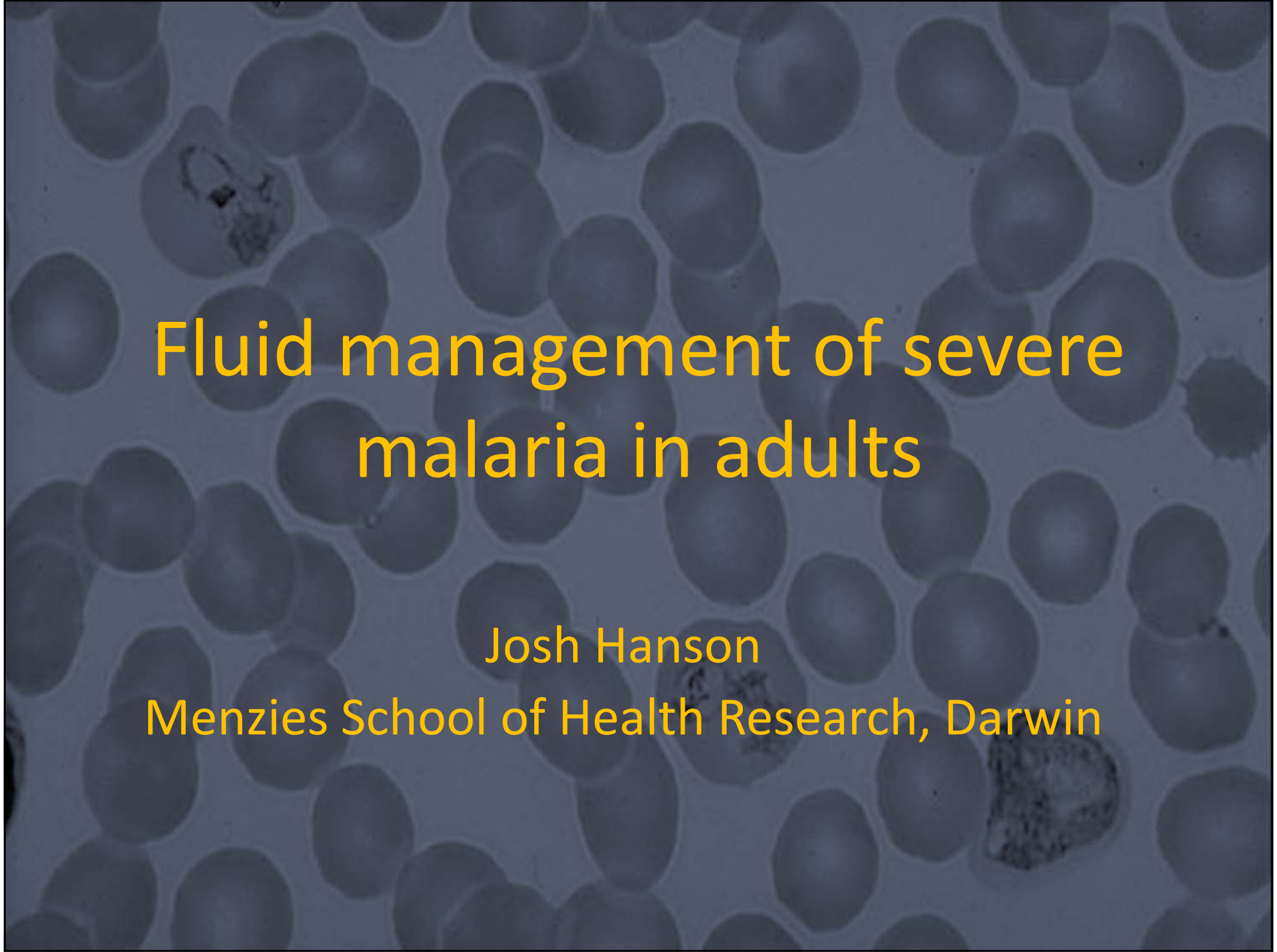
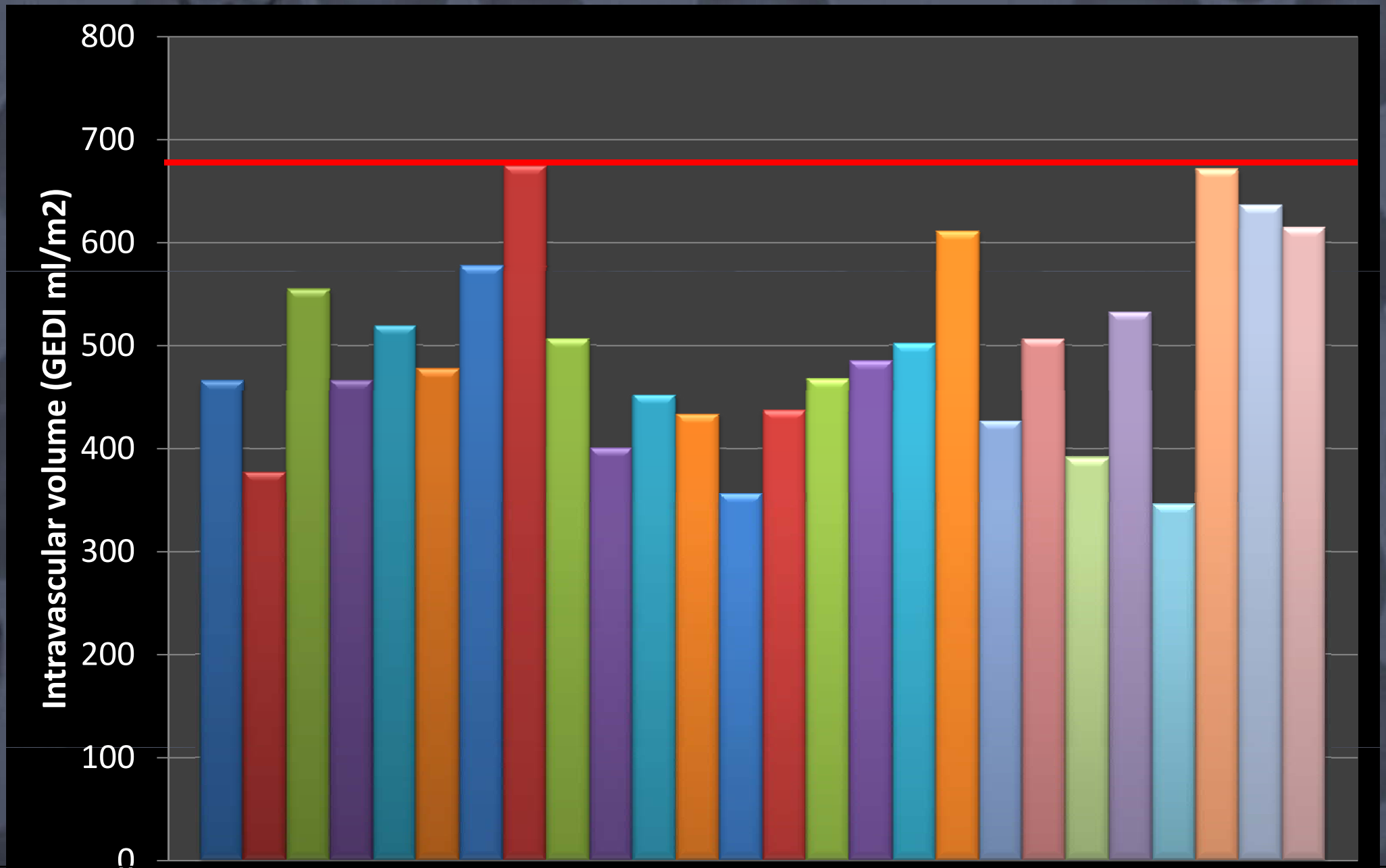
