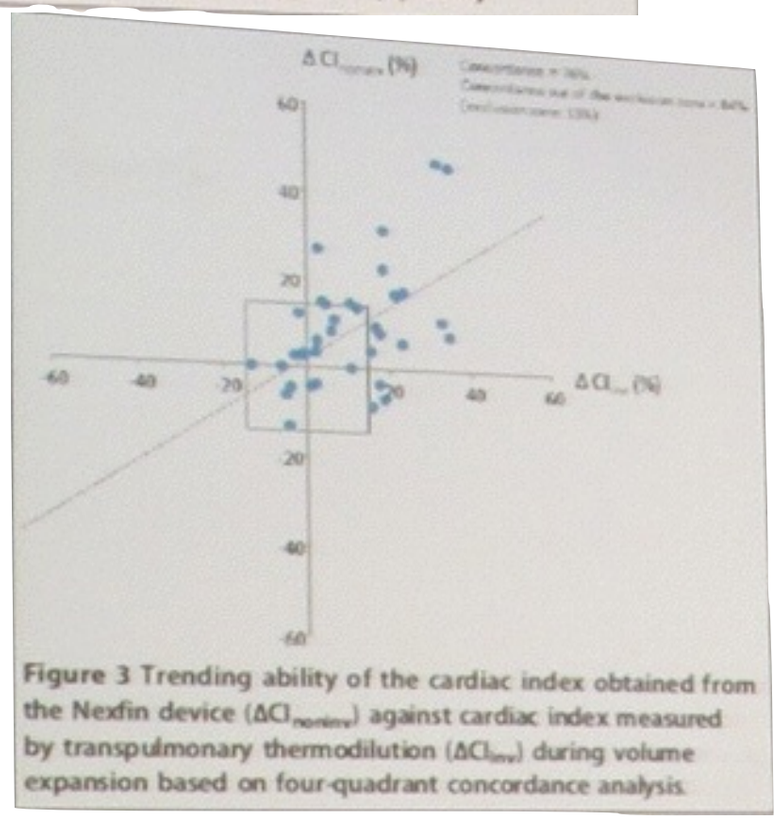
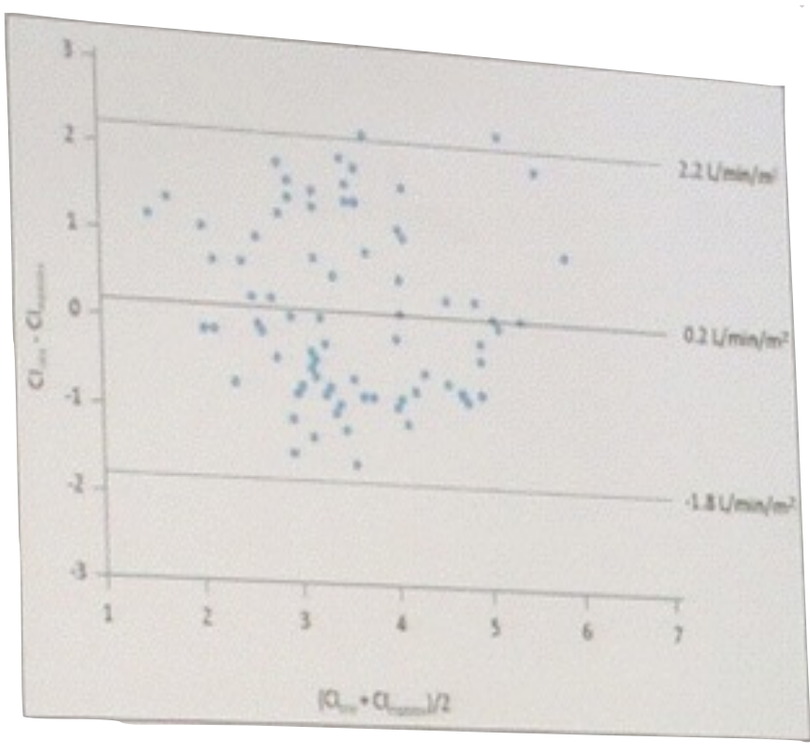


Figure 3 Trending ability of the cardiac index obtained from the Nexfin device (ΔCI_{noninv}) against cardiac index measured by transpulmonary thermodilution (ΔCI_{inv}) during volume expansion based on four-quadrant concordance analysis.



Chen et al J Clin Anesth 2013

But.....

- Main drawback is uncalibrated monitors are **highly dependent on vasomotor tone and on vascular compliance** (beware in sepsis!)

- It is surprising to observe that medicine is able to conduct clinical studies using devices that have been consistently demonstrated to be **inaccurate.**

- However, would any other industry dealing with life and death situations accept such a shortcoming?

Would an altimeter be used on a commercial passenger plane despite the fact that it has been demonstrated to be inaccurate?

Ramsingh et al. Critical Care 2013, 17:208

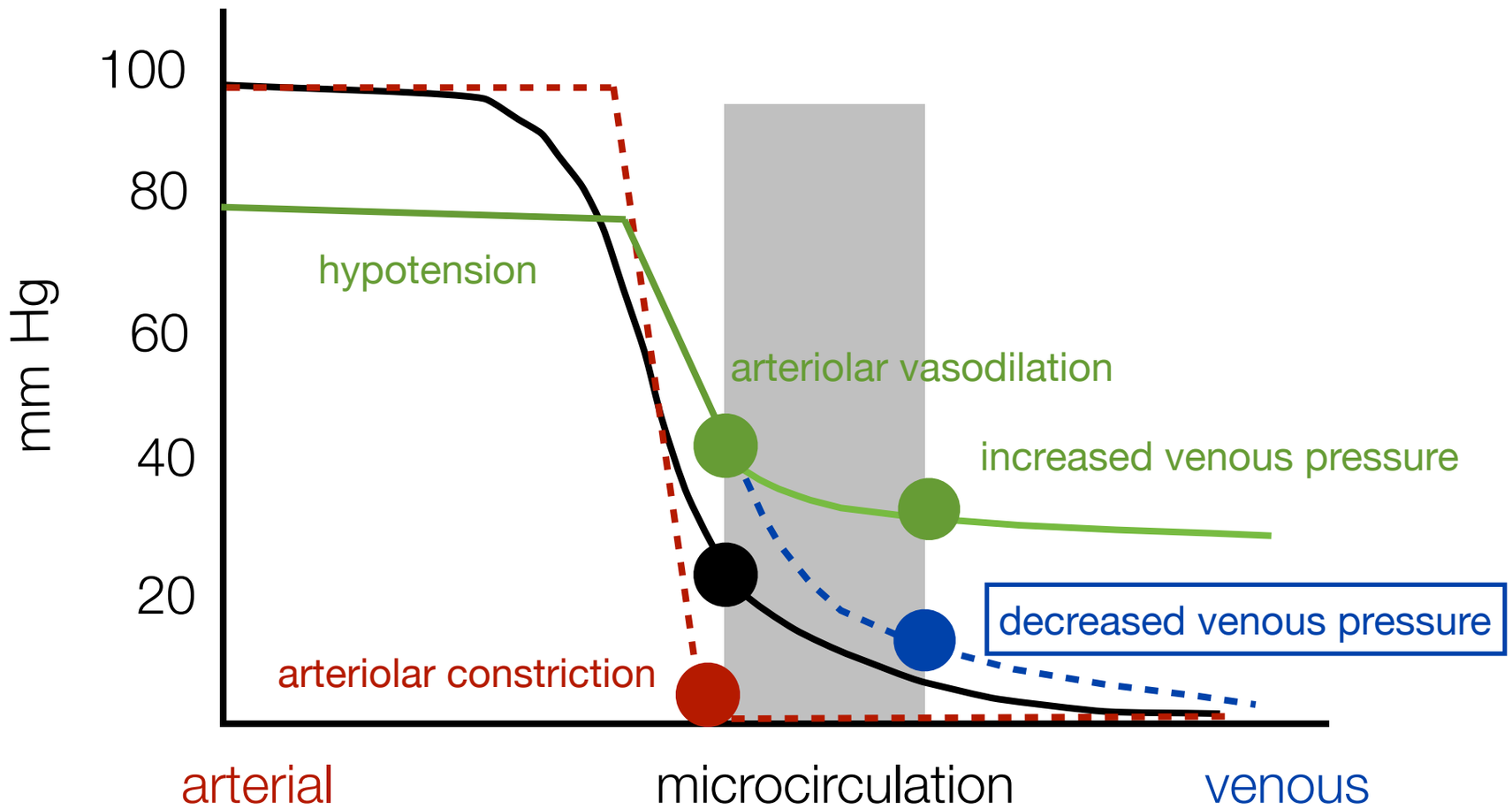
Microvascular flow

"...it seems likely that the circulatory defect is of the nature of a **distributional** change, since actual rates of blood **flow are not low.**

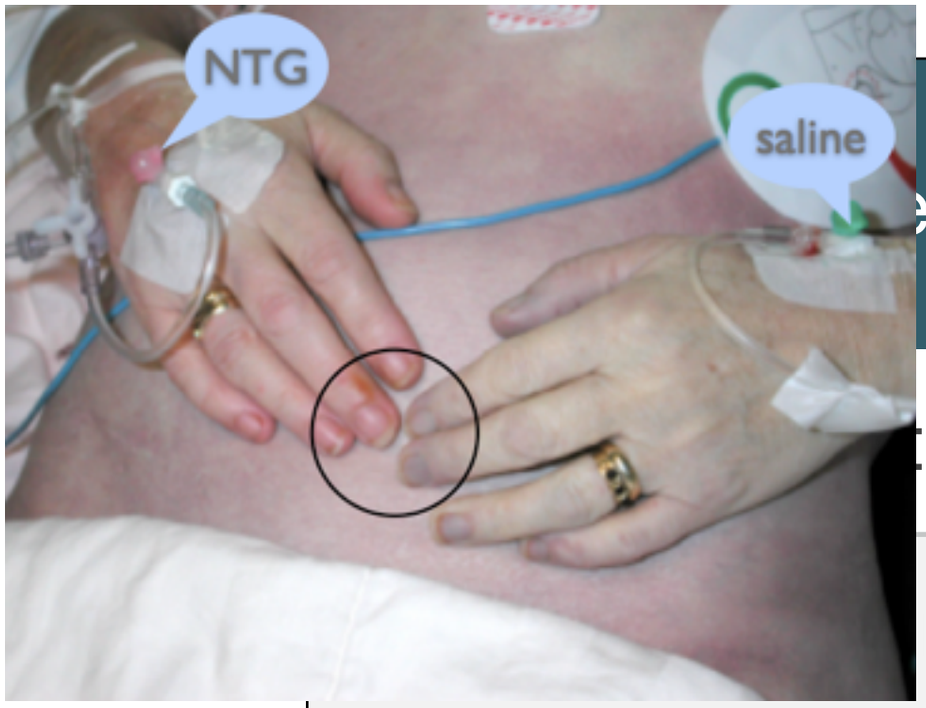
It might prove very **interesting if someone will try vasodilating drugs** in such a patient....."

"...it seems likely that the circulatory defect is of the nature of a **distributional** change, since actual rates of blood **flow are not low.** It might prove very **interesting if someone will try vasodilating drugs** in such a patient....."

Am J Cardiol 1963



Abnormal peripheral perfusion - effect of a stepwise increase of GTN



erfusion	T baseline	T max
time (sec)	9.4	4.8
ndex	-0.5	0.7
T skin-difference	3.3	0.7
StO2%	75	84
Upslope (%/sec)	1.9	2.8

Improvement in indices of perfusion with GTN

Prof Jan Bakker Personal communication

Conclusion

- Vasodilation and **optimizing venous pressure** makes sense even in patients with hypotension
- Impaired peripheral perfusion is associated with decreased clearance of lactate, increased organ failure and very high mortality
- Targeted infusion of NTG improves peripheral perfusion
- Outcome?

Detecting fluid responsiveness

CHEST Special Feature

Does Central Venous Pressure Predict Fluid Responsiveness?*

Conclusions: This systematic review (**24 studies**) demonstrated a very poor relationship between CVP and blood volume as well as the inability of CVP/ΔCVP to predict the hemodynamic response to a fluid challenge.

"CVP should **not be used** to make clinical decisions regarding fluid management."

CHEST **2008;** 134:172–178

Does the Central Venous Pressure Predict Fluid Responsiveness? An Updated Meta-Analysis

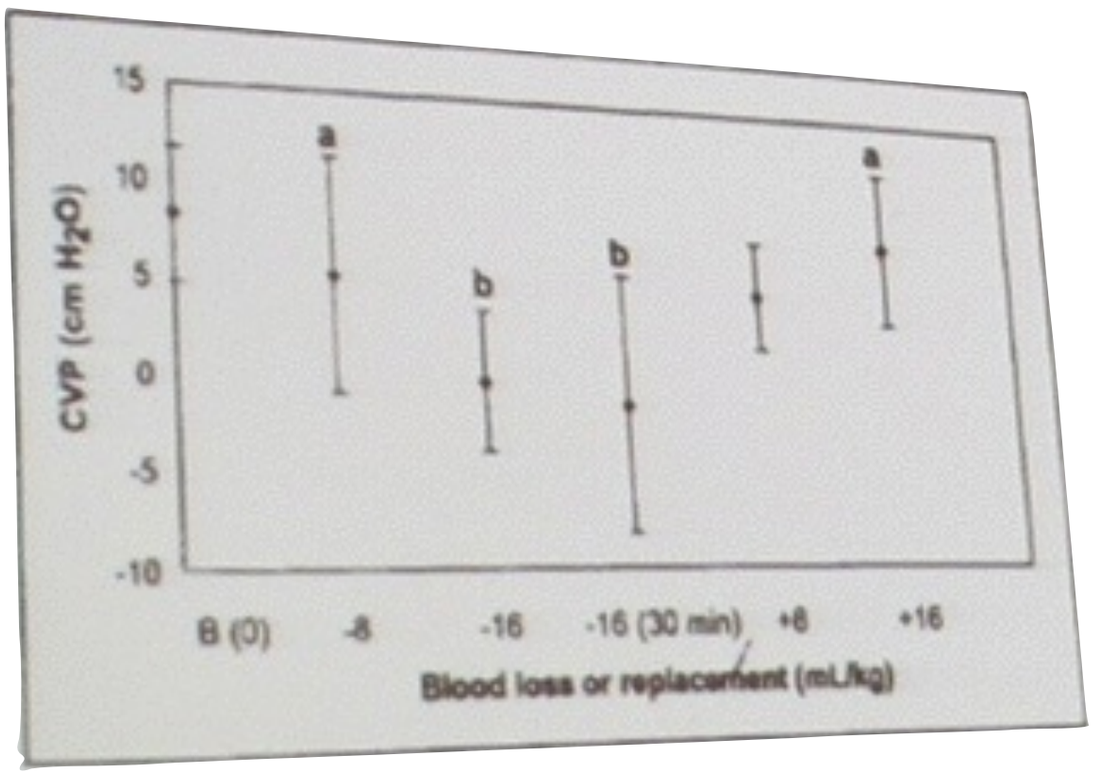
"43 studies : AUC was **0.56 (coin flip)**
There is no data in any group of patients to support using the CVP to guide fluid therapy. This approach must be **abandoned**."

CCM July **2013**; 41:7; 1774

But yes, the CVP works !

Changes in central venous pressure in response to acute blood loss **in horses**

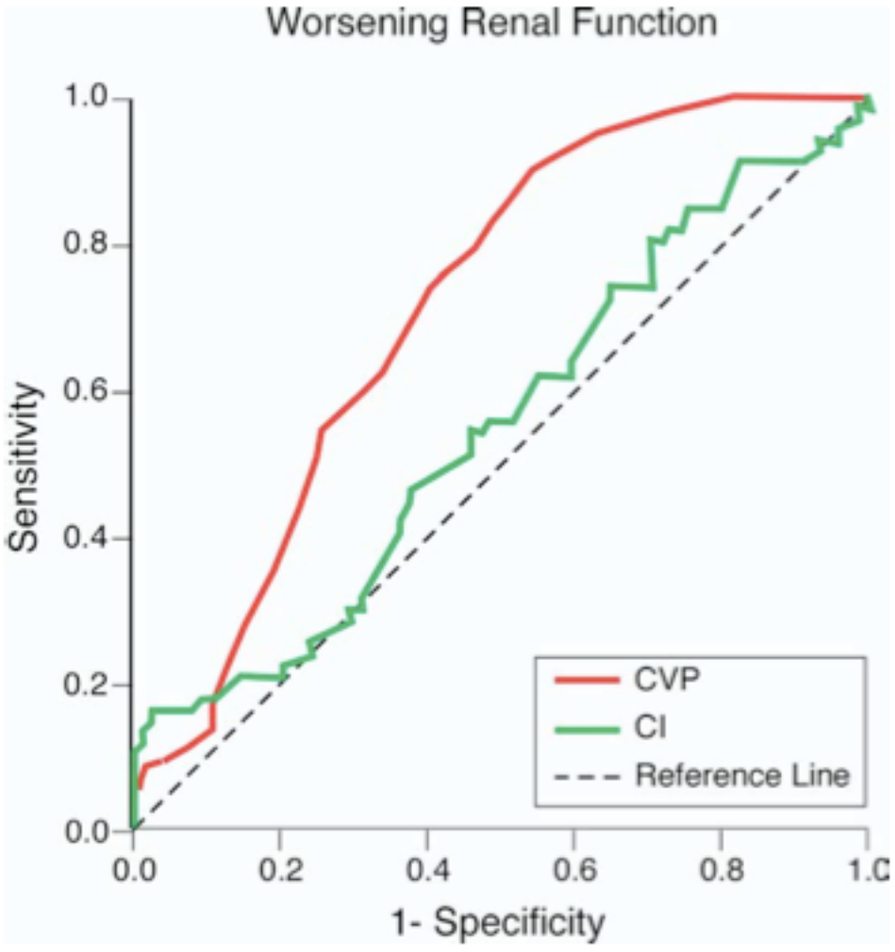
- 7 healthy, standing awake mares
- Graded haemorrhage

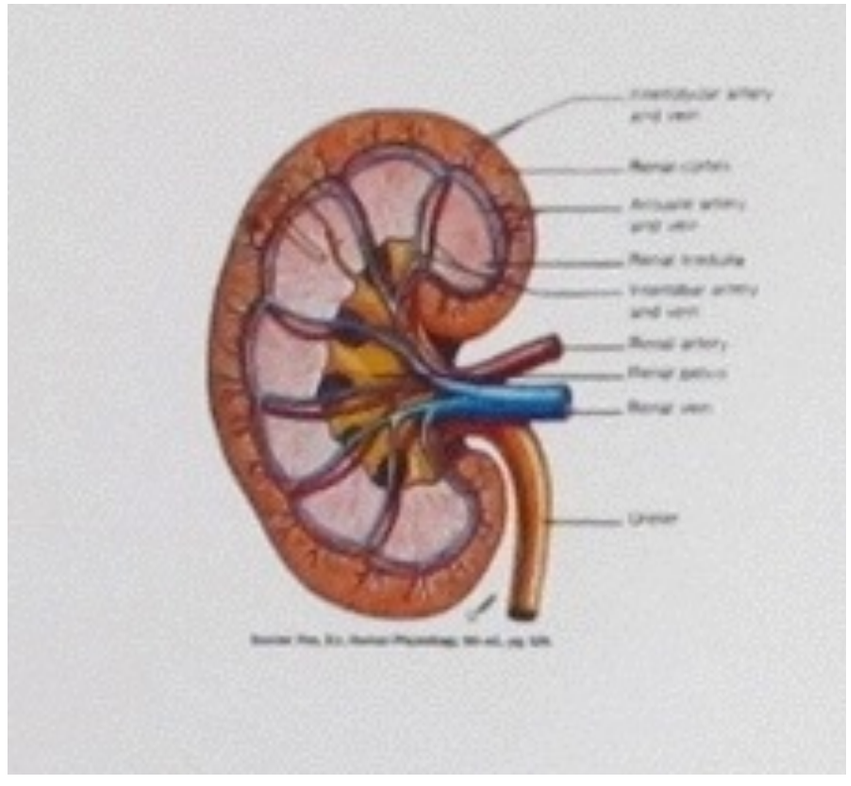


JAVMA 2006;228:1458

Negative effects of a raised CVP

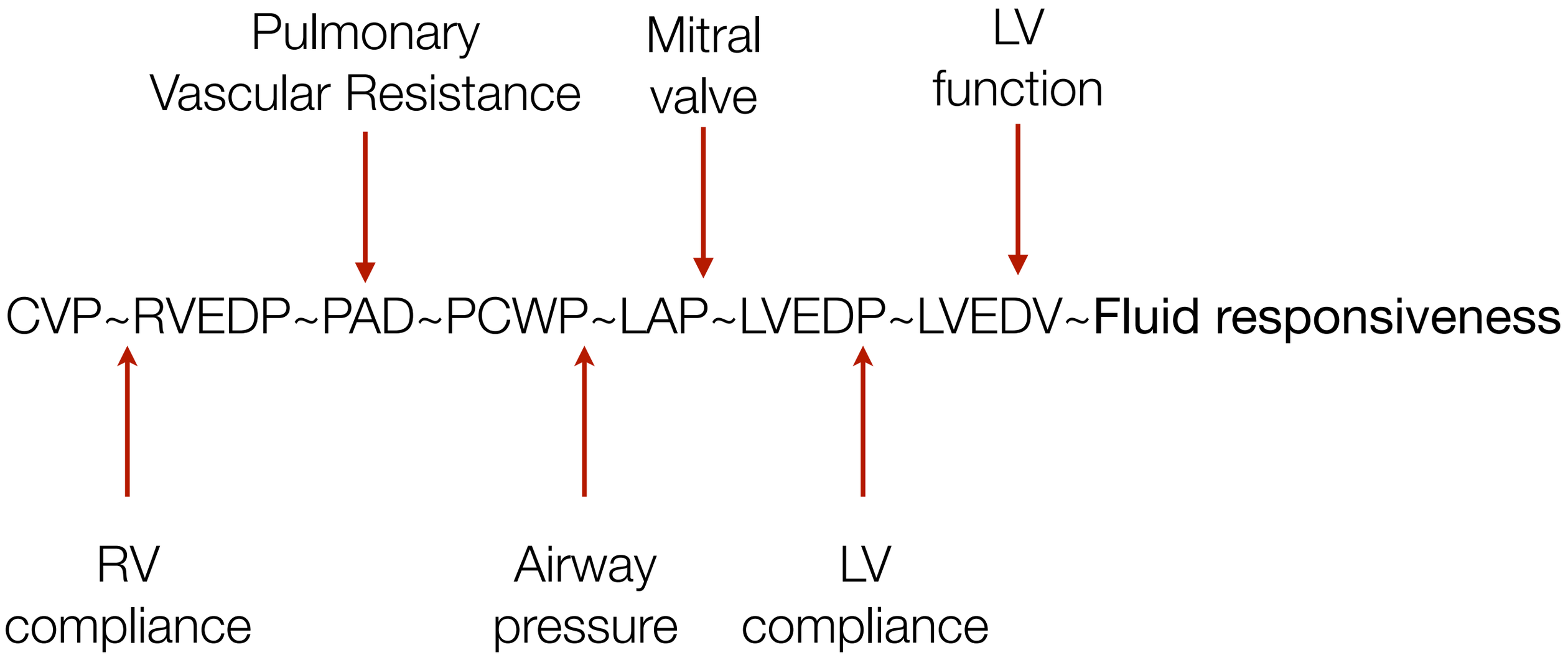
Importance of Venous Congestion for Worsening of Renal Function in Advanced Decompensated Heart Failure





JACC Vol. 53, No. 7, 2009

The 7 flawed assumptions in assuming that the CVP predicts fluid responsiveness



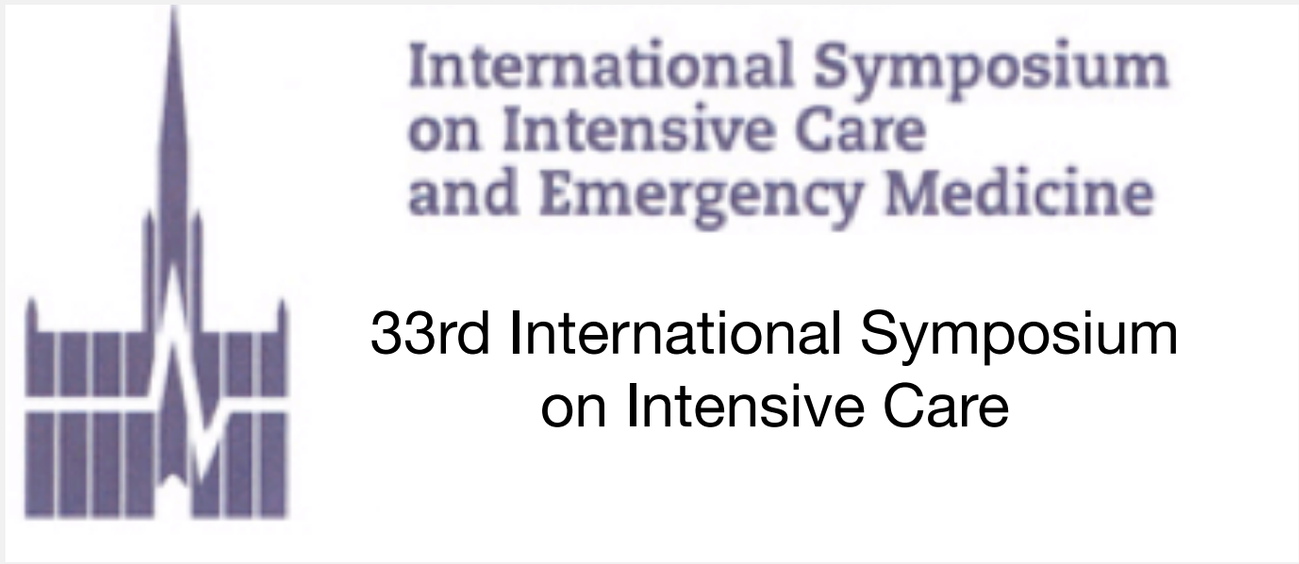
Kaplan's Cardiac Anesthesia 2006; pg 385, fig 14-11

???


KEEP
WELL
LEFT

Best of Brussels - 2013

Part 2



Best of Brussels - 2013

Part 1

- Surviving sepsis - Pro/Con
- CPR
- Glycocalyx
- Perioperative haemodynamic management
- Microvascular flow
- Detecting fluid responsiveness

Part 2

- Diastolic dysfunction
- Thermodilution derived variables
- Infections/Antibiotic pharmacokinetics
- Good medical websites
- Pancreatitis
- Obstetrics - PPH
- Obsterics - Amniotic fluid embolism

Diastolic dysfunction

Diastolic heart failure

- Diastolic heart failure increasingly more common -

  ~50% of heart failure cases

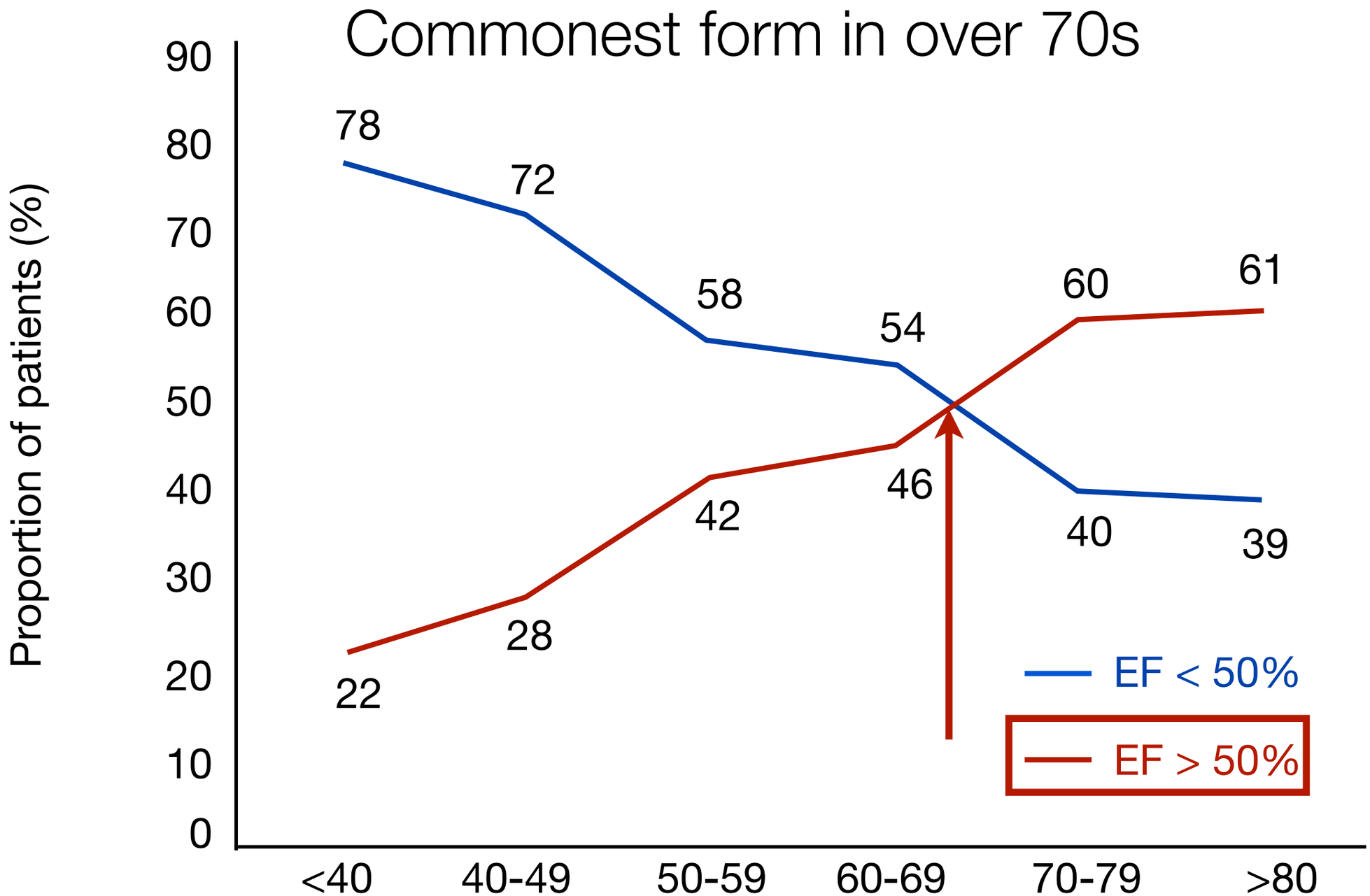
- **Prognosis** the **same** as systolic heart failure

- Patients often have **normal** ejection fraction

- **Difficult** to diagnose

- Appropriate treatment is not known

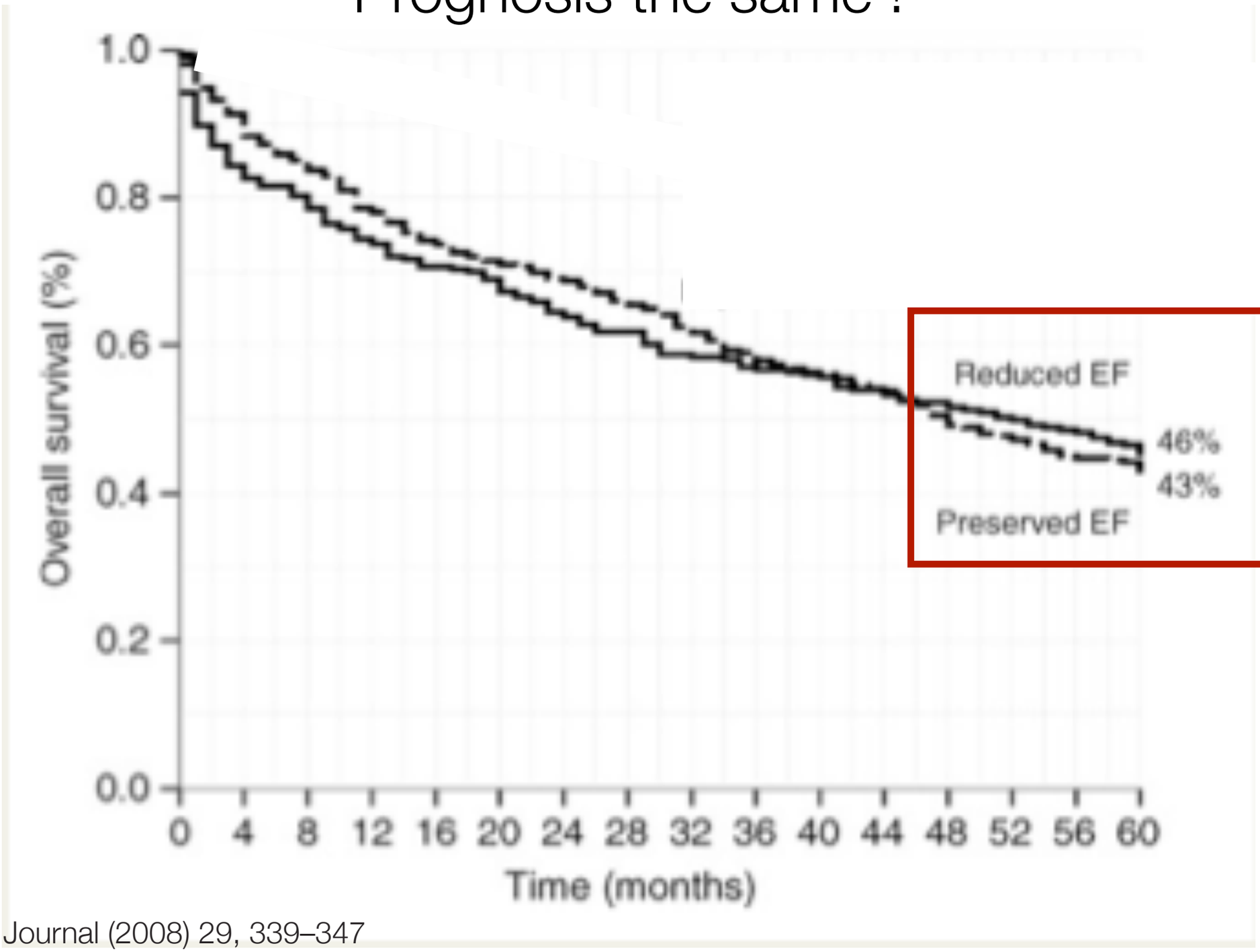
Diastolic heart failure (“failure with preserved ejection fraction”)



European Heart Journal (2008) 29, 339–347

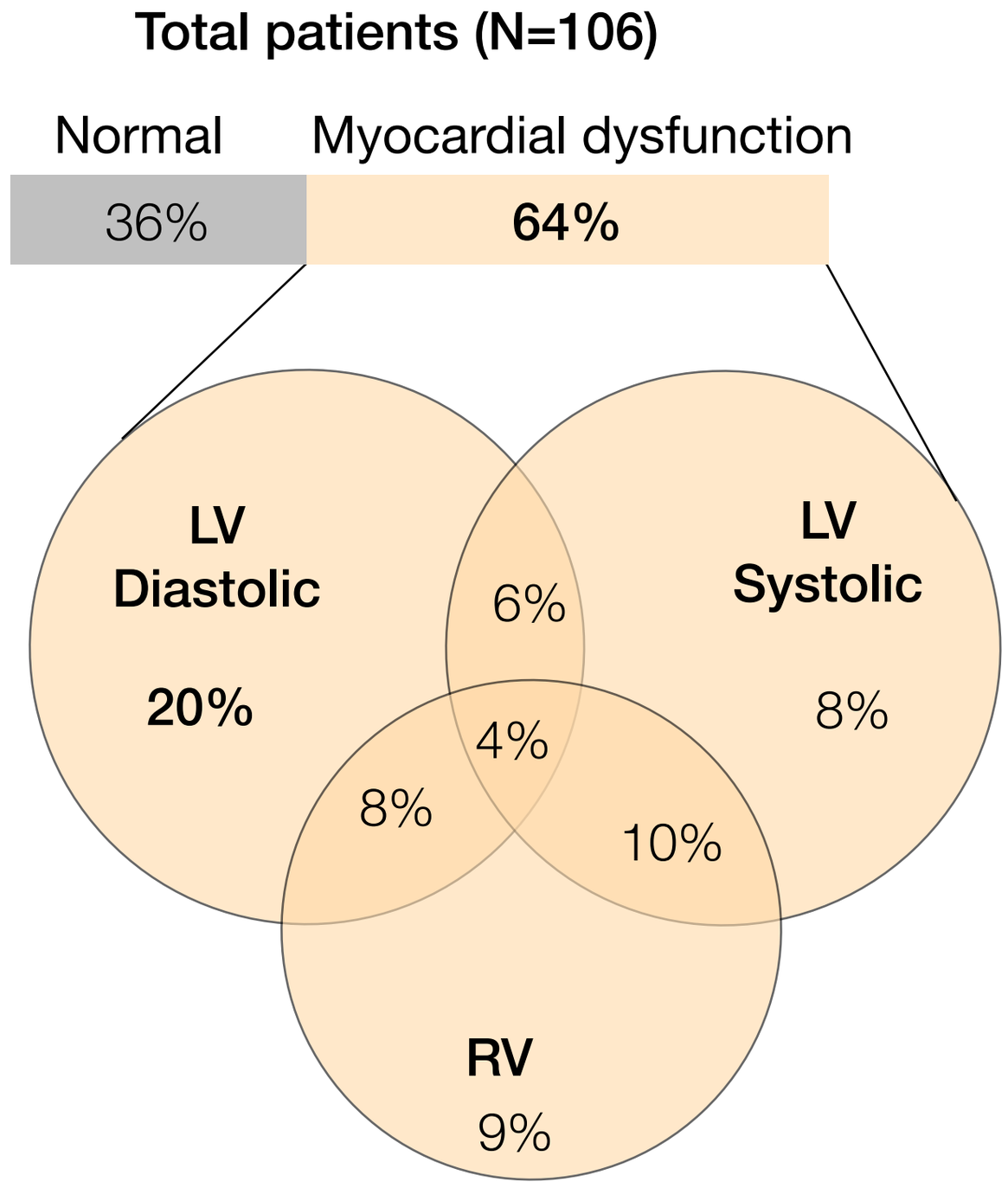
Diastolic heart failure (“failure with preserved ejection fraction”)

Prognosis the same !



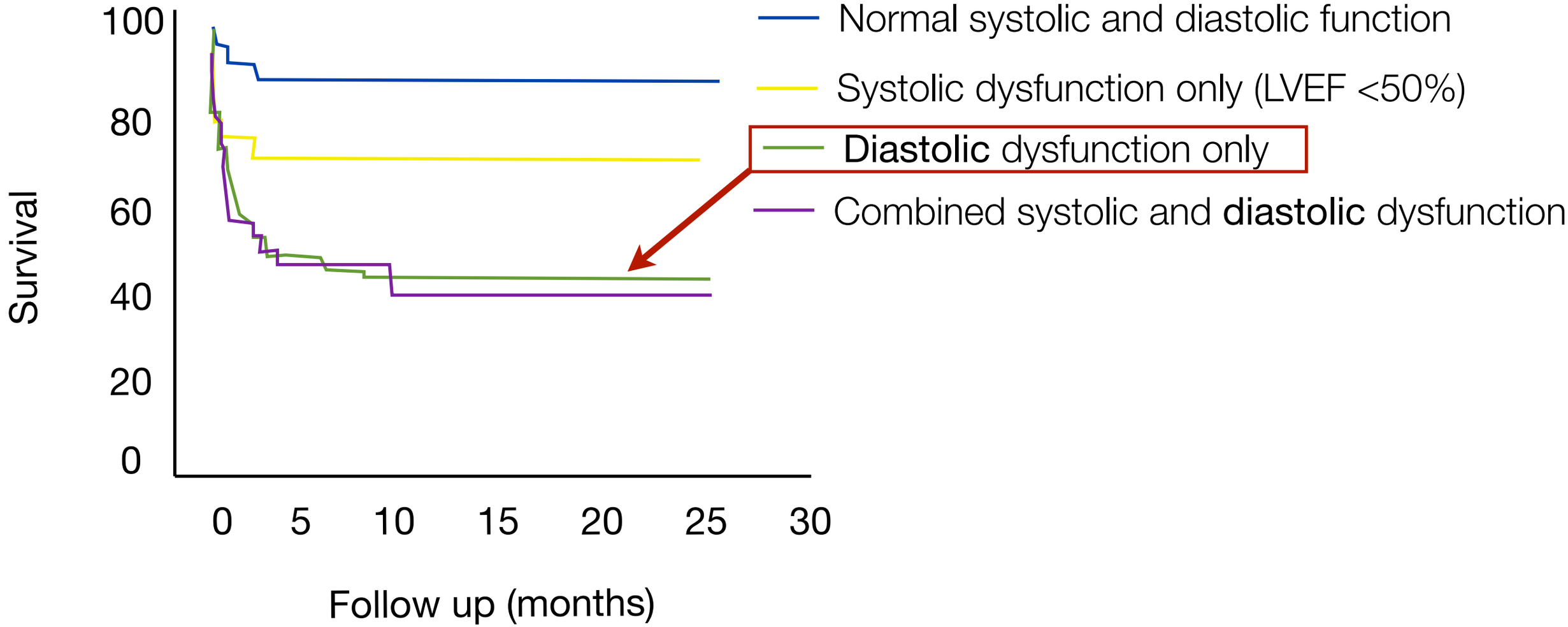
European Heart Journal (2008) 29, 339–347

Diastolic dysfunction **common** in **severe sepsis**

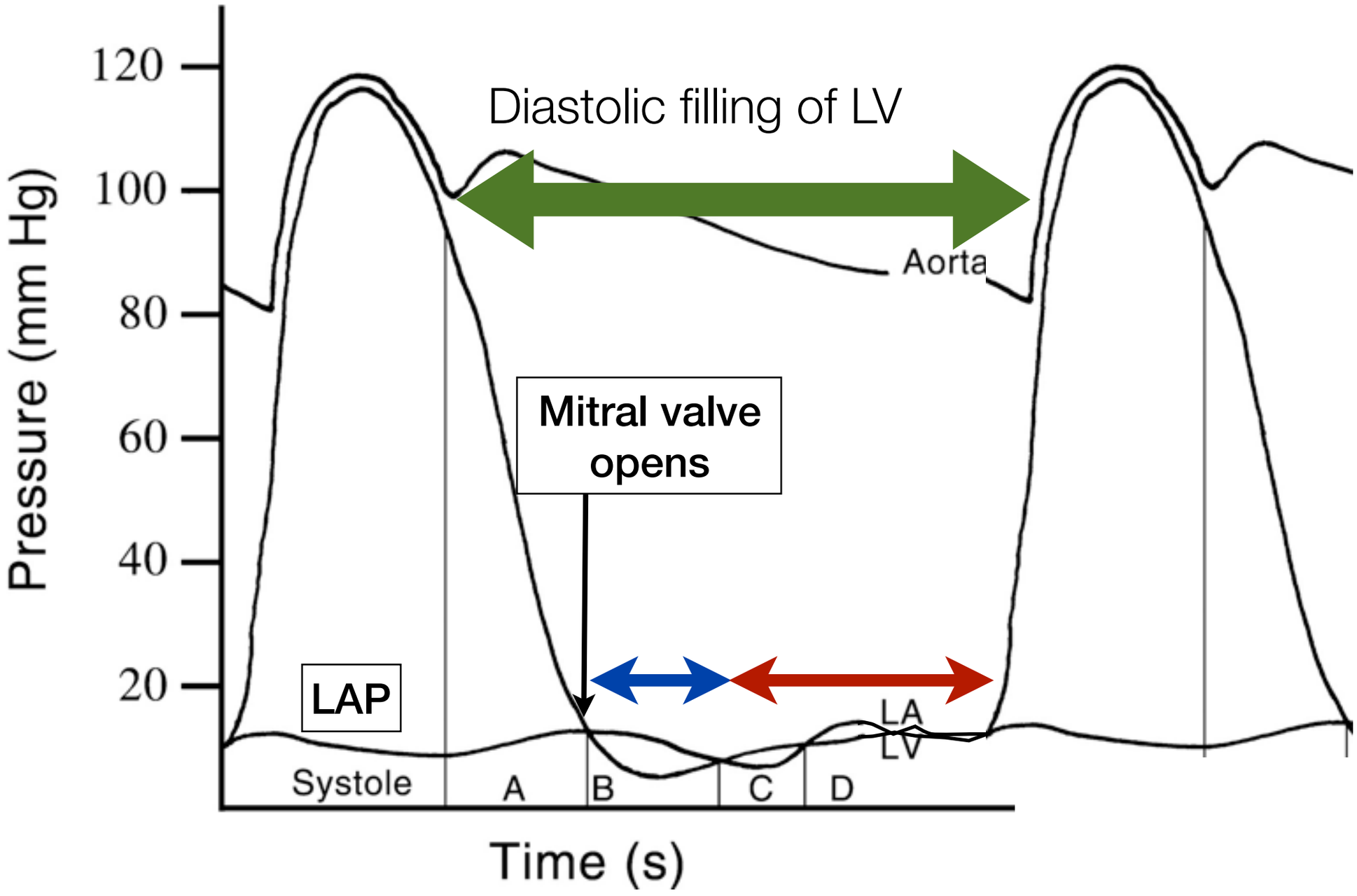


Mayo Clin Proc 2012; 87(7):620-628

Diastolic dysfunction and mortality in severe **sepsis** and septic shock

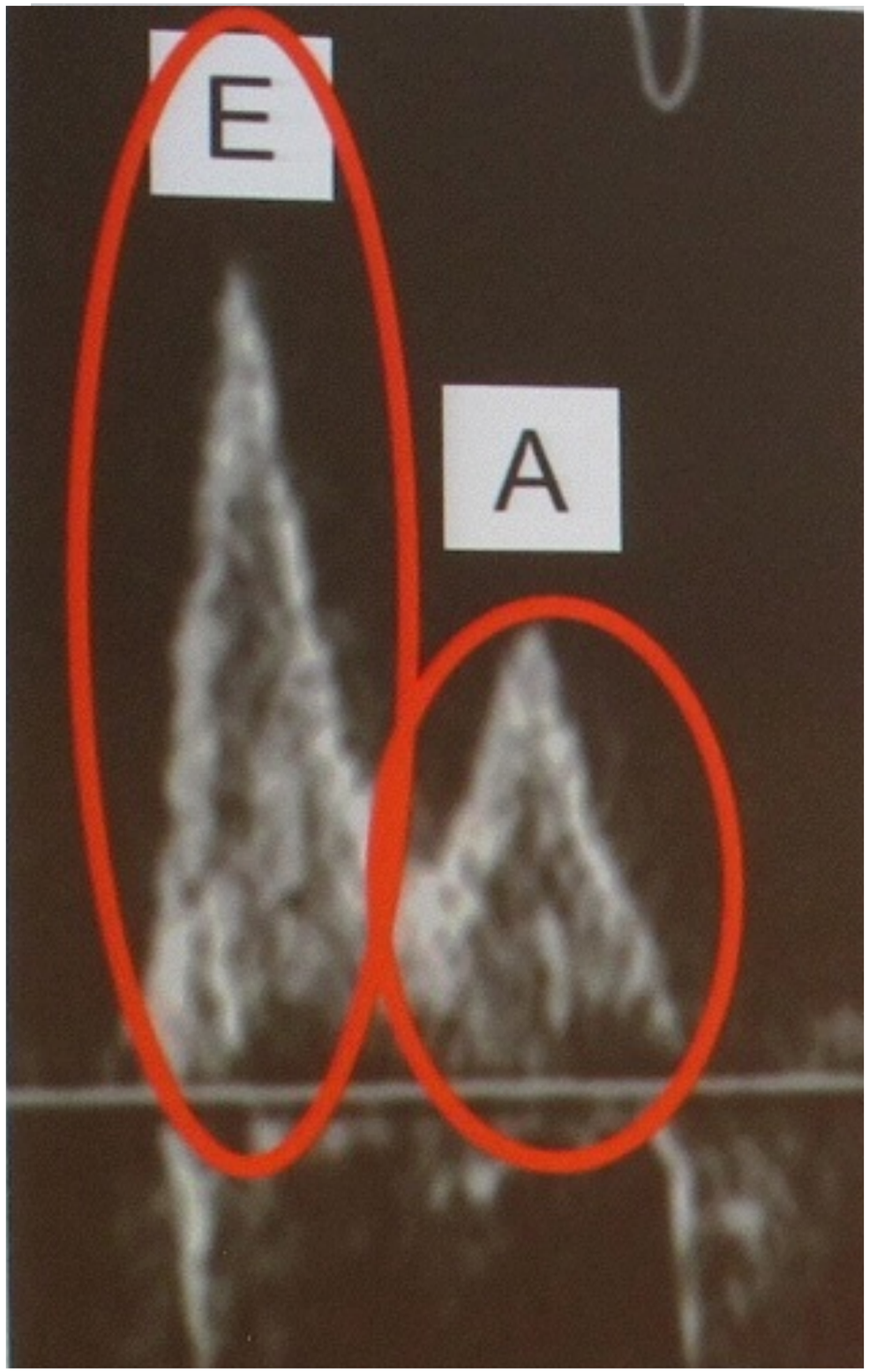


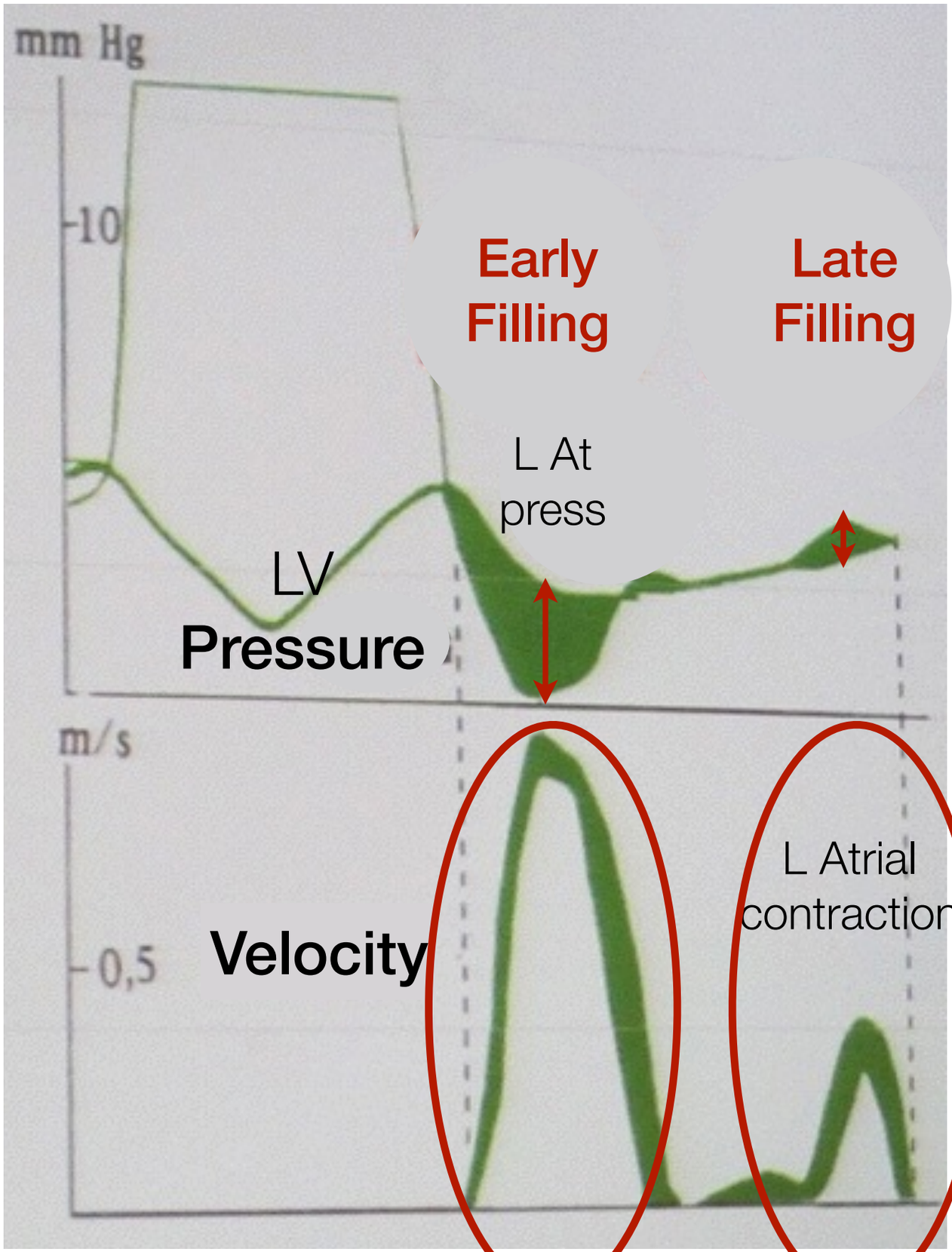
European Heart Journal (2012) 33, 895-903