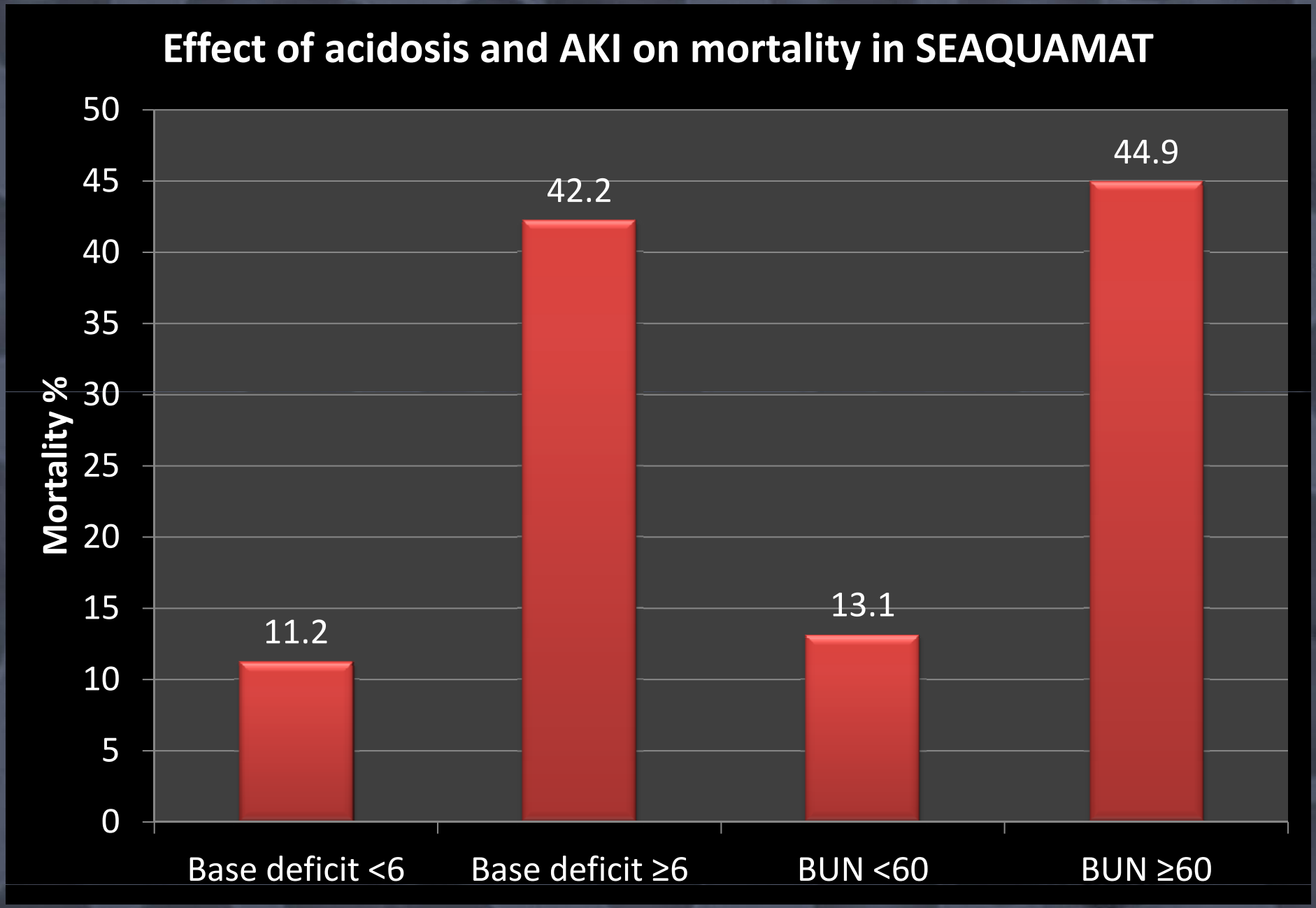


Fluid management of severe malaria in adults

Josh Hanson
Menzies School of Health Research, Darwin

Hypovolaemia is universal




Effect of acidosis and AKI on mortality in SEAQUAMAT
Mortality %
50
45
40
35
30
25
20
15
10
5
0
11.2
42.2
13.1
44.9
Base deficit <6
Base deficit ≥6
BUN <60
BUN ≥60

BLUE STAGE OF THE SPASMODIC CHOLERA.

Sketch of a Girl who died of Cholera, in Sunderland, November, 1831.

Wellcome Images

EXPERIMENTS ON THE BLOOD IN CHOLERA.

To the Editor of THE LANCET.

1. The blood drawn in the worst cases of *the* cholera, is unchanged in its anatomical or globular structure.

2. It has *lost a large proportion of its water*, 1000 parts of cholera serum having but the average of 860 *parts of water.*

3. *It has lost also a great proportion of its* NEUTRAL *saline ingredients.*

4. *Of the free alkali contained in healthy serum, not a particle is present in some cholera cases, and barely a trace in others.**

May I add, that until the publication of my report, I shall deem the suspension of discussion on the results now introduced as a matter of personal courtesy and obligation.

I am, Sir,

Your obedient servant,

W. B. O'SHAUGHNESSY, M.D.

London, 29 December, 1831.

His first patient was an elderly woman who had been given ‘all the usual remedies’ and who had ‘apparently reached the last moments of her earthly existence.’

Latta inserted a tube into the basilic vein and injected ounce after ounce of fluid ‘soon the sharpened features, and sunken eye, and fallen jaw, pale and cold, bearing the manifest imprint of death’s signet, began to glow with returning animation; the pulse returned to the wrist…’.

In the space of thirty minutes after six pints of fluid had been injected, the woman announced in a strong voice that she was now ‘free from all uneasiness’.