Relaxation= **active** phase ATP dependent

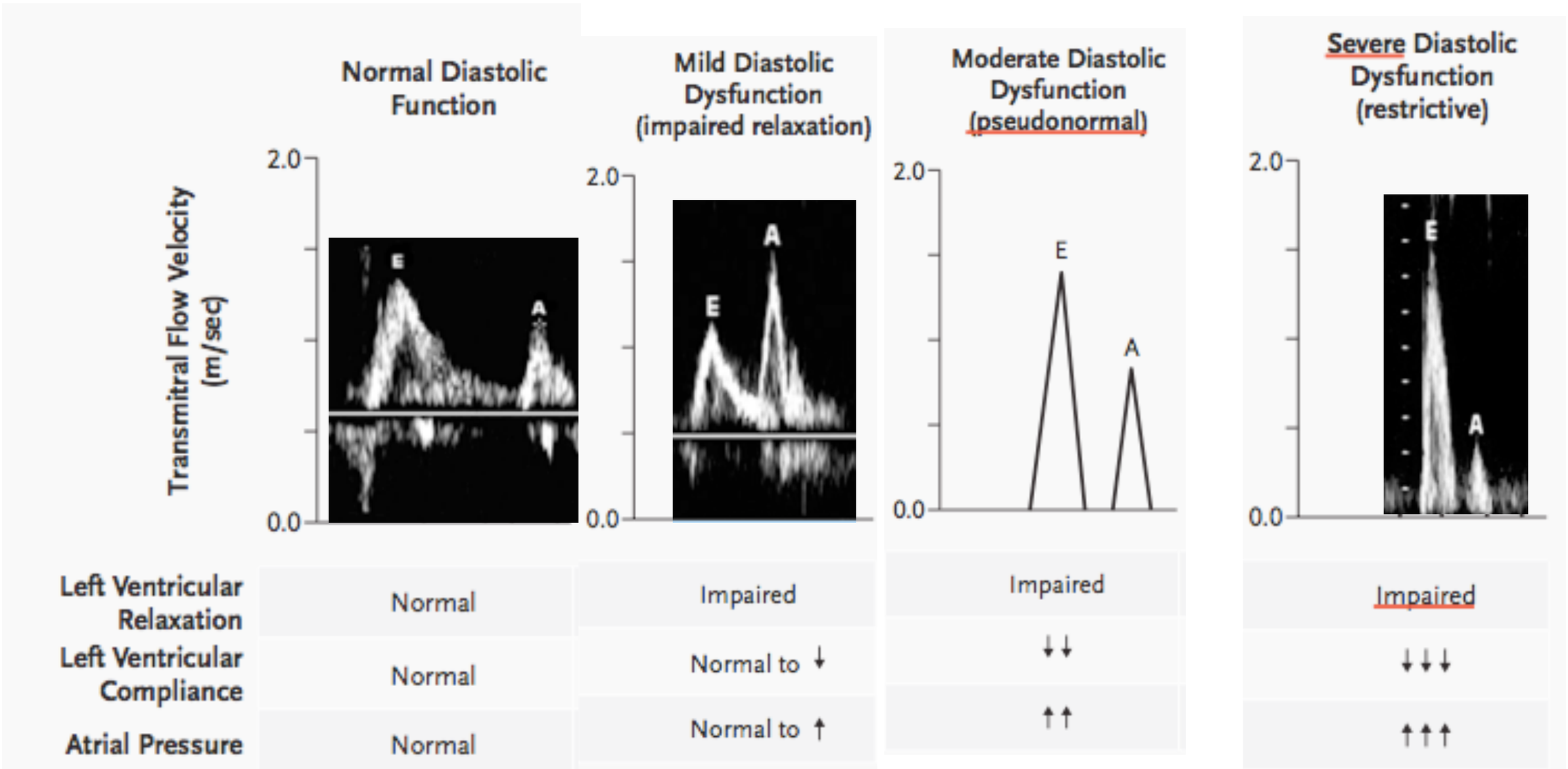
Relaxation= **passive** phase decreased LV compliance





$$\Delta \text{ Pressure} = 4 \text{ X Velocity}^2$$

Diagnosis of diastolic dysfunction-pulsed doppler

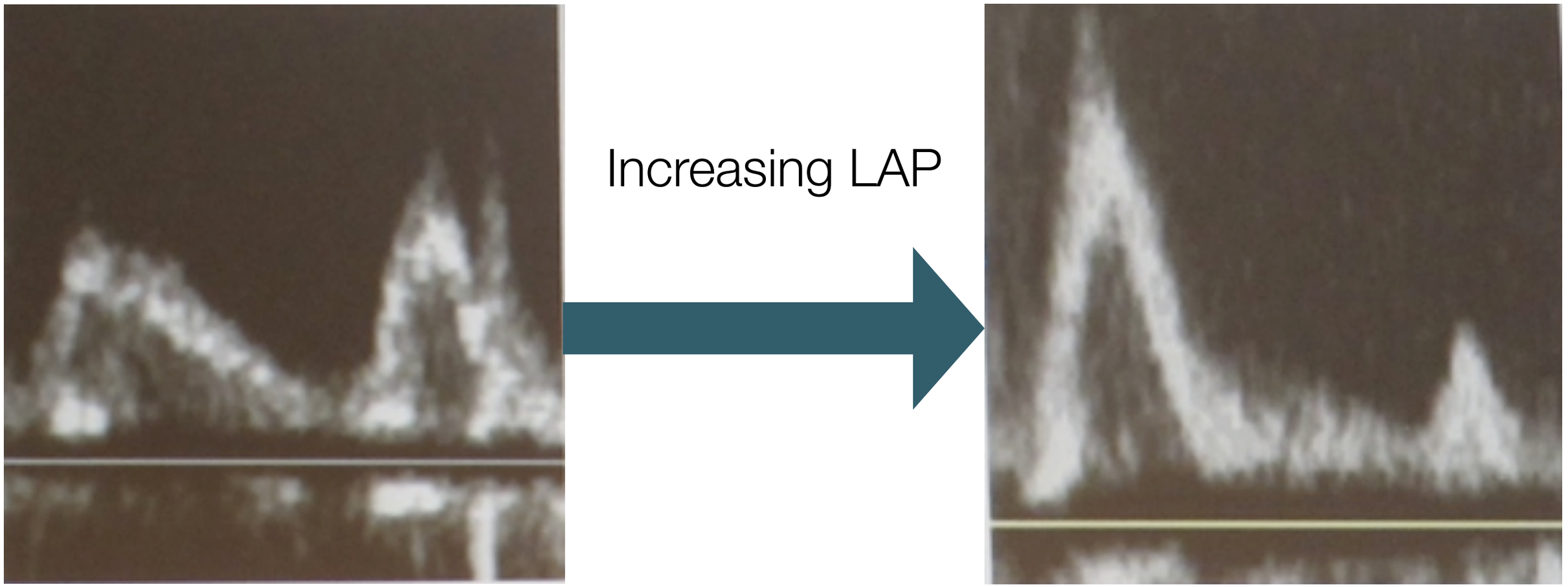


Reduced velocity of early filling (E wave), an **increase** in the **velocity** associated with **atrial contraction (A wave)**, and a **ratio of E to A that is lower** than normal

Moderate heart disease, when **left atrial pressure has risen**, the E-wave velocity and E:A ratio is **similar** to that in normal subjects (the **pseudonormal** pattern)

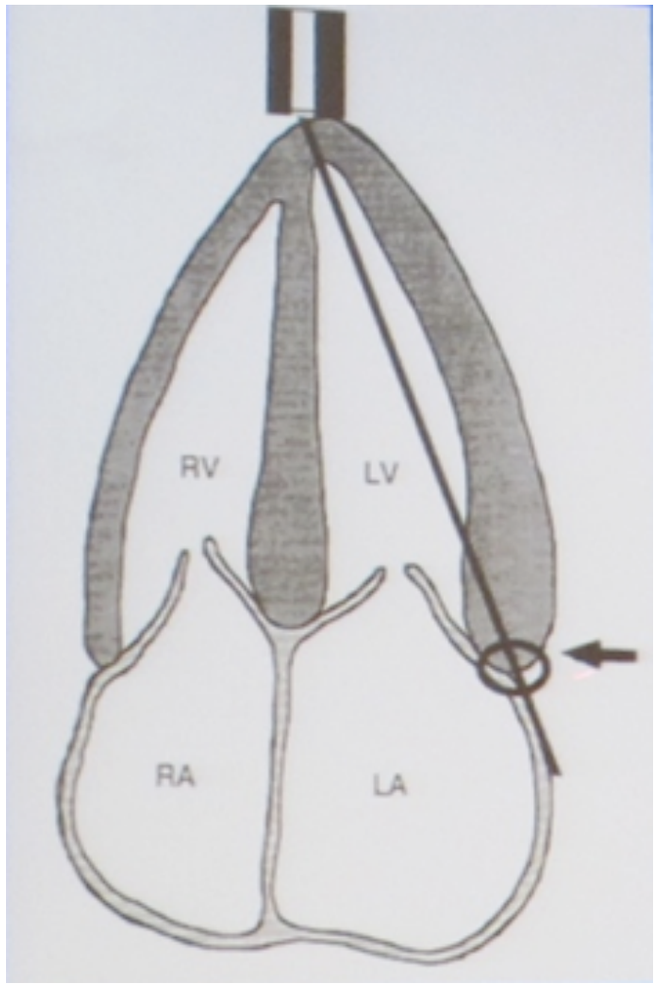
Advanced disease, Low ventricular compliance . The **E wave of normal to high velocity is a result of high left atrial pressure** and a **high transmitral pressure** gradient in **early diastole**

But...mitral flow is also sensitive to LAP

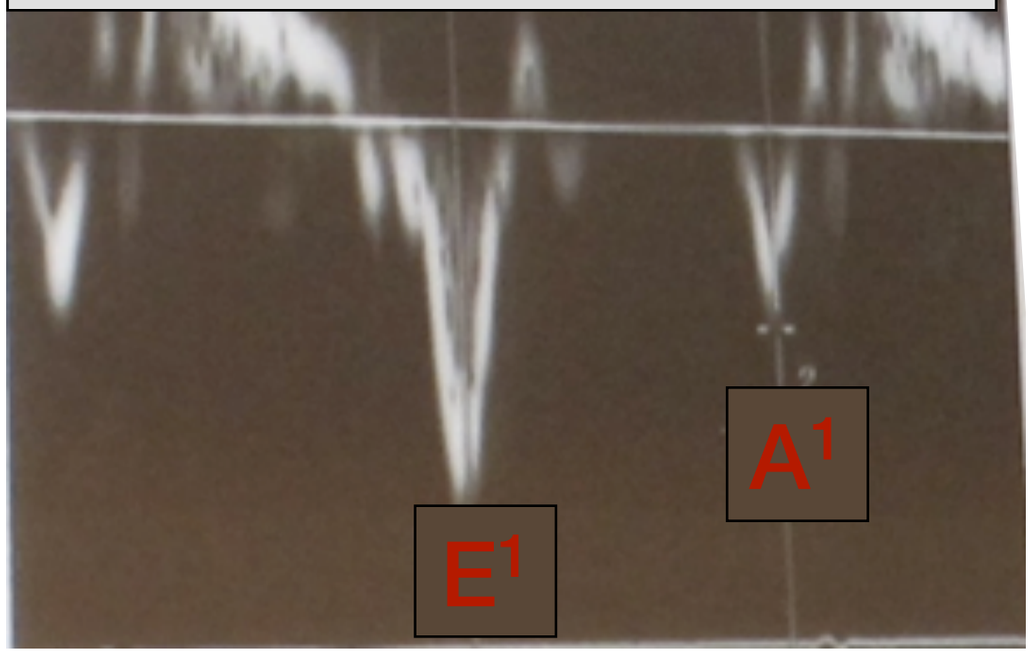


How do you assess diastolic function **independently** from LAP?

Tissue doppler of mitral annulus



E^1 **independent** of LAP
Normal values
E^1 > **8** cm/s and E^1 / A^1 > 1



The E/E^1 ratio most confidently **separates** normal filling pressures from elevated filling pressures

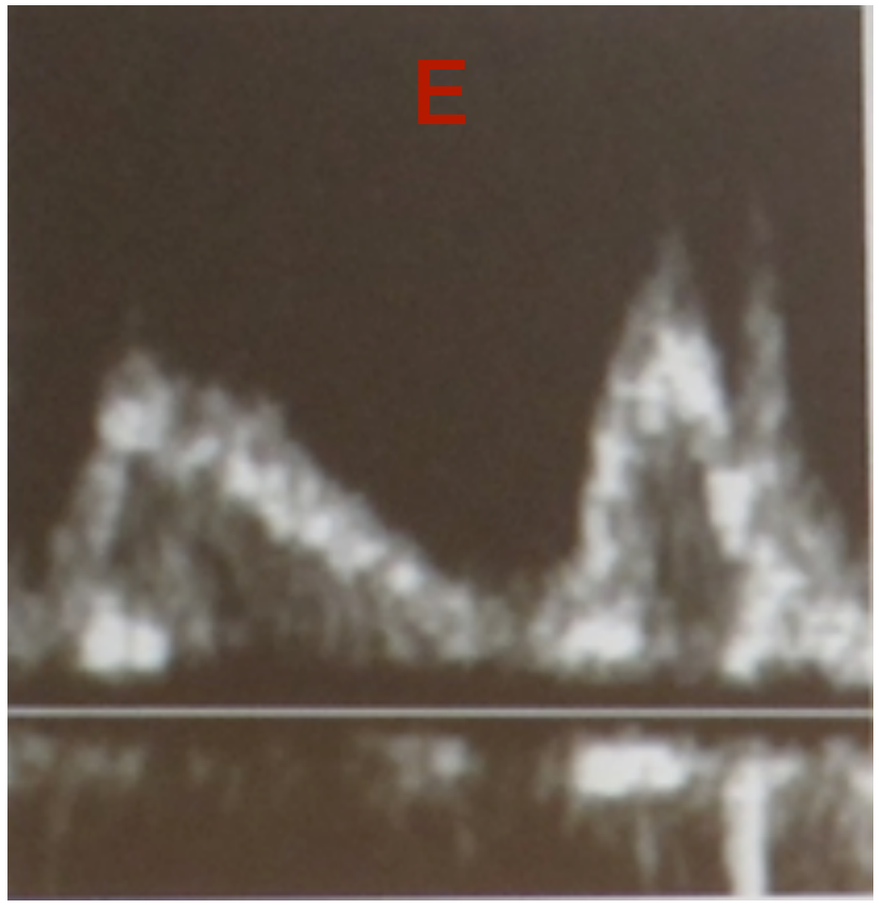
The **best index of diastolic function** is the **combined** assessment of transmitral flow and mitral annulus velocity

Conclusions

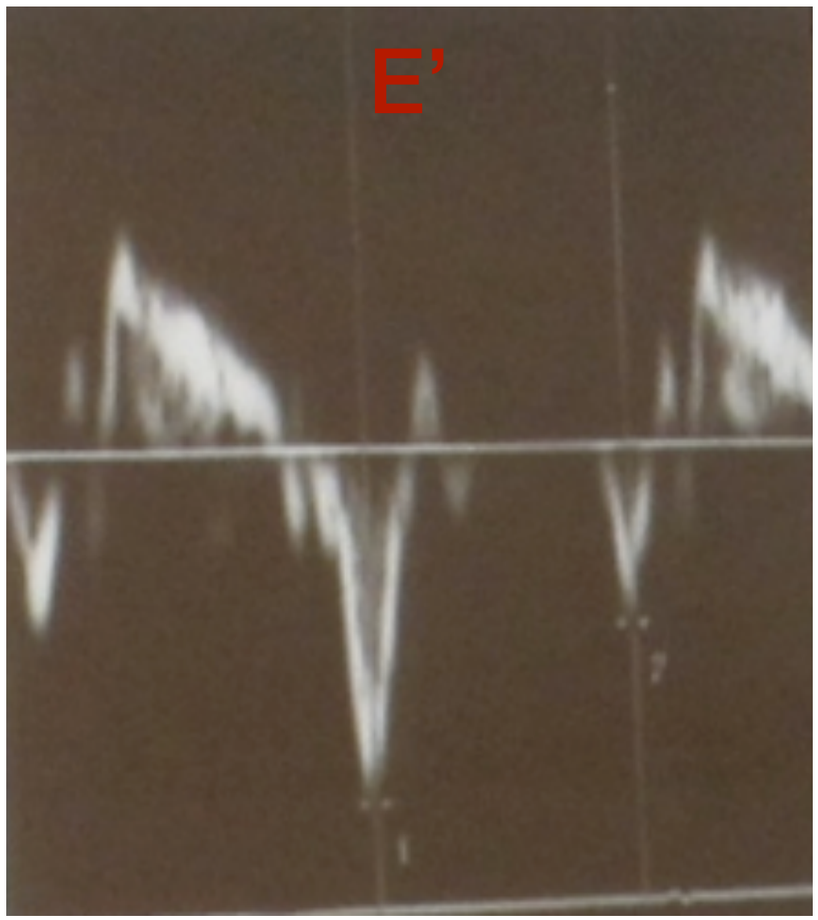
- Assessing diastolic function is critical in:
  - Unexplained pulmonary oedema with normal systolic function
  - Hypertensives to whom you decide to give fluid
  - Septic shock to predict prognosis
  - Weaning from mechanical ventilation
- Mitral flow is influenced by relaxation **AND** LAP
  - Therefore flow alone **cannot** be used to assess diastolic function
- To assess LV compliance : LA volume, Ea and **E/E'**

To assess diastolic function

Mitral **blood** flow (E wave)
but depends on relaxation
AND
preload (PAOP)



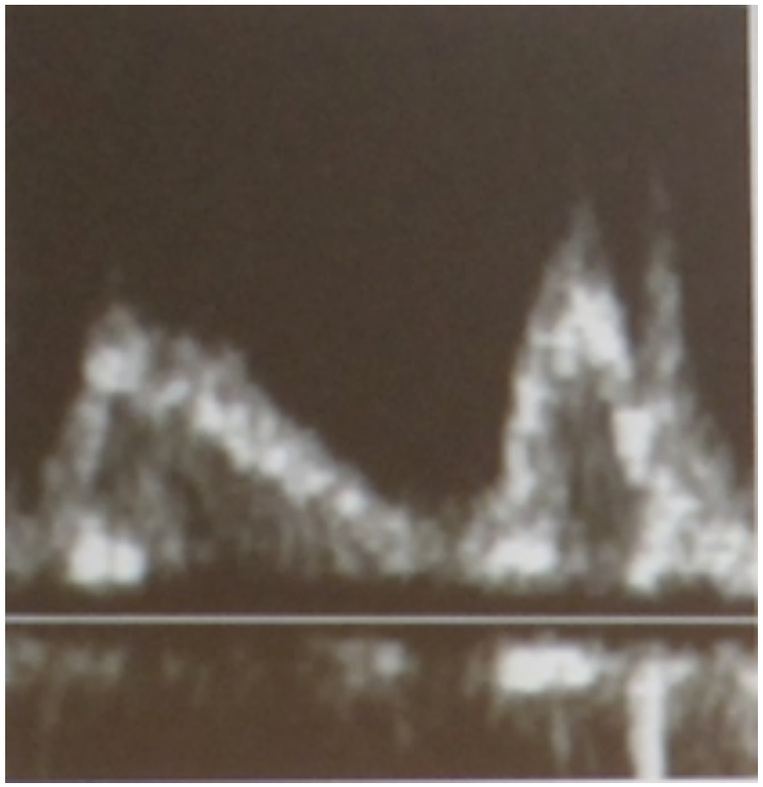
E’ - mitral annulus **tissue** velocity
which is **independent** of PAOP and depends only on LV relaxation and compliance



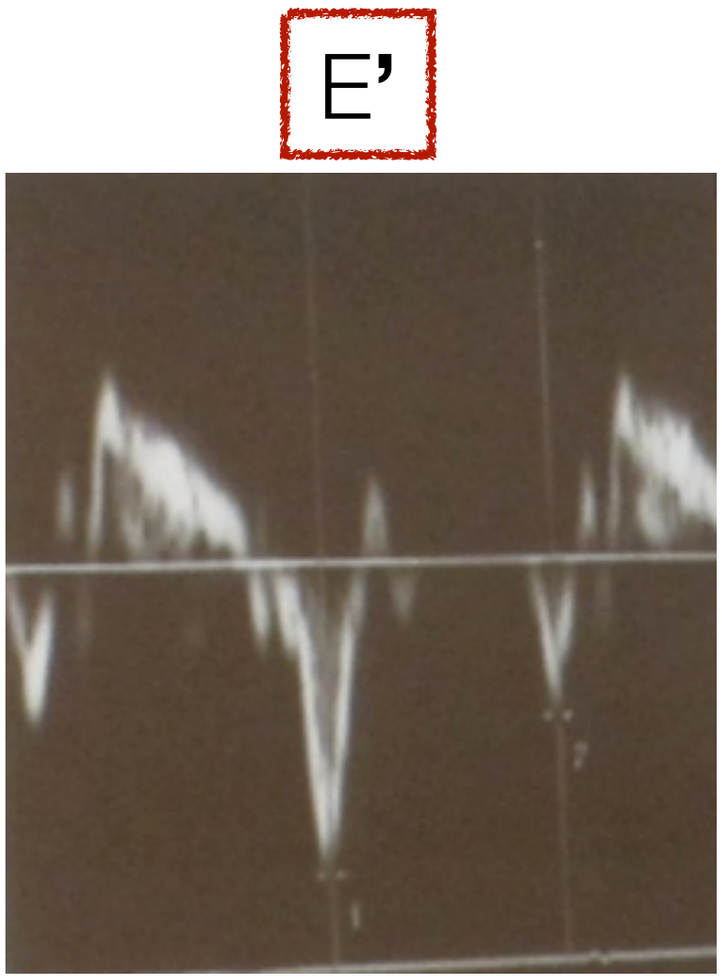
PAOP = E / E’

PAOP

LV relaxation



E



E’

LV relaxation

Thermodilution derived variables

Thermodilution derived variables

Transpulmonary thermodilution

- Cardiac output
- Global end-diastolic volume (GEDV)
- Extravascular lung water (EVLW)
- Pulmonary vascular permeability index (PVPI)
- Cardiac function index (CFI)

Volumetric indices

Pulse contour analysis

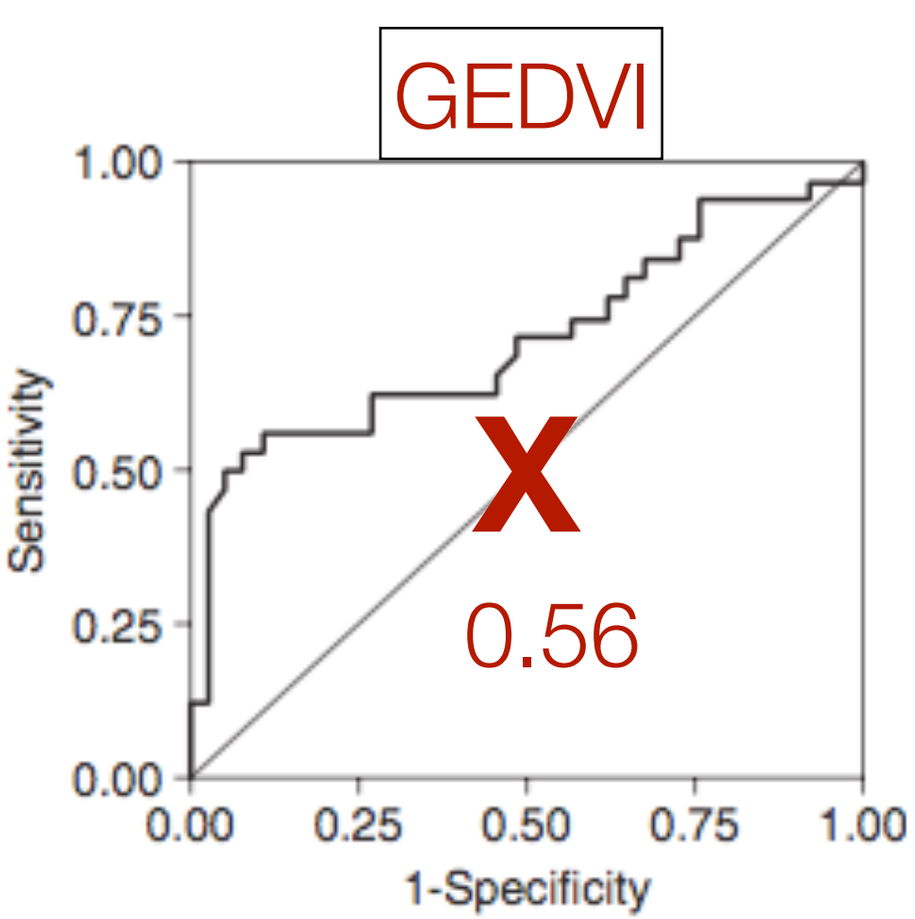
- Continuous cardiac output (CCO)
- Stroke volume variation (SVV)
- Pulse pressure variation (PPV)

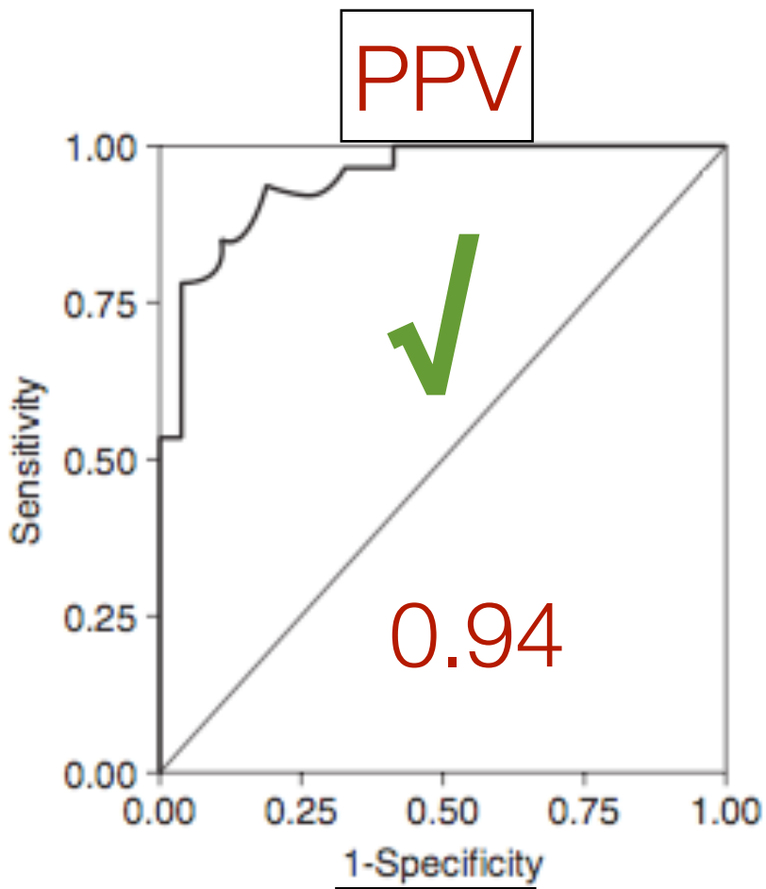
Limitations of GEDV

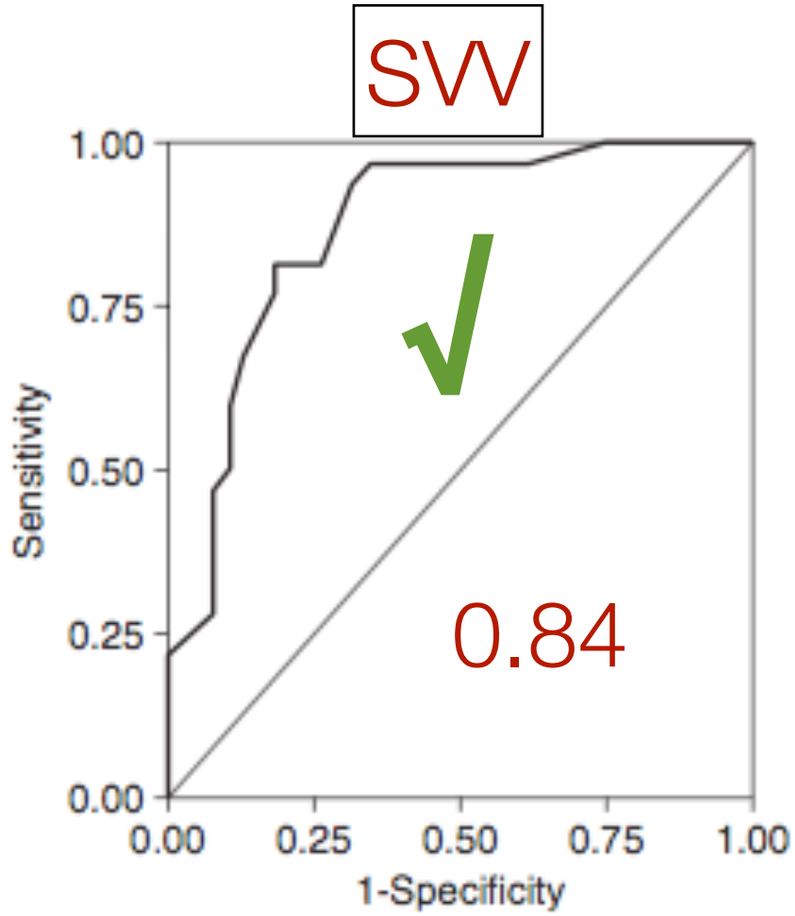
- GEDV could overestimate LV preload in case of dilated RV (as GEDV is a global volumetric index)

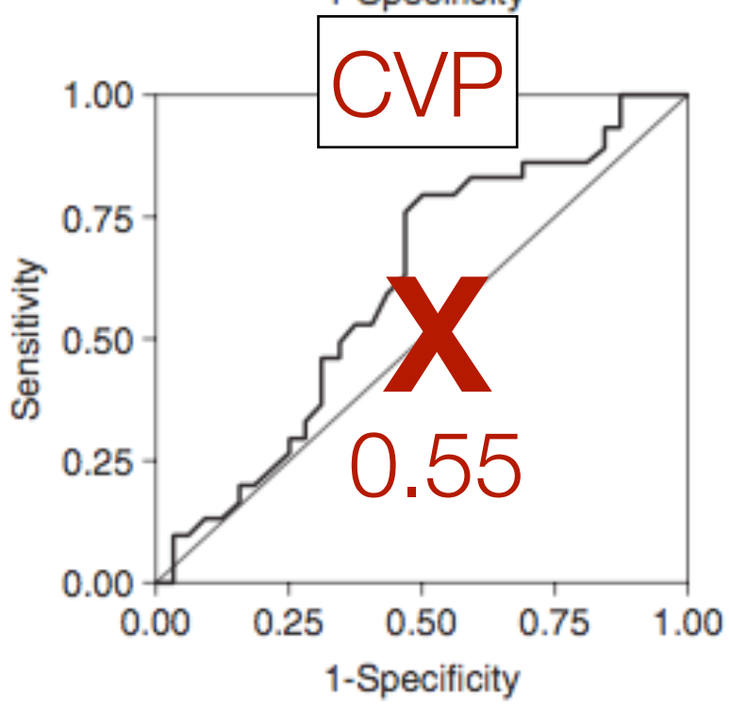
- GEDV is a **poor index of preload responsiveness**

Predicting fluid responsiveness





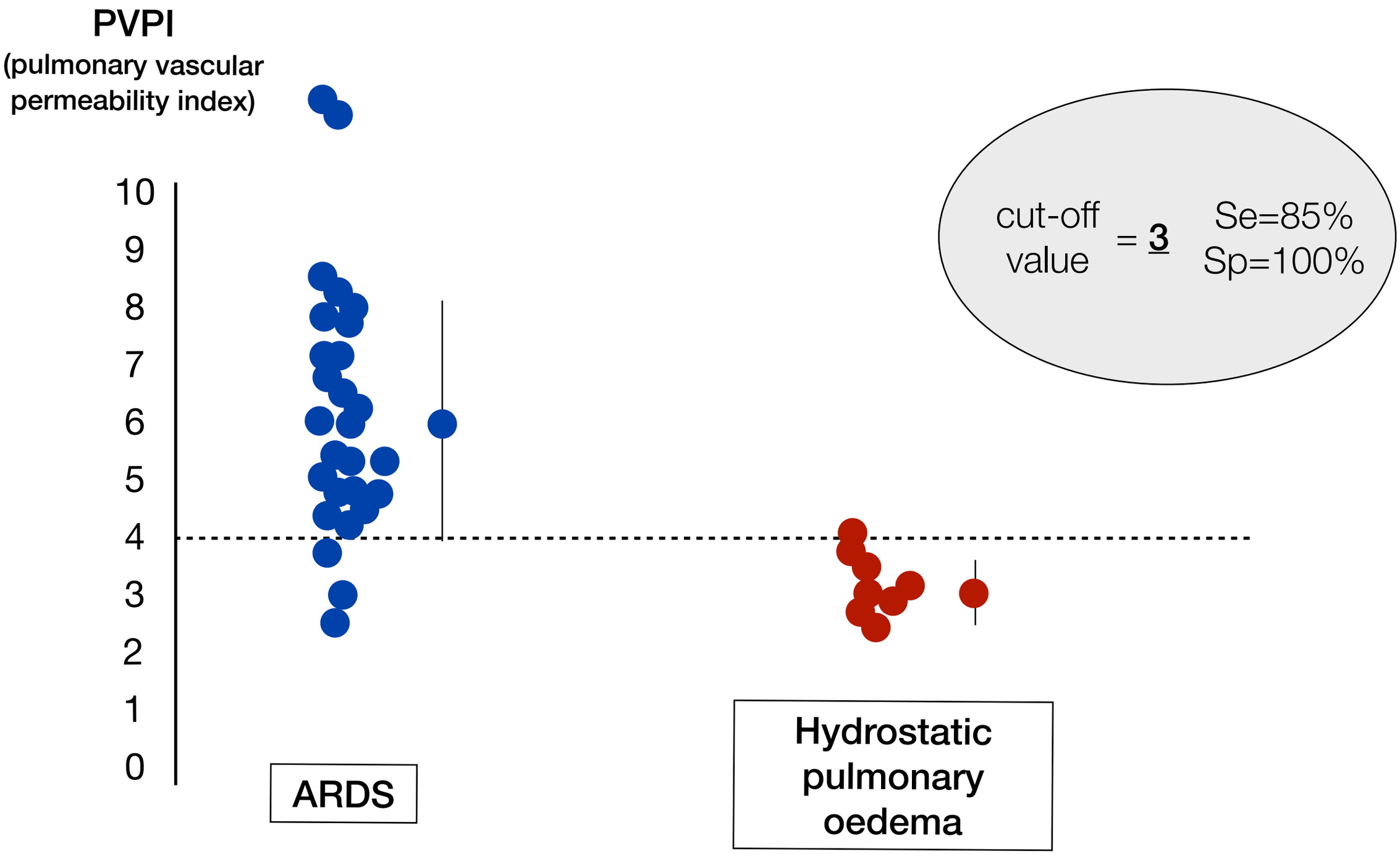




BJA 95 (6): 746–55 (2005)

CCM 2009; 37: 2642

Differentiation of hydrostatic pulmonary oedema from ARDS

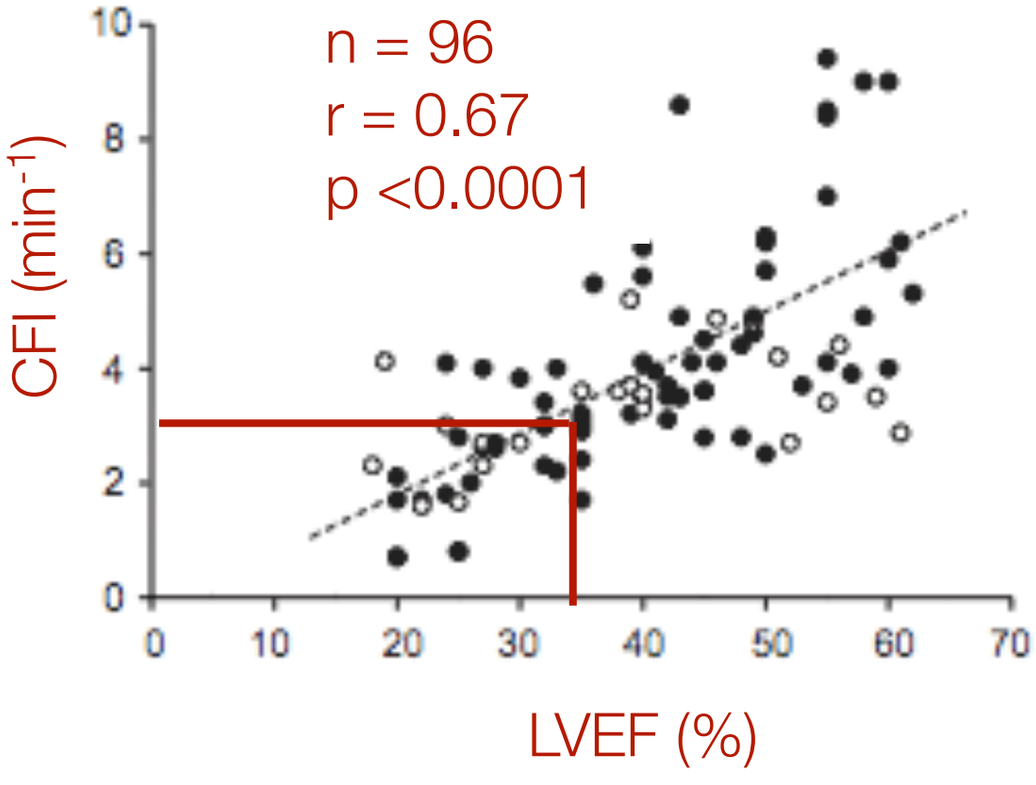


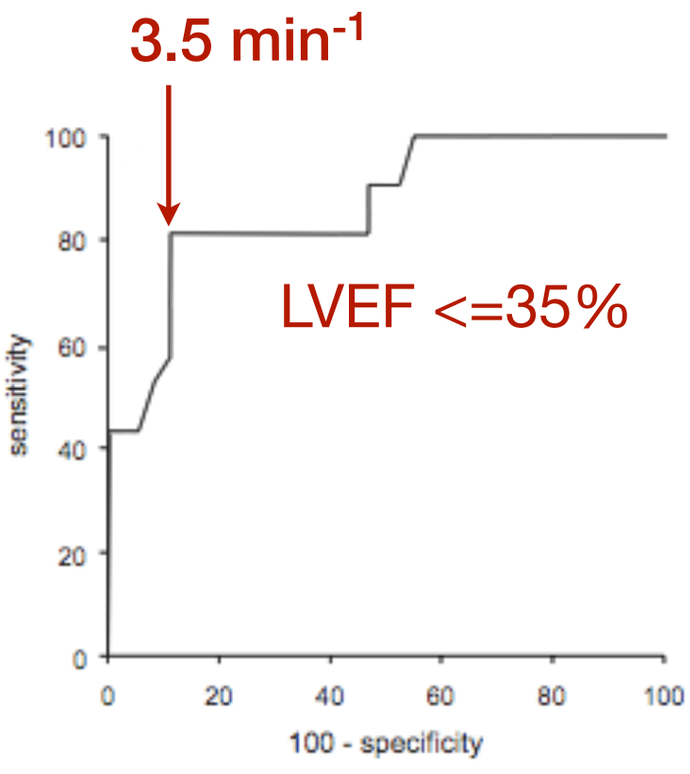
ICM 2007; 33: 448

Cardiac function index (CFI) as an indicator of LV systolic function

CFI = CO / GDEV

A low CFI can alert the clinician and incite to perform an echo



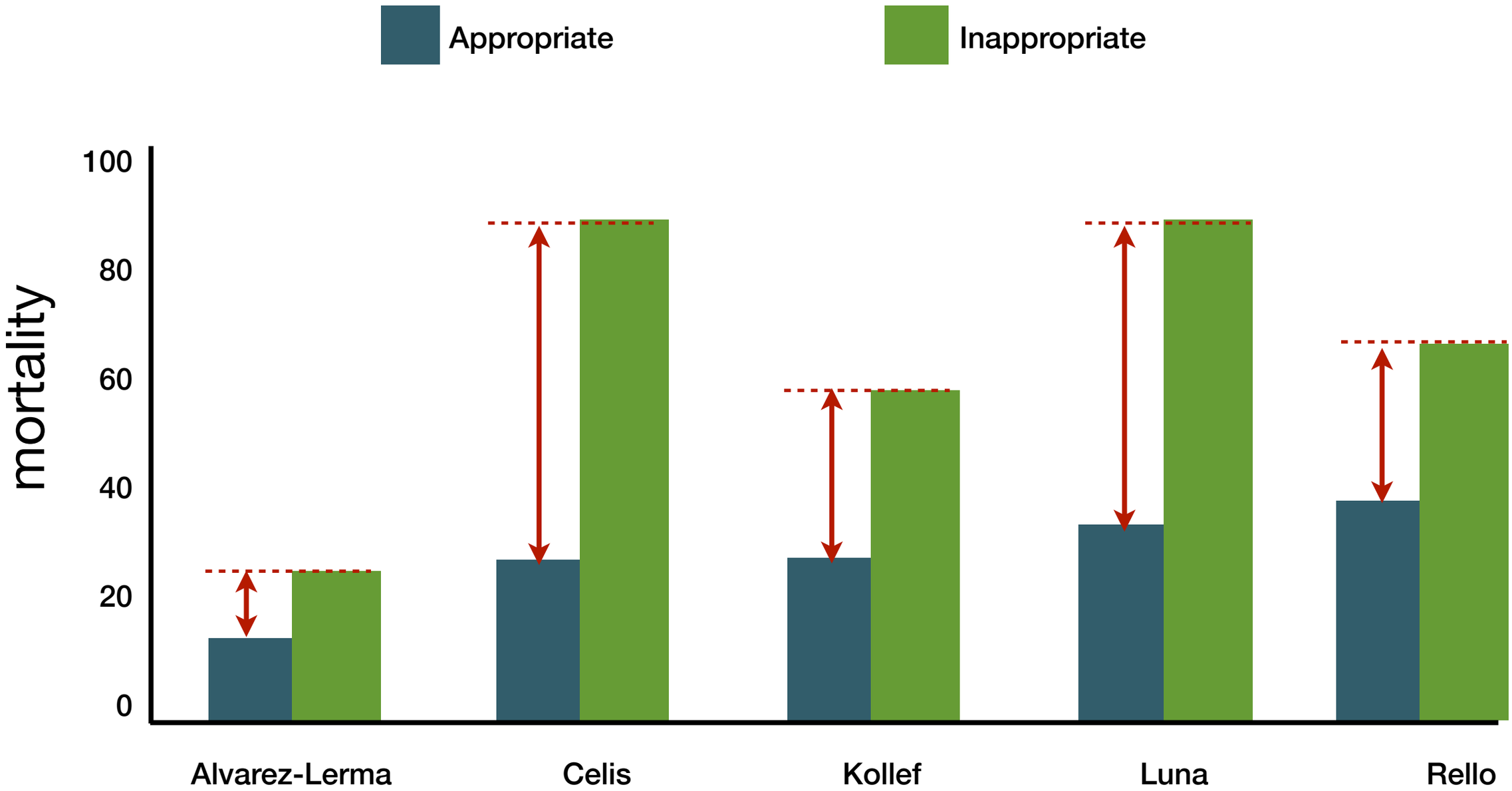


Ability of the CFI (**<3.5 min^{-1}**) to detect a LVEF <35%

Crit Care Med 2009; 37:2913–2918

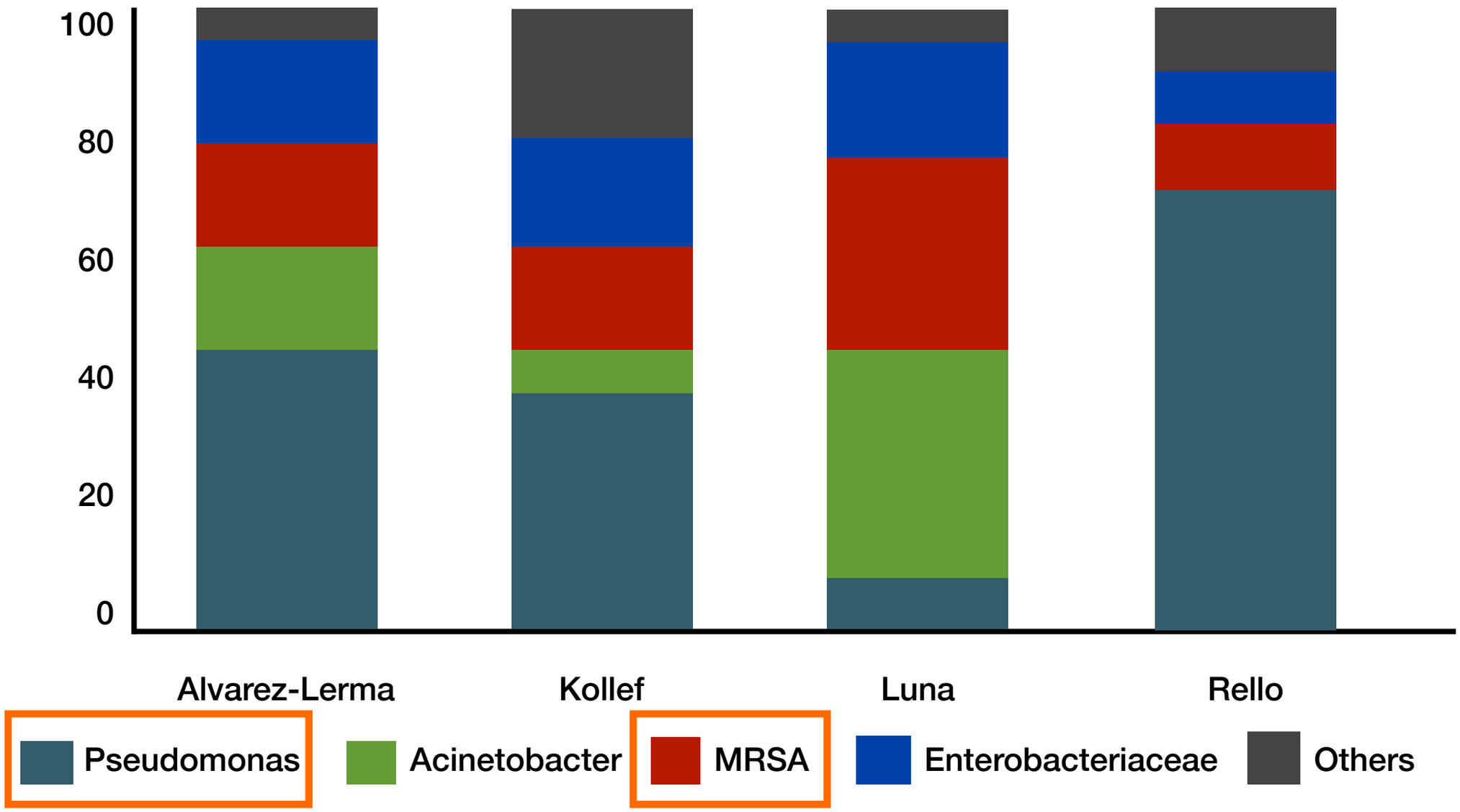
Infections

Inappropriate initial empirical therapy is associated with increased mortality in NP/VAP



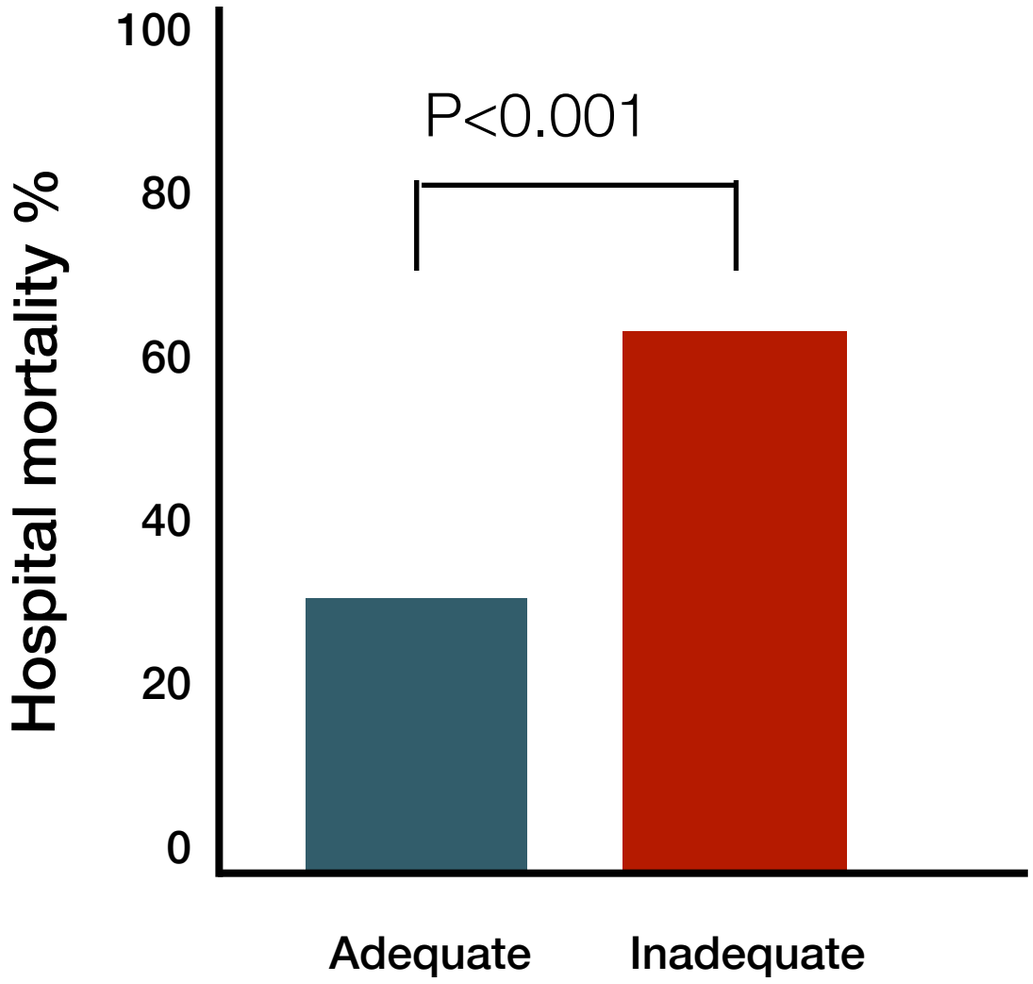
Alvarez et al Intensive Care Medicine 1996;22:387 Kollef Chest 1998,113:412 Luna Chest 1997,111:676 Rello AJRCCM 1997;196

Pathogens associated with **inappropriate** initial therapy for **VAP**



Alvarez et al Intensive Care Medicine 1996;22:387 Kollef Chest 1998,113:412 Luna Chest 1997,111:676 Rello AJRCCM 1997;196

Delay in appropriate antibiotic treatment and mortality



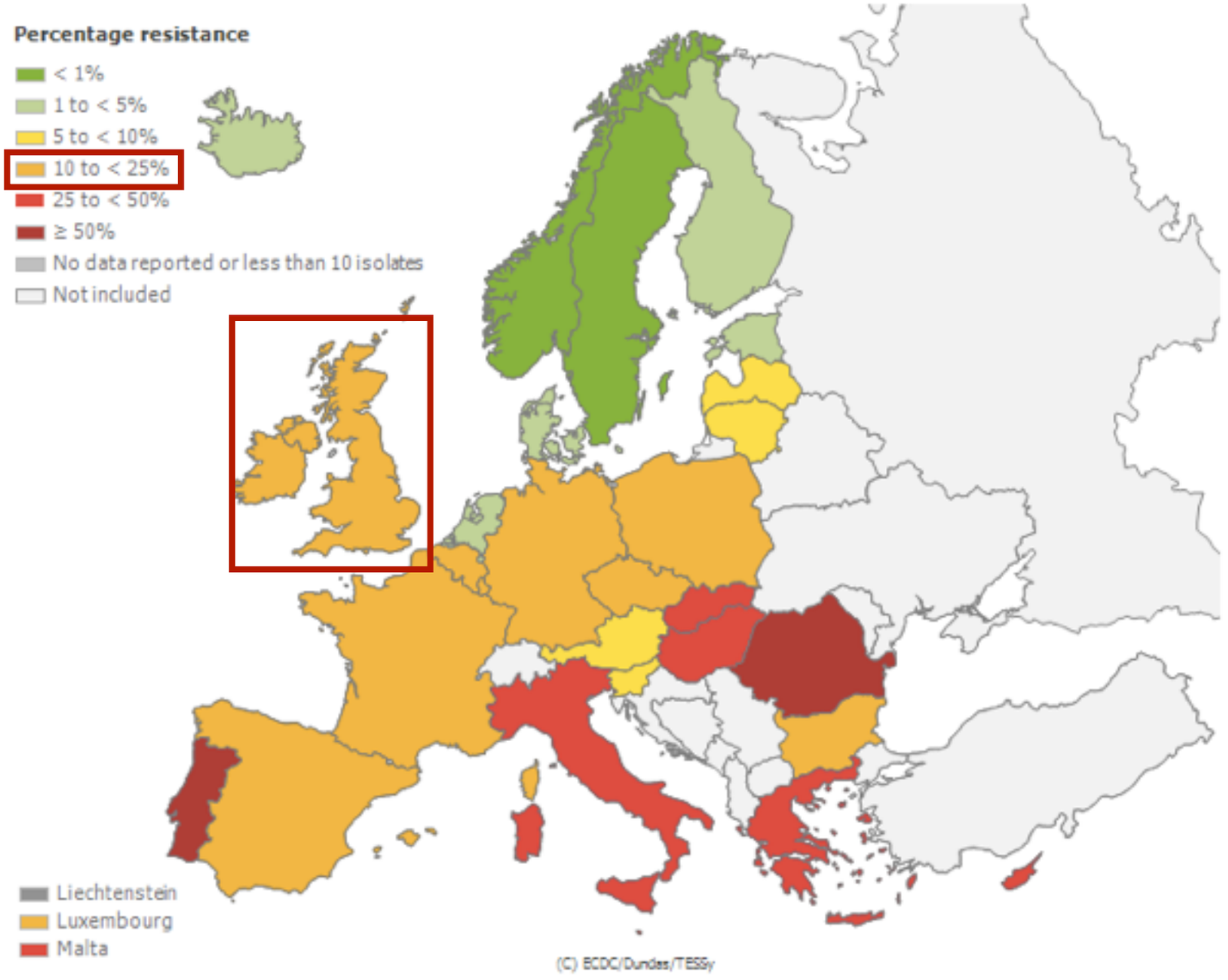
Initial antimicrobial treatment

	MSSA	MRSA
Pneumonia		
Nosocomial	13%	**60%**
Community acquired	13%	**42%**
Bloodstream		
Nosocomial	0	**73%**
Community acquired	15%	**50%**

% patients with delayed treatment

Kollef Chest 1999,115:462 Ibrahim et al Chest 2000,118:146

Staphylococcus aureus: percentage of invasive isolates resistant to methicillin 2011



http://ecdc.europa.eu/en/activities/surveillance/EARS-Net/database/Pages/maps_report.aspx

When is MRSA coverage required?

- In patients **previously identified** as colonized or infected by this strain
- When **local prevalence** is high
- In patients with **prior hospitalization** in **high-risk settings**, such as nursing homes or chronic haemodialysis centers
- When **Gram staining** of respiratory secretions shows G + cocci in a patient with a late onset infection and/ or **prior antimicrobial treatment**

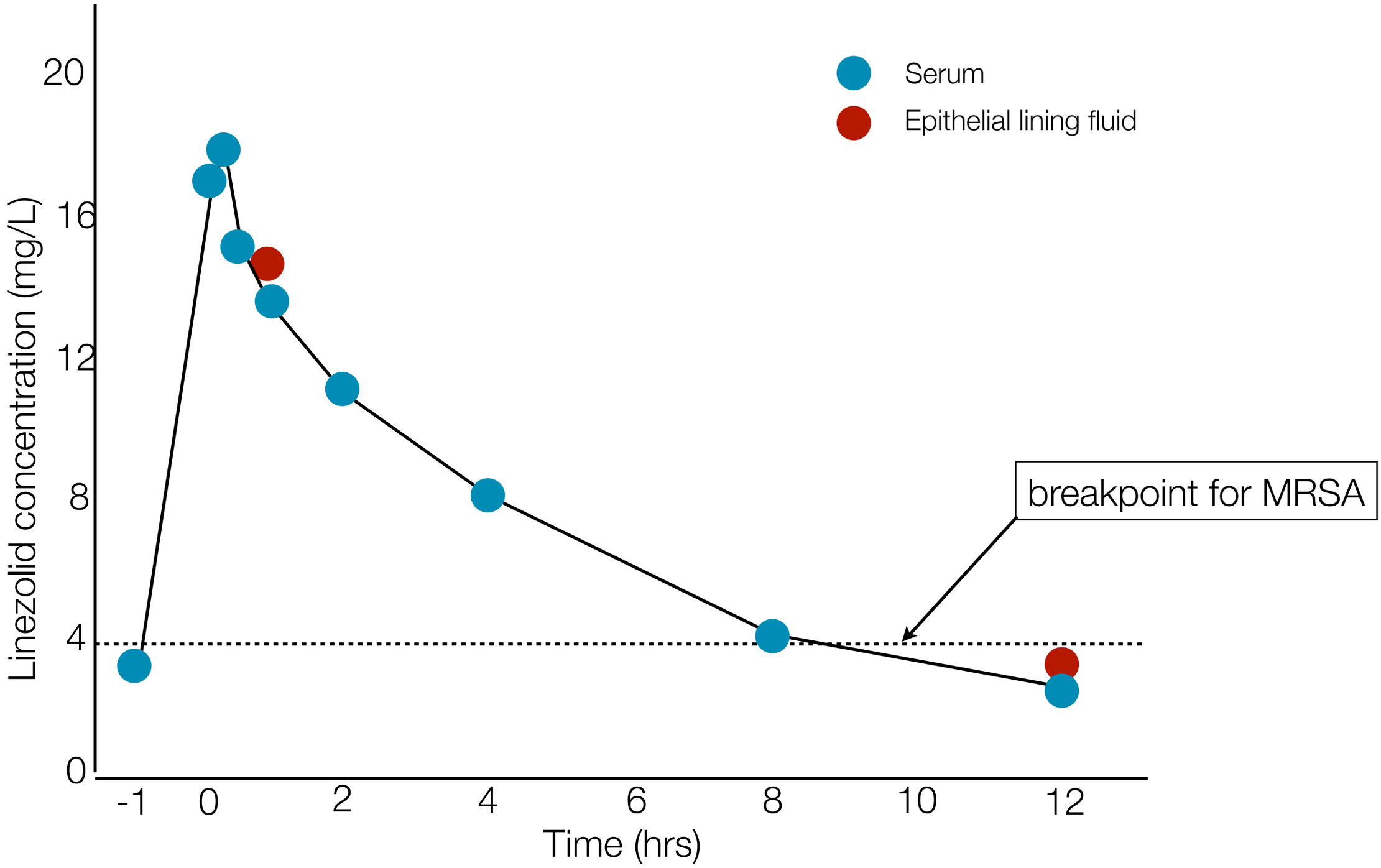
Chastre Clin Chest Med 2005 Dryden et al Clin Microbiol Infect 2010;16 Suppl 1:3-30 ATS, IDSA AJRCCM 2005;171:388

Potential advantages of linezolid in MRSA infection

- Good spectrum of activity covering MRSA
- 100% oral bioavailability
- Good **tissue penetration**, including the **lung**
- Low propensity for selecting resistant strains
- **Inhibits toxin** mediated effects of bacteria
- Proven clinical and microbiological efficacy in ZEPHyR study
- **Less nephrotoxicity** compared with vancomycin in ZEPHyR study

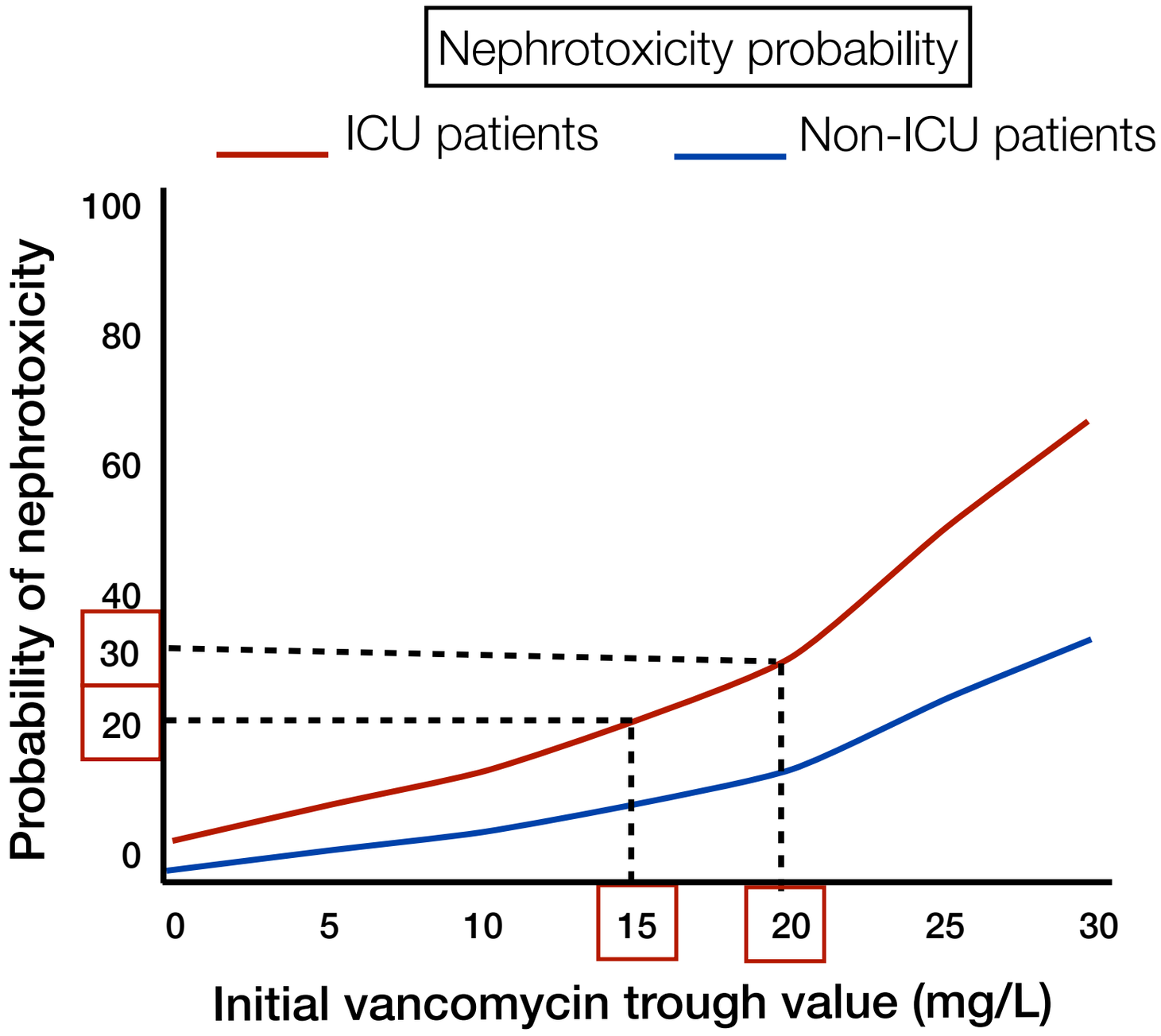
Boselli et al Crit Care Med 2005;33:1529
Ross et al J Chemother 2011; 23:71
Pichereau et al Antimicrob Agents Chemother 2012;56:140
Wunderink et al Clin Infect Dis 2012;54:621

Linezoloid penetrates well and rapidly into the lung



Boselli et al Crit Care Med 2005;33:1529

Vancomycin nephrotoxicity

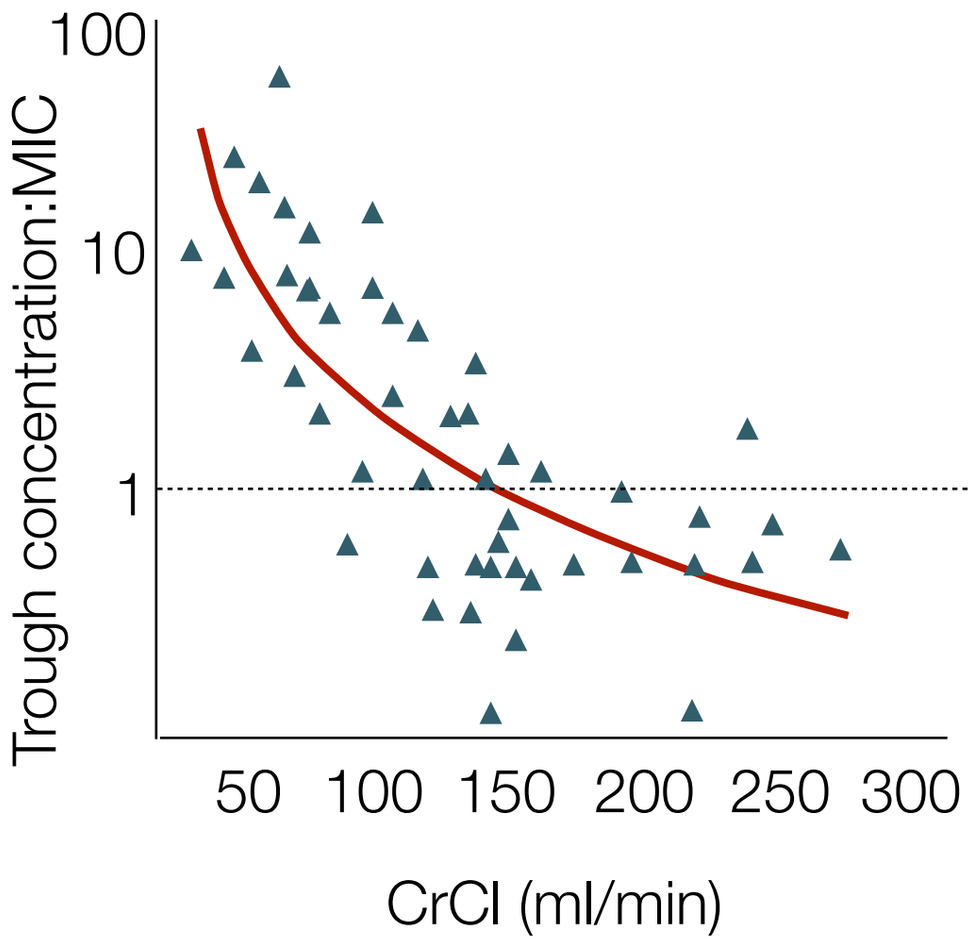


Lodise et al Clin Infect Dis 2009; 49:507-14

Antibiotic underdosing

Beta-lactam **underdosing** in patients with augmented renal clearance (ARC)

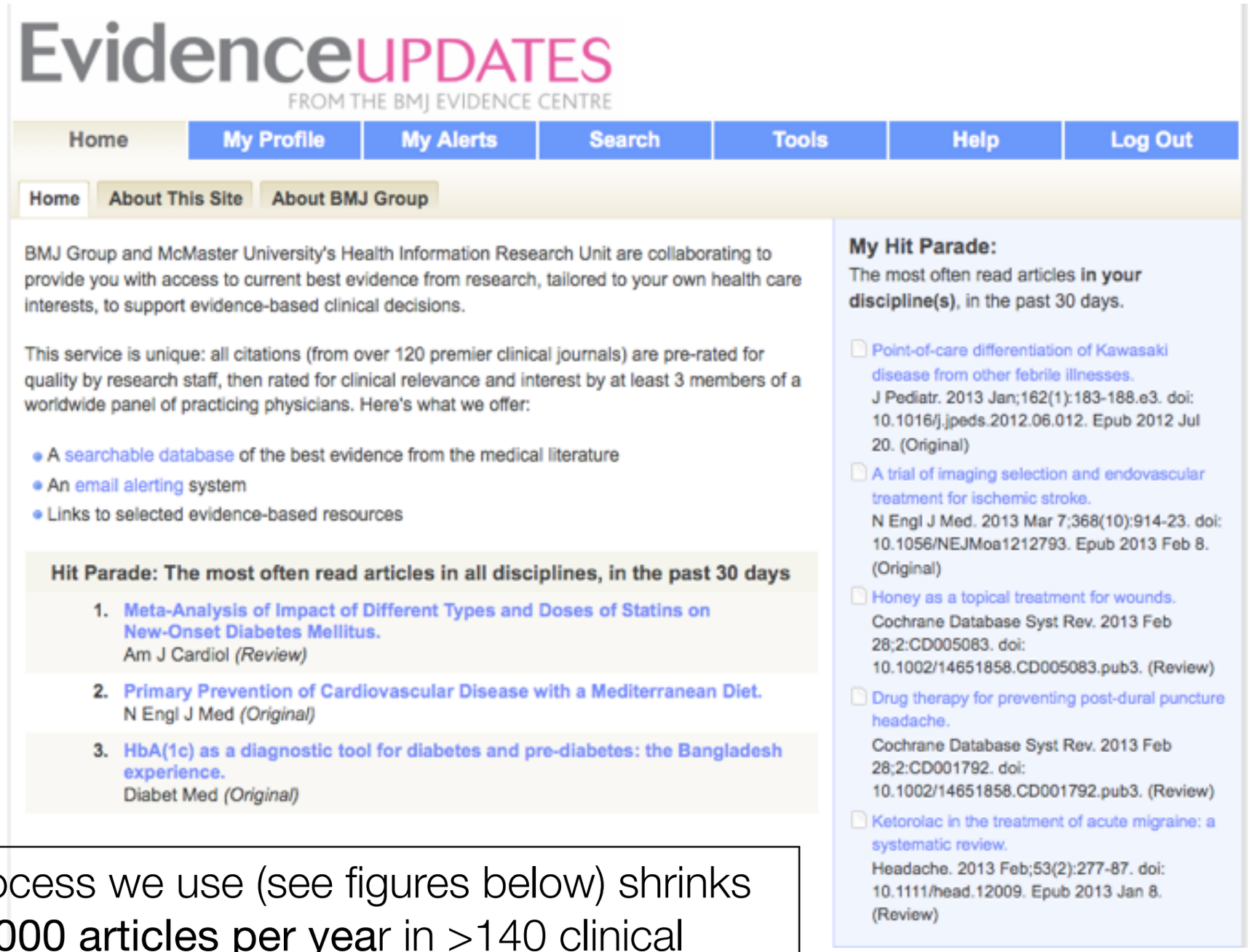
- ARC=**supra**normal GFR (>130ml/min)
- Most common in critically ill patients with :
  - SIRS/Sepsis
  - Trauma
  - Up to 30%



Anesth Intensive Care 2008;36: 674

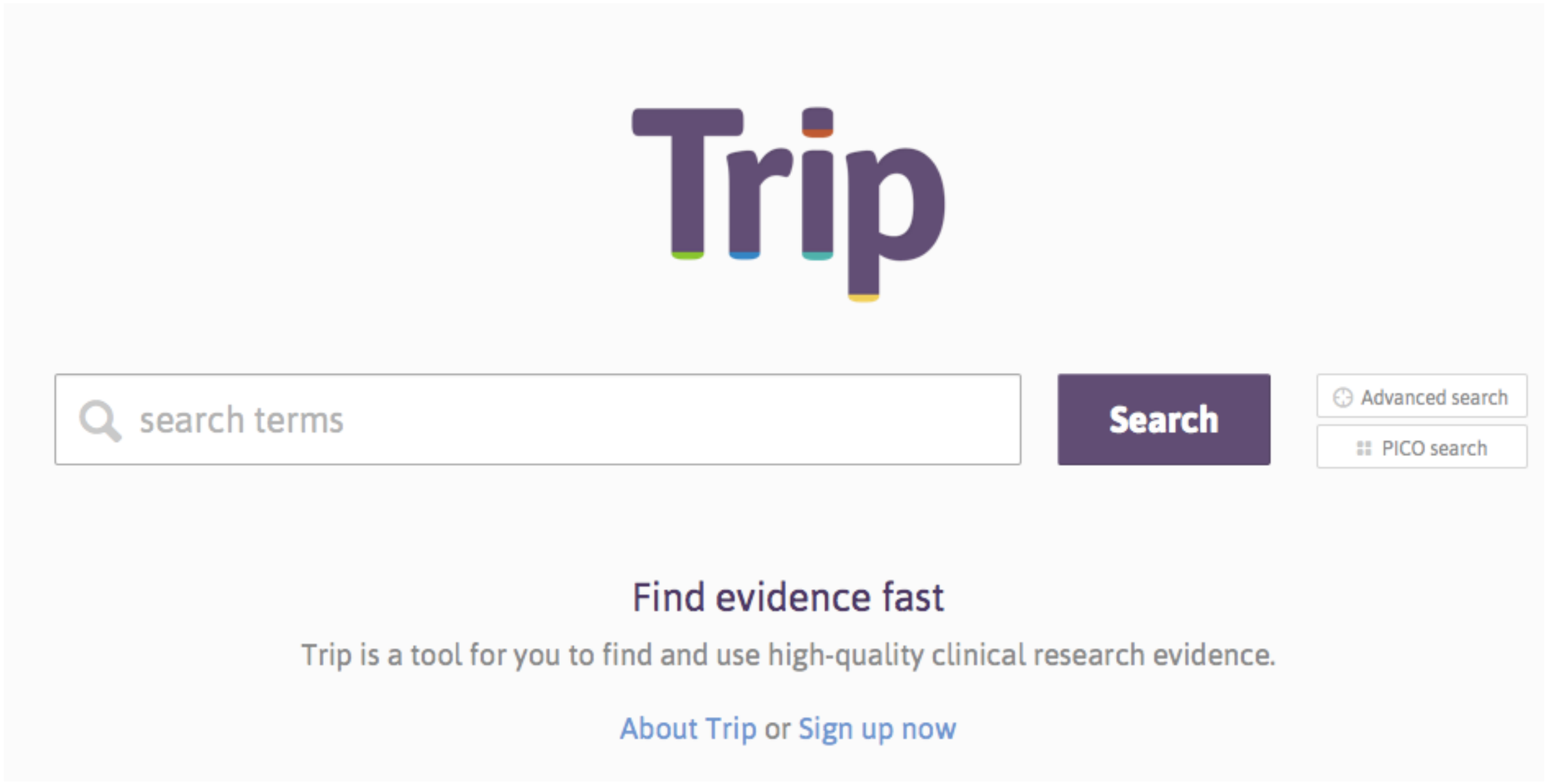
Good websites

http://plus.mcmaster.ca/evidenceupdates/

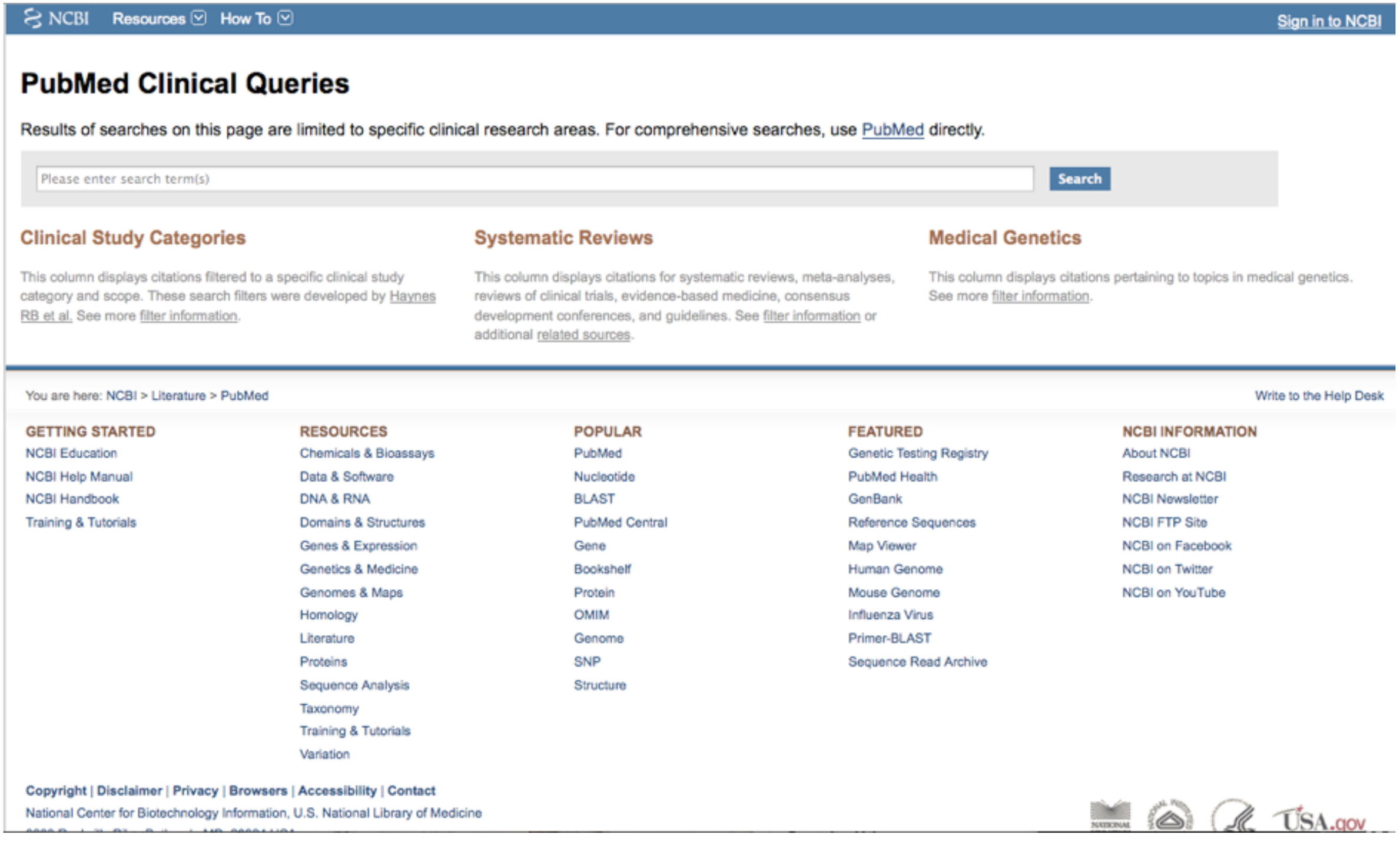


2-step process we use (see figures below) shrinks about **50,000 articles per year** in >140 clinical journals to the **most important 1 - 2 articles per month**, a "**noise reduction**" of over **99.9%.**

http://www.tripdatabase.com



http://www.ncbi.nlm.nih.gov/pubmed/clinical



Pancreatitis-new classification

Severe pancreatitis - updated classification

Severe pancreatitis

- **Persistent organ failure (>48hrs)**
- Usually local complications
- Increased mortality, even higher when **infected** necrosis

Severe pancreatitis - updated classification

Pancreatitis diagnosis

- 2/3 of the following
  - abdominal pain
  - lipase (or amylase) >3 x ULN
  - characteristic findings on CE-CT, MRI or U/S
- **Onset of pancreatitis; start of abdominal pain**

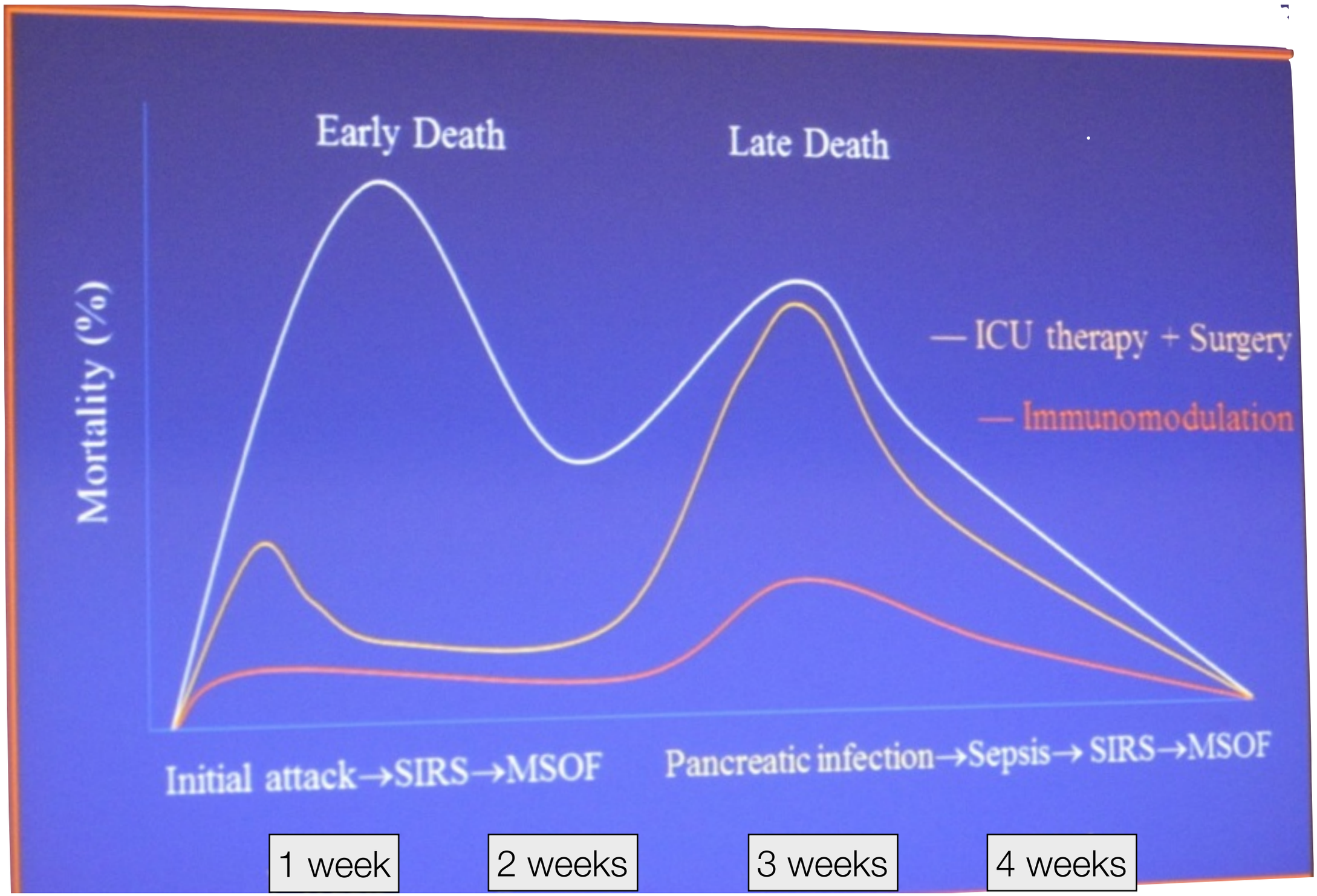
Banks et al Gut 2013:1;102-111

Determinant based severity classification

	Mild AP	Moderate AP	Severe AP	Critical AP
(peri)pancreatic necrosis	No	Sterile	Infected	Infected
	and	*and/or*	or	and
organ failure	No	Transient	Persistent	Persistent

Dellinger et al Ann Surg 2012 6:875-880

Time course of necrotising pancreatitis



Early vs late complications

Early (<2 weeks)

- “sepsis-like” syndrome,shock,DIC
- pleural effusion, ARDS
- renal failure and IAP
- nutrition and gut failure
- early perforations
- MSOF

Late (>2 weeks)

- necrosis infection
- extrapancreatic infection
- vascular (aneurysm, thrombosis)
- bowel ischaemia, necrosis, perforation
- fistula and nutrition

Banks et al Gut 2013:1;102-111

Cause of death in severe acute necrotizing pancreatitis

Mortality :9%

- sterile necrosis: 3%
- **infected necrosis 24%**

8 X higher mortality if infected

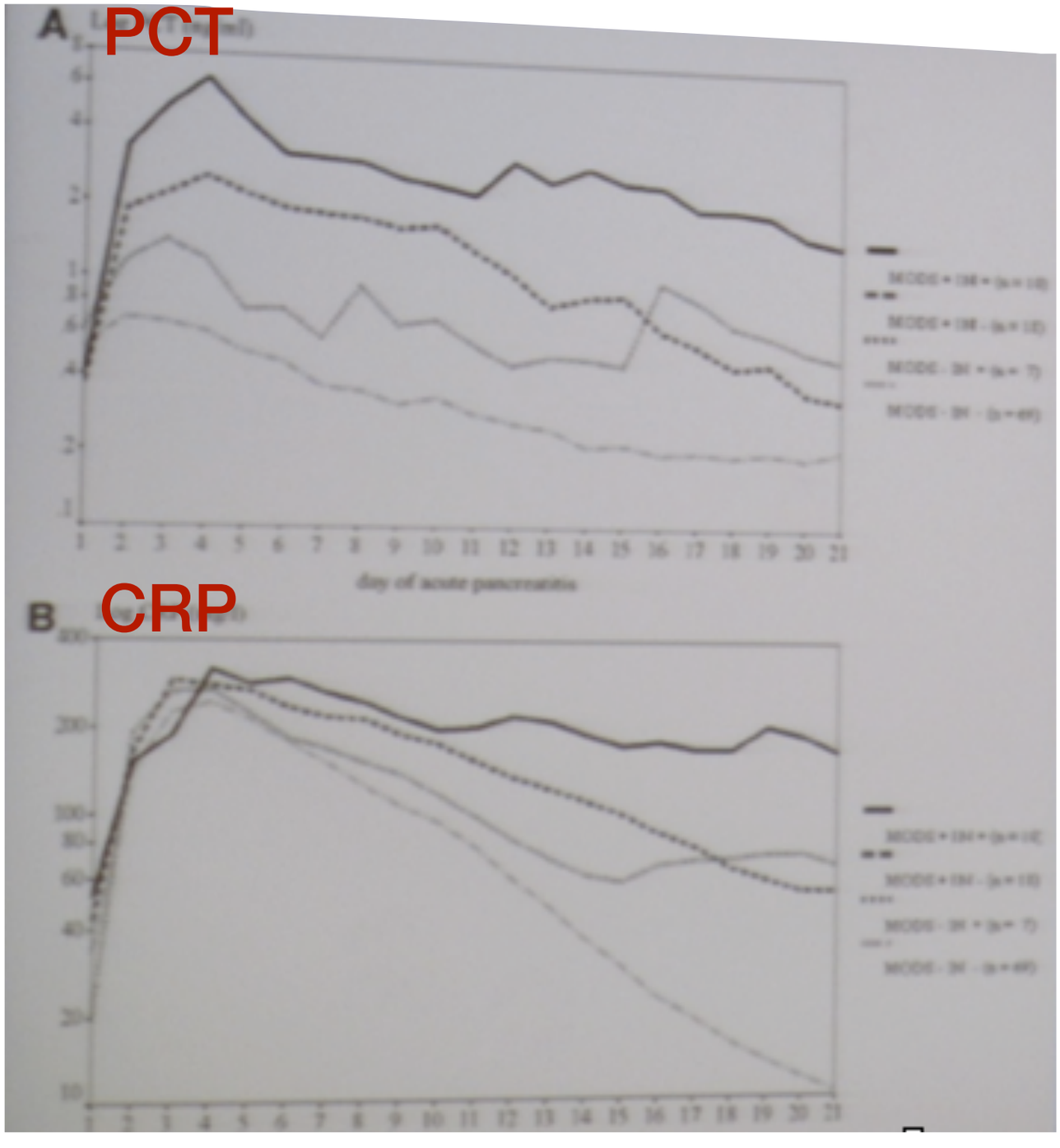
- cause of death: infected necrosis in 70%

Severe acute pancreatitis

- Necrosis occurs in 5-15%
- **Infection** of pancreatic/peripancreatic **necrosis** :**40-70%**
- Early diagnosis with **fine needle aspiration vital**
- Leading cause of death
- Mortality ranges from 20-30% when infection present
- Severity, presence of MOSF and necrosis extension are predictors of infection
- Rationale:Prophylactic antibiotics should reduce mortality???
- Antibiotic prophylaxis early???

Banks et al Gut 2013:1;102-111

Early assessment of pancreatic infections-PCT vs CRP

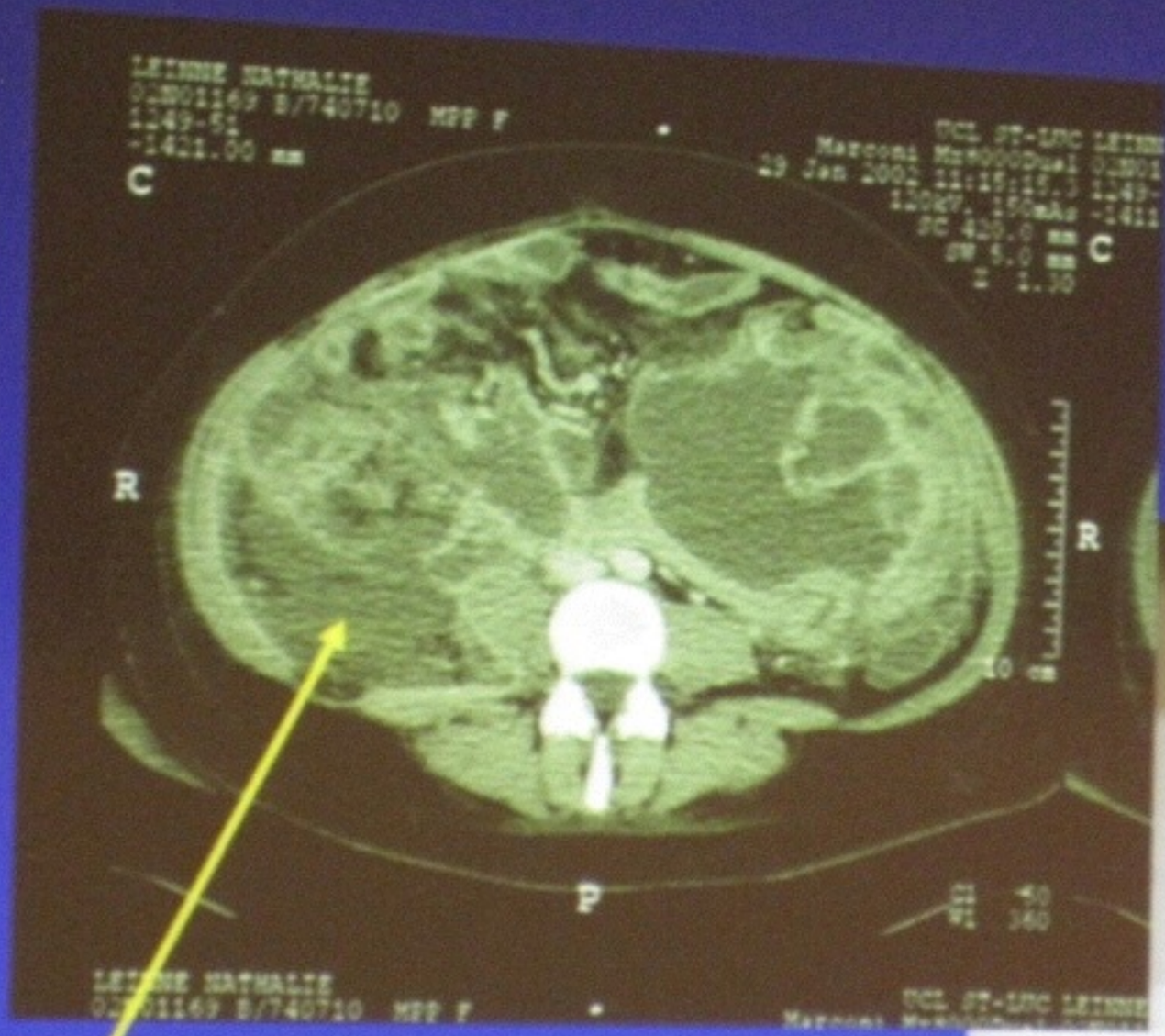


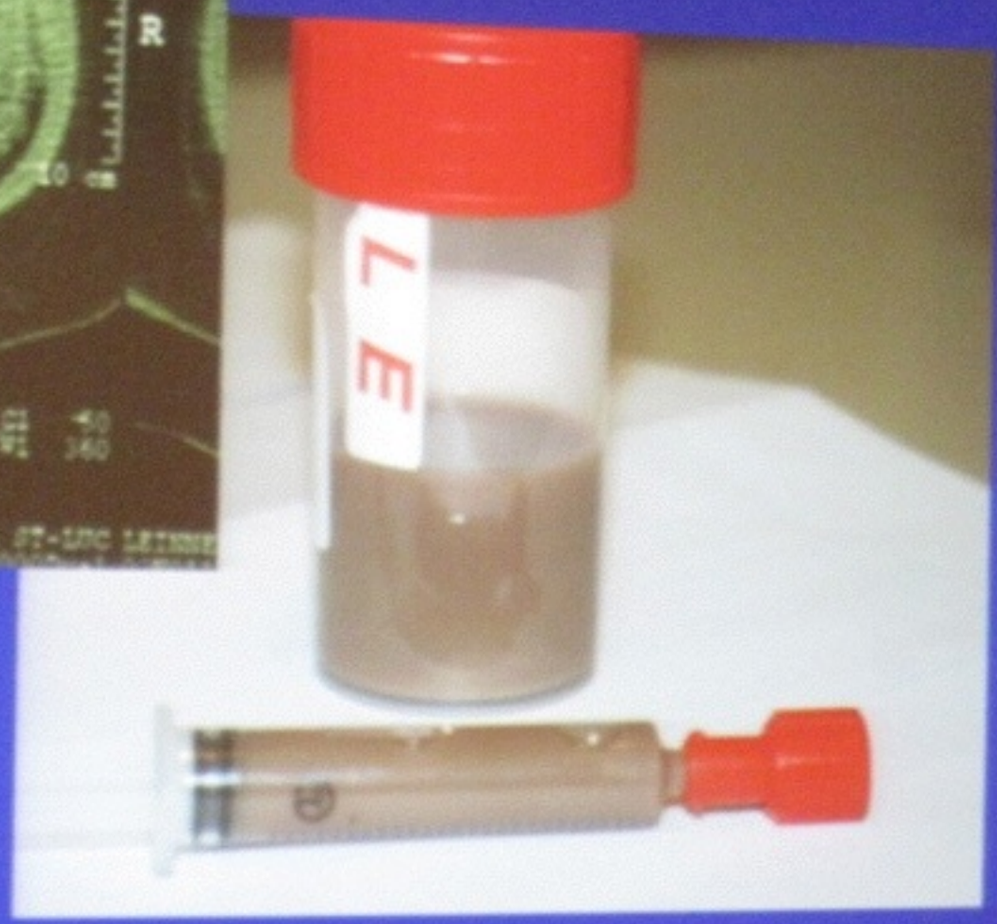
PCT and CRP in SAP

- **PCT** cutoff
  - 3.8 ng/mL
  - Sensitivity 80%, specificity 93%
- **CRP** cutoff
  - 430 mg/mL
  - Sensitivity 36%, specificity 97%

Rau et al Ann Surg 2007;245:745-754

Diagnostic work-up in Pancreatitis ?





CT/US guided puncture

Conclusions

- Incidence of SAP increasing
- Conservative approach in absence of infection
- Organ support, early fluids, early sphincerotomy
- Antibiotic prophylaxis???
- Suspect infection if sustained organ dysfunction

- **Early enteral nutrition**
- Delayed surgery
- Vascular complications?

Severe pancreatitis - updated classification

Necrotizing pancreatitis

- necrosis of the pancreatic and peripancreatic tissue
- peripancreatic necrosis may be isolated (15-20%)
- natural history variable

Banks et al Gut 2013:1;102-111

PPH

1. Detect PPH

Blood loss >500 ml after vaginal delivery or > 1000 mL after Cesarian section

Detection:

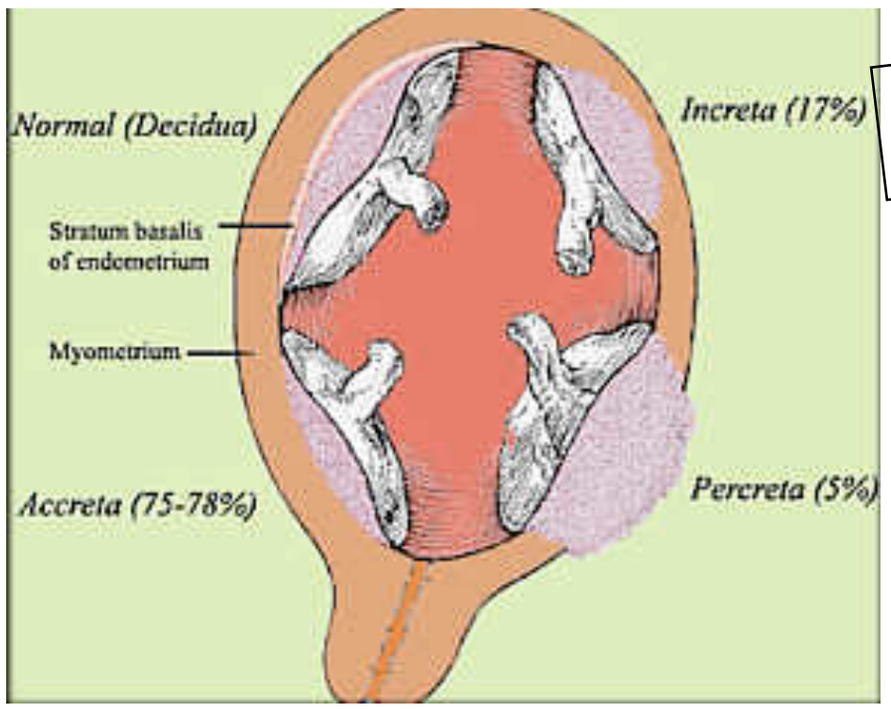
In delivery bag and by weighing the impregnated drapes

or

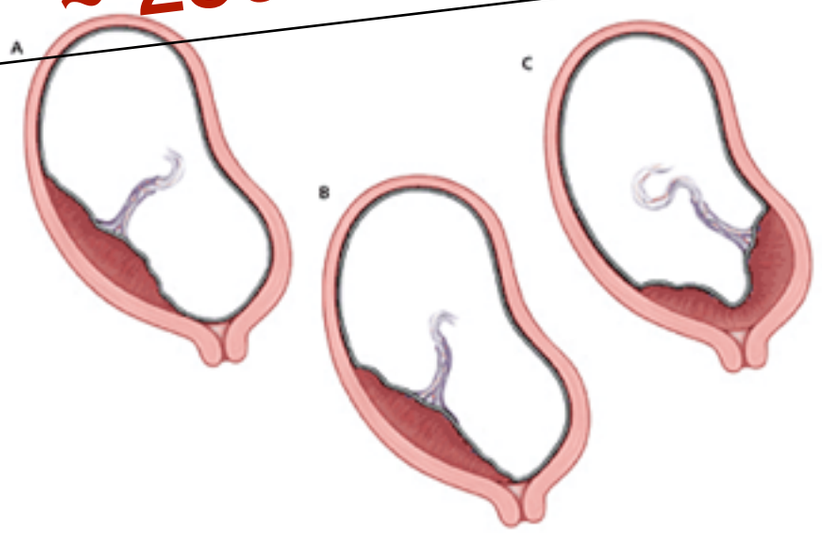
in surgical or intraoperative cell salvage aspiration system

Detection:

Abnormal placental insertion



Each "clot" ~ 250 ml blood



normal **low** **praevia**

2. Contract the uterine smooth muscle

Uterine contraction induces mechanical compression of the spinal arteries after delivery

Uterotonics : first step in PPH management

Prevention of atony

Oxytocin IV 5 IU after cord clamp

Misoprostol - 800 mcg PR

Treatment of atony

Oxytocin 30 IU per 30 minutes

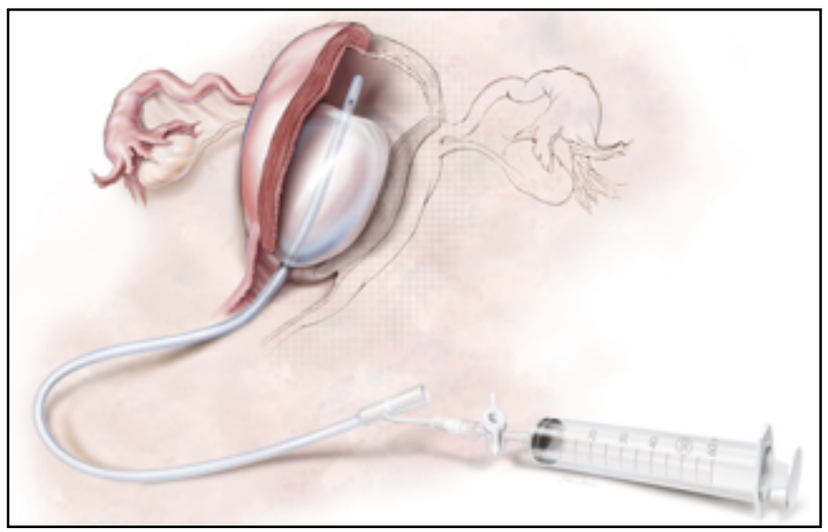
Sulprostone (PG2E) 500 mcg infusion per hour, 500 mcg every 6-12 hrs

Ergometrine 500 mg IV

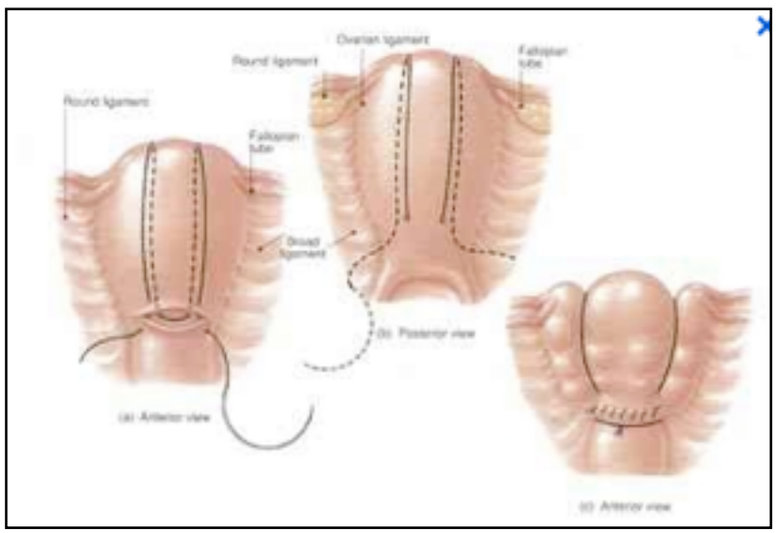
Misoprostol 800 mcg PR

3. Stop the uterine blood flow

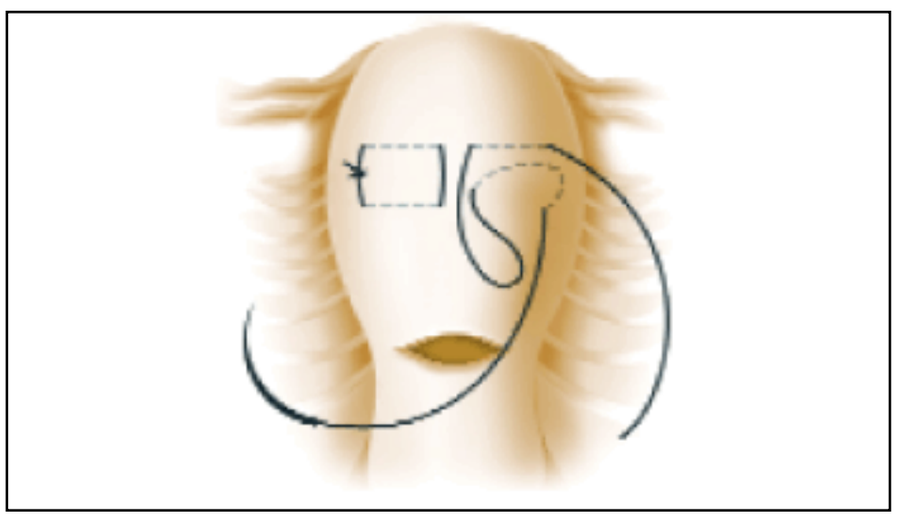
Bakri balloon



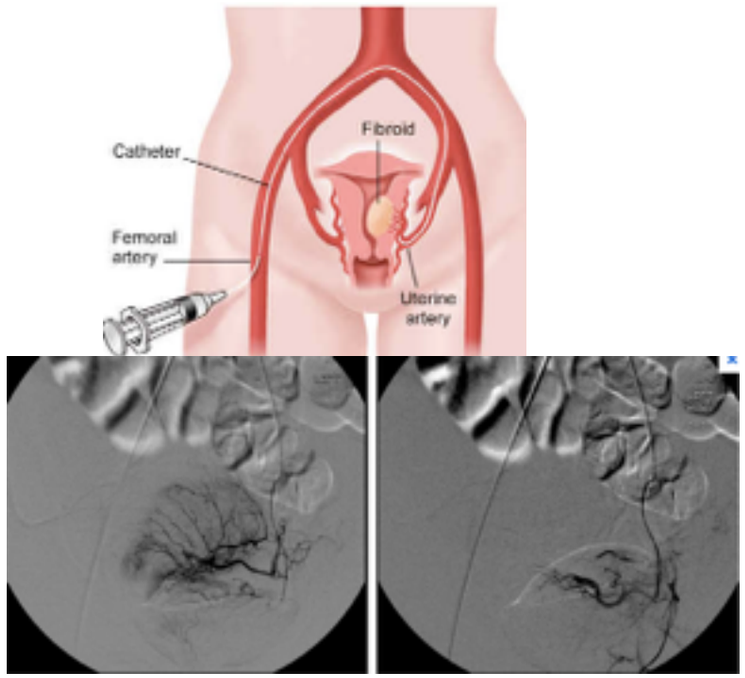
B-Lynch suture



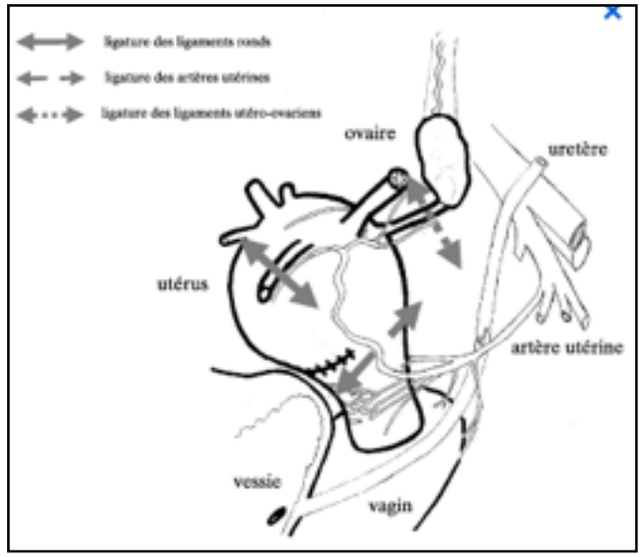
Cho suture



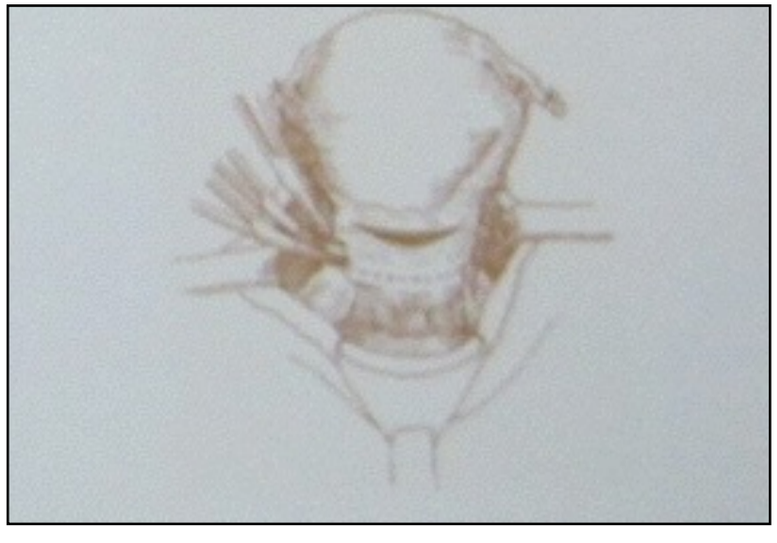
Embolisation



Triple ligature



Rescue hysterectomy



5. Transfusion strategies for massive PPH

Massive PPH: persistent bleeding > 500 ml/30 minutes
(Prostaglandins, Bakri, embolisation, B-Lynch)

Massive PPH
>2500mL
>500mL/30min

<u>Massive transfusion protocol</u>

-6 units PRBCs
- 4-6 units FFP
-4-8 units platelet concentrates

No biological monitoring

-rFVIIa if coagulopathy

<u>Monitored strategy</u>

-Continuous monitoring of Hb or HemoCue
-Non invasive hemodynamic monitoring
-Thromboelastography and laboratory monitoring

<u>Thresholds and objectives</u>

PRBC or Cell Saver - if Hb <7-1g/dL
Colloids - if MAP <65 mmHg; diuresis <1 ml/kg/h
Tranexamic acid: 1g/20 min then 0.5g/h
Fibrinogen concentrate: 3-12 g or **FFP** 30ml/kg
- If **fibrinogen** <3g/L and FIBTEM<18 mm
FFP - if factor V <30%
Platelets-if platelet count <50 x $10^9/mm^3$

6. PRBC transfusion for PPH acute anaemia

Haemoglobin target:
7 g/dL if bleeding has stopped
8-10 g/dL if bleeding is ongoing

Laboratory and point-of-care measurement of Hb may give faalsely stable or dereased readings in cases of haemoconcentration of haemodilution

7. Restore system regulation

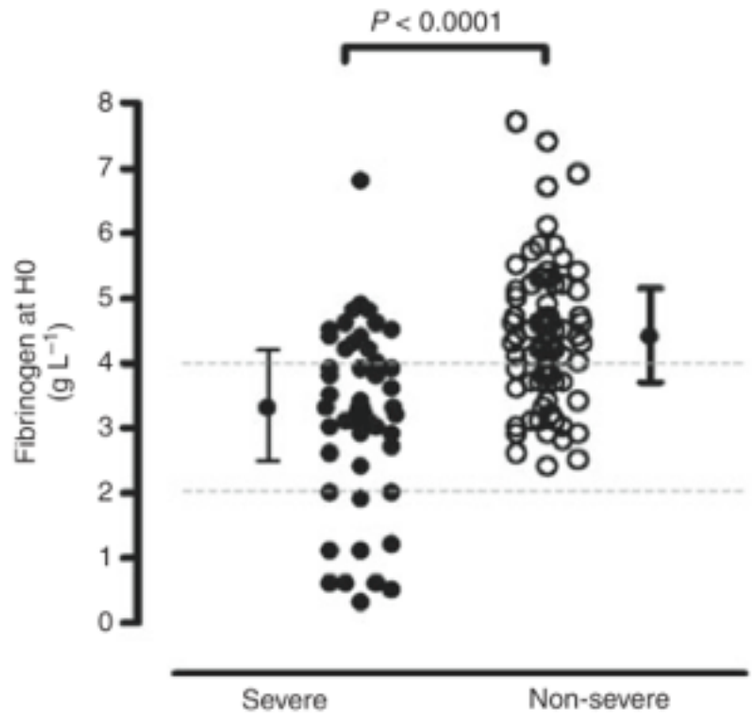
Non invasive haemodynamic monitoring
Fluid management: crystalloids + colloids vol/vol
but avoid haemodilution
Correct: acidosis, hypocacaemia
Calcium: Ca gluconate 10% 10 mL

8. Screen, monitor and treat coagulopathy

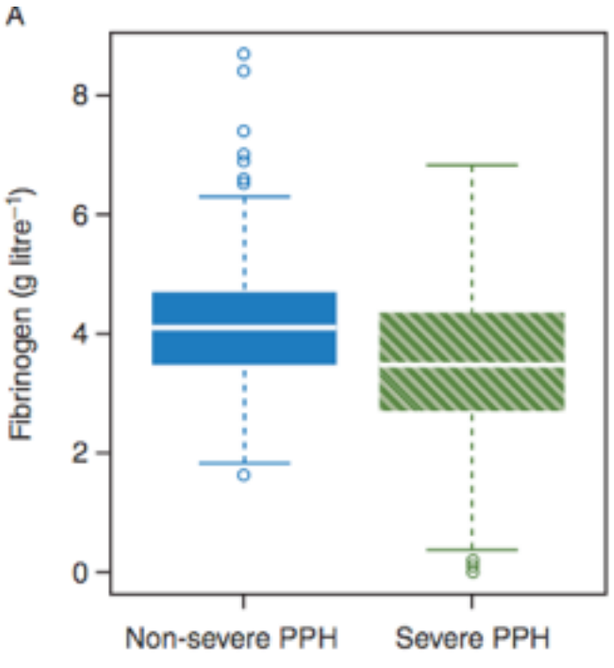
Decrease in fibrinogen is an early predictor of PPH poor outcome

Fibrinogen >4g/L = NPV 79%
Fibrinogen <2g/L = PPV 100%

Charbit et al J Thromb Haemost 2007;5:256



Low in fibrinogen predicts severity



Fibrinogen <3g/L = OR 1.9

Fibrinogen 2-3g/L = OR 11.99

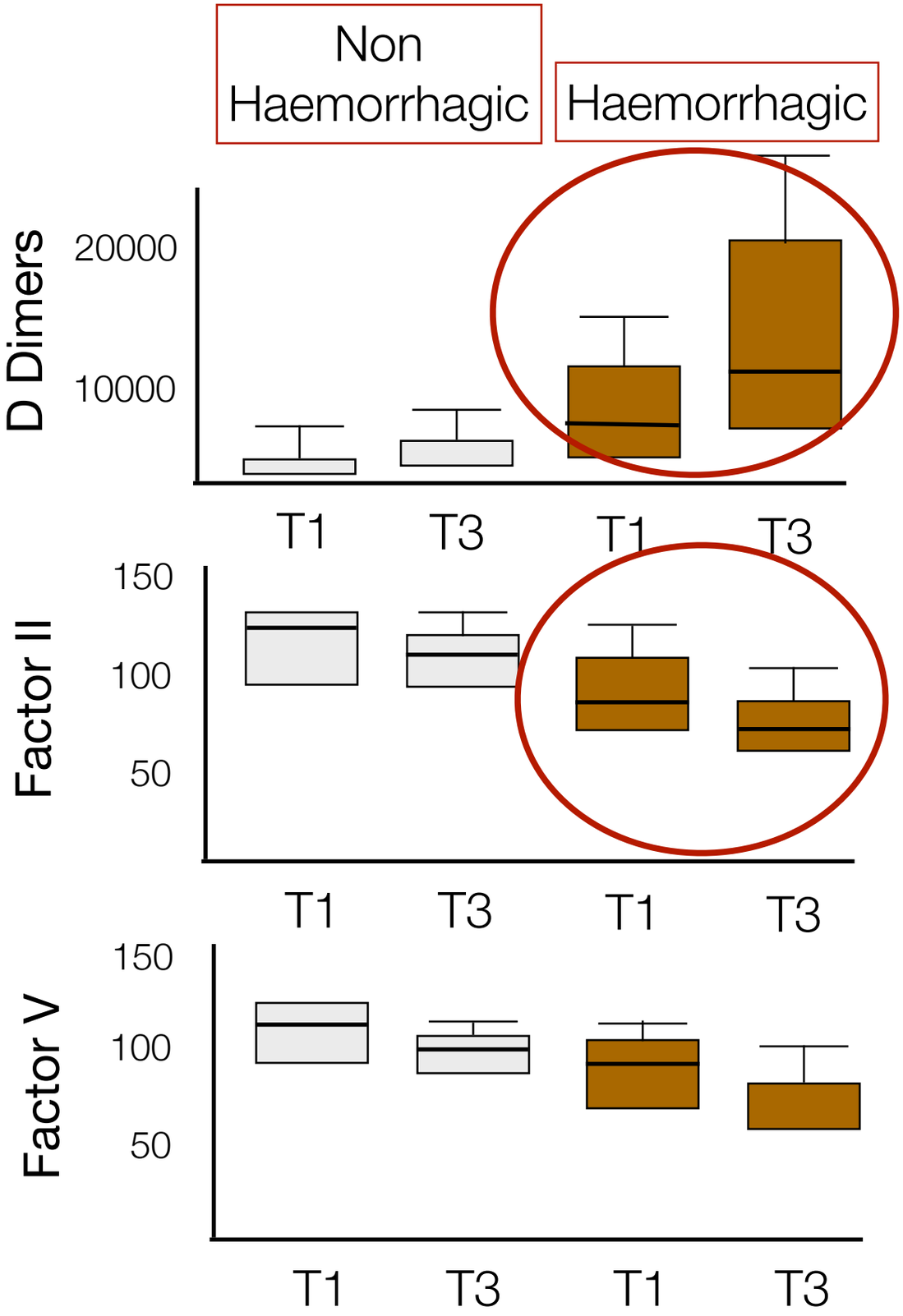
Remember:
Normal fibrinogen levels in pregnancy ~ 4.5 g/l in non-pregnant ~3 g/l

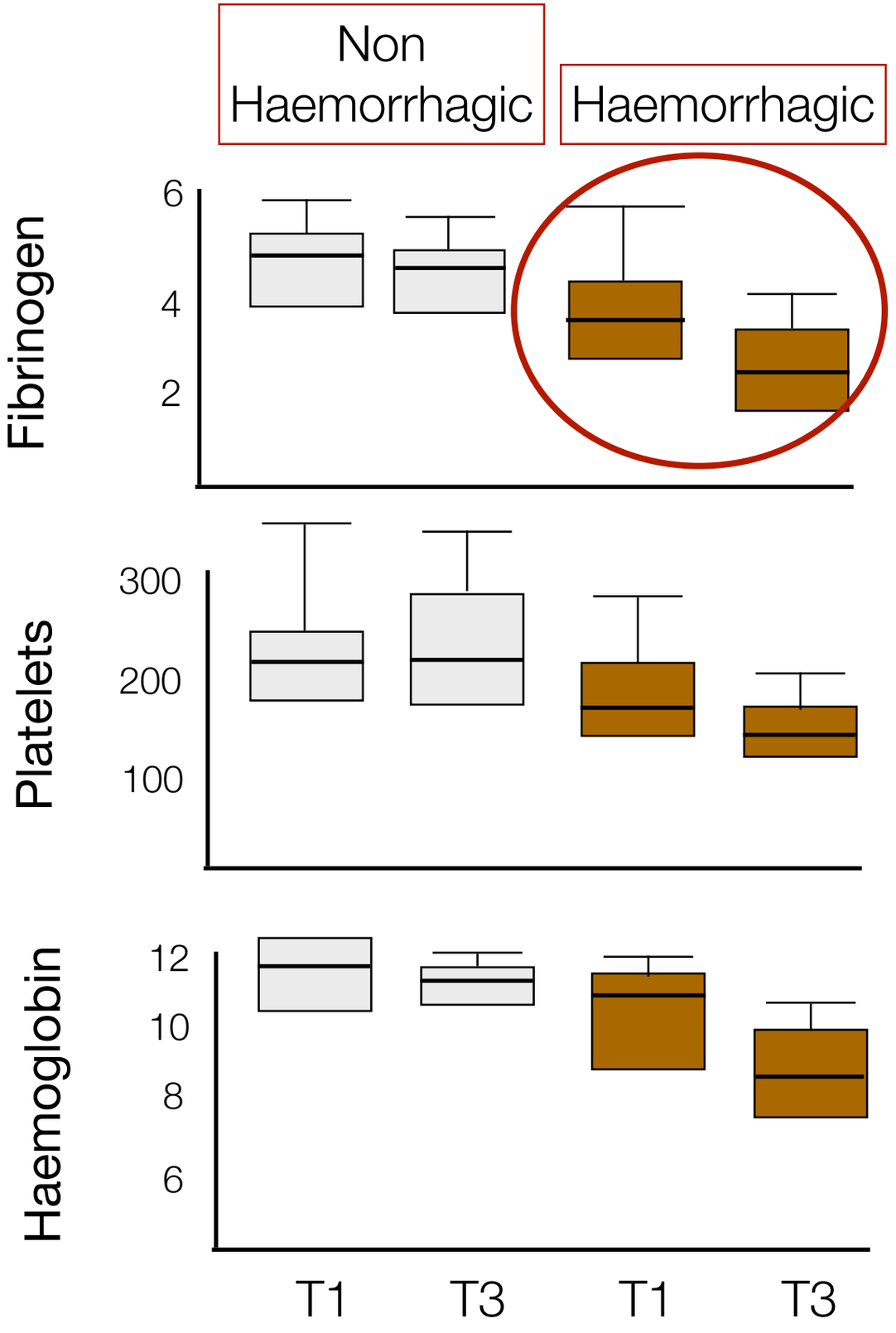
Cortet et al BJA; 108, 984-989

PPH induced coagulopathy

T1 - onset

T3 - 2 hrs later



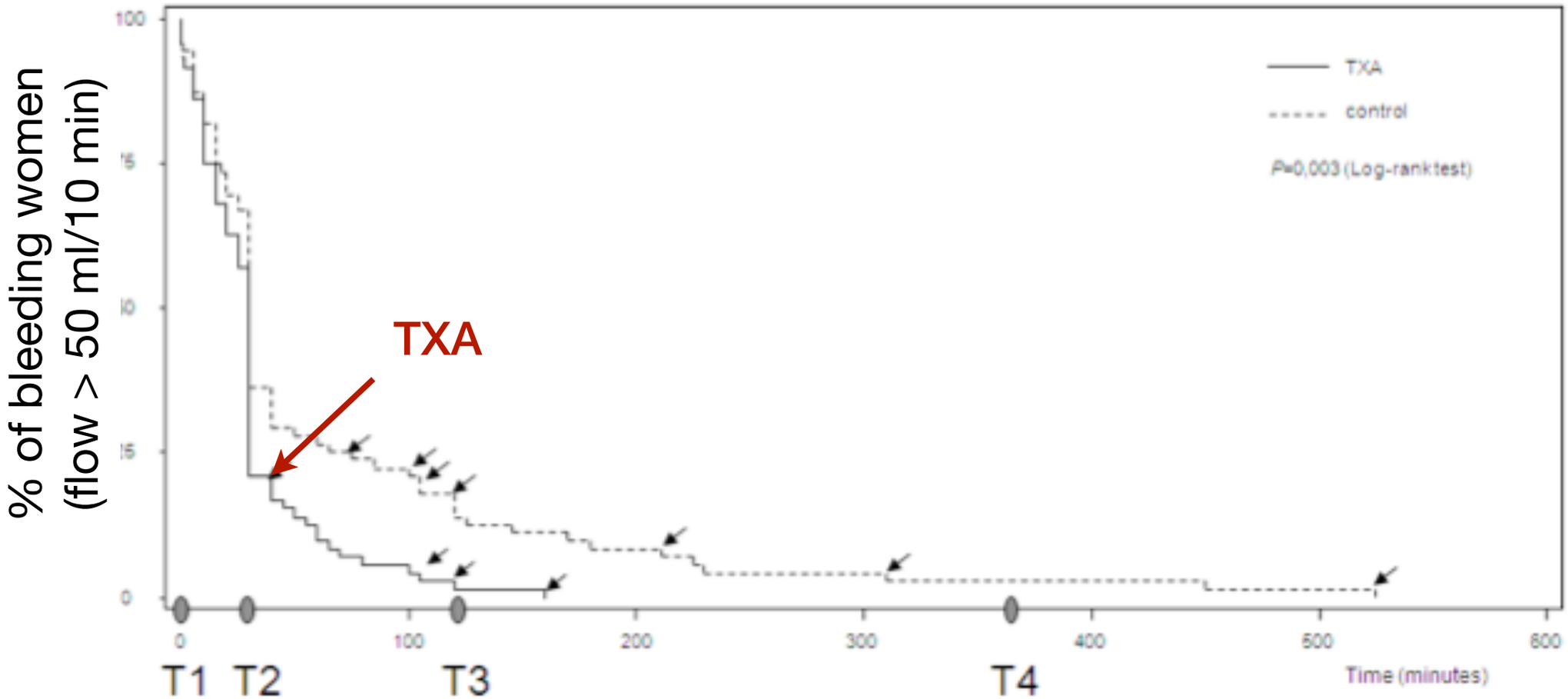


8b. Treat the coagulopathy early with targeted therapies

Stop the hyperfibrinolysis: tranexamic acid
EXADELI trial: efficacy of TXA to reduce PPH blood loss

High dose TXA **reduces**:
measured blood loss, duration of bleeding Hb drop> 4g/dL
The need for transfusion and evolution to severity

Side effects were minor (vomiting)



Graph showing time from enrolment until PPH cessation in the two groups

Ducloy-Bouthors et al. Critical Care 2011, 15:R117

8c. Restore plasma coagulation

Restore fibrinogen level
Fibrinogen concentrates
To raise fibrinogen concentration by 1 g/L in a 70 kg adult

FFP 4 units (1000 mL) £384 <-->cryoprecipitate 13 units (260 mL) £478
<--> Fibrinogen concentrate 2 gm (100 mL) £440

Bell et al Int J Obstet Anesth 2010; 19:218-23

9. Prevent maternal morbidity and reduce PPH induced thrombotic risk with thromboprophylaxis

Severe PPH increases the risk of post partum DVT

In one study: 32,463 women
-317 severe PPH
-11 post partum VTE
-60 superficial vein thrombosis

Chaleur et al Thromb Haemost 2008; 100:773-9

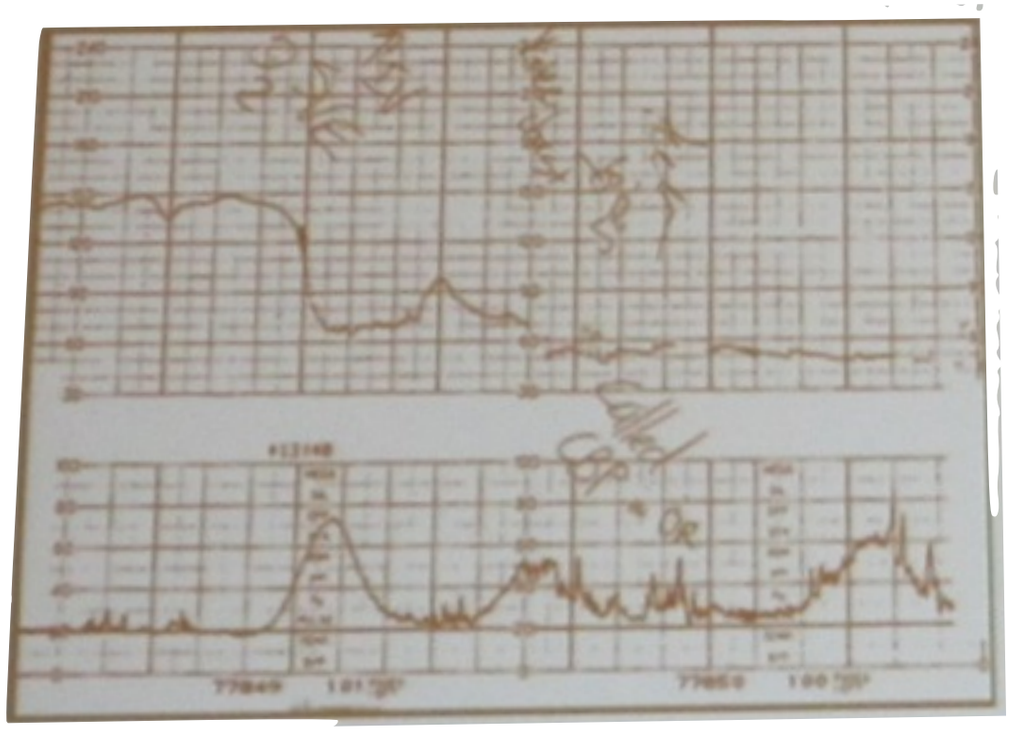
Amniotic fluid embolism

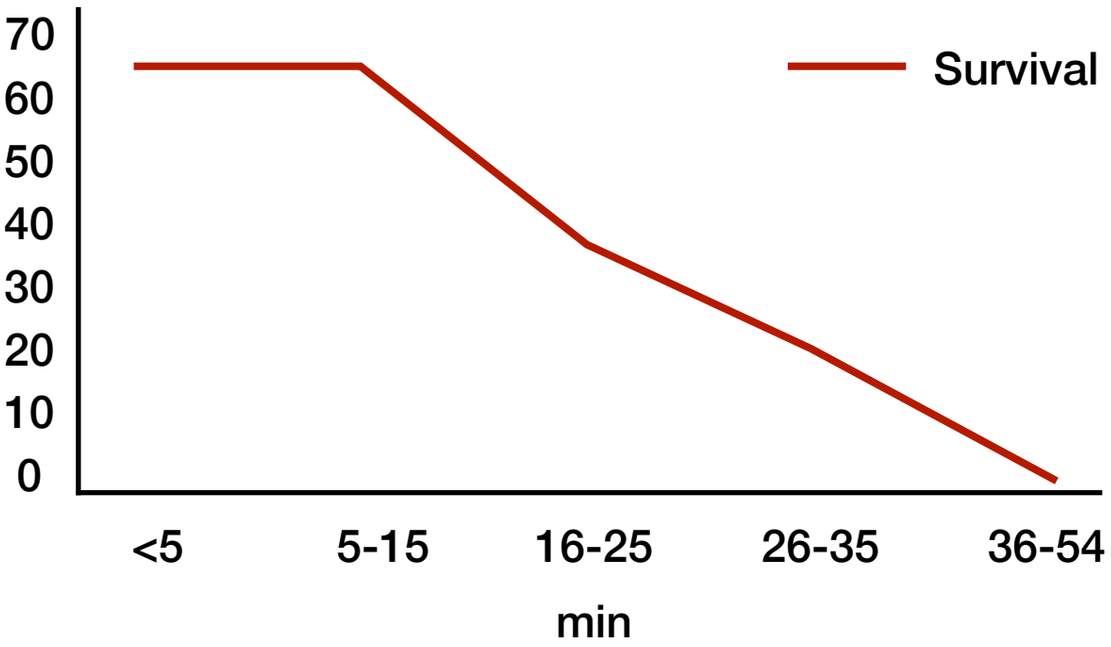
Amniotic fluid embolism

- AFE is **not constantly fatal**
- AFE is **not an anaphylactic** reaction
- AFE is not a physiological process during normal labour

- Diagnosis remains often based on clinical evaluation and exclusion - histology rarely available
  - **IGFBP-1 a new biomarker**

Acute foetal compromise - 49-100%



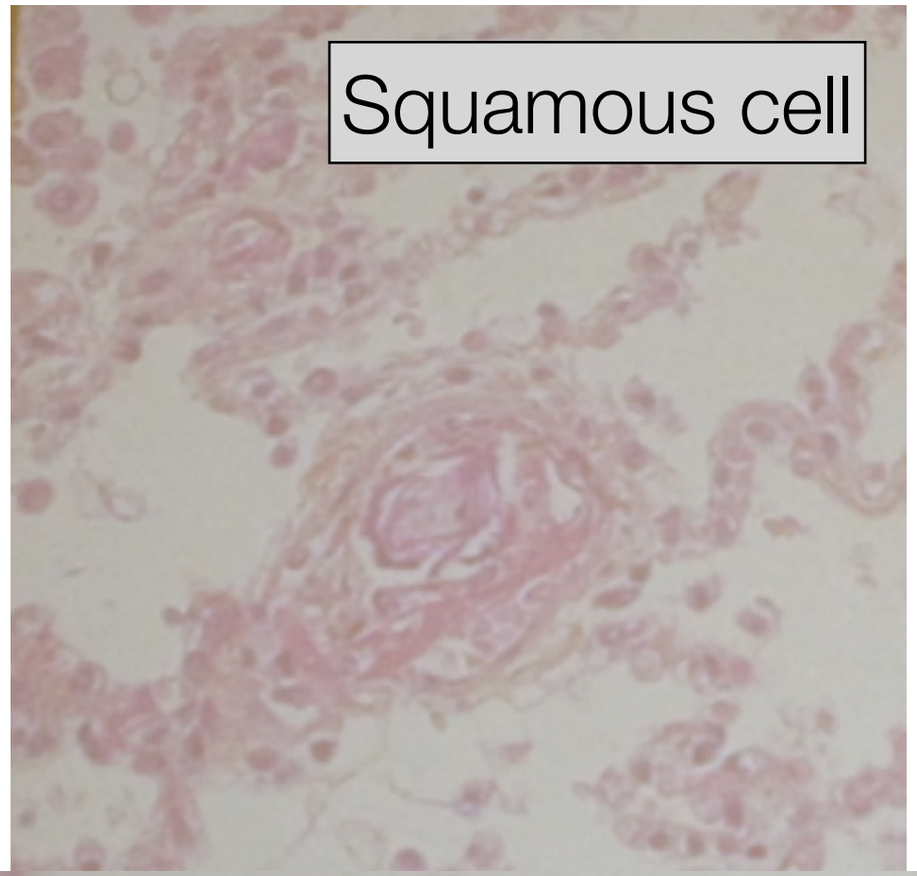


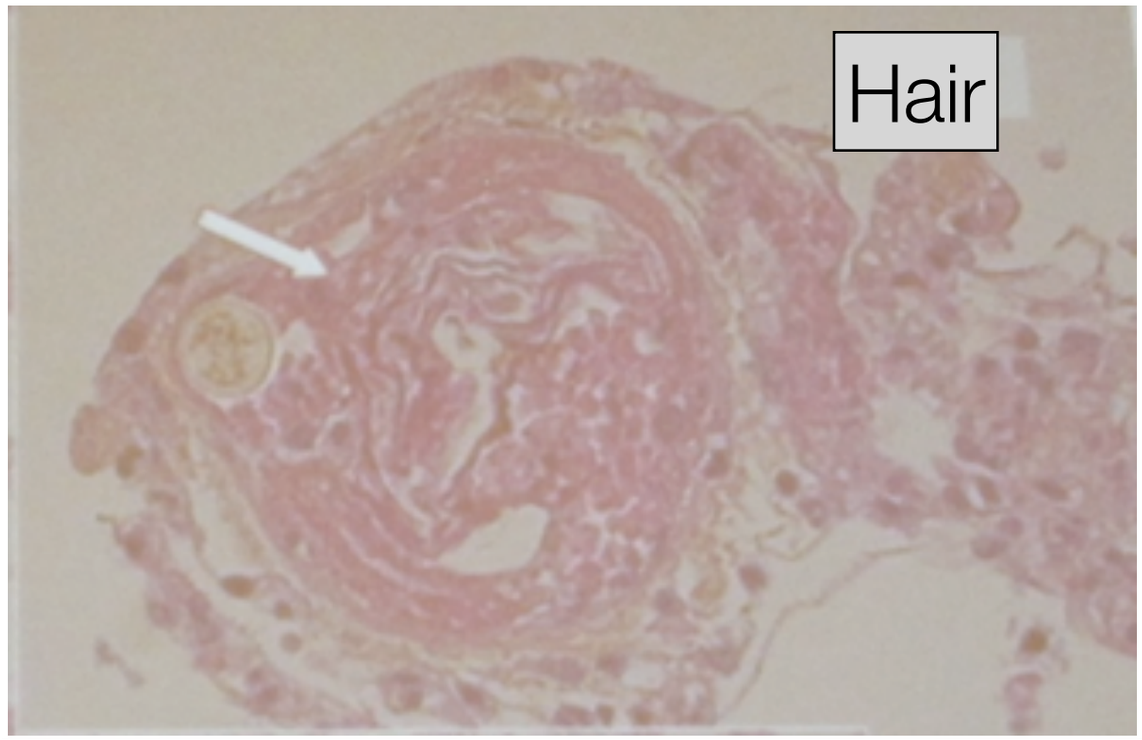
- 79% foetus alive (32% when cardiac arrest)
- 50% neurologic sequelae

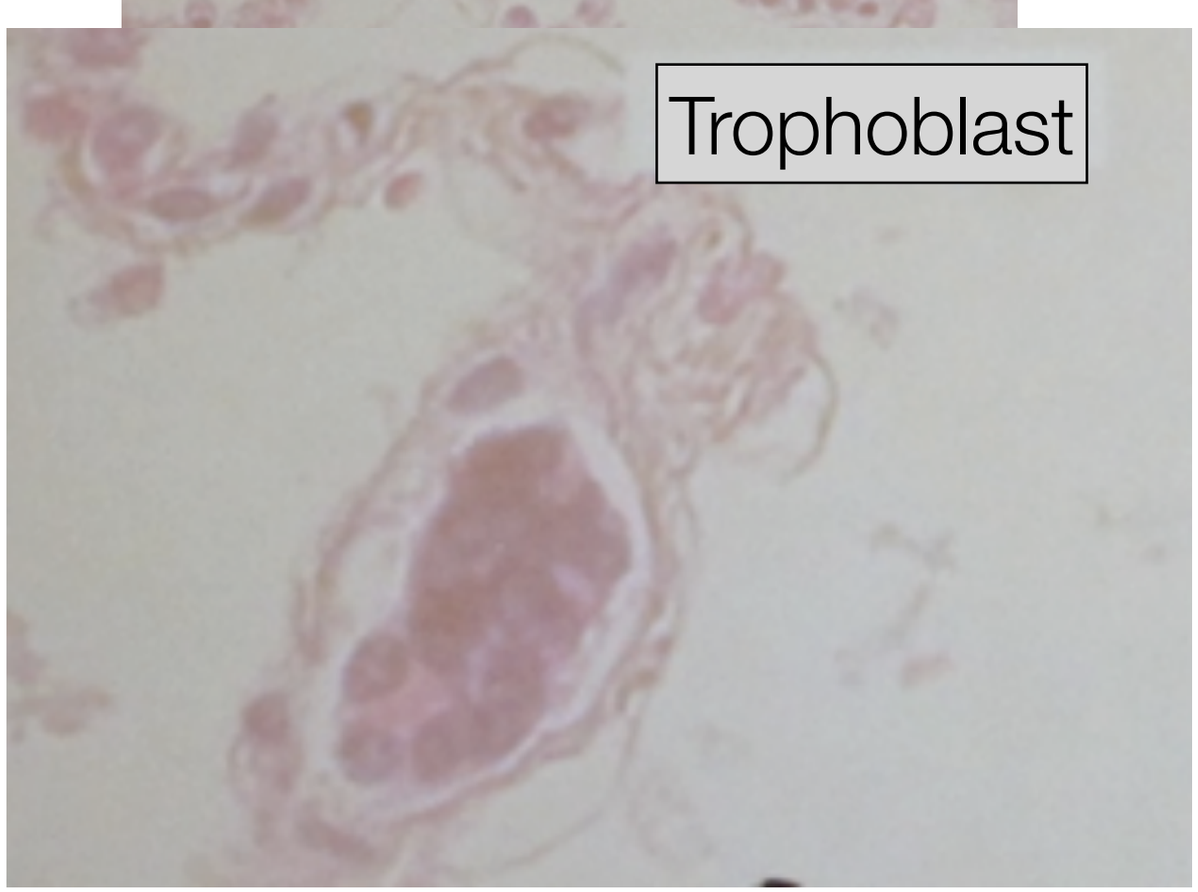
Clark Am J Obstet Gynecol 1995

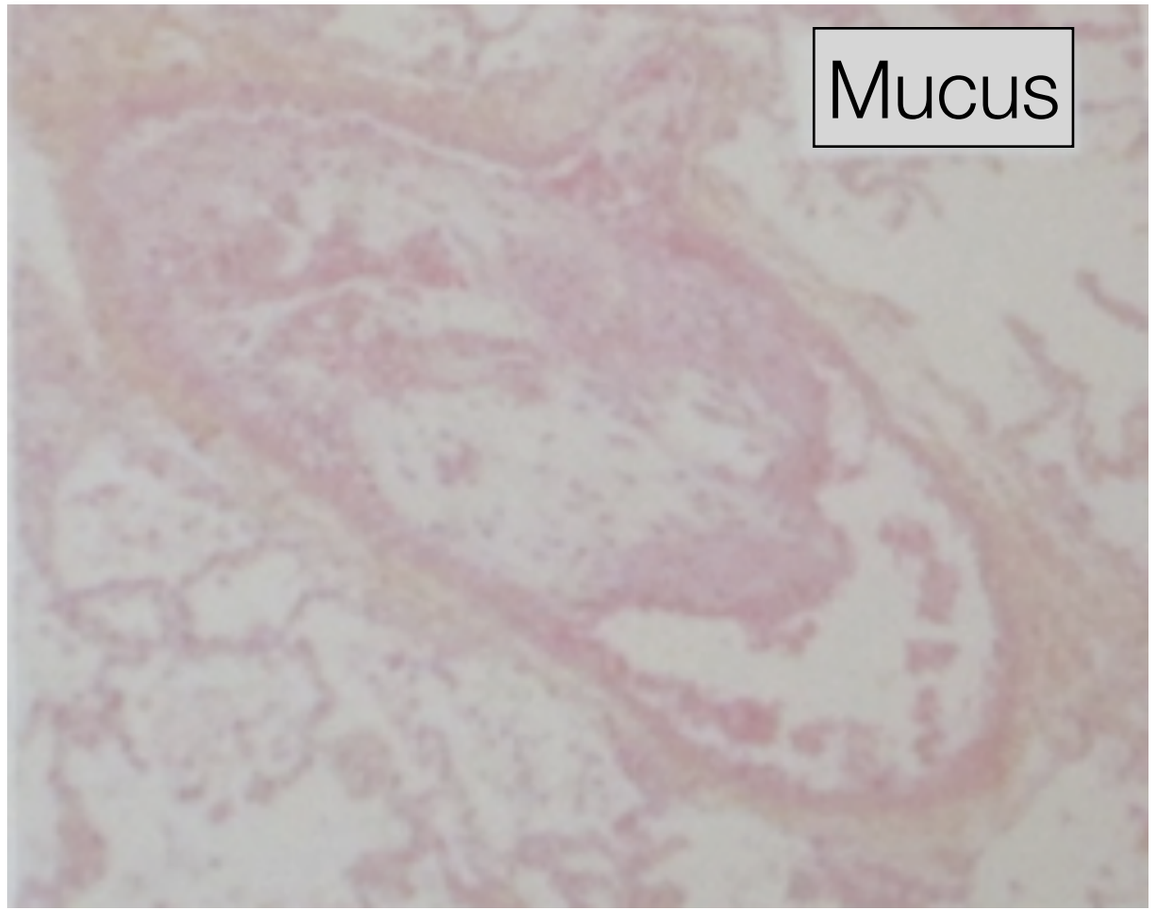
Gilbert Obstet Gynecol 1999

Amniotic fluid embolism

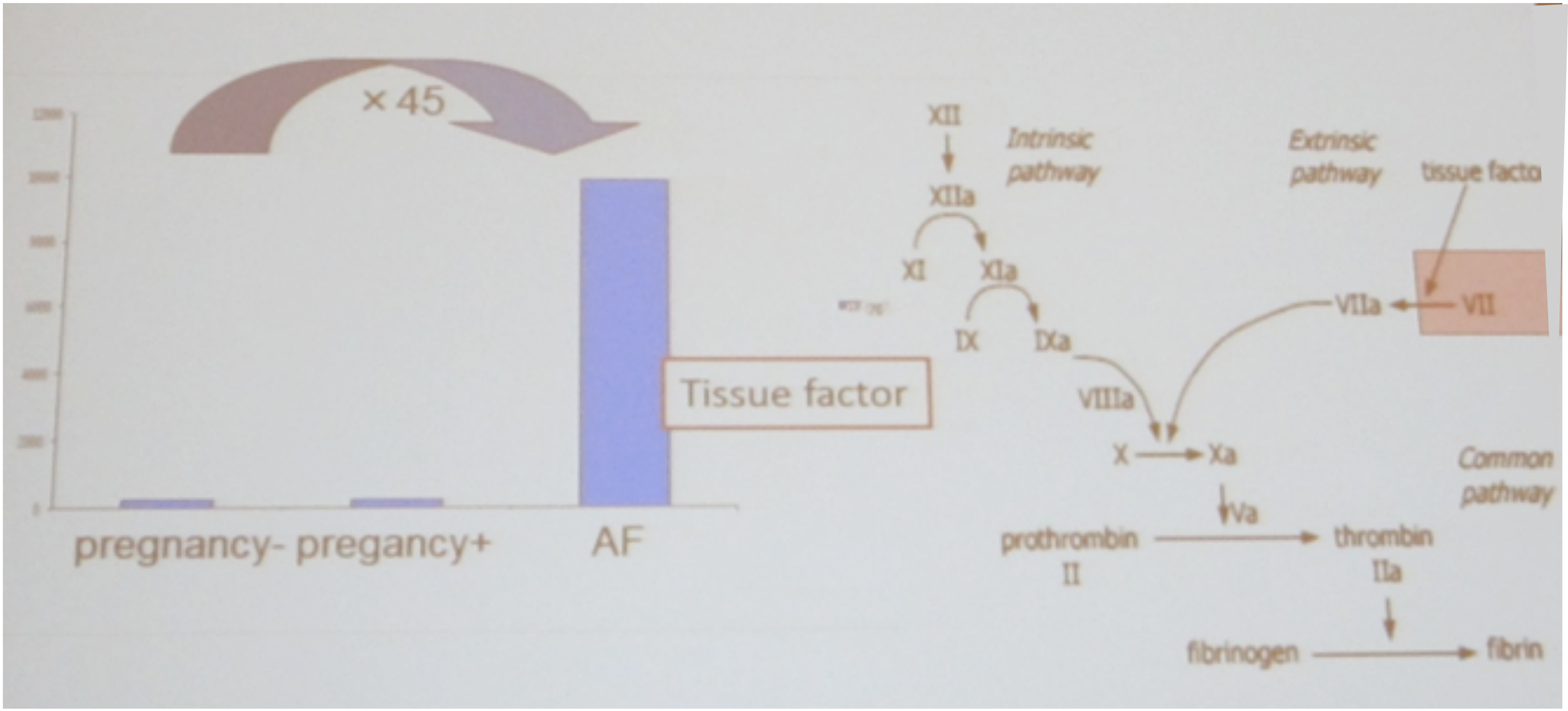








AFE-Fibrinolysis - DIC



Biron et al Pathophysiol Haemost Thromb 2003

Biomarkers of AFE

- Plasma mast cell tryptase
  - Biomarker of anaphylaxis
  - Slightly elevated in AFE, very high levels in anaphylactic shock
    - Neither specific nor sensitive
- Mild increase of serum tryptase in AFE

  67 ng/mL in AFE

  <10 ng/mL in controls

  648 ng/mL in anaphylactic shock

Nishio Forensic Science International Volume 126, Issue 1, 28 March 2002

Why do we need biomarkers?

CMAJ. 1993 March 1; 148(5): 806–809.

Medicolegal nightmare: a tragic case, a needless trial.

J St-Amand

CASE REPORT PATHOLOGY/BIOLOGY

Medical Responsibility in the Operating Room: The Example of an Amniotic Fluid Embolism

Journal of Forensic Sciences

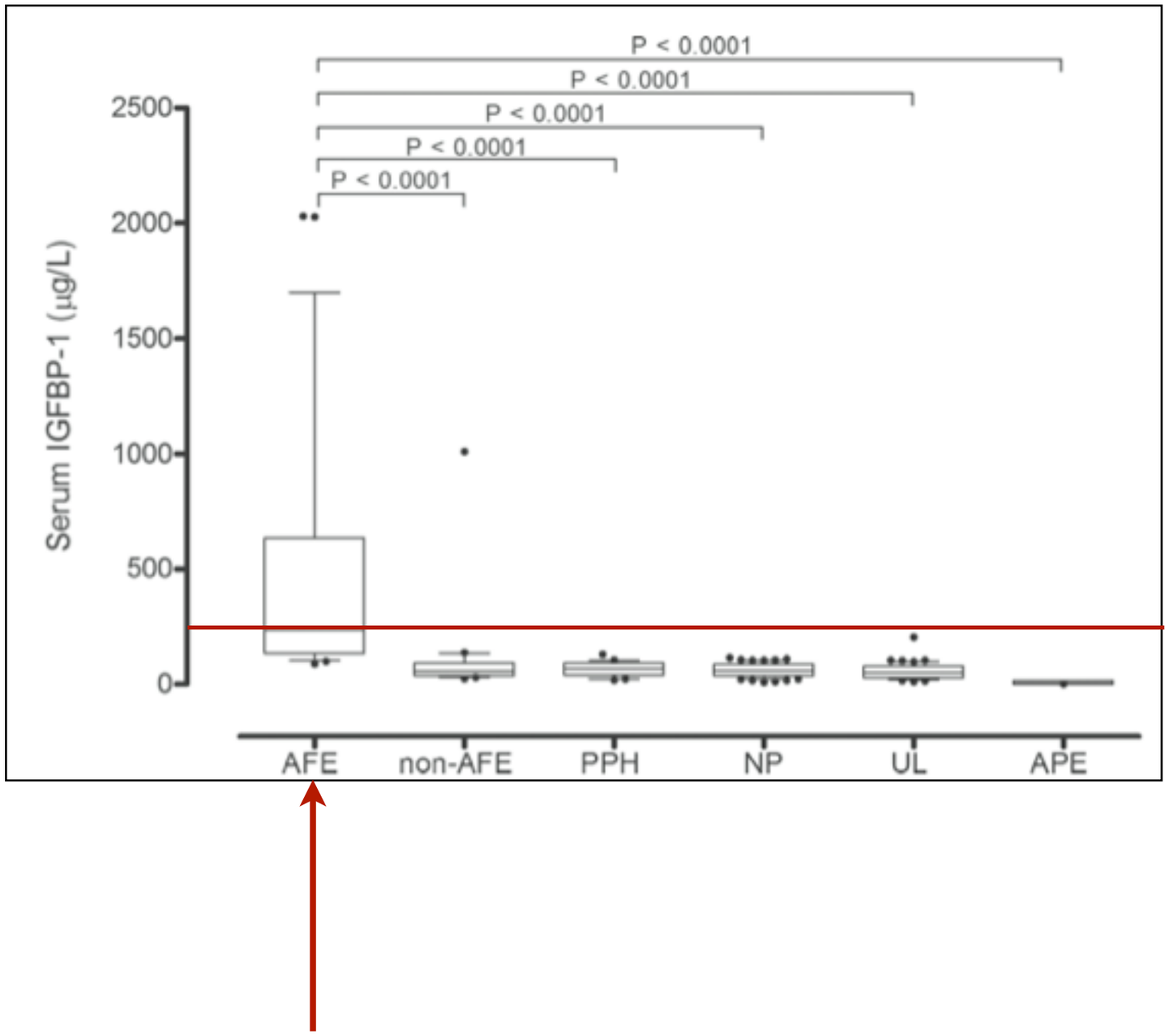
Volume 57, Issue 4, pages 1120–1123, July 2012

Diagnostic accuracy of **insulin-like growth factor binding protein-1** for amniotic fluid embolism

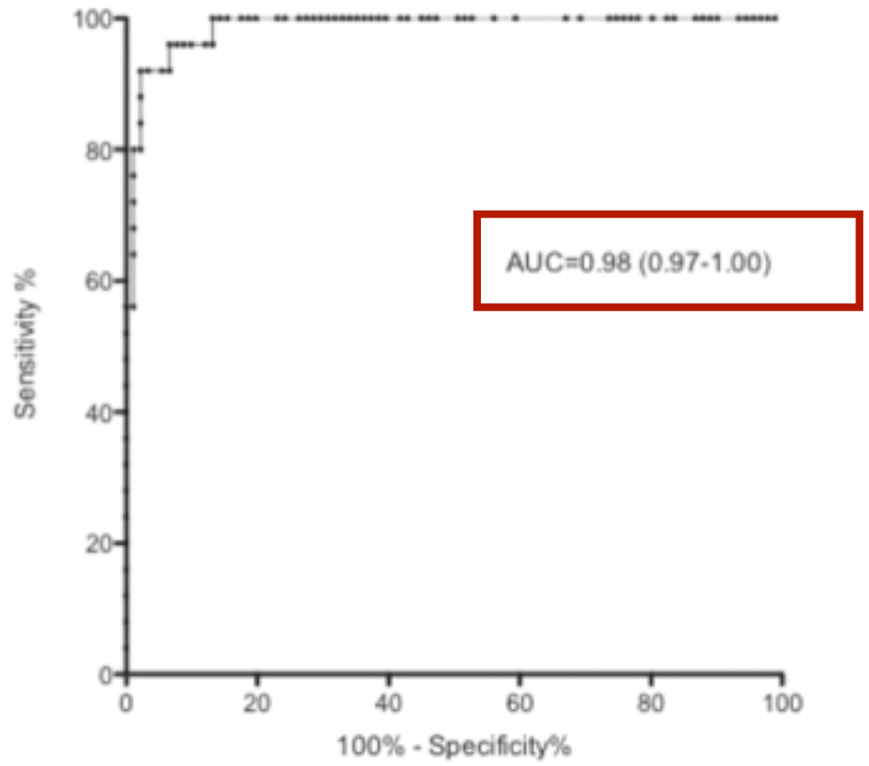
- The insulin-like growth factor binding proteins are a family of structurally related binding proteins that complex the insulin-like growth factors
- **IGFBP-1** is considered to be a **specific protein marker of amniotic fluid**, which is **500 to 1000-fold higher concentration** compared with normal plasma

CCM 2012 Vol 40, No.7

Diagnostic accuracy of insulin-like growth factor binding protein-1 for amniotic fluid embolism



AFE	**234 µg/L**
Control	56 µg/L
PPH	65 µg/L
Normal labour	49 µg/L
PE	5 µg/L



CCM 2012 Vol 40, No.7

Amniotic fluid embolism

- AFE is rare
- AFE is severe
- AFE is **not** a death sentence
- Clinical diagnosis and exclusion criteria
- Histology
- New biomarker - **IGFBP-1**

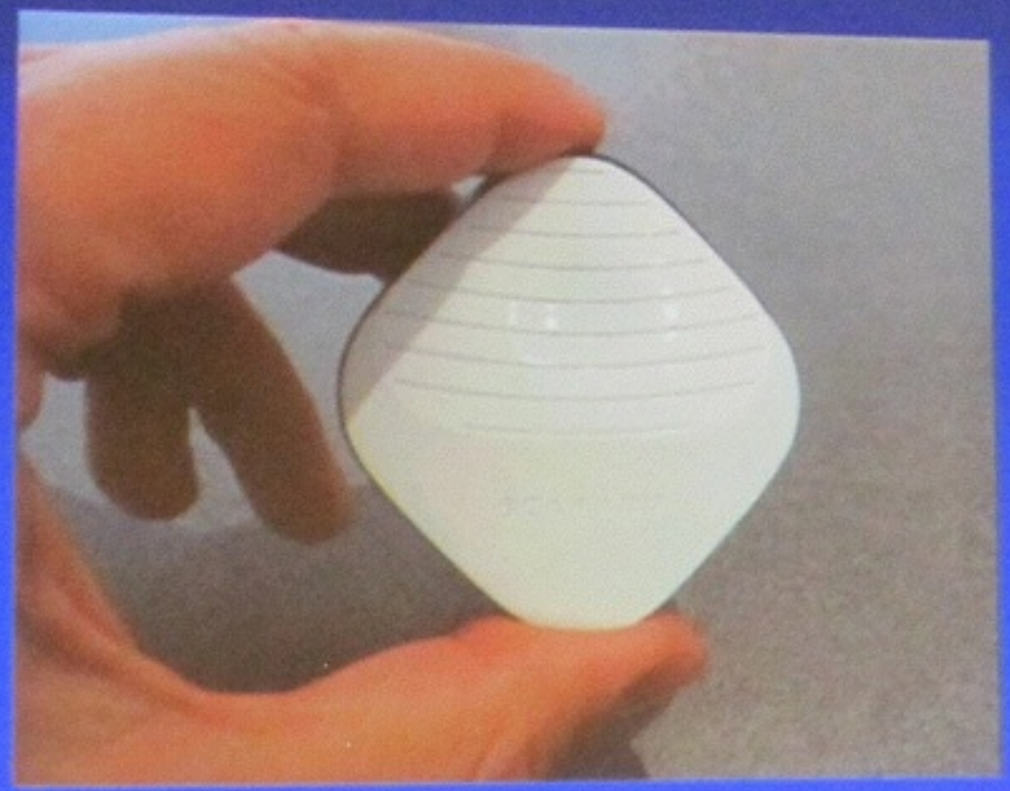
???


KEEP
WELL
LEFT

Holy Spock! The *Star Trek* Medical Tricorder Is Real And It's Only $150

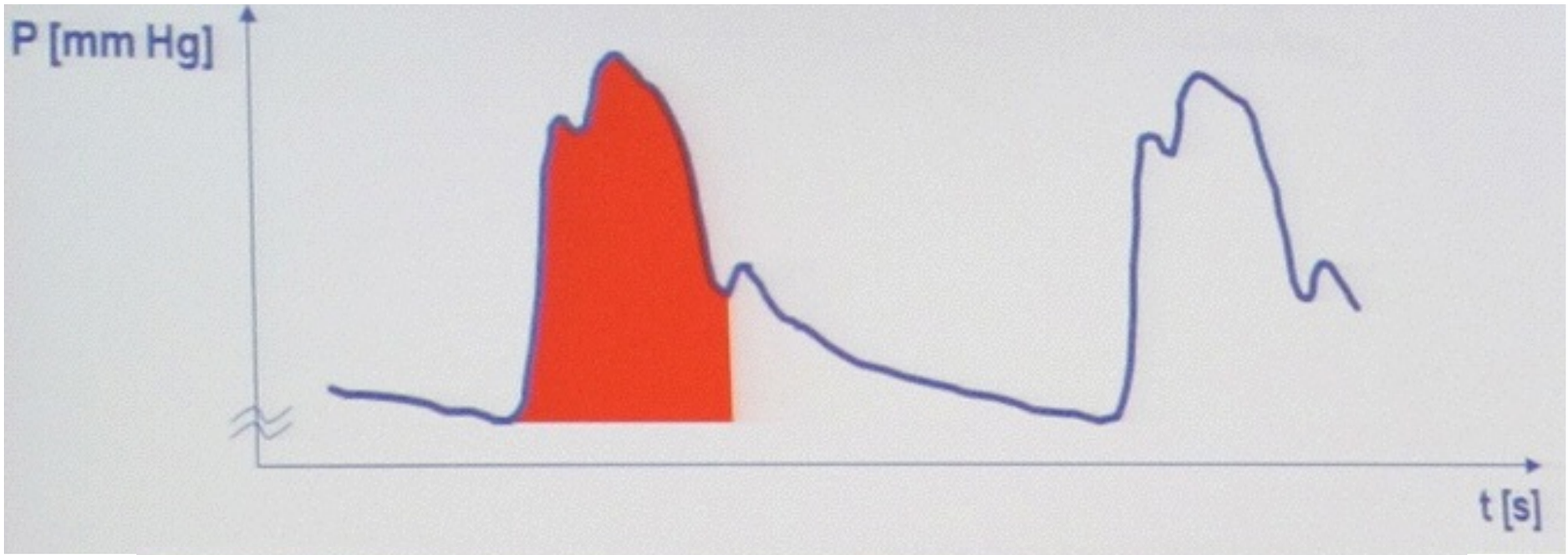
By Jesus Diaz January 2013, Gizmodo Blog

Scanadu's Tricorder, the Scout



Heart rate, electrical heart activity, pulse transit time, temperature, heart rate variability, and blood oxygenation. It then transmits this information to an iOS app via Bluetooth.

Pulse contour analysis



$$CO = cal \cdot HR \cdot \int_{Systole} \left(\frac{P(t)}{SVR} + C(p) \cdot \frac{dP}{dt} \right) dt$$

Noninvasive Hemodynamic Profiling in Emergency Medicine

Richard M Nowak MD, MBA, FACEP, FAAEM

Past Chairperson
Emergency Medicine
Henry Ford Health System
Detroit, Michigan

Clinical Professor
Emergency Medicine
Wayne State University
Detroit, Michigan, USA
University of Michigan
Ann Arbor, Michigan, USA

Henry Ford Health System

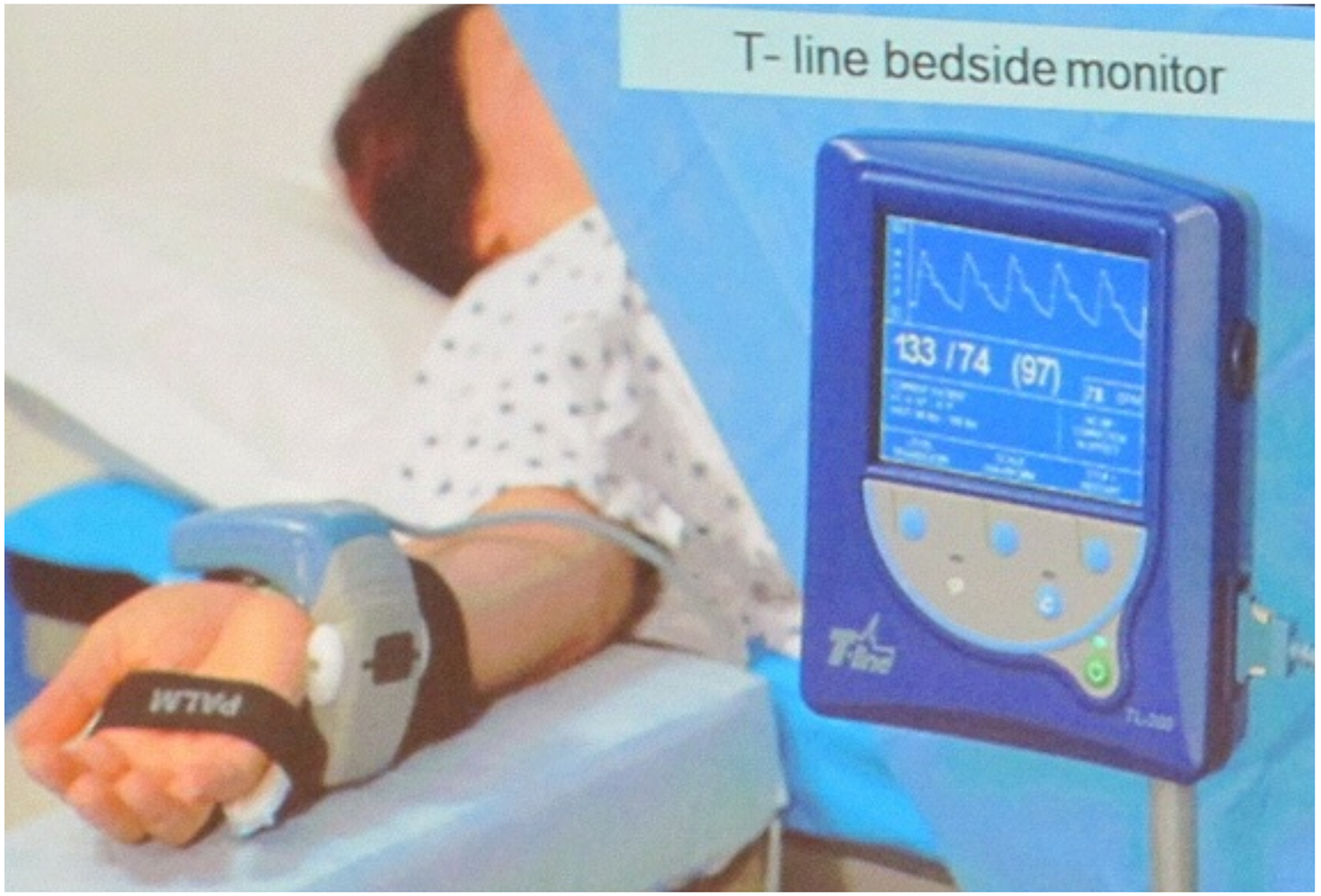
University of Michigan

Wayne State University

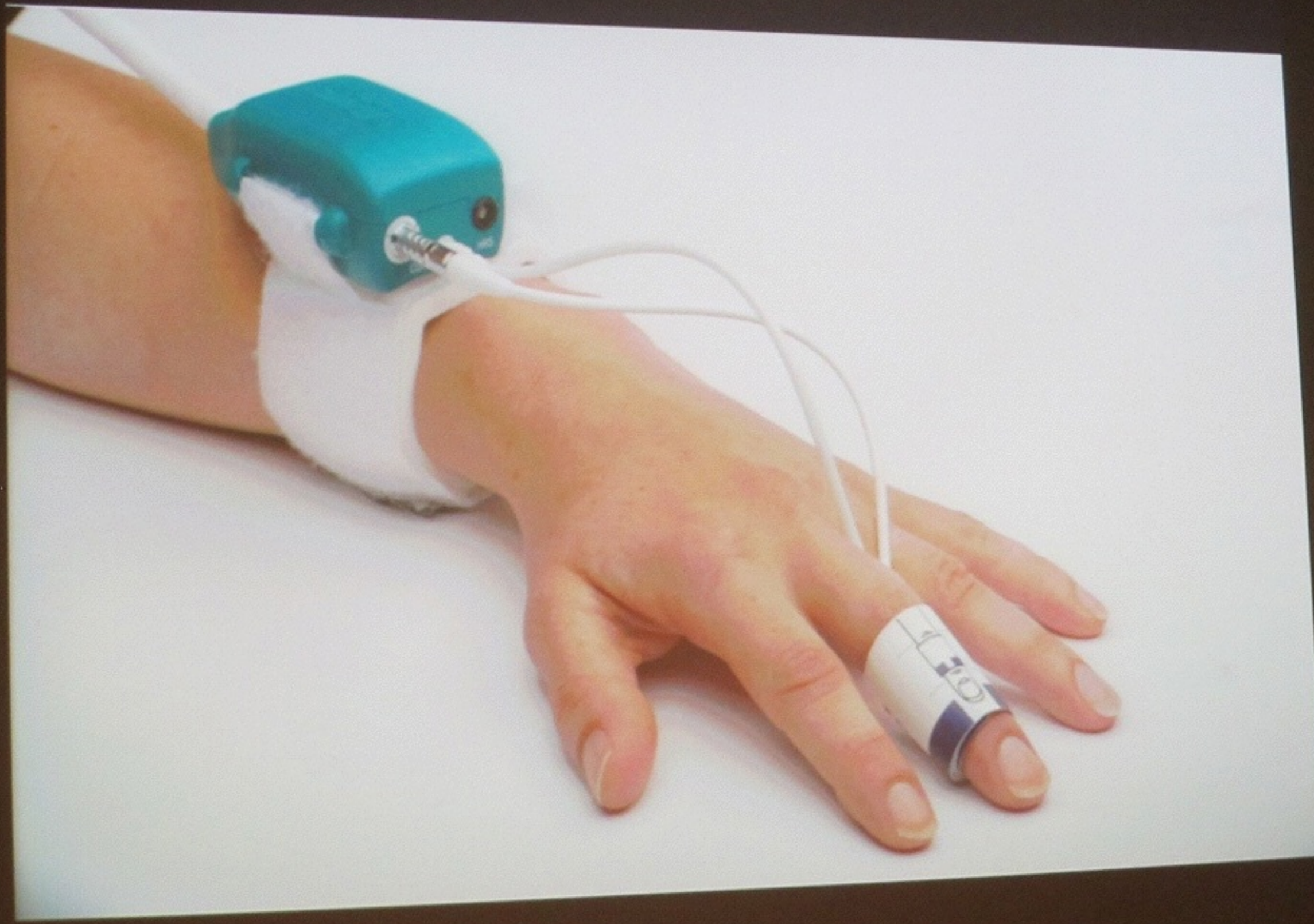
Emergency department hemodynamic monitoring needs

- Any hemodynamic monitoring device that will be used frequently must be totally non invasive, **reasonably accurate** (trending) and be easily applied by non physician staff
- Minimally invasive (arterial line) is too invasive for routine ED hemodynamic profiling

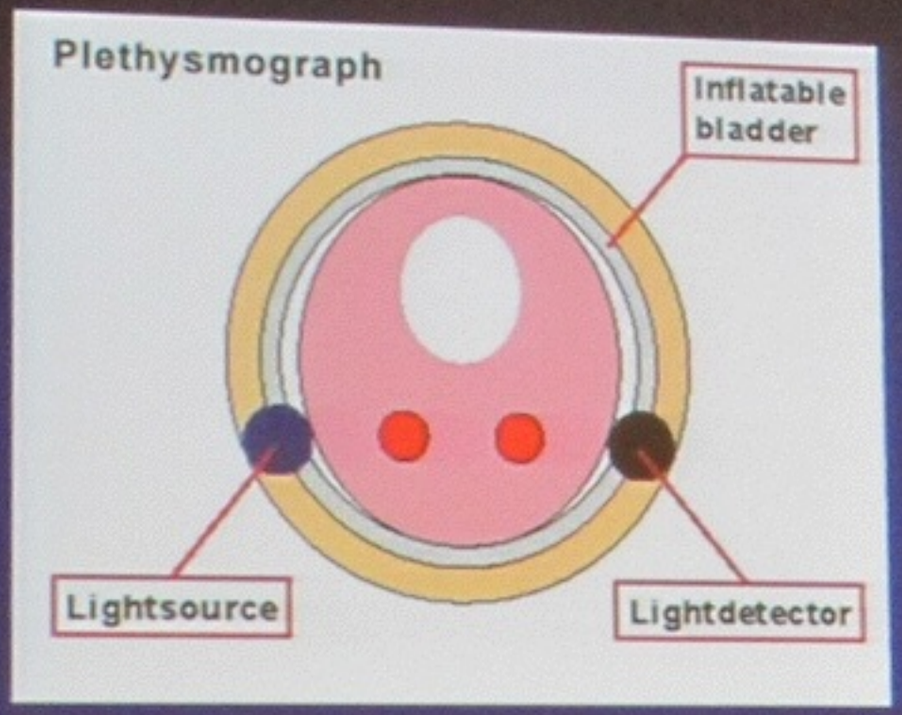
T-line non invasive bedside monitor

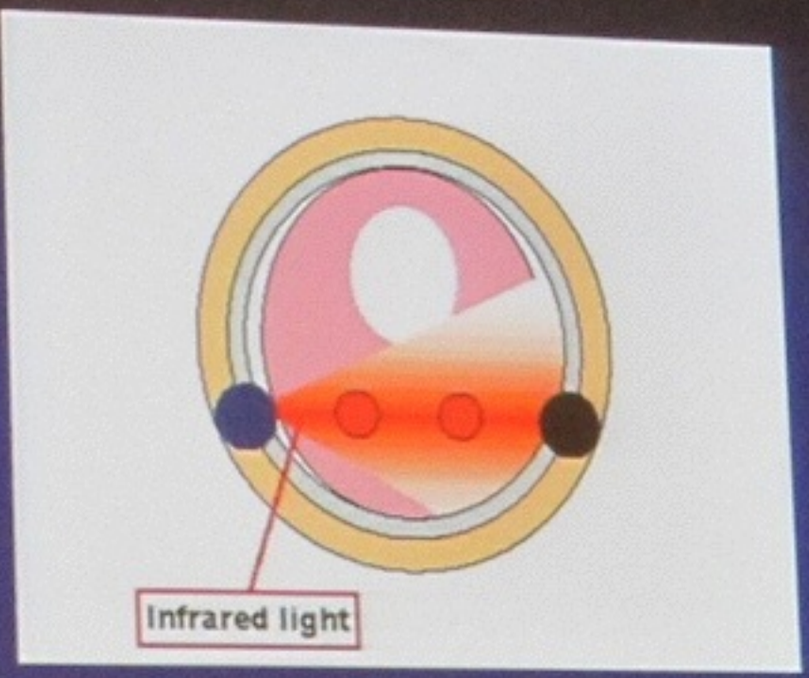


Nexfin Finger cuff and wrist unit



Nexfin Measurement Principles





- In order to determine beat-to-beat stroke volume and cardiac output from noninvasive continuous blood pressure a pulse contour method based on a physiological model of the circulation is used

British Journal of Anaesthesia Page 1 of 6
doi:10.1093/bja/aet025

BJA

Non-invasive continuous arterial pressure measurement based on radial artery tonometry in the intensive care unit: a method comparison study using the T-Line TL-200pro device

B. Saugel[1*†], A. S. Meidert[1†], A. Hapfelmeier[2], F. Eyer[3], R. M. Schmid[1] and W. Huber[1]

Arterial pressure, $n=4502$ averaged 10-beat epochs	Femoral arterial catheter	TL-200pro device	Bias [mean (SD) of the difference]	95% limits of agreement
Mean arterial pressure (mm Hg)	82.3 (11.3)	83.0 (11.4)	+0.72 (5.15)	−9.37 to +10.82
Systolic arterial pressure (mm Hg)	123.6 (17.8)	122.2 (16.6)	−1.39 (8.85)	−18.74 to +15.96
Diastolic arterial pressure (mm Hg)	60.1 (8.8)	64.5 (9.6)	+4.36 (6.64)	−8.66 to +17.38

BJA Advance Access published March 13, 2013

Emergency Medicine Hemodynamic Questions

- What are the underlying presenting and post treatment hemodynamic profiles of acutely ill ED patients?
- Can these profiles predict patient outcomes?
- How should any individual hemodynamic profile be altered in order to improve patient care?

Hemodynamic Profile of an ED Patient

I20

	A	B	C	D	E	F	G	H	I	J	K	L	M
1	A009	Timepoint	0-15	15-30	30-45	45-1hr	1hr-1:15	1:15-1:30	1:30-1:45	1:45-2hr	2hr-2:15	2:15-2:30	2:30-2:45
2	SJJ	Systolic	160	167	165	166	161	162	168	167	166	162	158
3	11/1/2010	Diastolic	83	83	83	85	84	87	90	92	88	88	85
4	CHF	MAP	113	115	115	116	114	116	121	122	119	118	114
5		PP	76	83	81	81	76	75	78	75	77	73	75
6		CO	8.4	8.9	8.7	8.7	8.5	8.1	8.2	7.9	8.7	8.4	8.6
7		CI	3.8	4.0	3.9	3.9	3.8	3.6	3.7	3.5	3.9	3.8	3.8
8		HR	81	81	82	82	84	83	84	84	87	86	87
9		IBI	0.744	0.749	0.745	0.737	0.729	0.726	0.725	0.718	0.695	0.694	0.694
10		SV	103	109	107	105	102	98	97	94	100	98	99
11		SVI	46	49	48	47	45	44	43	42	45	44	44
12		SVR	1094	1062	1096	1157	1297	1167	1288	1285	1132	1134	1079
13		SVRI	2438	2366	2442	2577	2873	2600	2870	2861	2521	2525	2404
14		dP/dt	1304	1648	1543	1434	1291	1218	1438	1430	1487	1481	1476
15		HRS	-8	-11	-3	3	2	7	-2	-2	0	-1	0
16		Recording	#81										
17													

PREMIUM Registry

Primary objectives

The primary objectives of this study are to:

1. Describe the 4 hour continuous ED hemodynamic profiles of patients treated under current clinical standards with acute CHF, stroke syndromes and systemic infection.
2. Describe the clinical outcomes for differing hemodynamic profiles and the respective changes in these profiles over the 4 hour observation period in these 3 acute disease states.

PREMIUM Registry

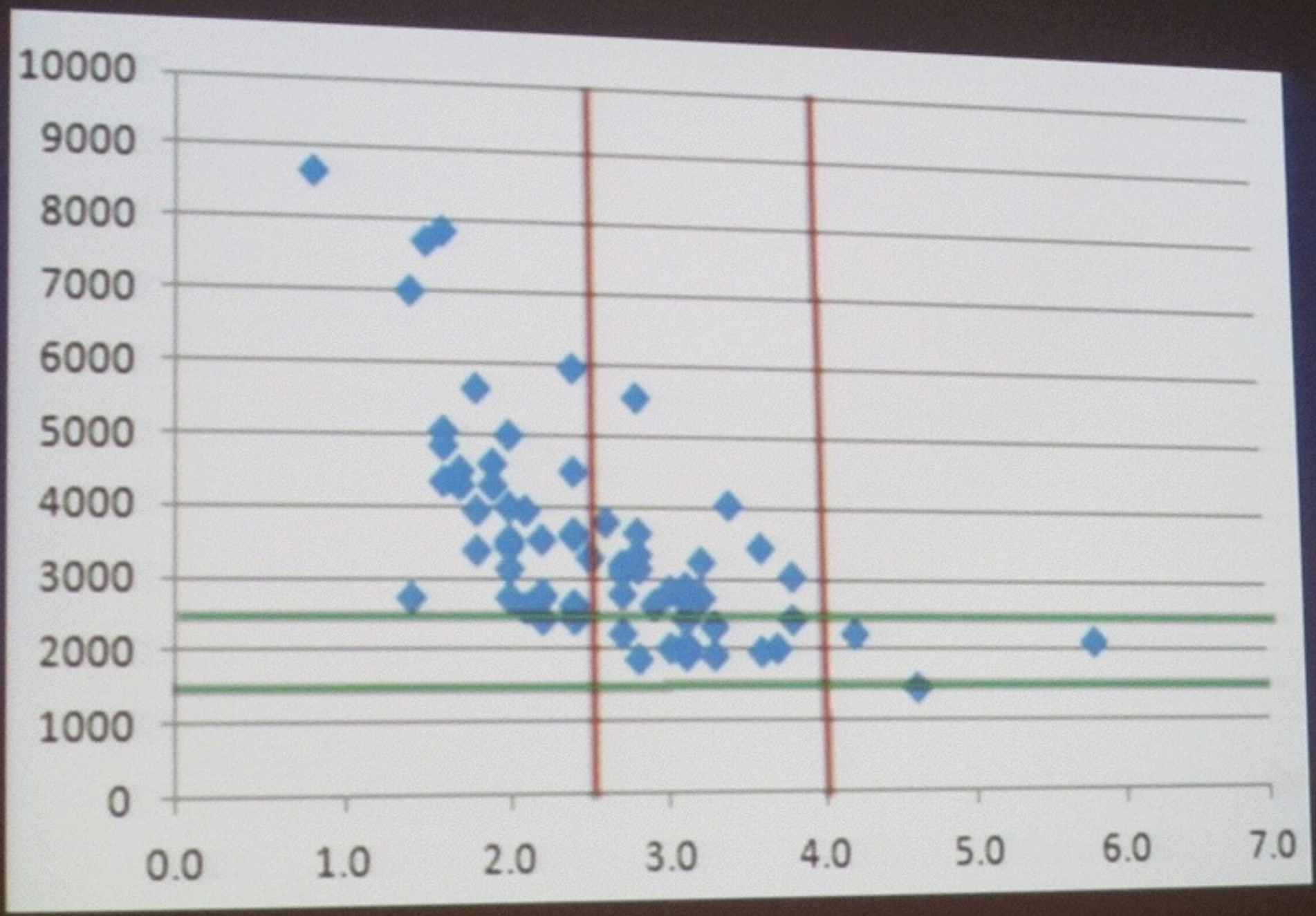
Study Groups

Choose One Group:	Inclusion Criteria	'Yes'	No
☐ CHF	Recurrent or worsening (**within 3 days**) shortness of breath (SOB) as the primary presenting complaint.	☐	☐
	Initial impression by treating physician that the worsening SOB is most likely caused by decompensated CHF.	☐	☐
	Known history of physician diagnosed CHF	☐	☐
	Natriuretic peptide (BNP, MR-pro ANP, NT pro BNP) level *will be* ordered by the treating physician as part of the patient's work up.	☐	☐
☐ **Stroke** NIH Stroke Scale ☐☐ (upon arrival) (NO 'blank', 00-42)	Onset of abnormal neurological symptoms consistent with possible stroke, within the prior **24 hours**, as the primary ED complaint.	☐	☐
	Initial treating ED physician impression that the abnormal neurological symptoms/signs are most likely caused by an acute stroke syndrome.	☐	☐
	Non-contrast head CT *will be* ordered by the treating physician as part of the patient's work up.	☐	☐
☐ **Systemic Infection**	Any combination of acute (**within 3 days**) symptoms or signs that the treating ED physician, after initial hx & physical exam, attributes to a systemic infection	☐	☐
	Blood Cultures and/or a blood lactate *will be* ordered by the treating physician as part of the patient's work up.	☐	☐

Presenting Averaged 15 Min Hemodynamic Variables

Variable	AHF (n=183) Mean ± SD (Min, Max)	SEPSIS (n=194) Mean ± SD (Min, Max)	STROKE (n=130) Mean ± SD (Min, Max)	p-value
Systolic BP	125.7 ± 29.1 (55.9, 233.2)	115.6 ± 28.4 (39.1, 233.2)	142.8 ± 30.6 (76.2, 240.8)	**<0.0001**
Diastolic BP	69.5 ± 16.0 (32.5, 114.3)	65.0 ± 13.4 (31.8, 106.6)	78.0 ± 16.5 (44.6, 142.1)	**<0.0001**
Mean BP	89.4 ± 19.5 (43.9, 154.9)	84.3 ± 18.4 (39.8, 152.1)	102.4 ± 20.6 (57.1, 178.4)	**<0.0001**
Cardiac Output	5.4 ± 1.9 (1.1, 12.3)	6.5 ± 2.0 (0.9, 11.7)	5.5 ± 2.1 (2.0, 12.6)	**<0.0001**
Heart Rate	83.0 ± 17.6 (47.4, 144.6)	96.6 ± 18.5 (41.7, 159.0)	77.6 ± 15.6 (44.4, 117.8)	**<0.0001**
Stroke Volume	67.0 ± 23.9 (13.1, 155.1)	68.5 ± 22.5 (11.5, 141.4)	70.7 ± 22.8 (22.4, 132.1)	0.3737
Systemic Vascular Resistance	1483.7 ± 613.7 (660.6, 5216.8)	1172.1 ± 618.4 (525.6, 6173.9)	1787.6 ± 927.4 (630.7, 7235.5)	**<0.0001**
Dp/dt	875.3 ± 425.3 (204.5, 2330.5)	953.7 ± 477.1 (134.1, 3029.1)	967.5 ± 426.1 (160.4, 2499.8)	0.1225

Initial SVRI v CI in CHF Patients



SVRI

CI

Acute CHF Individualized Therapy Based on Initial ED Hemodynamic Profile

	SVRI Low	SVRI Normal	SVRI High
CI Low	? Fluids ? Inotropes	Vasodilators ? Inotropes ? Diuretics	High dose vasodilators
CI Normal	? Fluids ? Inotropes	Vasodilators ? Diuretics	High dose vasodilators
CI High	Consider high output CHF	Consider high output CHF	?

To also be done for sepsis and stroke groups, suspected and confirmed disease

Case A035 CHF (ED Course)

- 65 yr old AA male presented with SOB/chest pain
  Hx of CHF, ETOH abuse, hyperlipidemia

- BP 154/70, HR 94, RR 20, O2 Sat 96%
  Lungs reported clear, no peripheral edema

- BNP 1258, Trop 0.06, BUN 11, Creat 1.1
  Chest xray: borderline cardiomegaly and CHF

- Given lasix 20 mg IV with 1 L urine output
  Admitted to telemetry for acute CHF

Case A035 CHF (Hospital Course)

- ECHO day 2: EF 15%. Patient not improving: Day 3 had R & L cardiac cath showing normal filling pressures, severely decreased CI (1.48) and increased SVR with non ischemic cardiomyopathy

- Transferred to the CICU

  Treated with after load (Nipride) reduction as BP would tolerate

- 5 days later returned to GPU, discharged after 11 days IPD

ED Hemodynamic Assessment Future

The PREMUIM Registry evaluation is a work in progress: Additional predictive analyses

Confirmed (not just suspected) diagnoses

Changes in hemodynamic profiles over time/with therapy and final ED profile

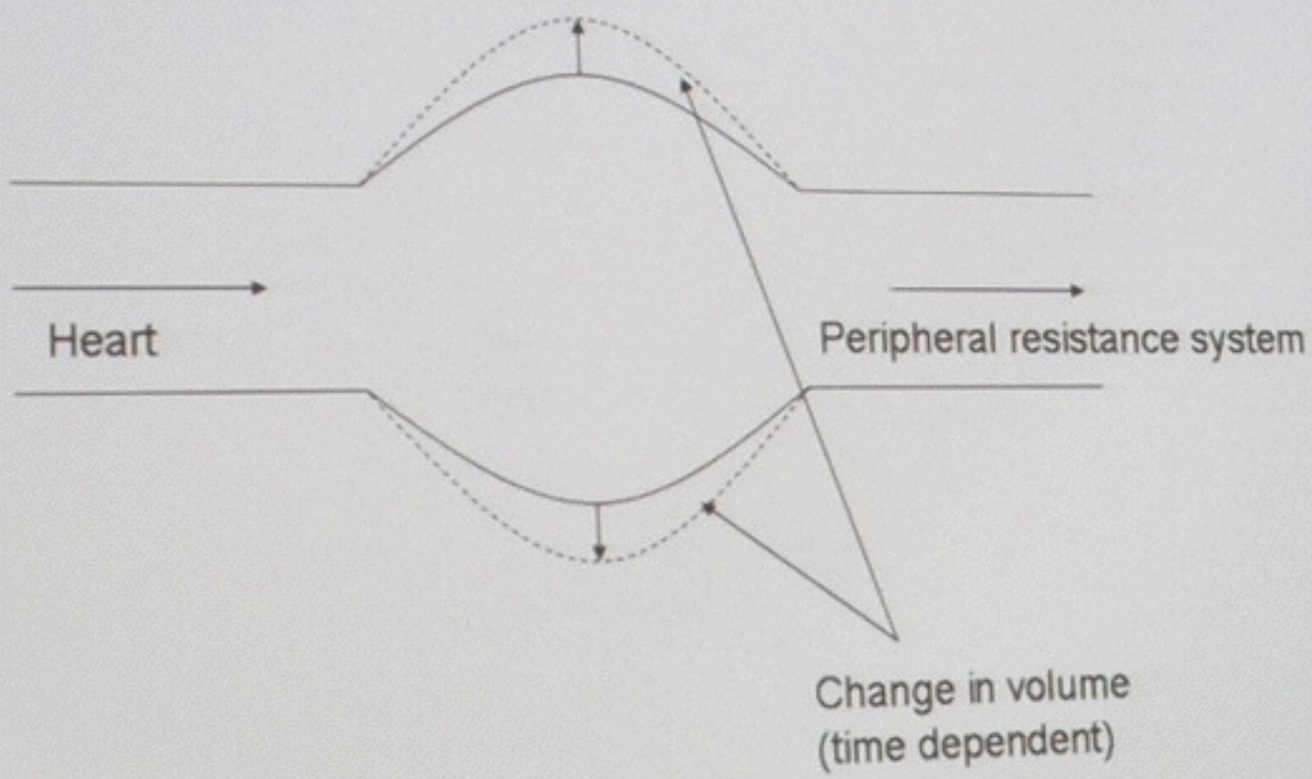
Determine the additive predictive value of profiling to conventional VS and other clinical assessments

Use of profiles to distinguish amongst different diseases with similar clinical presentations

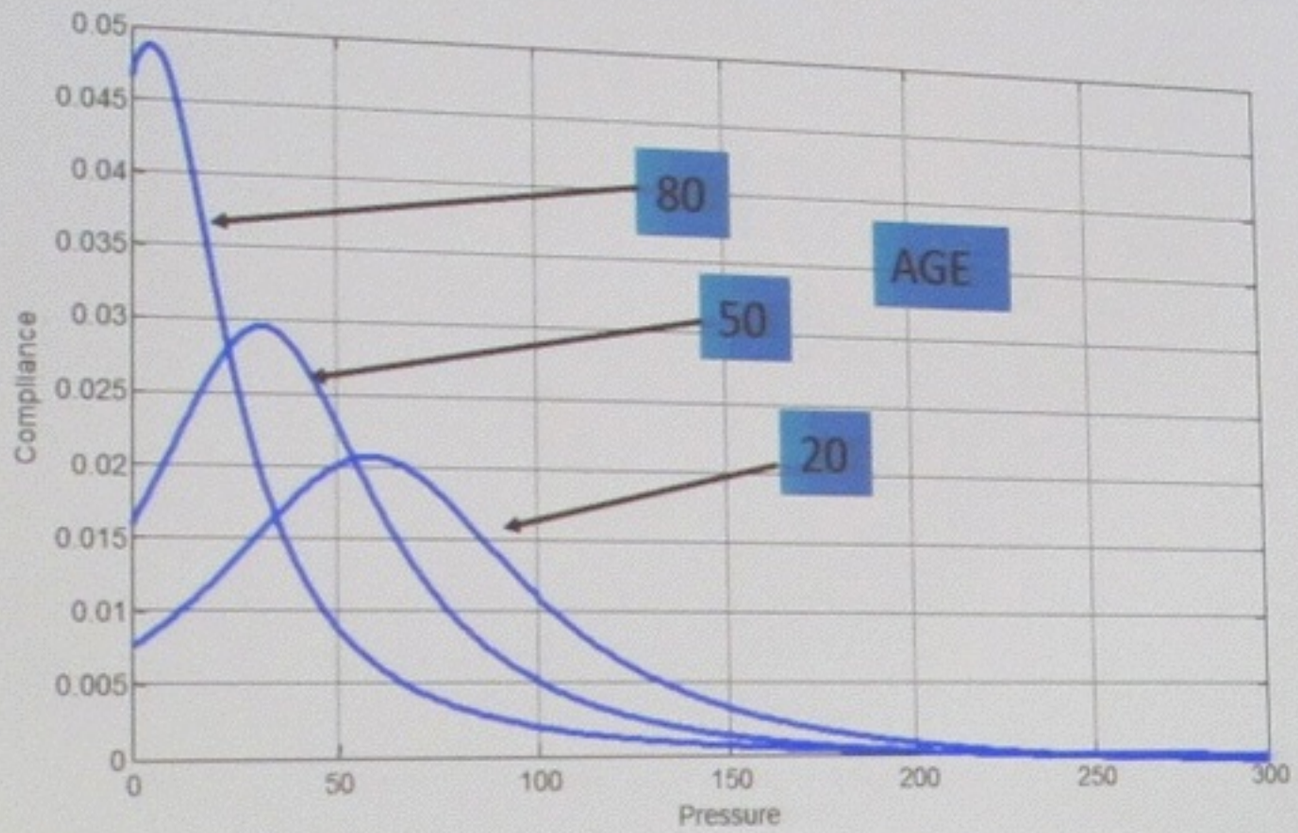
Consider therapeutic trial guided by hemodynamic profiling using the GREAT network (Rome, Italy)

Relationship between Flow and Pressure

Flow waves
≠
Pressure Waves

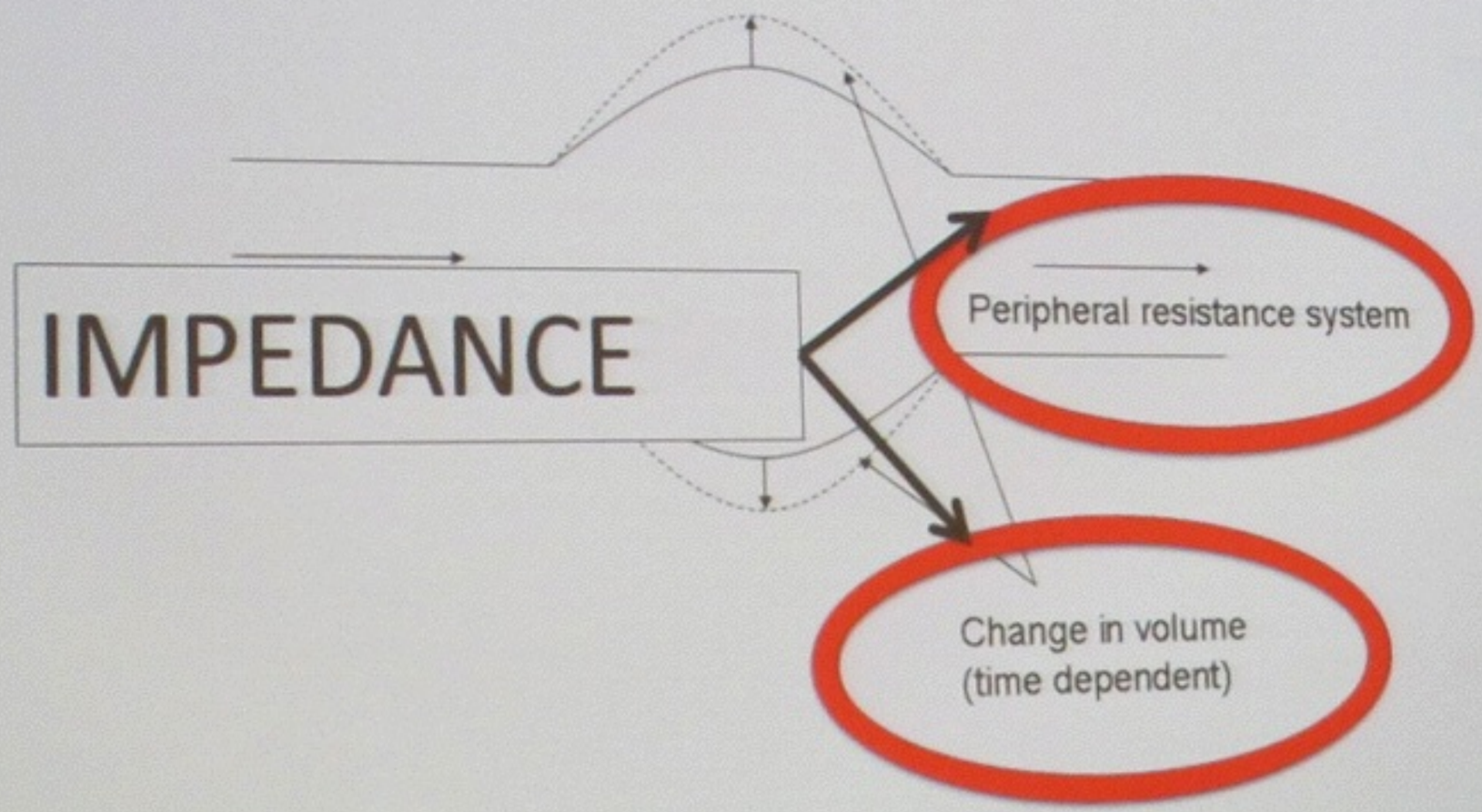


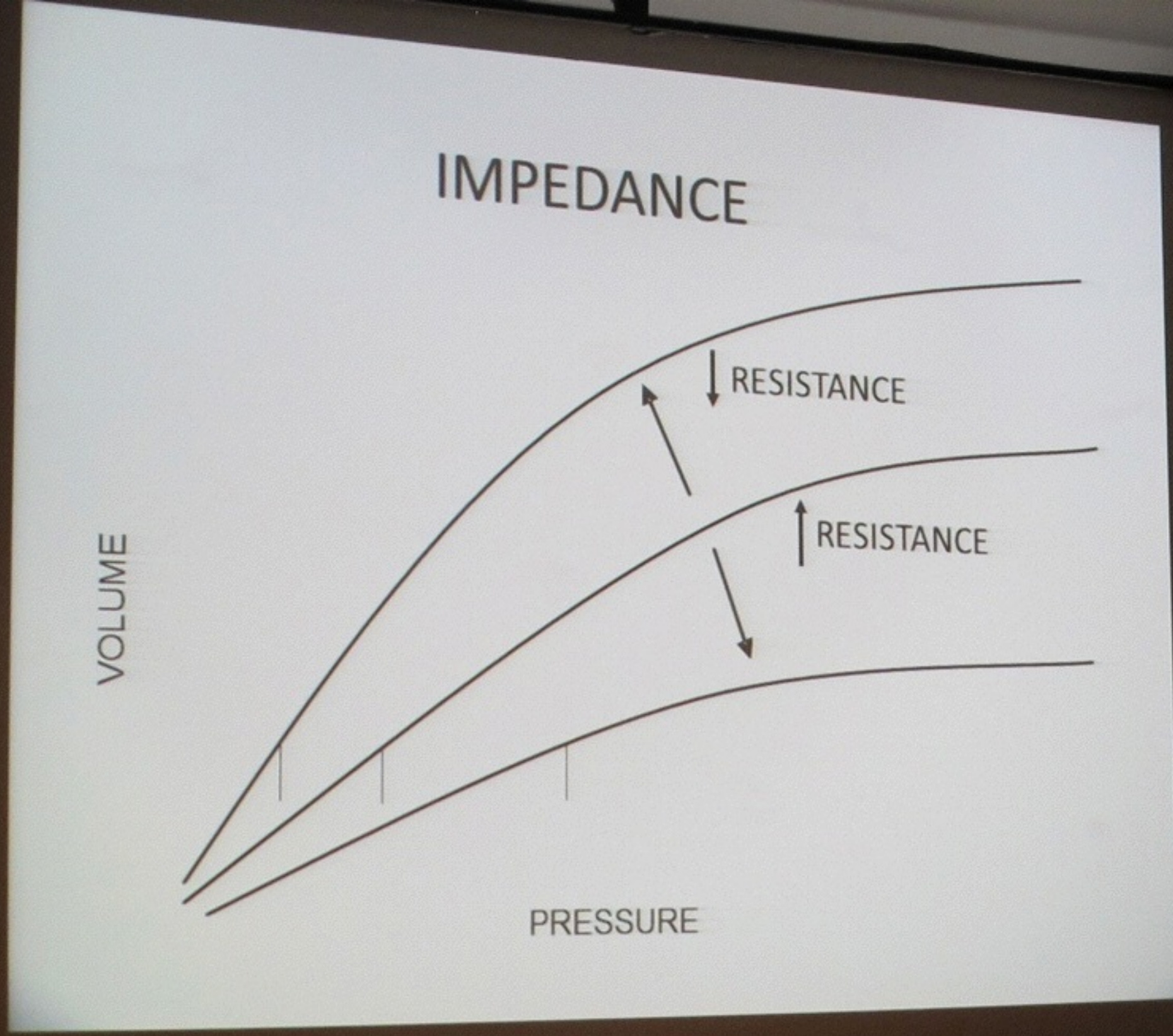
Change of Arterial Compliance with Age



Langouwouters J Biomechan 1984

Relationship between Flow and Pressure



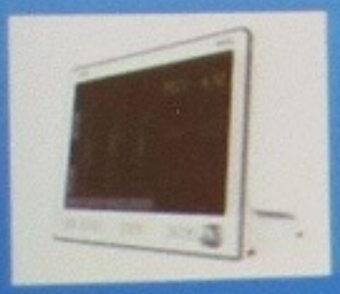

IMPEDANCE
RESISTANCE
RESISTANCE
VOLUME
PRESSURE

- PiCCO*plus* and PiCCO2 *(Pulsion, Munich, Germany),*
- *LiDCOTMplus and* LiDCOTMrapid *(LidCO, Cambridge, UK),*
- *Flotrac Vigileo, EV1000 (Edwards Lifesciences, Irvine, USA)*
- MostCare PRAM (Vytech, Padova, Italy)

EV1000

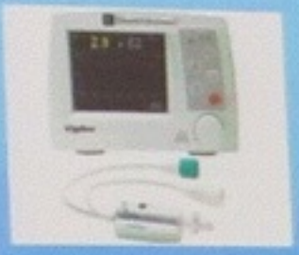
LiDCO*plus*

PiCCO2



CALIBRATED

Vigileo



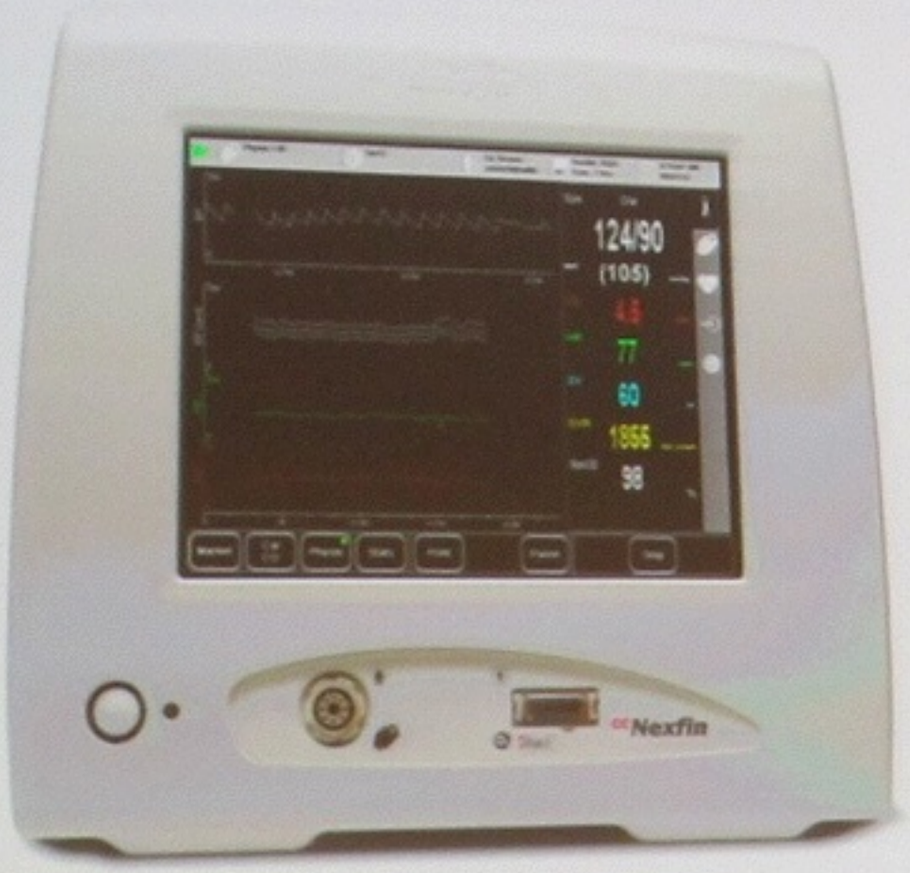
MostCare

LiDCO*rapid*

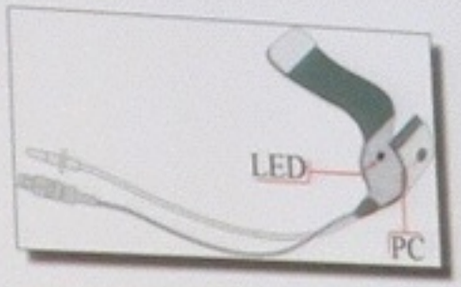
UNCALIBRATED

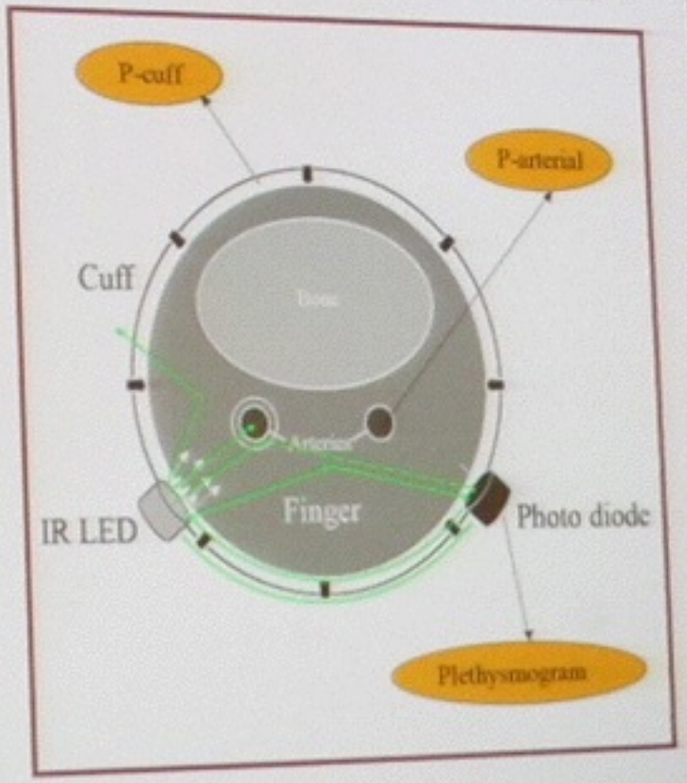
1. Measurement of continuous beat-by-beat finger BP

Volume Clamp Technology



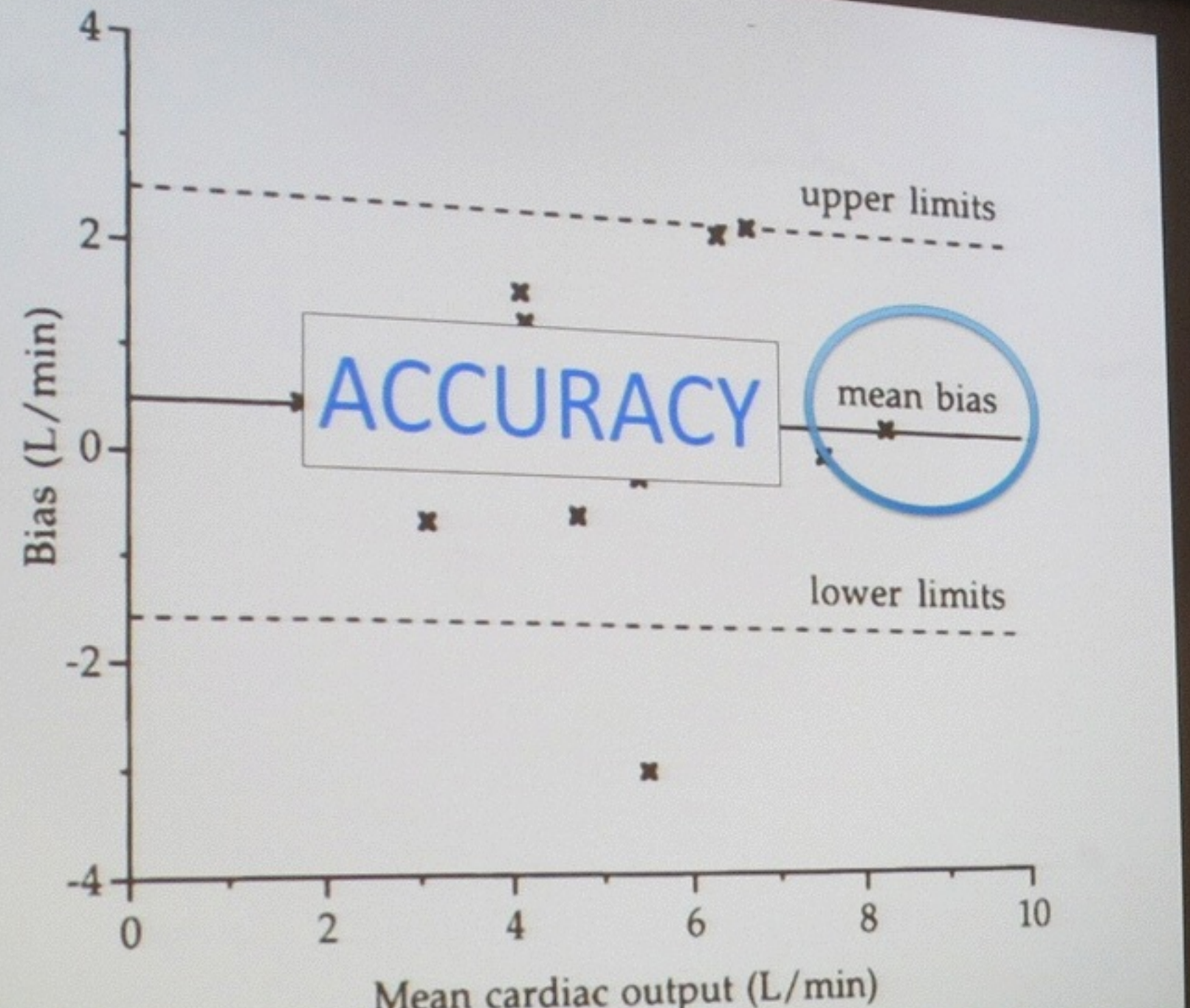
ccNexfin



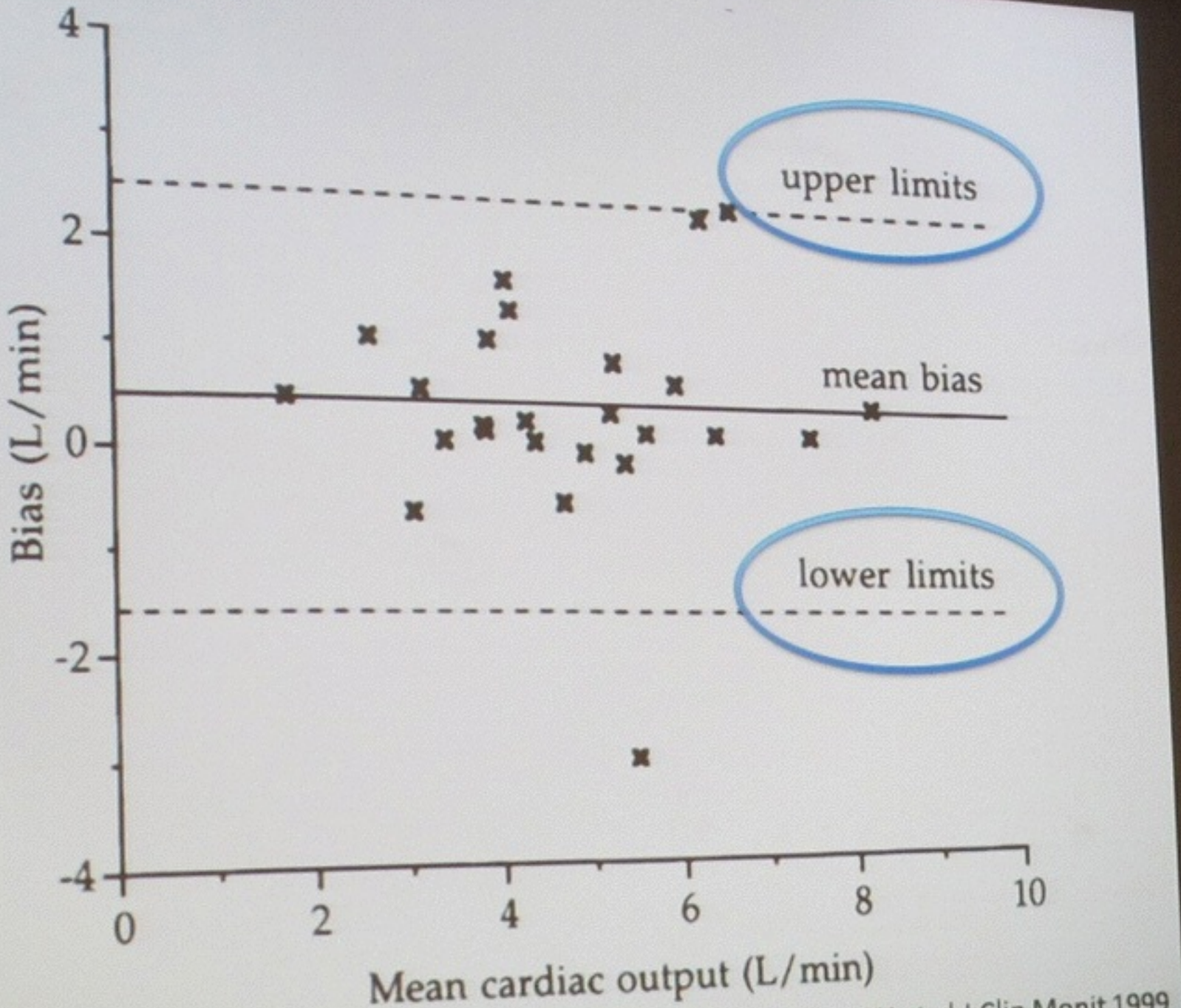


Azriel Perel 2011

Author	Setting	Technique Compared	Bias L/min	Percentage Error %
Broch O et al (120)	Cardiac Surgery	PiCCO	-0.1	23
Broch O et al (120)	Cardiac Surgery	PiCCO	-0.1	26
Fischer M.O et al (119)	Critical Care	PiCCO	n.r	50
Monet X et al (116)	Critical Care	PiCCO	0.2	57
Peetermans M et al (122)	Critical Care	PiCCO	0.7	58
Peetermans M et al (122)	Critical Care	PiCCO	0.01	29
Stover JF et al (118)	Critical Care	PAC	0.23	29
Van de Vivier K et al (117)	Critical Care	PiCCO	0.4	36
Van de Vivier K et al (117)	Critical Care	PiCCO	0.2	37
	Mean		**0.25**	**36**

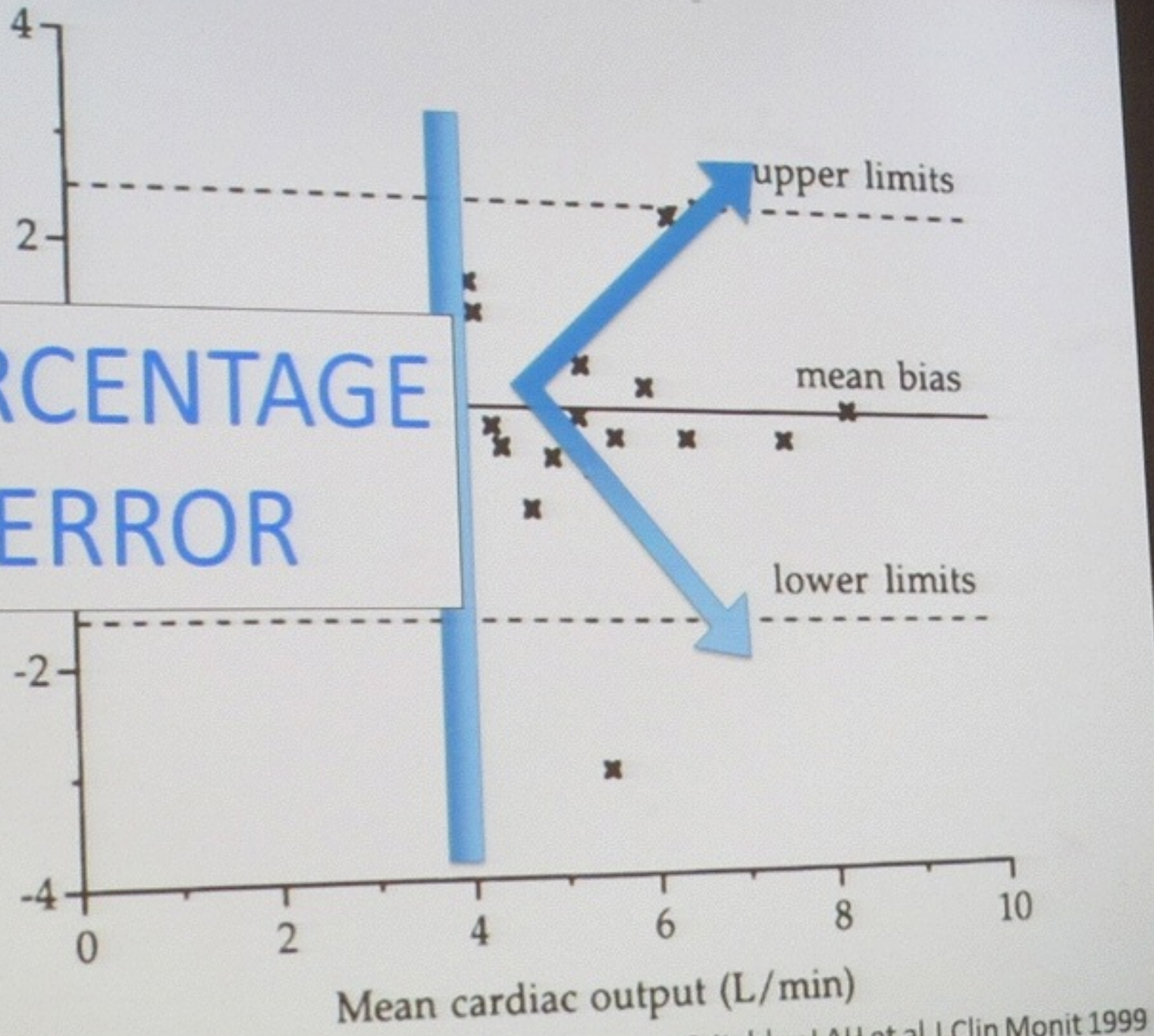


Critchleyy LAH et al J Clin Monit 1999



Critchleyy LAH et al J Clin Monit 1999

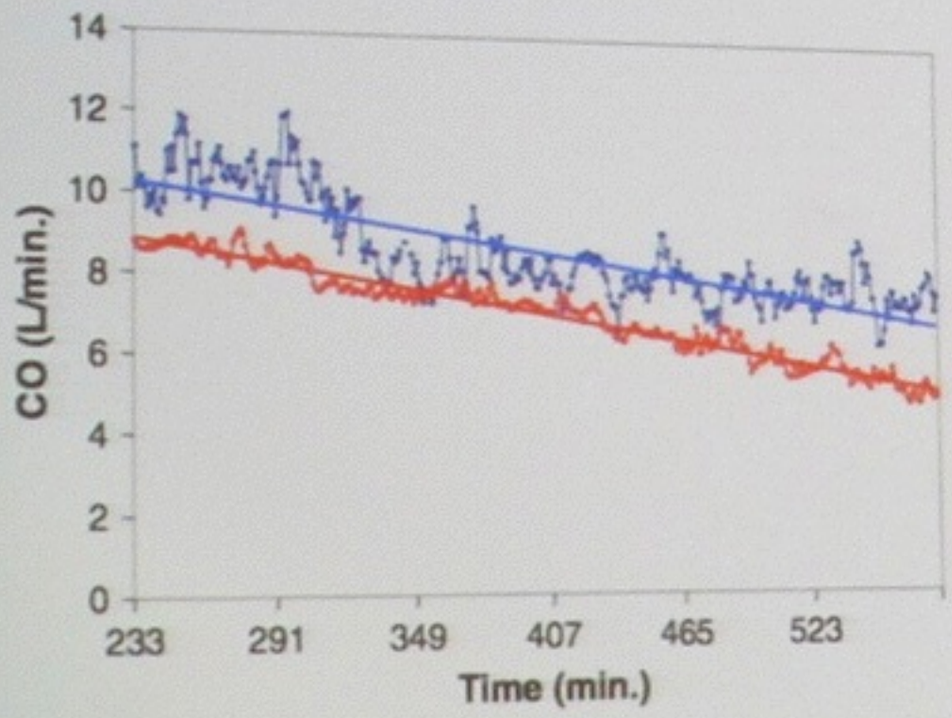
PERCENTAGE ERROR

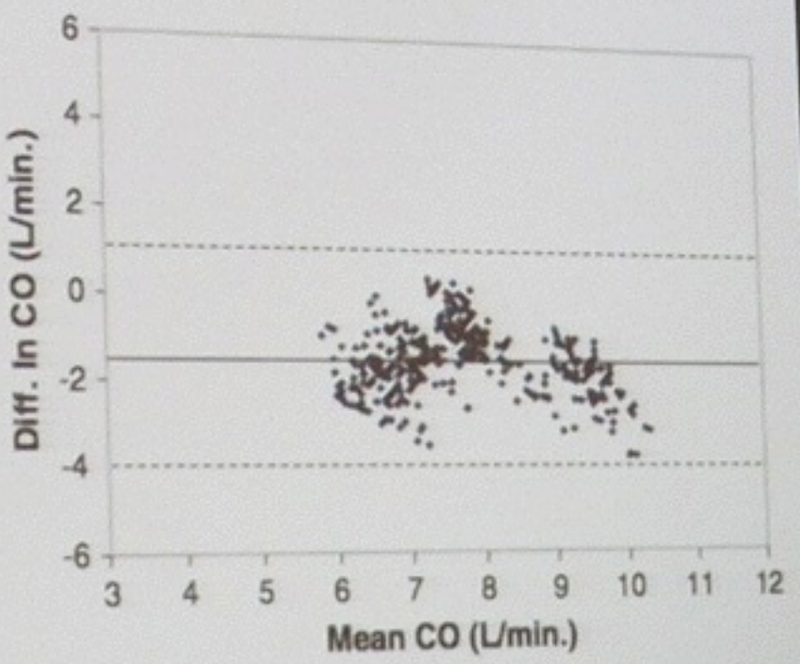


Critchley LAH et al J Clin Monit 1999

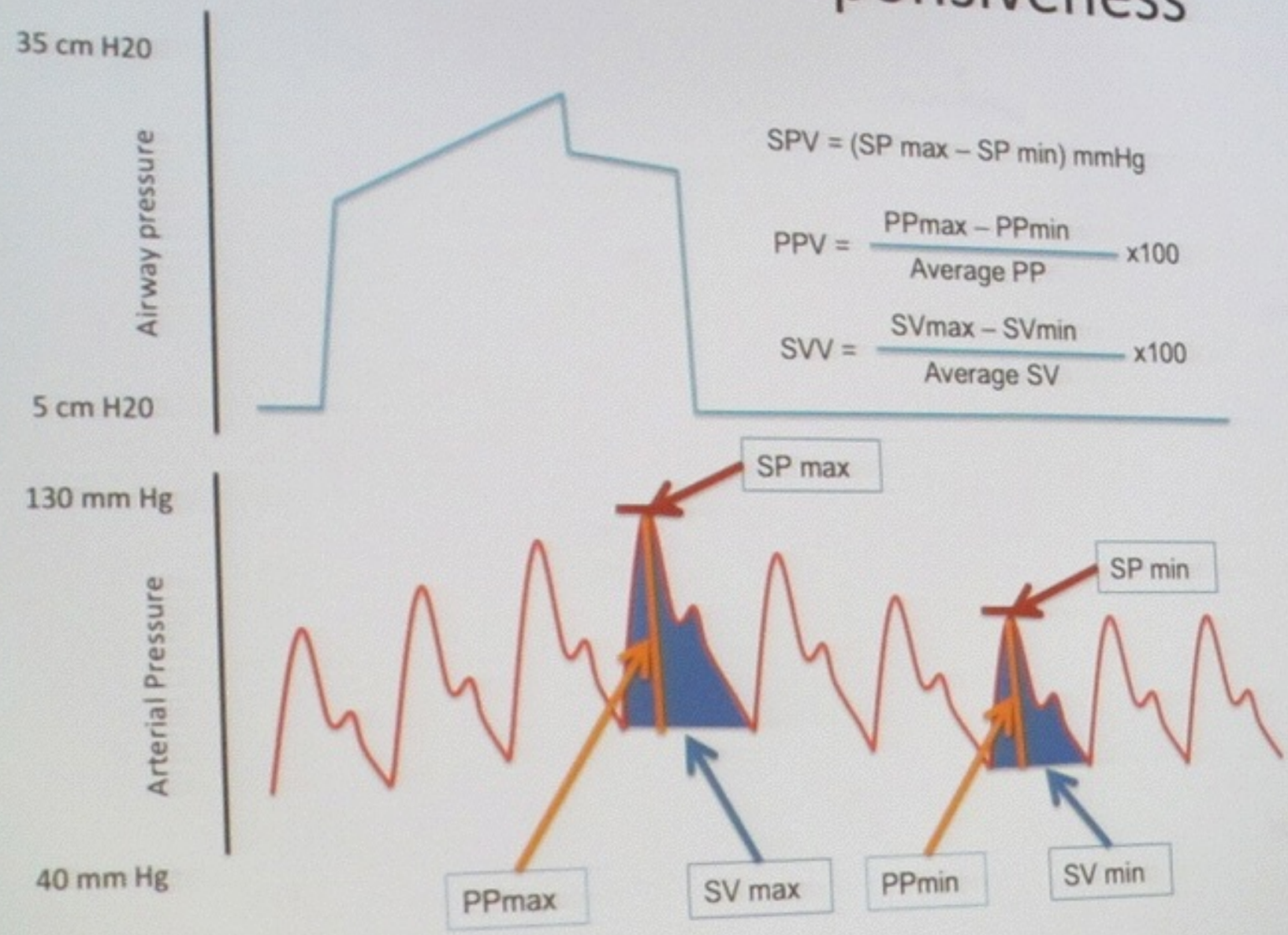
Tracking Changes in Cardiac Output: Methodological Considerations for the validation of monitoring devices

Pierre Squara, Maurizio Cecconi, Andrew Rhodes, Mervyn Singer, Jean-Daniel Chiche
ICM 2009

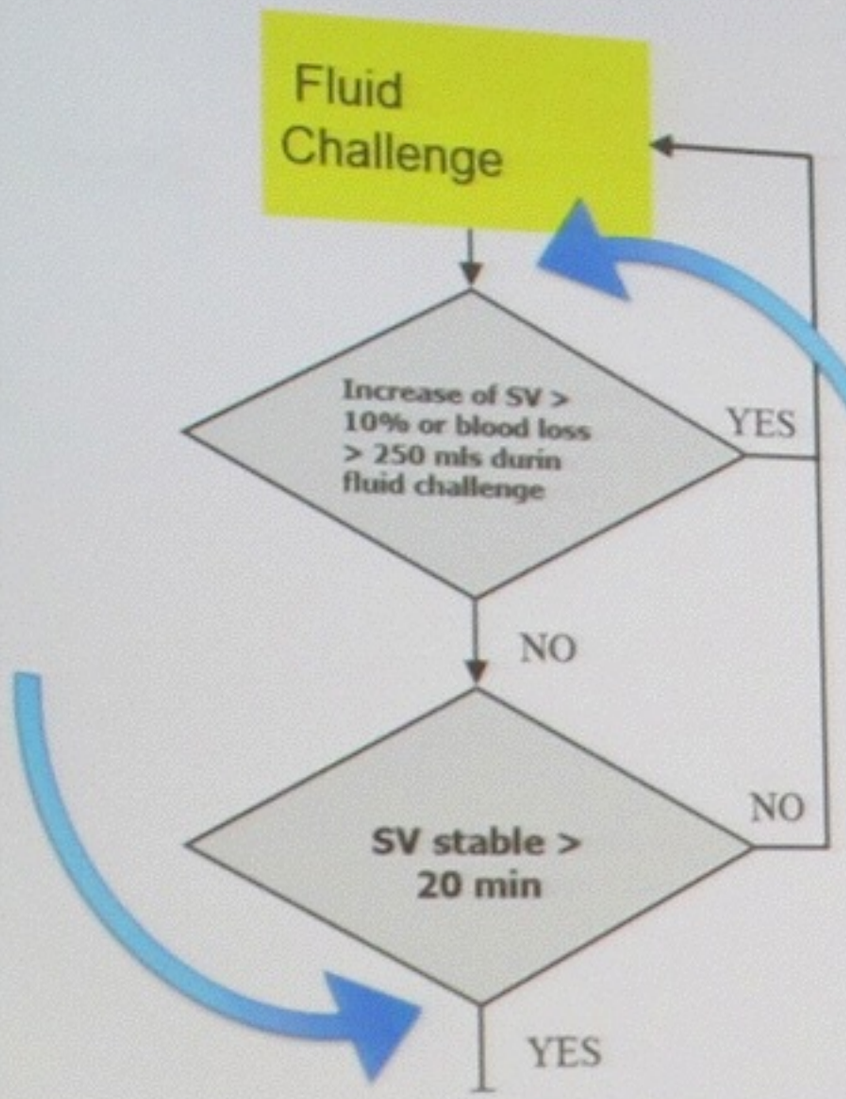


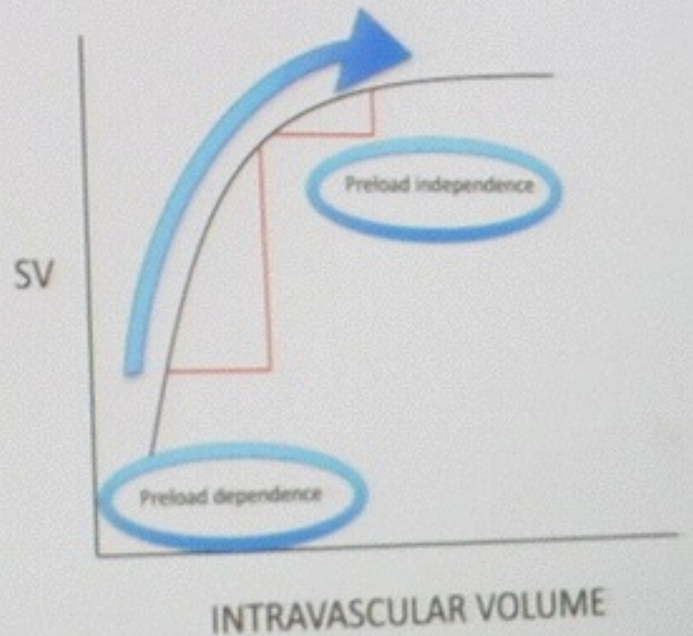


Prediction of Fluid Responsiveness



SV OPTIMISATION





The estimation of cardiac output by the Nexfin device is of poor reliability for tracking the effect of a fluid challenge

Xavier Monnet, Fabien Picard, Elsa Lidzborski, Malcie Mesnil, Jacques Duranteau, Christian Richard and Jean Louis Teboul

Crit Care 2012

Critically Ill Patients

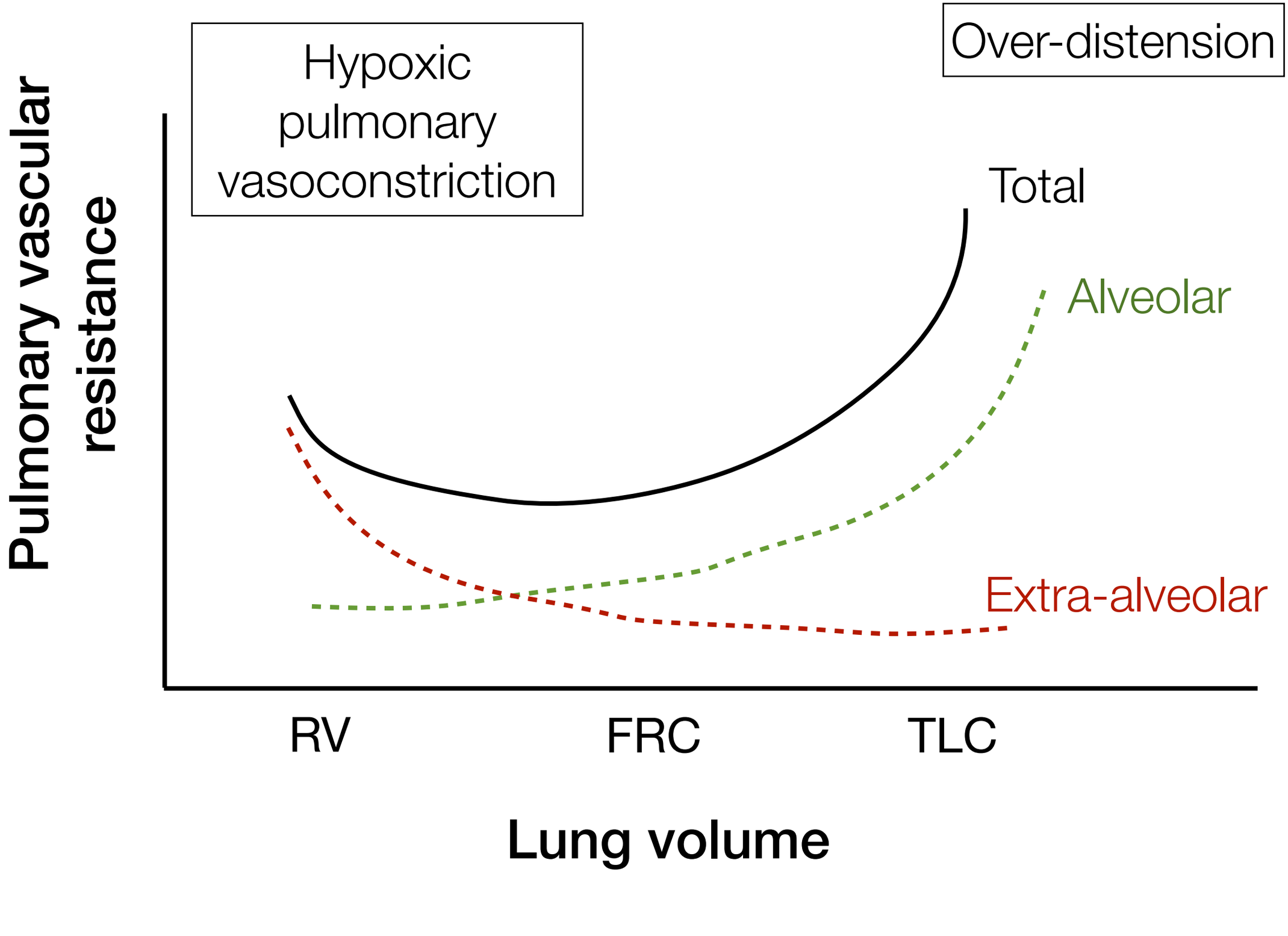
Nexfin vs PiCCO

Comparison during Fluid Challenge

Absolute values

Trend Analysis

Lung volume and PVR



Afterload induced RV failure

Pulmonary hypertension

1) thrombolytic therapy, iNO, FRC, pH, hypoxaemia, PGI_2, low tidal volumes

Increased contractility

2) Dobutamine, noradrenaline, levosimendan

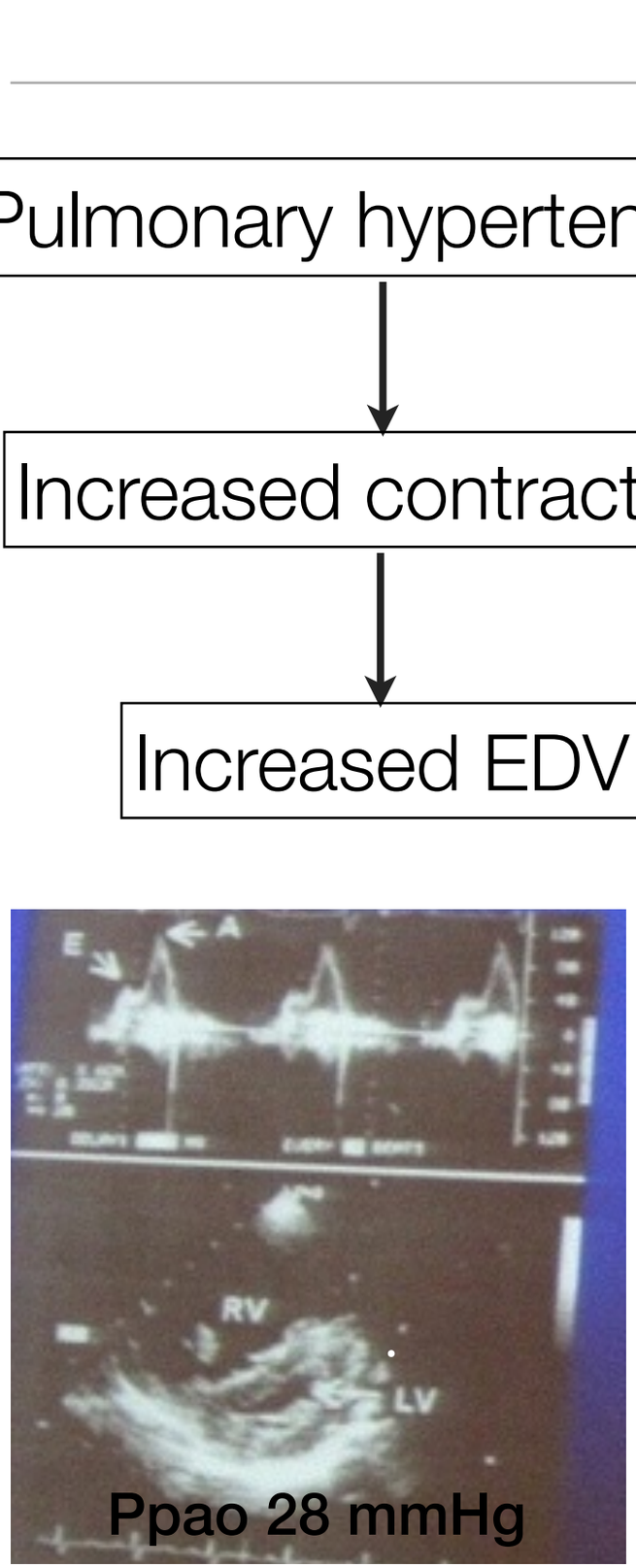
Increased EDV

diastolic failure

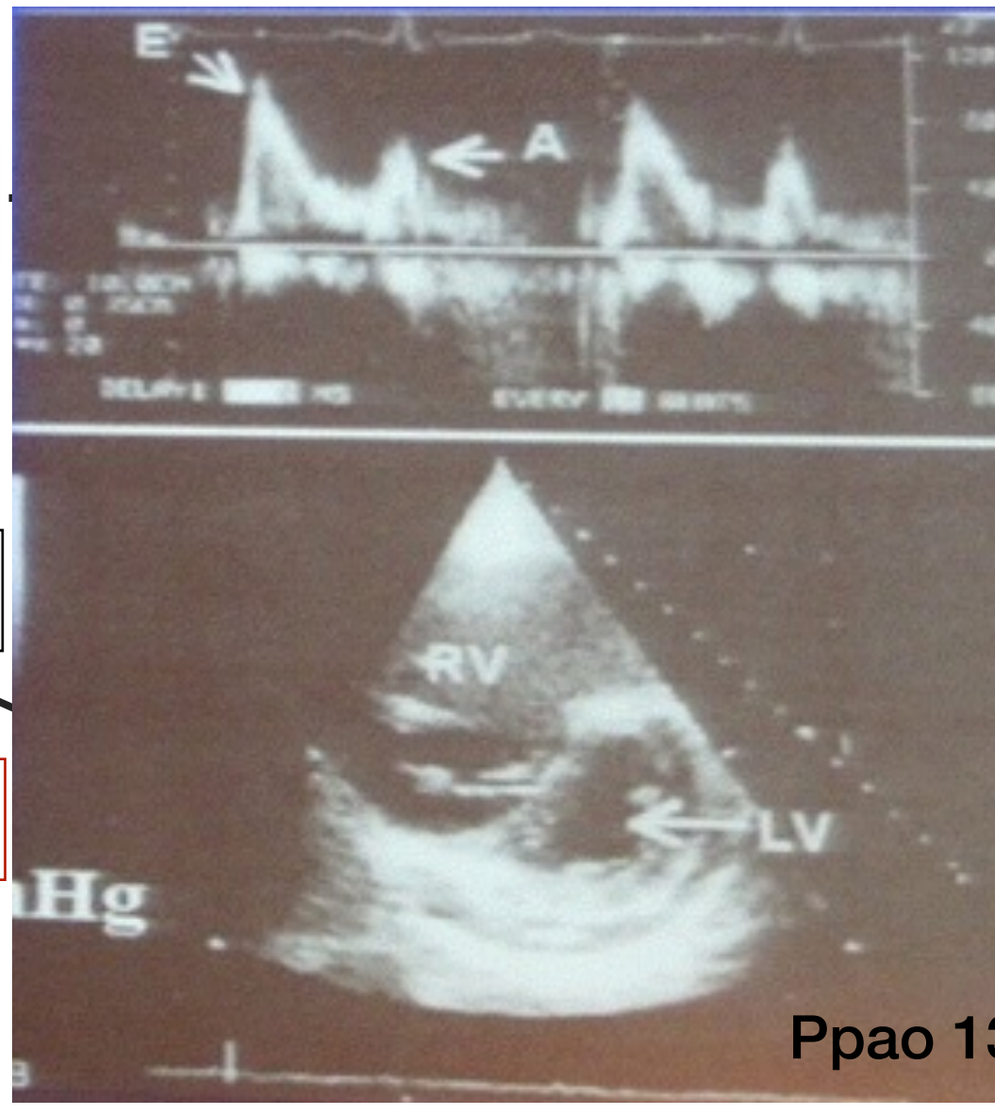
3) Diuretics

systolic failure

4) Noradrenaline

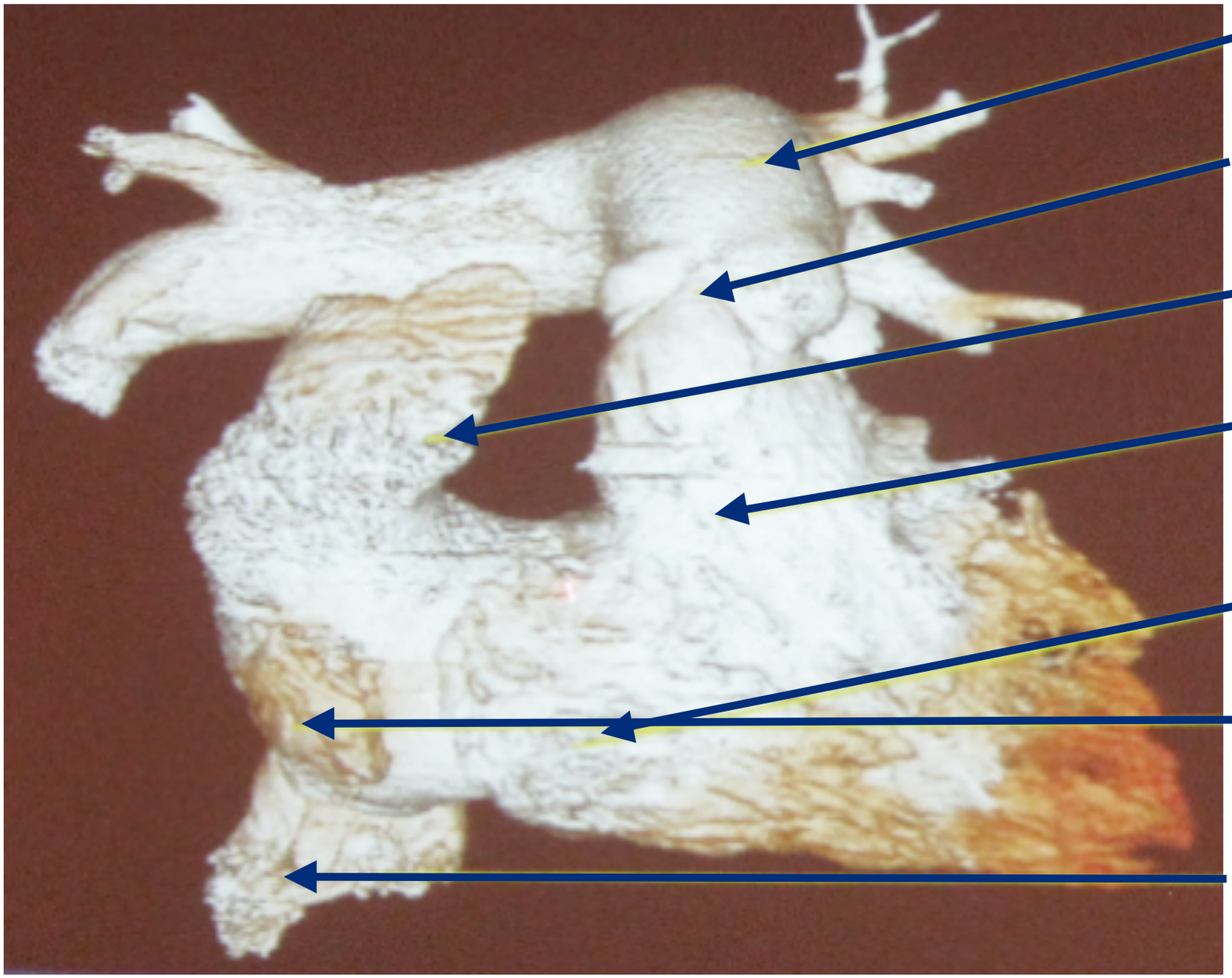


Ppao 28 mmHg

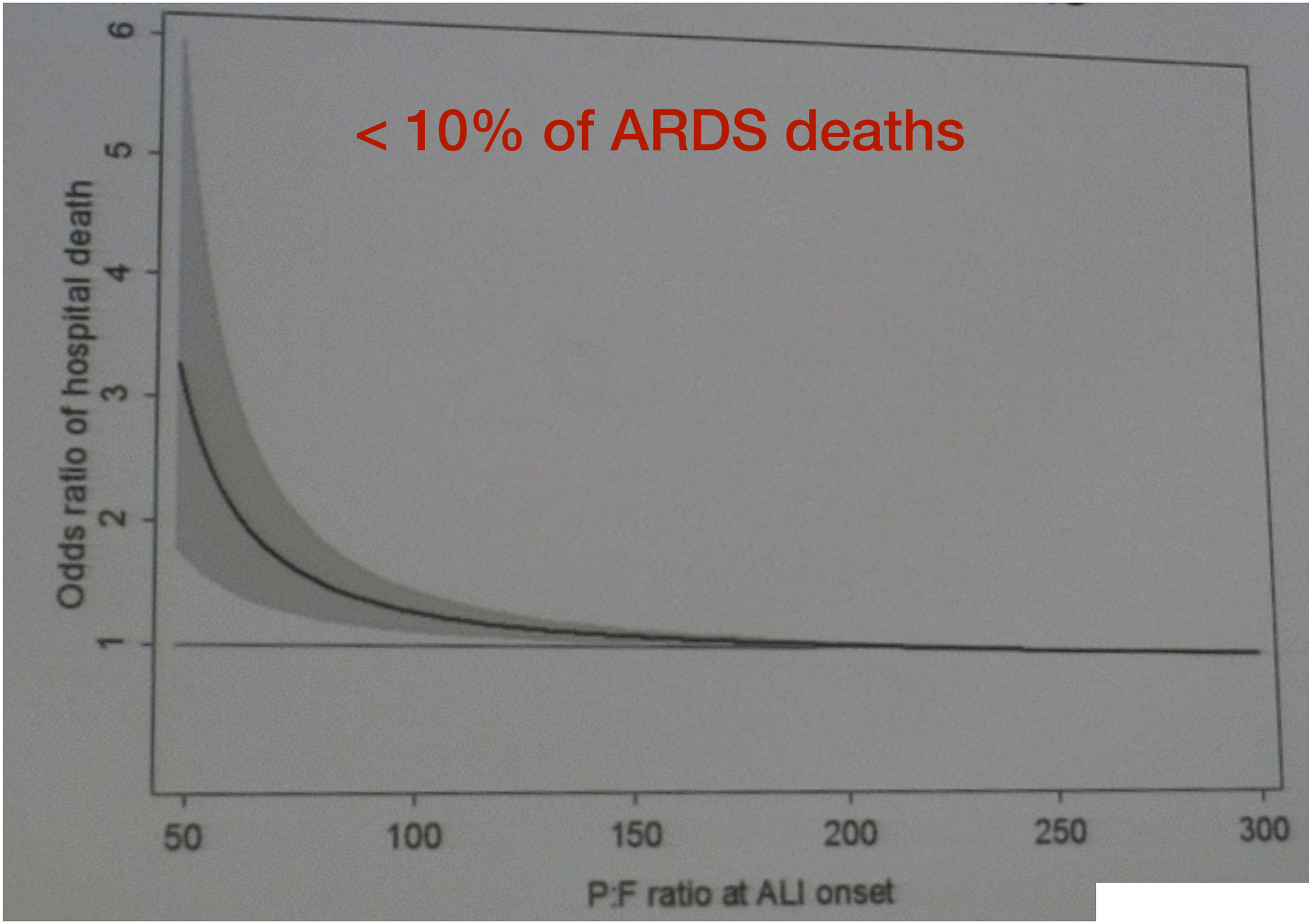


Ppao 13

Anatomy of the Right Ventricle



Hypoxaemia associated with increased mortality but a rare cause of death



Montgomery et al ARRD 1985; 146:486 Estenssorro et al CCM 2002; 30:2450 Stapleton et al Chest 2005; 128:525

What is the attributable mortality/morbidity of refractory hypoxaemia

- Unclear
- Rare cause
- Associated with some cognitive abnormalities after critical illness in 1 study
- Hypoxaemia associated with cognitive abnormalities in other diseases but causal link unclear

Permissive hypoxemia?

0090-3493/84/1201-0075$02.00/0
CRITICAL CARE MEDICINE

Vol. 12, No. 1
Printed in U.S.A.

Severe hypoxemia without evidence of tissue hypoxia in adult respiratory distress syndrome

TJØSTOLV LUND, MD; MAI-ELIN KOLLER, MD, PhD; JOHAN KOFSTAD, MD

CHEST

Official publication of the American College of Chest Physicians

Permissive Hypoxemia : Is It Time To Change Our Approach?

Mohamed Abdelsalam

Chest 2006;129;210-211

Is permissive hypoxemia (SaO2 8X%-90%) safe and even beneficial in ARDS?

- Respiratory acidosis from hypercapnia shifts oxygen dissociation to promote tissue unloading
- Hyperoxia may be harmful
  - Increases infarct size after MI
  - Worsens outcome after cardiac arrest
- Hypoxic and ischemic preconditioning causes hypoxia-inducible factors and enhances stem cell production

Heart. 2009 Mar;95(3):198-202
Crit Care. 2010; 14(4): 315

What are the treatment options for refractory hypoxemia?

- Rule out readily reversible causes
  - Mucus plugging/lobar collapse
  - Pneumothorax
  - Systemic vasodilators enhancing shunt
  - Pulmonary embolism
  - Intra-cardiac R > L shunt
  - Circulatory collapse (low SvO2)
- Recruitment and ventilator interventions
- Pharmacologic
- ECLS
- Permissive hypoxemia

"Stable" mechanically ventilated patients have 5-7% variation in PaO2

Higher % variation in hypoxemic patients

Variability of Arterial Blood Gas Values Over Time in Stable Medical ICU Patients*

Chest 1994; 106:187-93

Scott A. Sasse, M.D.; Priscilla A. Chen, M.D.; and Cornelis K. Mahutte, M.D., Ph.D., F.C.C.P.

Y.-H. Tsai
M.-C. Lin
M.-J. Hsieh
N.-H. Chen
T.C.Y. Tsao
C.-H. Lee
C.-C. Huang

Spontaneous variability of arterial oxygenation in critically ill mechanically ventilated patients

Intensive Care Med (1999) 25: 37–43

Respiratory and cardiac cycle

Look for changes larger than this for signal from interventions

HFO: ineffective or harmful
but not tested in "refractory" hypoxemia

ESTABLISHED IN 1812 FEBRUARY 28, 2013 VOL. 368 NO. 9

PF<200
FiO2 0.60
PEEP 10

High-Frequency Oscillation in Early Acute Respiratory Distress Syndrome

Niall D. Ferguson, M.D., Deborah J. Cook, M.D., Gordon H. Guyatt, M.D., Sangeeta Mehta, M.D., Lori Hand, R.R.T., Peggy Austin, C.C.R.A., Qi Zhou, Ph.D., Andrea Matte, R.R.T., Stephen D. Walter, Ph.D., Francois Lamontagne, M.D., John T. Granton, M.D., Yaseen M. Arabi, M.D., Alejandro C. Arroliga, M.D., Thomas E. Stewart, M.D., Arthur S. Slutsky, M.D., and Maureen O. Meade, M.D., for the OSCILLATE Trial Investigators and the Canadian Critical Care Trials Group*

High-Frequency Oscillation for Acute Respiratory Distress Syndrome

PF<200

Duncan Young, D.M., Sarah E. Lamb, D.Phil., Sanjoy Shah, M.D., Iain MacKenzie, M.D., William Tunnicliffe, M.Sc., Ranjit Lall, Ph.D., Kathy Rowan, D.Phil., and Brian H. Cuthbertson, M.D., for the OSCAR Study Group*

Routine Approaches to Severe Hypoxemia

What about transfusion?
What about increasing cardiac output?

- DO2 directly proportional to Hgb
- Unfortunately, transfused blood is not 'normal'
- Transfusion from Hgb 7-9 to > 10 does not clearly improve (and may actually worsen) DO2
- Serum free hemoglobin may worsen VQ
- Do not 'routinely' transfuse patients above Hgb 7 just because they have refractory hypoxemia

Crit Care Med. 2004 Feb;32(2):364-71
JAMA. 1993 Jun 16;269(23):3024-9

UNIVERSITE DE GENÈVE

HUG Hôpitaux Universitaires de Genève

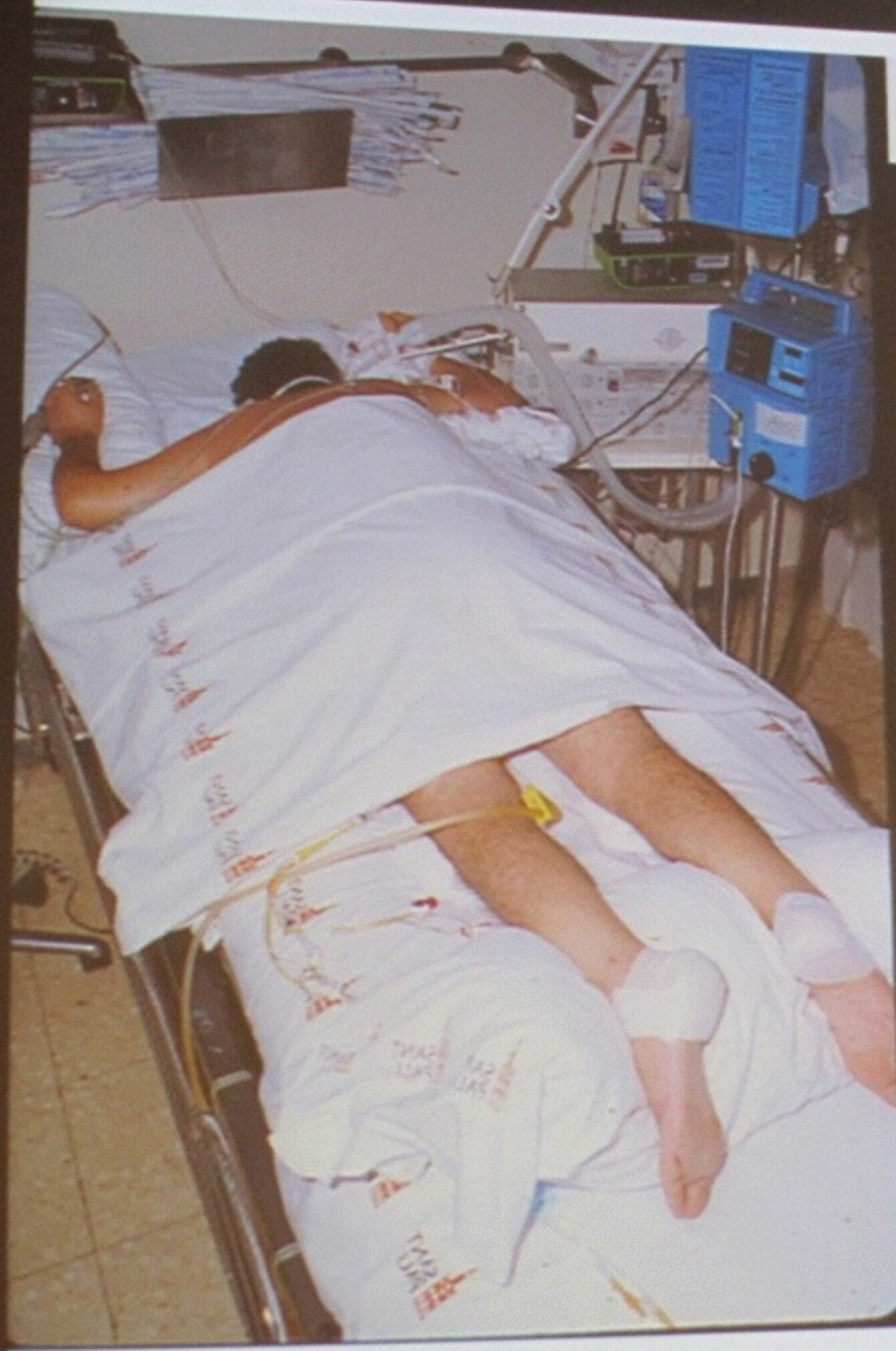
Salvage therapies in ARDS

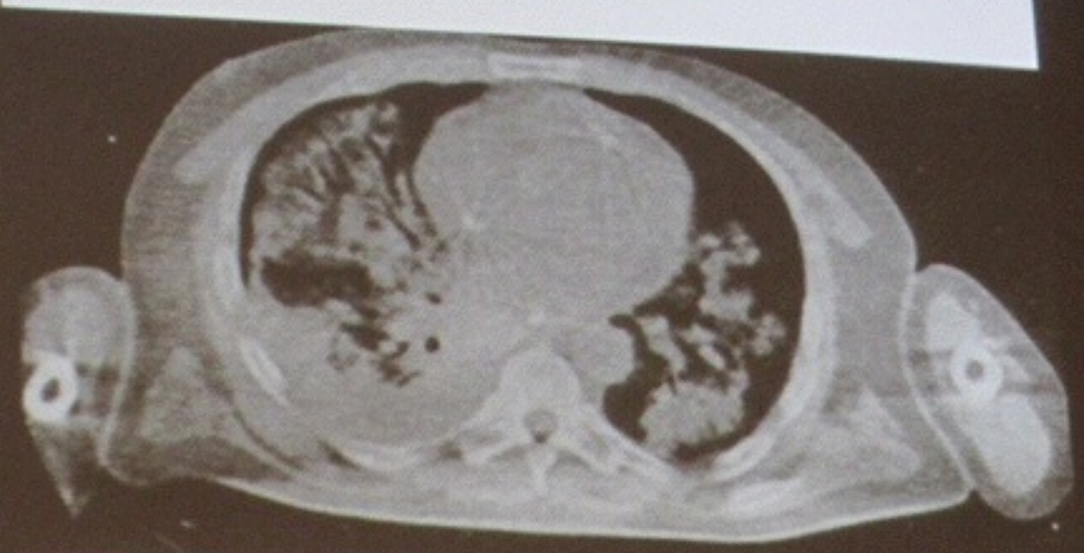
Prone positioning

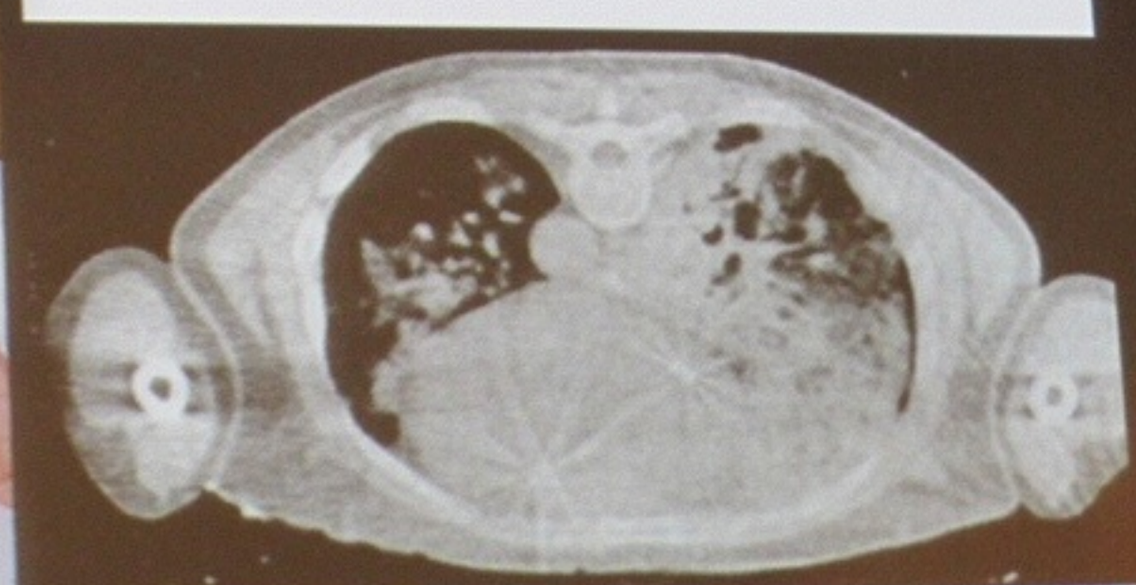
Laurent Brochard
ICU - Geneva

Réseau Européen de Ventilation Artificielle
REVA

ReVA

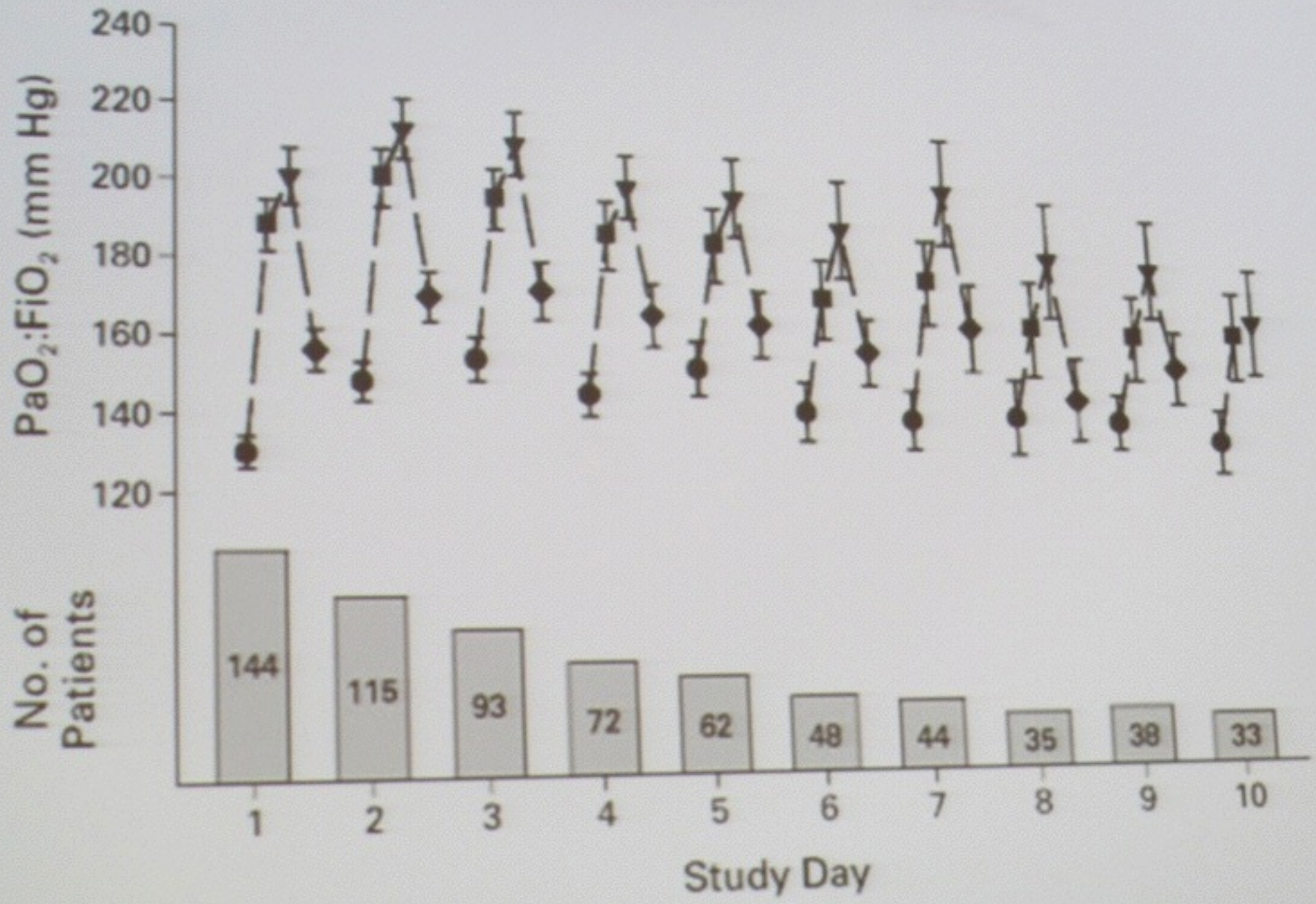






Gattinoni L, *et al*. Anesthesiology 1991;74:15-23

Gattinoni L, *et al*. NEJM 2001;345:568-73



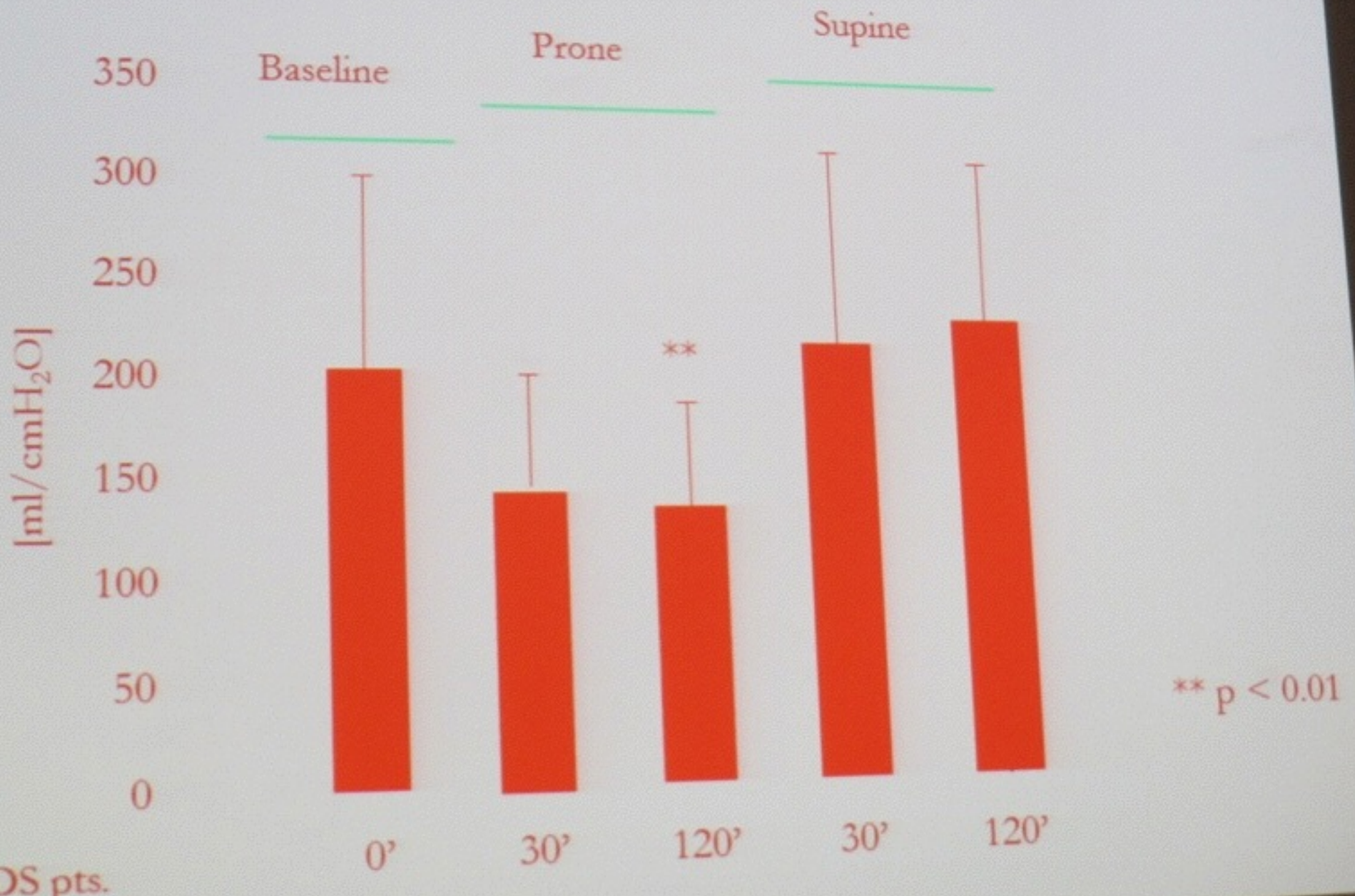
Chest wall compliance in prone

Pelosi P et al. *Am J Respir Crit Care Med* 1998;157:387-393

16 ARDS pts.

Chest wall compliance in prone

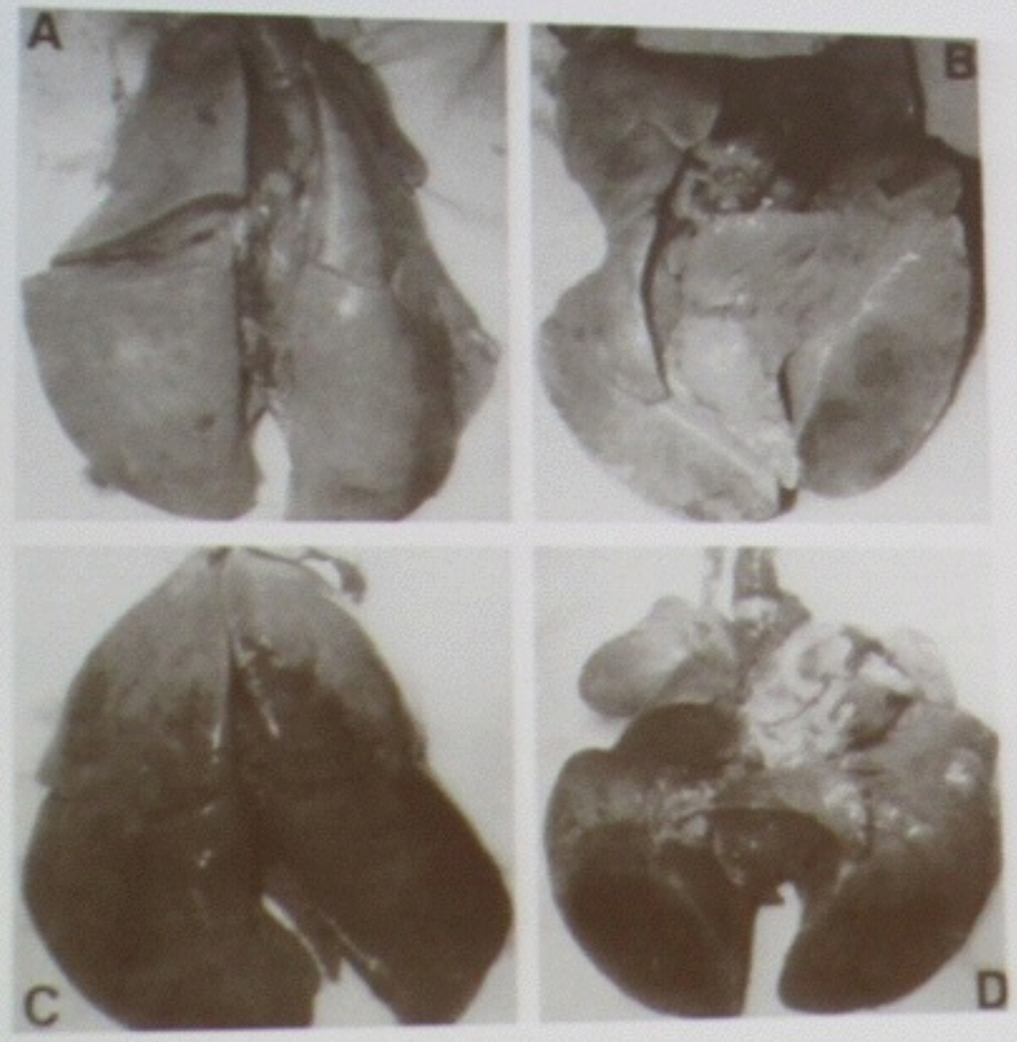
Pelosi P et al. *Am J Respir Crit Care Med* 1998;157:387-393



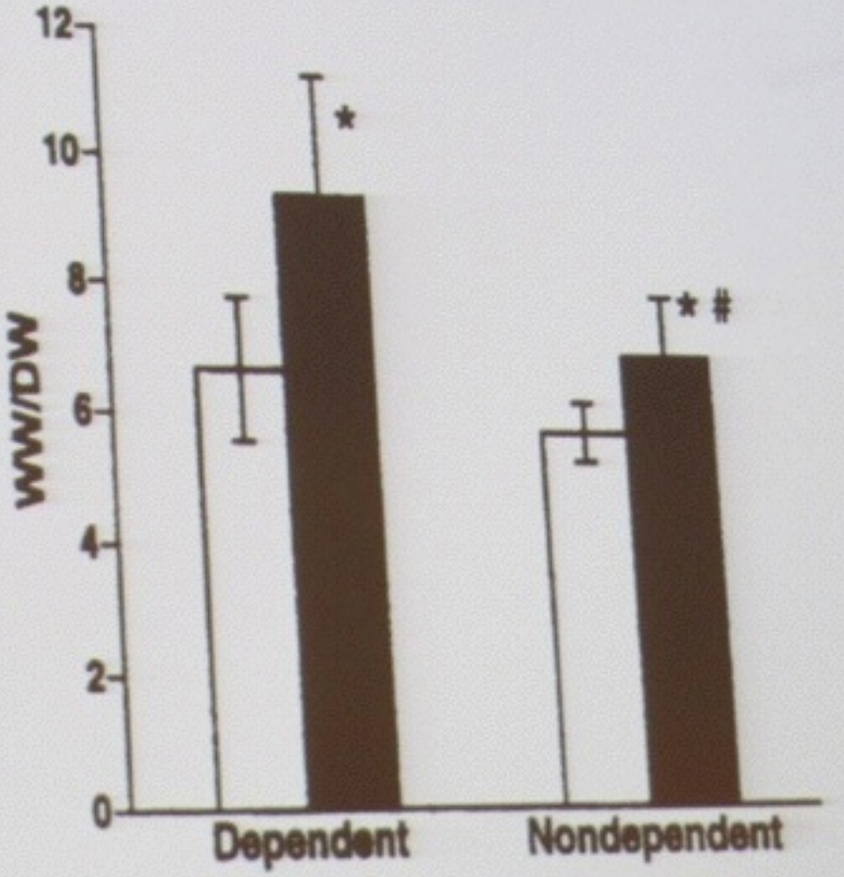
16 ARDS pts.

Prone position: effect on VILI

Proning allow to reduce PEEP and FiO_2



Lim et al ICM 2001;27:477

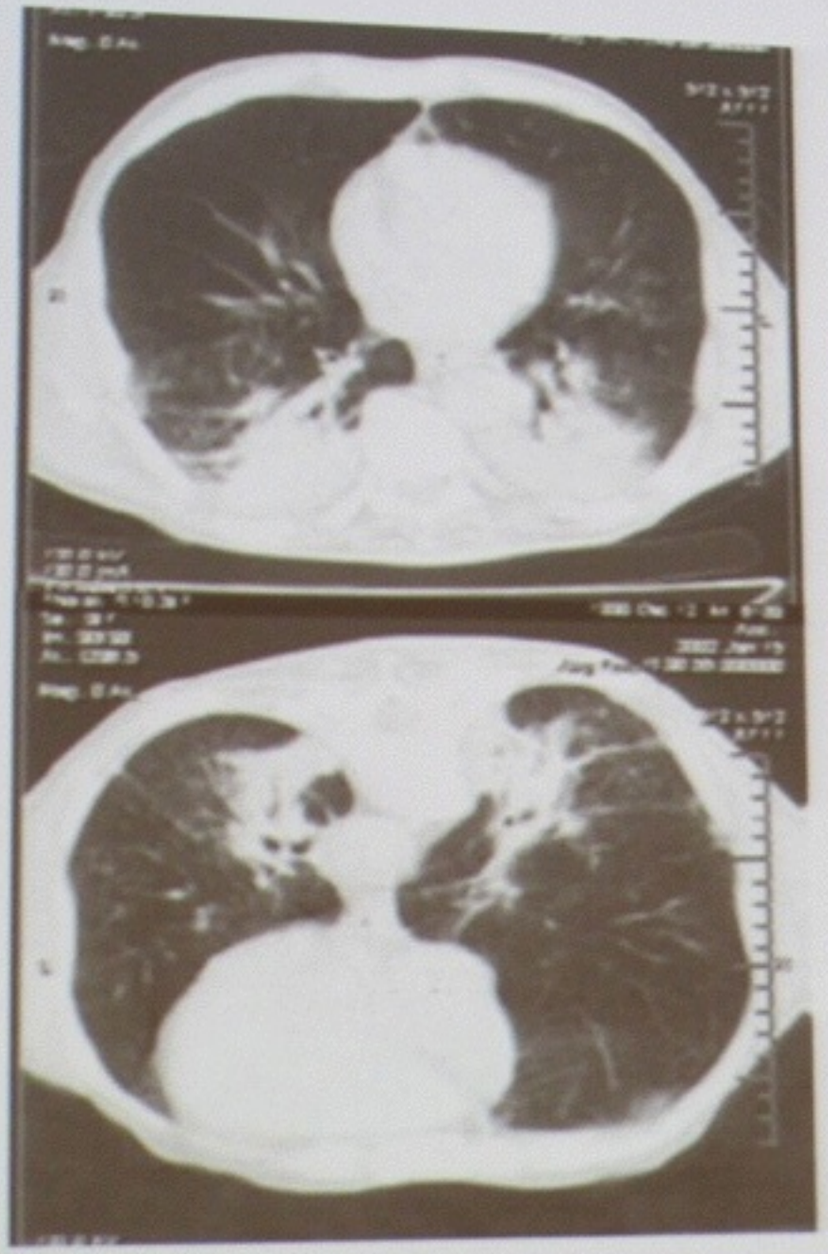


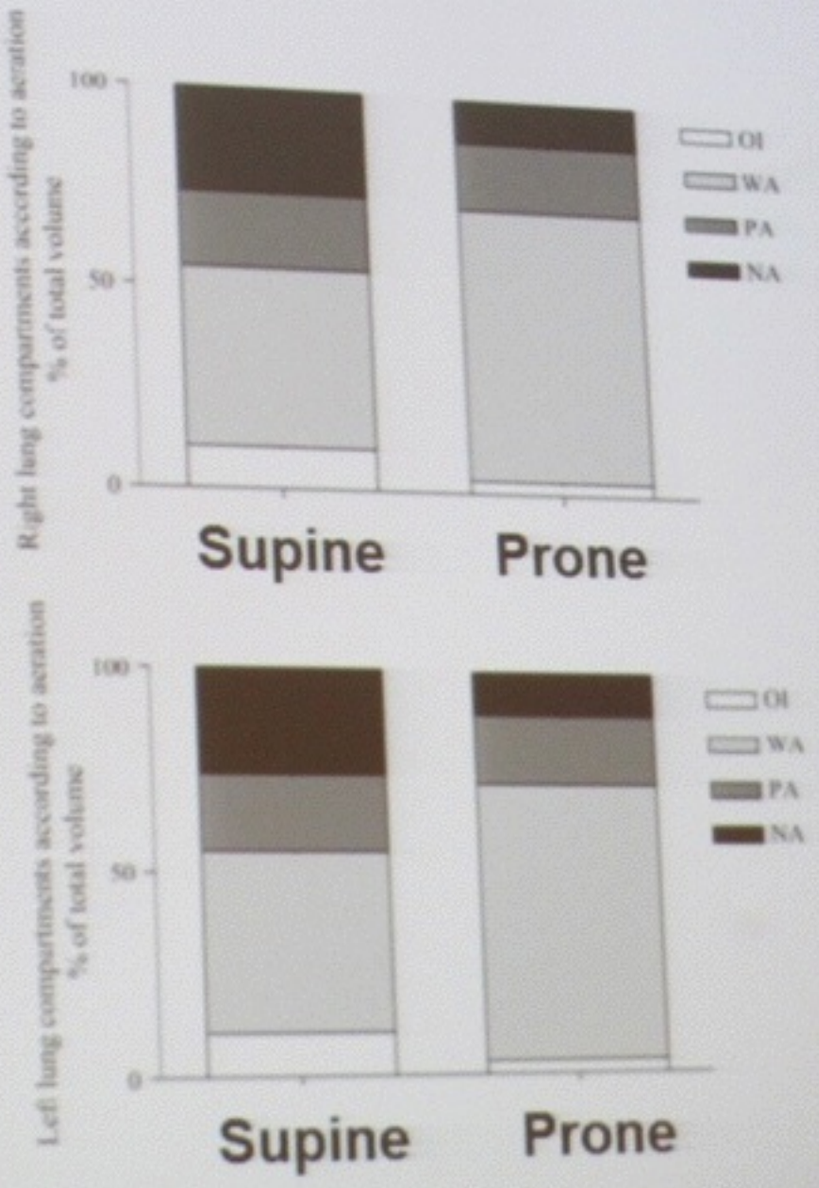
Broccard et al CCM 1997;21:210
Broccard et al CCM 2000;28:295

Prone Position Augments Recruitment and Prevents Alveolar Overinflation in Acute Lung Injury

Eftichia Galiatsou, Eleonora Kostanti, Eugenia Svarna, Athanasios Kitsakos, Vasilios Koulouras, Stauros C. Efremidis, and Georgios Nakos

Am J Respir Crit Care Med Vol 174. pp 187–197, 2006

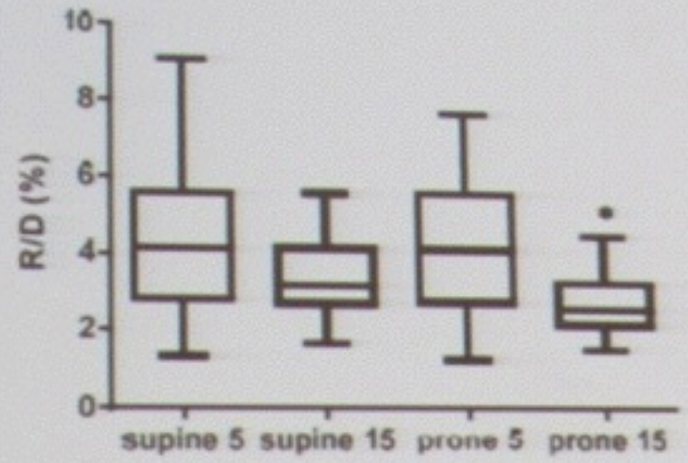


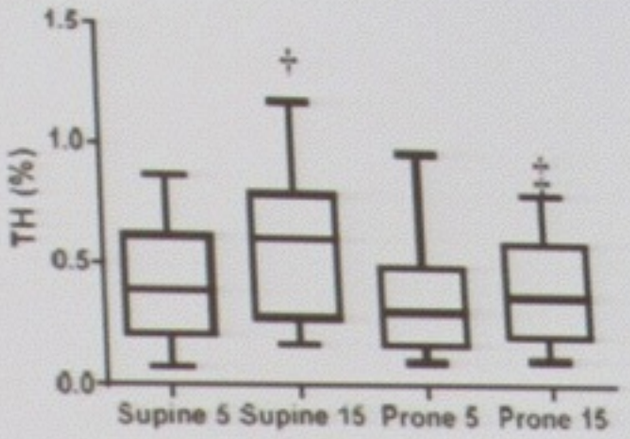


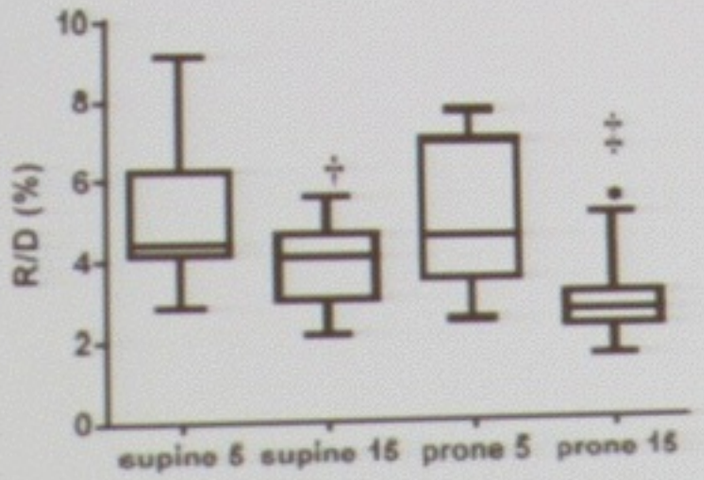
Effects of prone positioning on lung protection in patients with Acute Respiratory Distress Syndrome

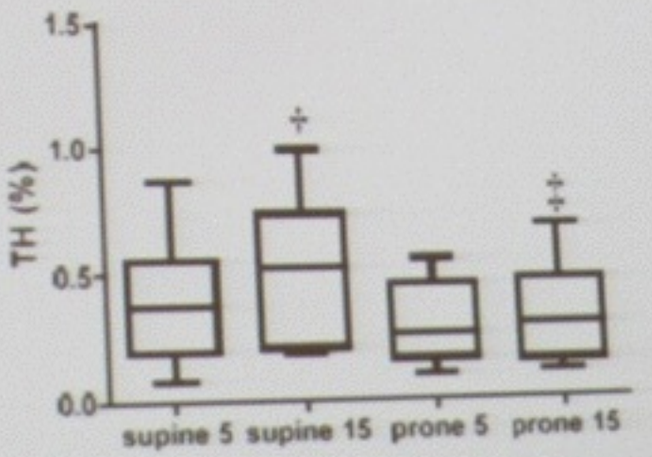
Cornejo RA et al AJRCCM 2013

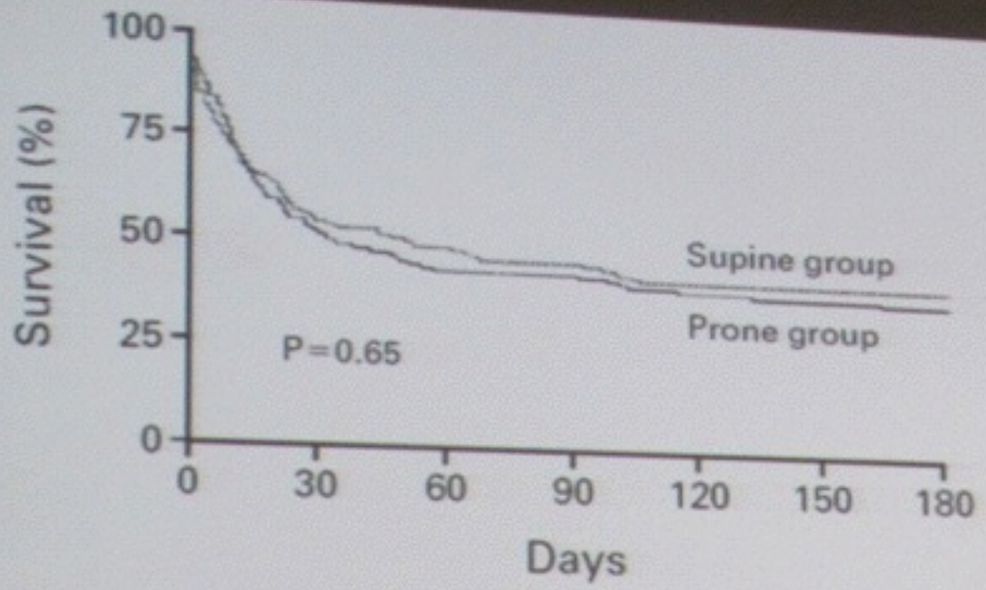
A - Overall population (n = 24)



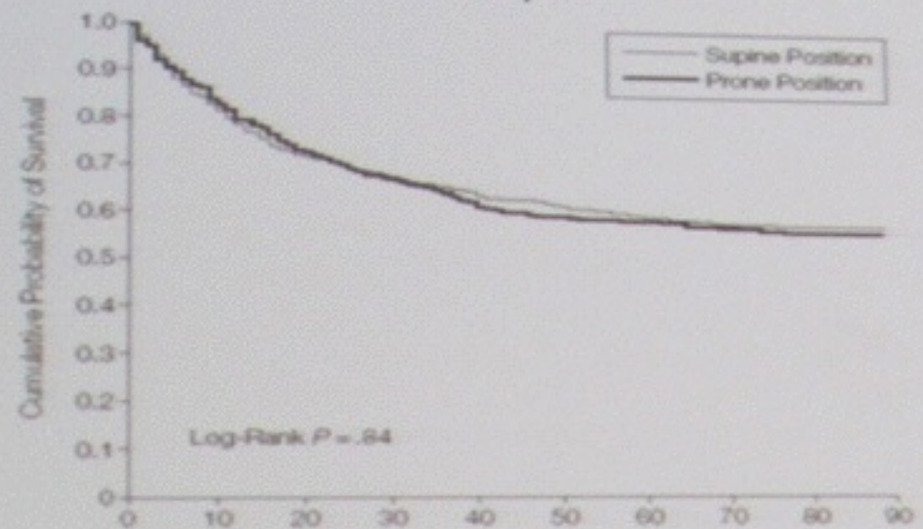




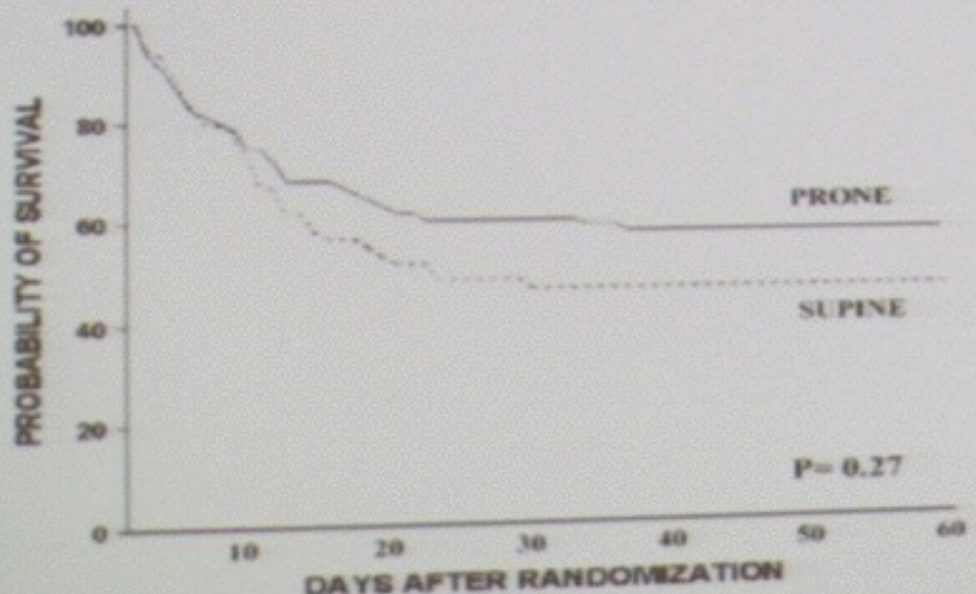




Gattinoni et al. NEJM 2001



Guérin et al. JAMA 2004

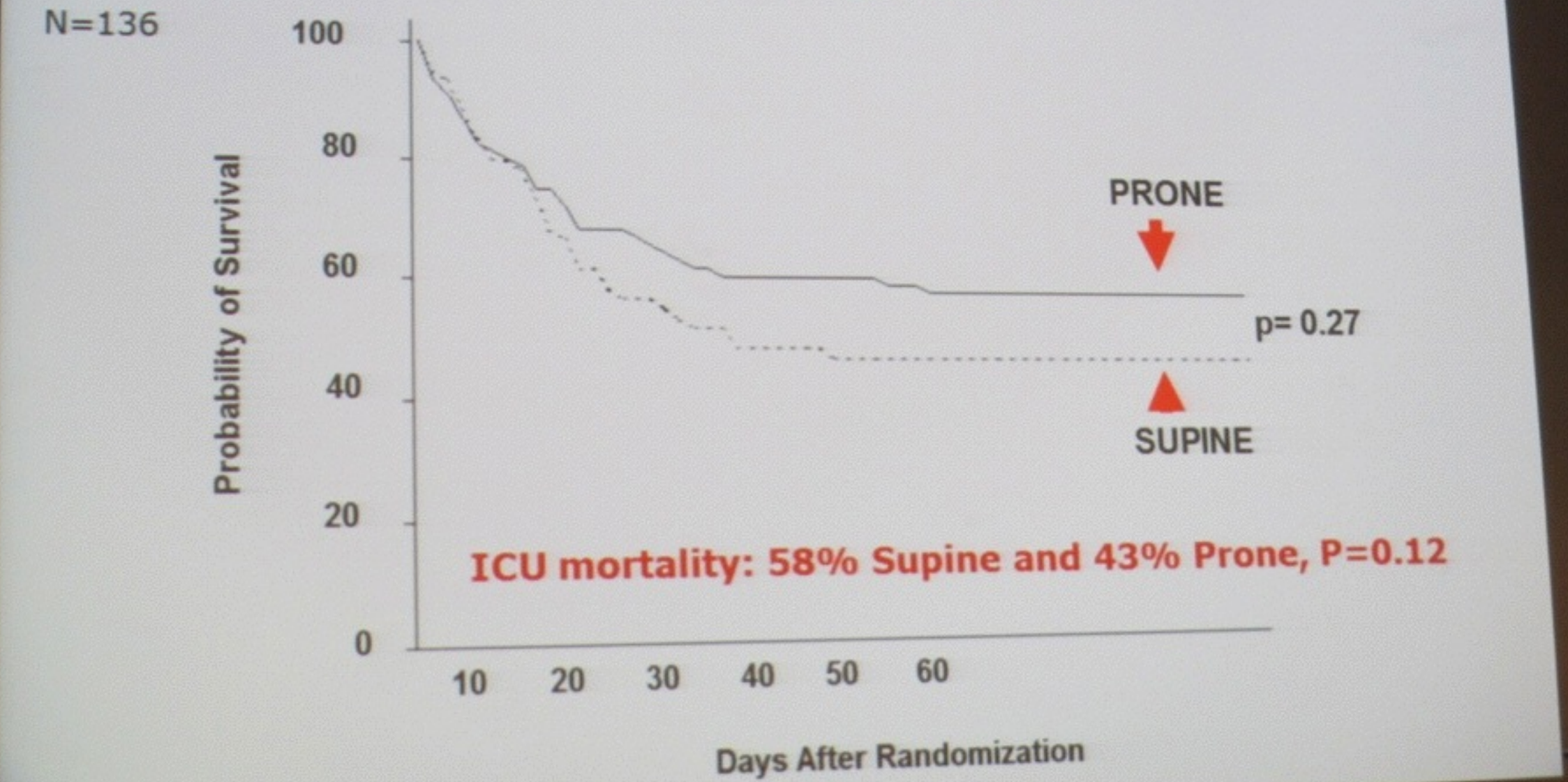


Mancebo et al. AJRCCM 2006

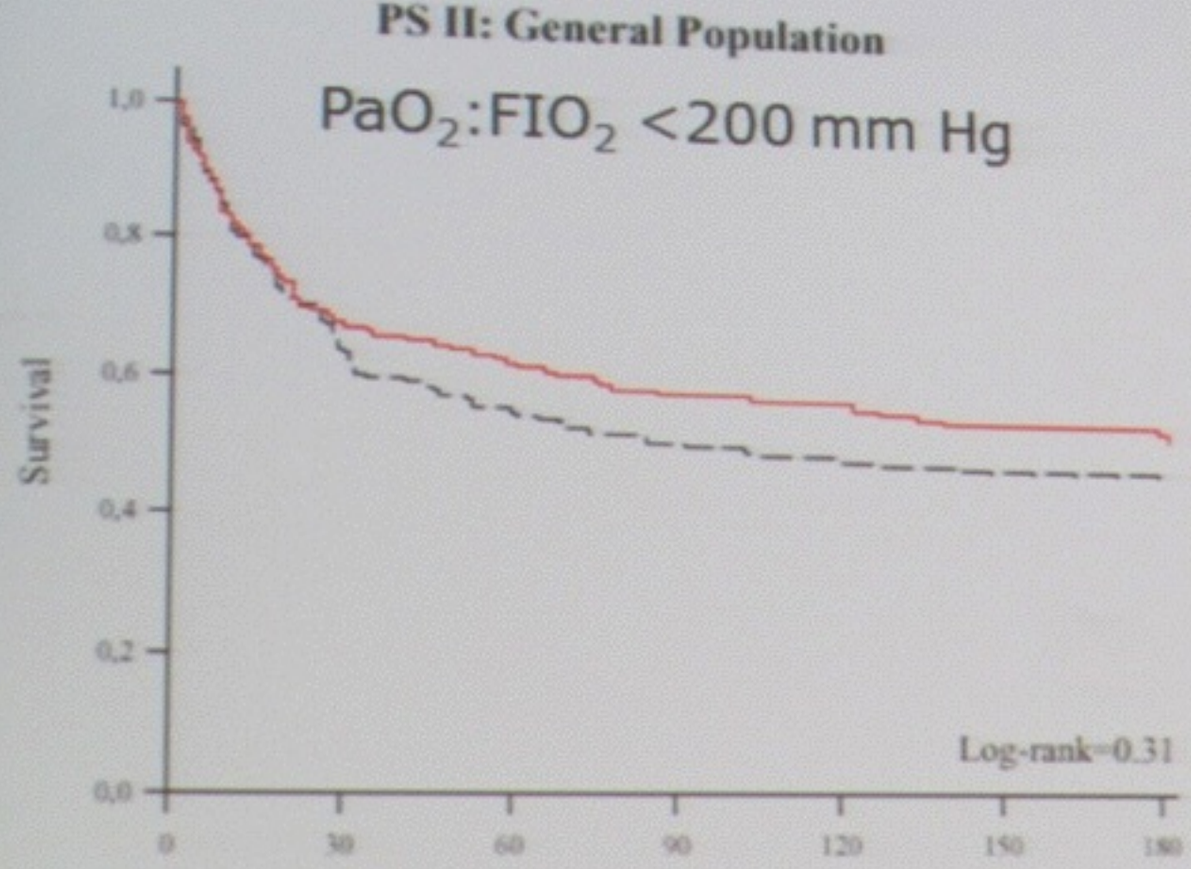
A Multicenter Trial of Prolonged Prone Ventilation in Severe Acute Respiratory Distress Syndrome

Jordi Mancebo, Rafael Fernández, Lluis Blanch, Gemma Rialp, Federico Gordo, Miquel Ferrer, Fernando Rodríguez, Pau Garro, Pilar Ricart, Immaculada Vallverdú, Ignasi Gich, José Castaño, Pilar Saura, Guillermo Domínguez, Alfons Bonet, and Richard K. Albert

Am J Respir Crit Care Med Vol 173. pp 1233–1239, 2006

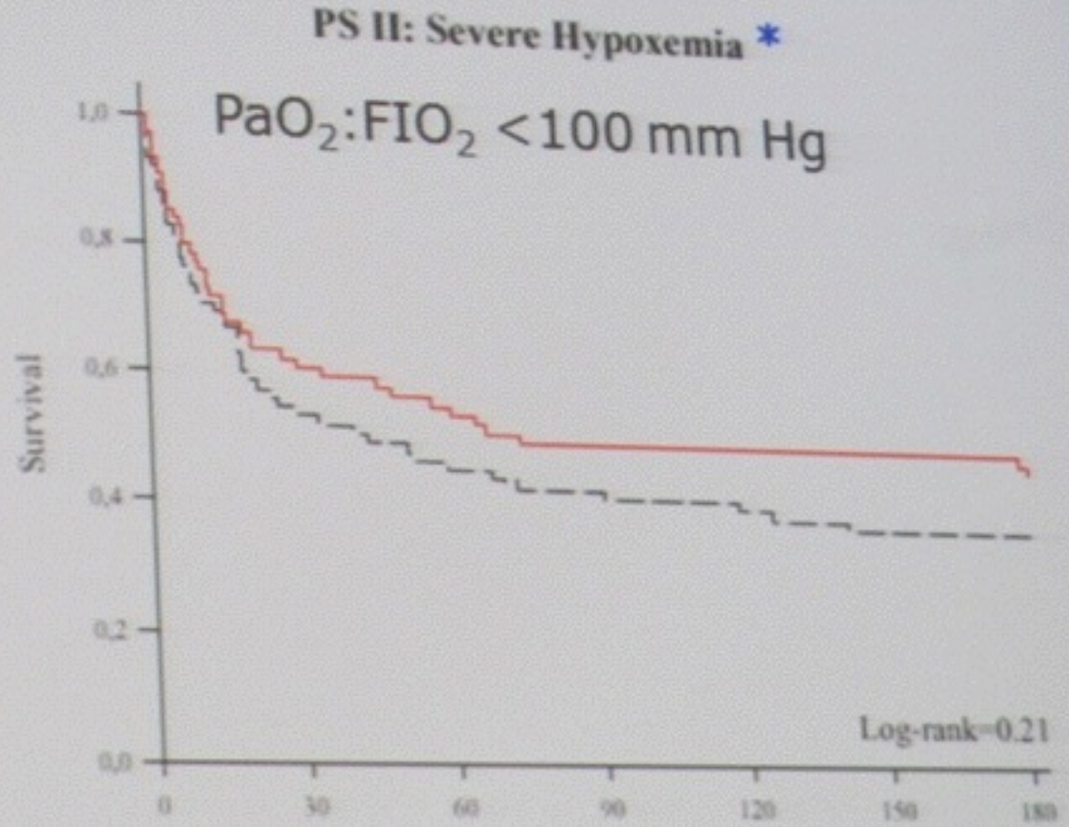


Taccone P, *et al*. JAMA 2009;302:1977-84



No. at risk

Supine	174	110	95	87	84	81	81
Prone	168	113	104	96	95	90	90



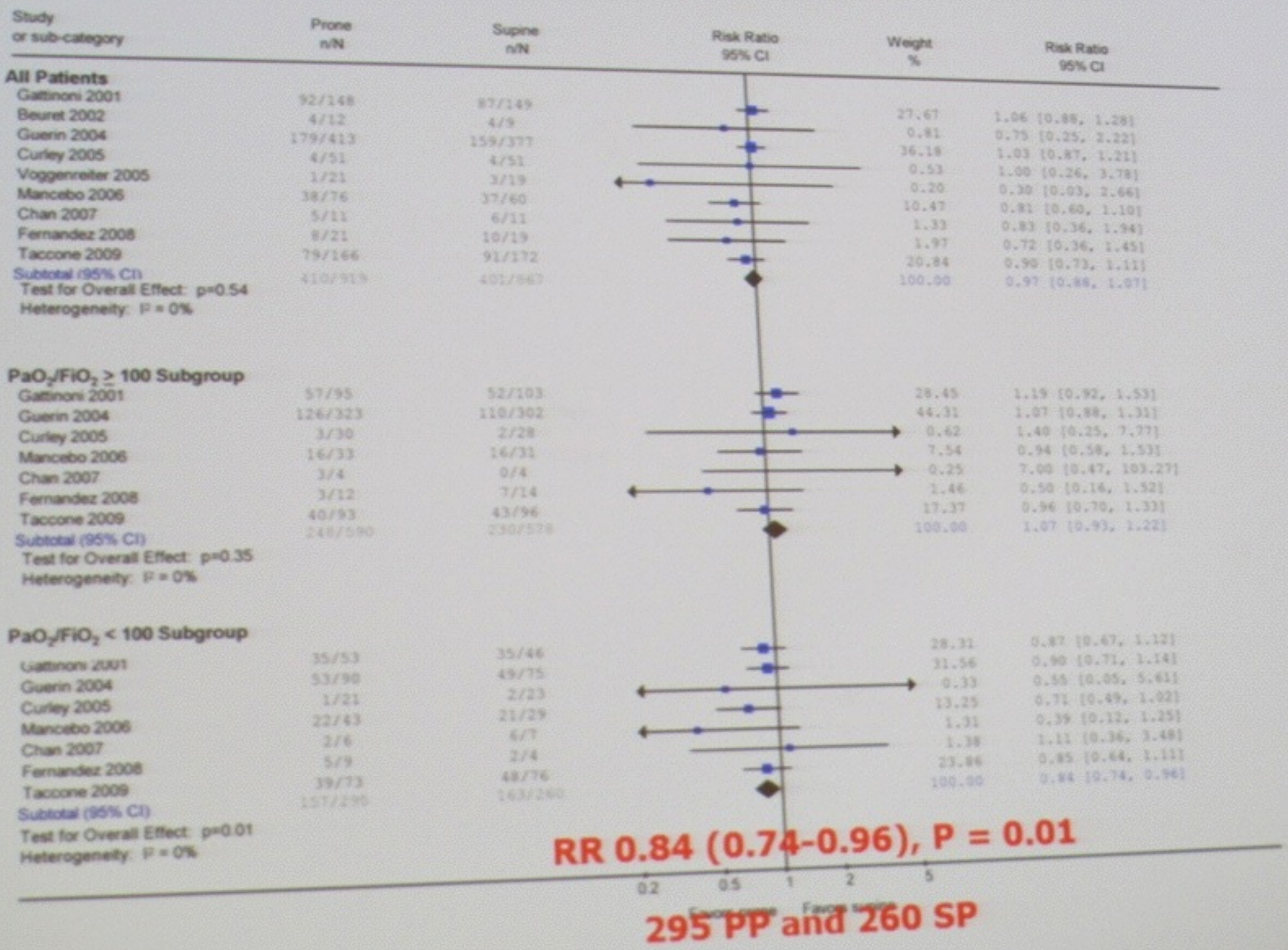
No. at risk

Supine	76	40	35	32	31	28	28
Prone	74	45	40	36	36	36	36

Prone Group (31%; 48%) **Supine group (33%; 52%)**

***Prone Group (38%; 53%)** **Supine group (46%; 63%)**

Sud S, *et al*. ICM 2010;36:585-99
Individual Metaanalysis



Abroug F, *et al*. CC 2011

Group by Patient Type	Study name	Odds ratio	Lower limit	Upper limit	p-Value
ALI/ARDS	Gattinoni_2001	1,111	0,709	1,742	0,646
ALI/ARDS	Guerin_2004	1,045	0,775	1,410	0,772
ALI/ARDS	Voggenreiter_2005	0,267	0,025	2,815	0,272
All studies with ALI/ARDS		1,049	0,819	1,344	0,706
ARDS	Mancebo_2006	0,548	0,276	1,087	0,085
ARDS	Chan_2007	0,593	0,078	4,498	0,613
ARDS	Fernandez_2008	0,554	0,157	1,952	0,358
ARDS	Taccone_2009	0,810	0,530	1,238	0,330
All studies with ARDS		0,708	0,503	0,997	0,048
Overall		0,916	0,750	1,120	0,392

Statistics for each study

Odds ratio and 95% CI

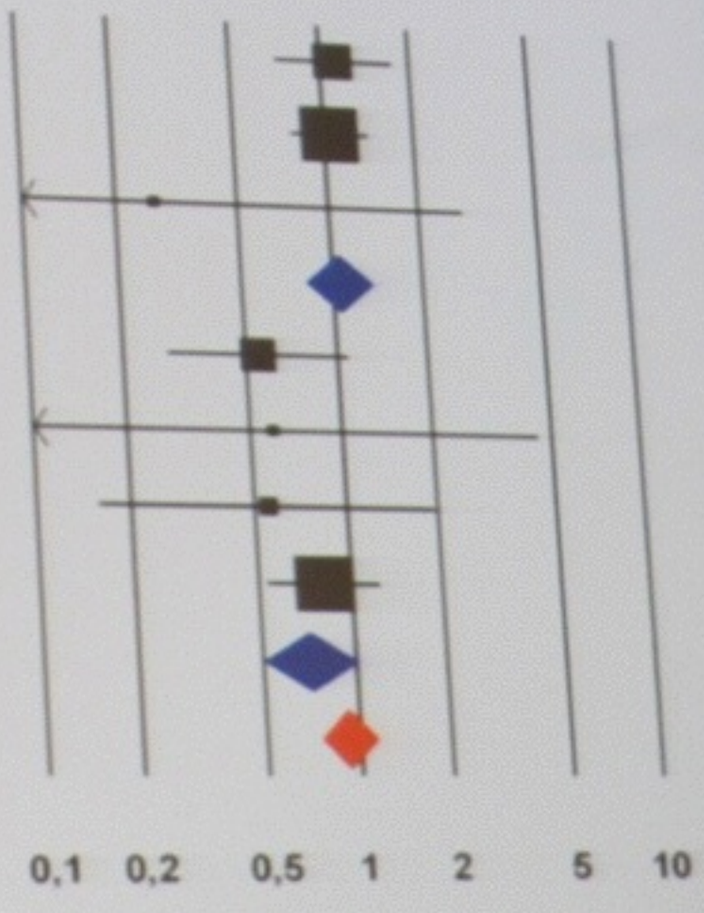
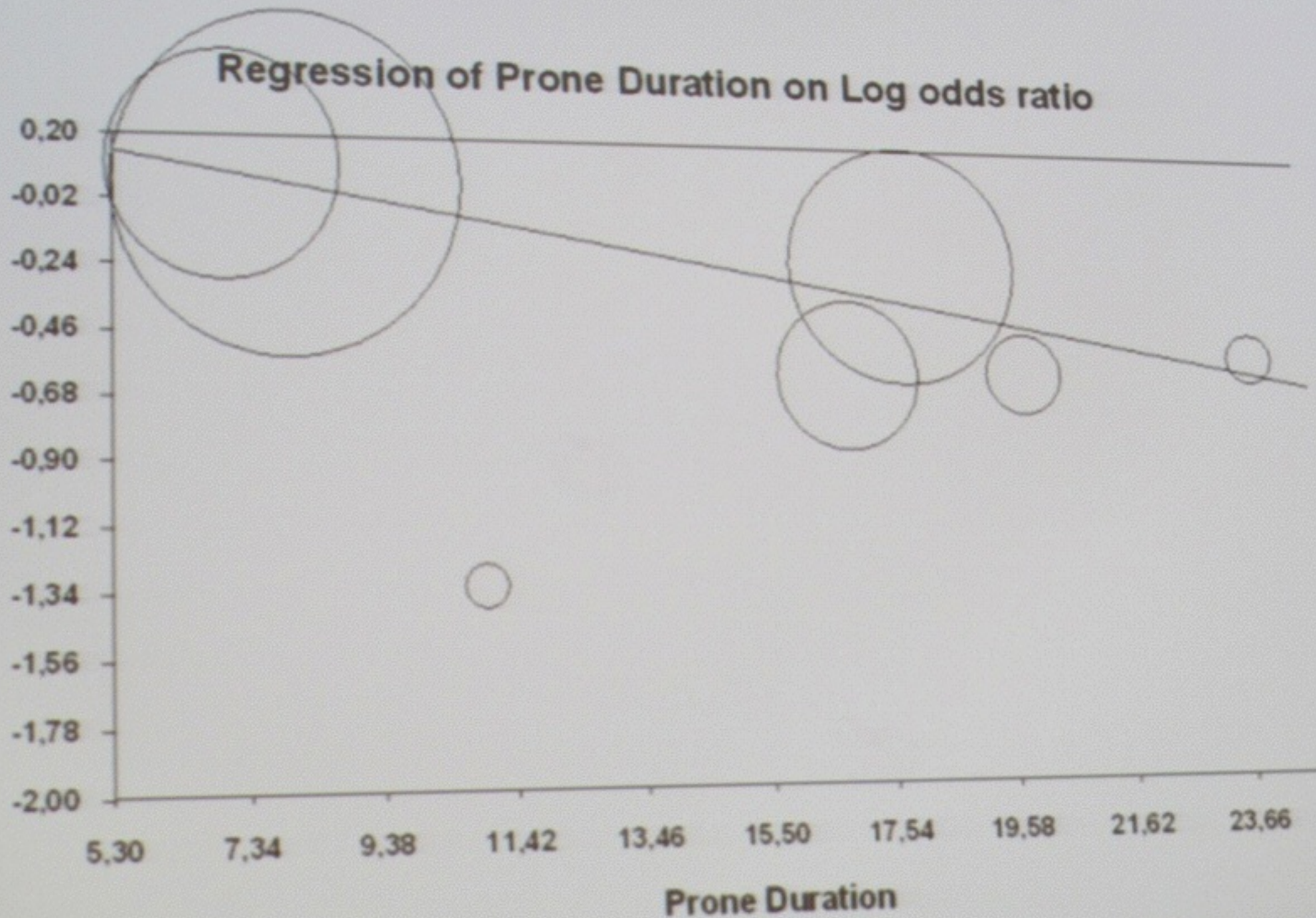


Figure 3

Abroug F et al. CC 2011



PROSEVA Flow Chart

51 189 Admissions to the 27 ICUs in the study period (January 1st, 2008 to July 25th, 2011

76% Not eligible*

24% Eligible*

44.5% Not included*

474 included

234 SP group

240 PP group

5 excluded:
3 P/F > 150
1 persistent < 12 hrs
1 guardianship

3 excluded:
2 persistent < 12 hrs
1 NIV > 24 hrs

- From a sample of 2405 patients

= 4.7% of all admissions

466 analyzed in an intention-to-treat manner

229 SP

237 PP

466 at the last follow-up (90 days)

229 SP

237 PP

Guerin C et al PROSEVA

Inclusion criteria

1. Aged 18 years or more
2. Both genders
3. Intubated for ARDS for < 36 hours
4. ARDS according to AECC criteria
5. Criteria confirmed 12-24 hours later
6. AND severity criteria at that time
   - $PaO_2/FiO_2 < 150$ with $F_IO_2 \geq 0.6$ + PEEP ≥ 5 cm H_2O + VT 6 ml/kg IBW
7. Information notice given to next of kin

Guerin C et al PROSEVA

Dose of proning in PP group

- Time from randomization to first PP session = 55 ± 55 minutes
- Number of PP sessions per patient = 4 ± 4
- PP session duration = 17±3 hours
- Time in PP = 16,304 hours x patient
  - (73% of time between onset of first and end of last PP session)

Guerin C et al PROSEVA

Primary outcome: Mortality at D28

	SP group (n=229)	PP group (n=237)	P value
No. deaths	75	38	
% death [95% CI]	32.8 [26.4-38.6]	16.0 [11.3-20.7]	0.0000256
Unadjusted HR with PP [95% CI]	0.39 [0.25-0.63]		
Adjusted HR for SOFA score with PP [95% CI]	0.42 [0.26-0.66]		0.0002

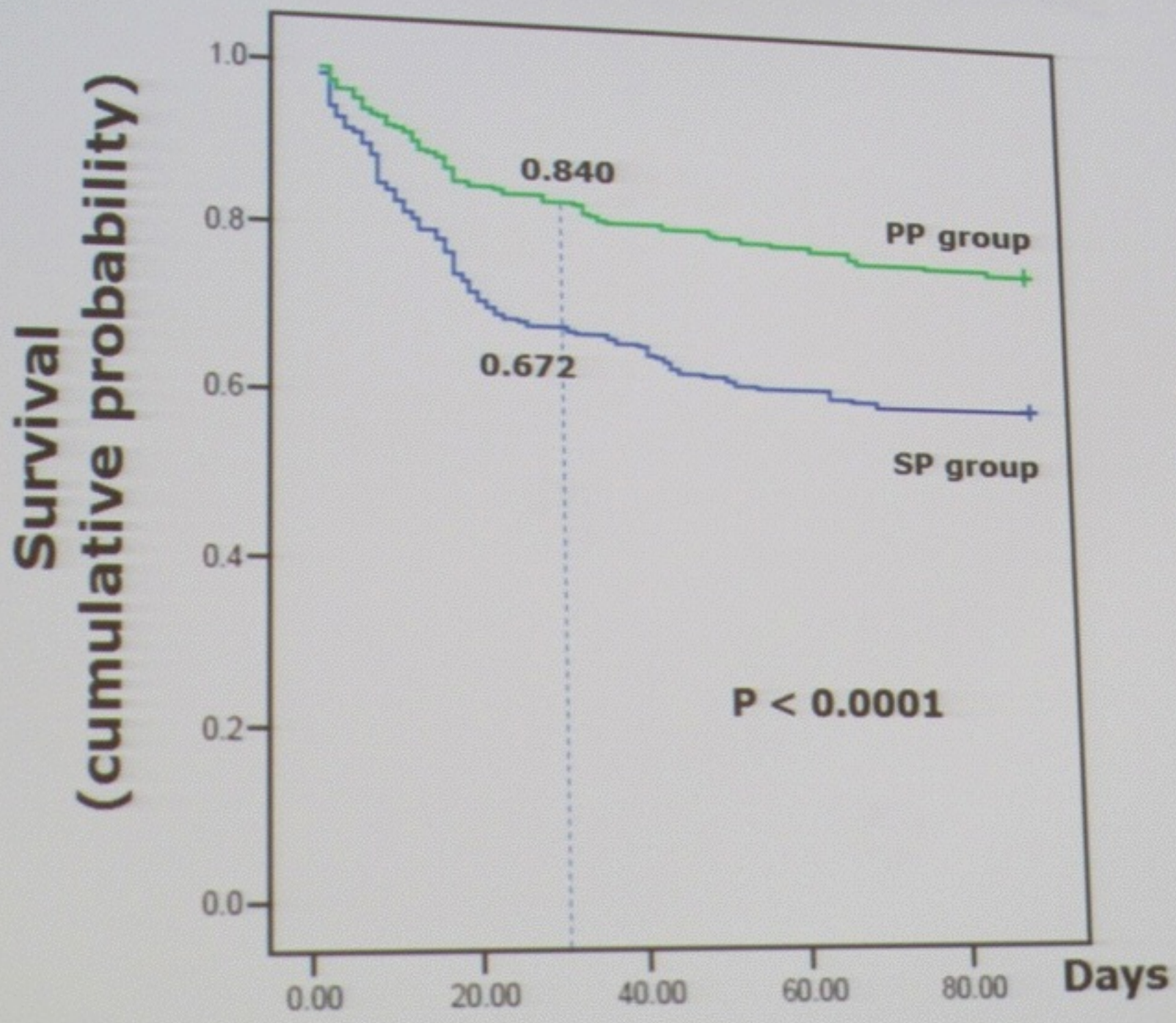
Guerin C et al PROSEVA

Secondary outcome: Mortality at D90

	SP group (n=229)	PP group (n=237)	P value
No. deaths	94	56	
% death [95% CI]	41.0 [34.6-47.4]	23.6 [18.2-29.0]	0.0000573
Unadjusted HR with PP [95% CI]	0.44 [0.29-0.67]		
Adjusted HR for SOFA score with PP [95% CI]	0.48 [0.32-0.72]		0.0004

Guerin C et al PROSEVA

Survival



Guerin C et al PROSEVA

Prone position

- Refractory hypoxemia: PP should be the number one rescue therapy
- Severe confirmed ARDS PP may offer a great survival benefit
- The rationale may be a more homogeneous ventilation reducing the risk of VILI

Alteration of RBC's with Storage

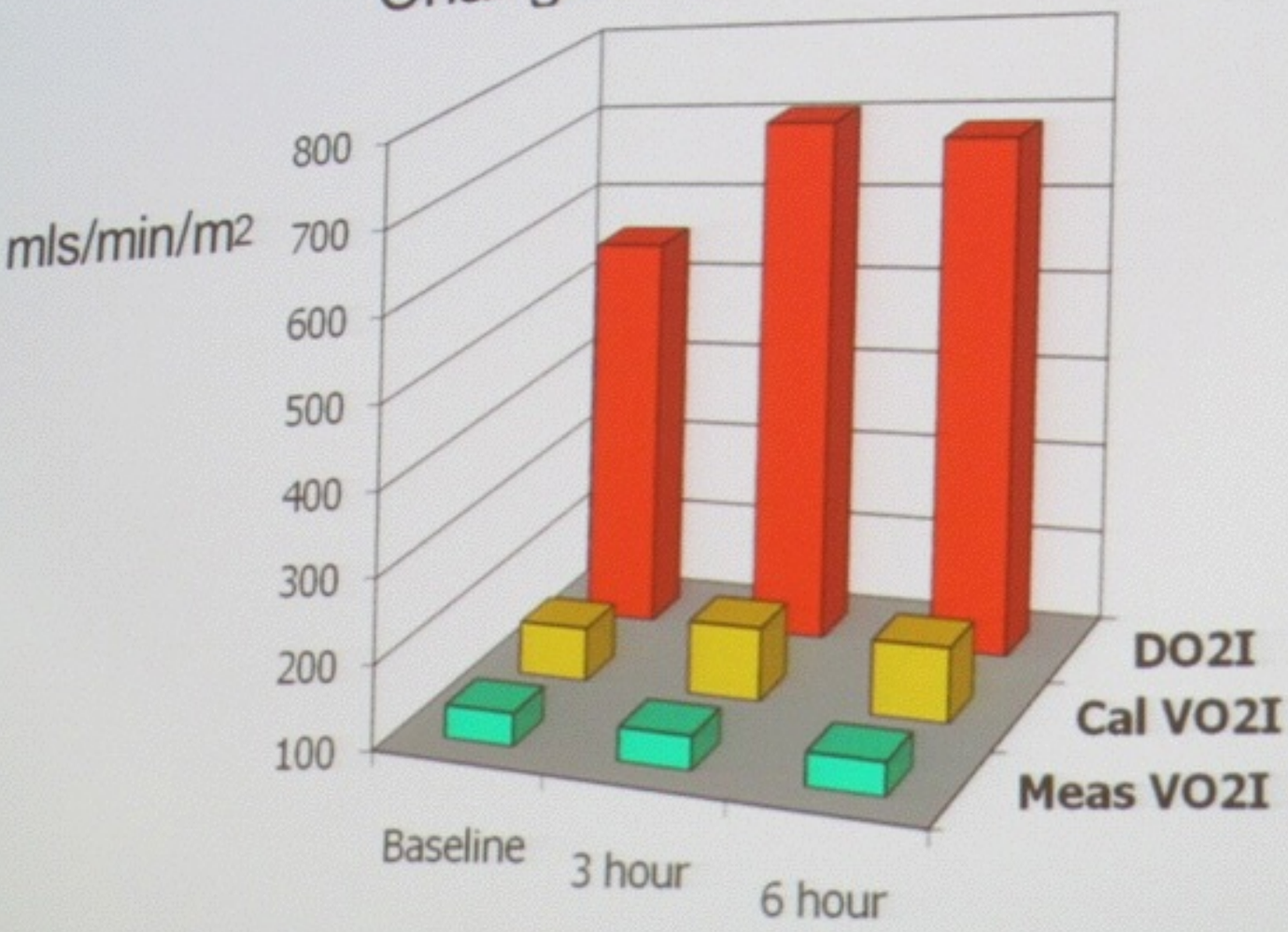
Day 1

Day 21

Effect of Stored-Blood Transfusion on Oxygen Delivery in Patients With Sepsis

Paul E. Marik, MMed, William J. Sibbald, MD, FRCPC

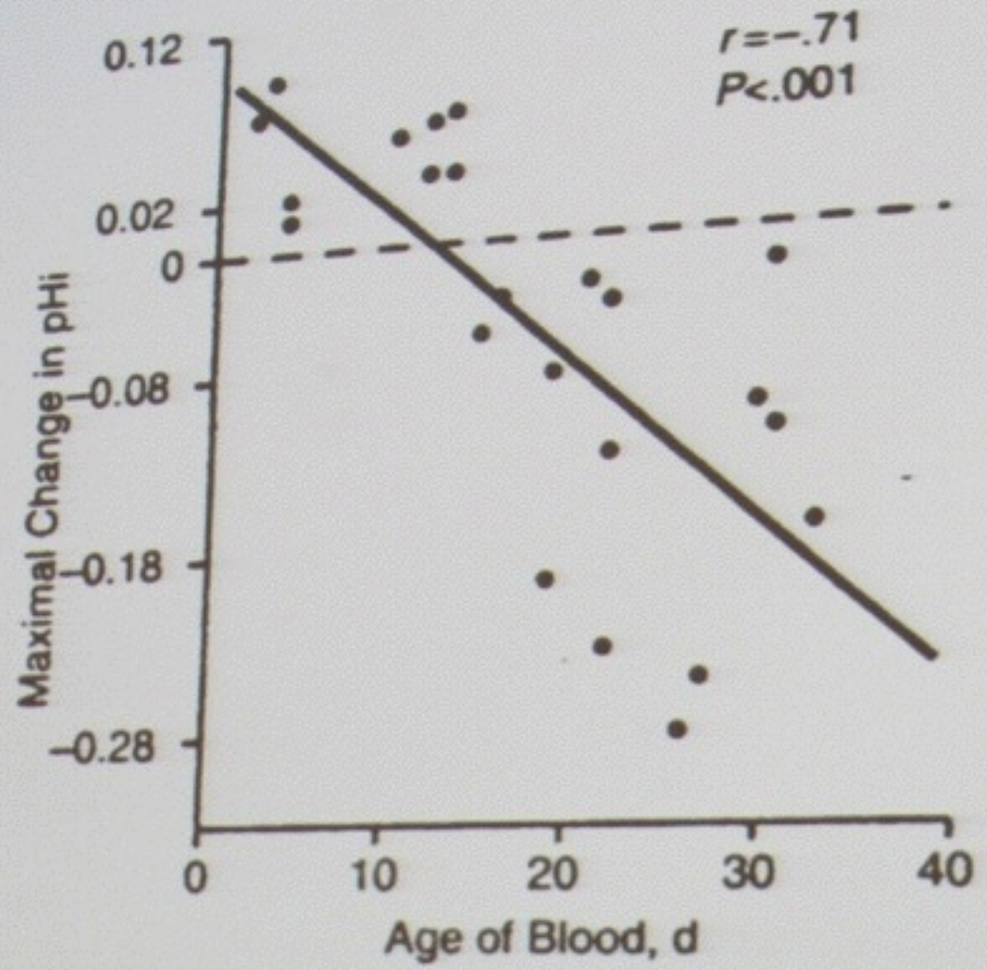
Change in DO2I and



JAMA 19

Effect of Stored-Blood Transfusion on Oxygen Delivery in Patients With Sepsis

Paul E. Marik, MMed, William J. Sibbald, MD, FRCPC



JAMA 19

Effect of Red Cell Transfusion on Oxygen Consumption Following Fluid Resuscitation in Septic Shock

Variable	Pretransfusion	Posttransfusion
Hb g/dl	8.3 ± 0.3	10.7 ± 0.3
DO2 ml/min/m2	482 ± 28	621 ± 32*
VO2 ml/minM2	124 ± 12	125 ± 10
Lactate meq/l	4.6 ± 1.0	4.1± 1.3

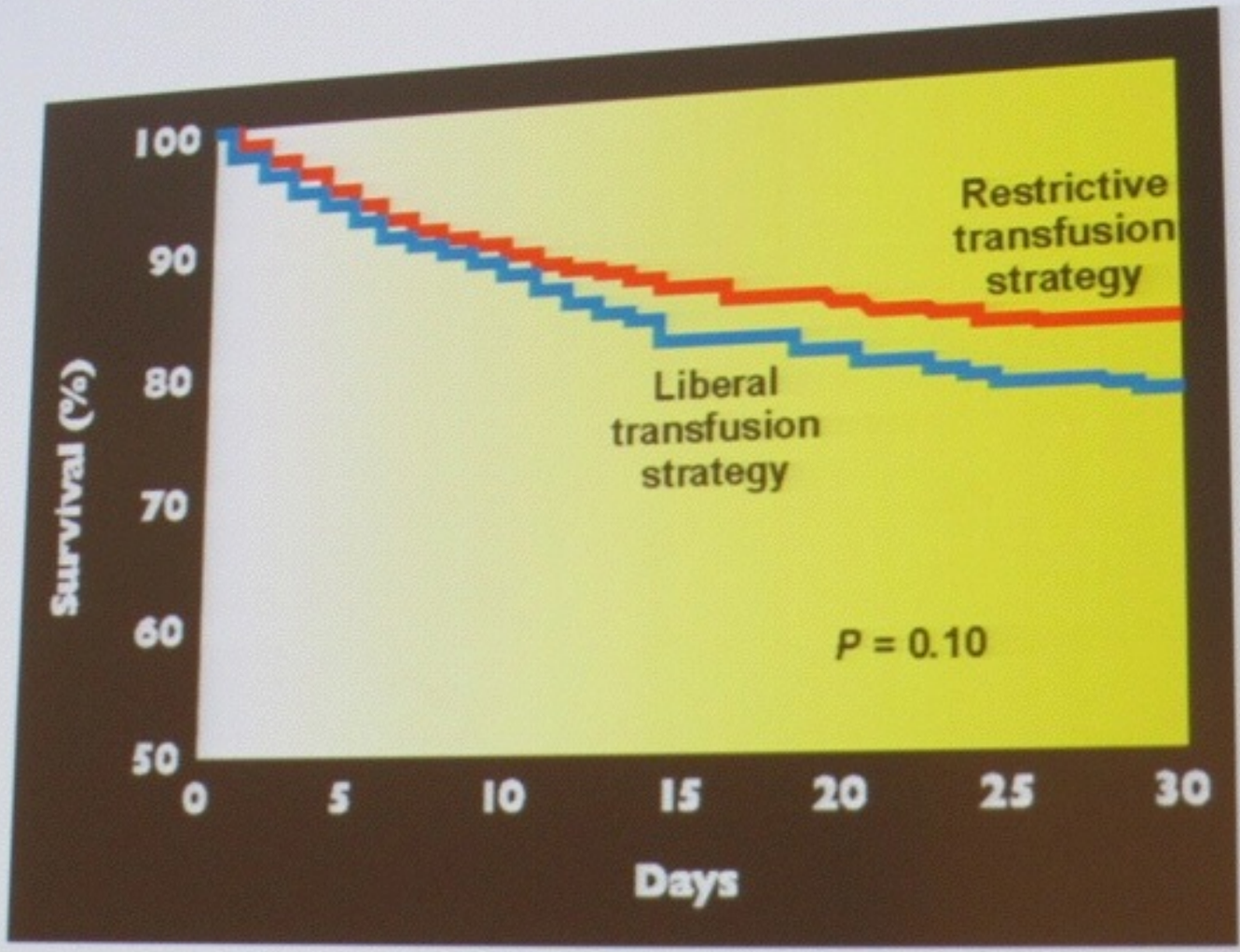
* < 0.0001

Conrad SA, et al. *Circ Shock*

VOLUME 340 FEBRUARY 11, 1999 NUMBER 6

A MULTICENTER, RANDOMIZED, CONTROLLED CLINICAL TRIAL OF TRANSFUSION REQUIREMENTS IN CRITICAL CARE

- 838 patients Hb < 9
- Restrictive
  - T/f HB < 7 g/dl
  - HB 7-9 g/dl
- Liberal
  - T/f Hb < 10 g/dl
  - Hb 10-12 g/dl



VOLUME 340 · FEBRUARY 11, 1999 · NUMBER 6

A MULTICENTER, RANDOMIZED, CONTROLLED CLINICAL TRIAL OF TRANSFUSION REQUIREMENTS IN CRITICAL CARE

30 day mortality: Severe sepsis and septic shock

Restrictive	Liberal
22.8%	29.7%

p=0.36

IJCCM
Indian Journal of Critical Care Medicine
Official Publication of Indian Society of Critical Care Medicine

The impact of packed red blood cell transfusion on clinical outcomes in patients with septic shock treated with early goal directed therapy

Brian M. Fuller, Mithil Gajera,[1] Christa Schorr,[1] David Gerber,[1] R. Phillip Dellinger,[1] Joseph Parrillo,[1] and Sergio Zanotti[1]

Variable	PRBC (n = 34)	No PRBC (n = 59)	*P* value
Age (years)	63.5	59.3	0.199
Gender			
Male	22 (64.7)	33 (55.9)	0.512
Female	12 (35.3)	26 (44.1)	
Race			
Black	15 (44.1)	22 (37.3)	0.676
Hispanic	3 (8.8)	9 (15.3)	
White	16 (47.1)	27 (45.8)	
Other	0 (0)	1 (1.7)	
APACHE II	21.1	20.3	0.682
Lactate (mmol/l)	6.0	5.4	0.463

Indian J Crit Care Med 2010;14:16

Anesthesiology 2008; 108:3–4

Liars, Damn Liars, and Propensity Scores