Guidelines for Management of Severe Sepsis and Septic Shock

Surviving Sepsis Campaign This is a summary of the Surviving Sepsis Campaign International Guidelines for Management of Severe Sepsis and Septic Shock: 2008, condensed from Dellinger RP, Levy MM, Carlet JM, et al: Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock. Intensive Care Medicine (2008) 34:17-60 and Crit Care Med 2008; 36(1) 296-327. This version does not contain the rationale or appendices contained in the primary publication. The SSC guidelines do not cover every aspect of managing critically ill patients, and their application should be supplemented by generic best practice and specific treatment as required. Please refer to the guidelines for additional information at www.survivingsepsis.org

Strength of recommendation and quality of evidence have been assessed using the GRADE criteria, presented in brackets after each guideline.
For added clarity:
- ◆ Indicates a strong recommendation or "we recommend"
- ◇ Indicates a weak recommendation or "we suggest"

SSC GUIDELINES HAVE BEEN ENDORSED BY

American Association of Critical-Care Nurses
American College of Chest Physicians
American College of Emergency Physicians
Canadian Critical Care Society
European Society of Clinical Microbiology and Infectious Diseases
European Society of Intensive Care Medicine
European Respiratory Society
Indian Society of Critical Care Medicine
International Sepsis Forum
Japanese Association for Acute Medicine
Japanese Society of Intensive Care Medicine
Society of Critical Care Medicine
Society of Hospital Medicine
Surgical Infection Society
World Federation of Critical Care Nurses
World Federation of Societies of Intensive and Critical Care Medicine.
Participation and endorsement by German Sepsis Society and Latin American Sepsis Institute.

The Surviving Sepsis Campaign is a collaboration of the European Society of Intensive Care Medicine, the International Sepsis Forum, and the Society of Critical Care Medicine.

EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

Society of Critical Care Medicine
The Intensivist Care Professionals

INTERNATIONAL SEPSIS FORUM

January 2008

Initial resuscitation (first 6 hours)

- ◆ Begin resuscitation immediately in patients with hypotension or elevated serum lactate Ω4mmol/L; do not delay pending ICU admission. (1C)
- ◆ Resuscitation goals: (1C)
  - Central venous pressure (CVP) 8–12 mm Hg*
  - Mean arterial pressure ≥65 mm Hg
  - Urine output ≥0.5 mL.kg^{-1}.hr^{-1}
  - Central venous (superior vena cava) oxygen saturation ≥70%, or mixed venous ≥65%
- ◇ If venous O_2 saturation target not achieved: (2C)
  - consider further fluid
  - transfuse packed red blood cells if required to hematocrit of ≥30% and/or
  - dobutamine infusion max 20 µg.kg^{-1}.min^{-1}

* A higher target CVP of 12-15 mm Hg is recommended in the presence of mechanical ventilation or pre-existing decreased ventricular compliance.

Diagnosis

- ◆ Obtain appropriate cultures before starting antibiotics provided this does not significantly delay antimicrobial administration (1C)
  - Obtain two or more blood cultures (BCs)
  - One or more BCs should be percutaneous
  - One BC from each vascular access device in place Ω48 hours
  - Culture other sites as clinically indicated
- ◆ Perform imaging studies promptly in order to confirm and sample any source of infection if safe to do so. (1C)

Antibiotic therapy

- ◆ Begin intravenous antibiotics as early as possible, and always within the first hour of recognizing severe sepsis (1D) and septic shock. (1B)
- ◆ Broad-spectrum: one or more agents active against likely bacterial/fungal pathogens and with good penetration into presumed source. (1B)
- ◆ Reassess antimicrobial regimen daily to optimize efficacy, prevent resistance, avoid toxicity, & minimize costs. (1C)
- ◇ Consider combination therapy in Pseudomonas infections. (2D)
- ◇ Consider combination empiric therapy in neutropenic patients. (2D)
- ◇ Combination therapy no more than 3-5 days and de-escalation following susceptibilities. (2D)
- ◆ Duration of therapy typically limited to 7–10 days; longer if response slow, undrainable foci of infection, or immunologic deficiencies. (1D)
- ◆ Stop antimicrobial therapy if cause is found to be non-infectious. (1D)

Source identification and control

- ◆ A specific anatomic site of infection should be established as rapidly as possible, (1D) and within the first 6 hours of presentation. (2D)
- ◆ Formally evaluate patient for a focus of infection amenable to source control measures (eg: abscess drainage, tissue debridement). (1C)
- ◆ Implement source control measures as soon as possible following successful initial resuscitation. (1C)
- ◇ Exception: infected pancreatic necrosis, where surgical intervention best delayed. (2B)
- ◆ Choose source control measure with maximum efficacy and minimal physiologic upset. (1D)
- ◆ Remove intravascular access devices if potentially infected. (2C)

Fluid therapy

- ◆ Fluid-resuscitate using crystalloids or colloids. (1B)
- ◆ Target a CVP of ≥ 8mmHg (≥12mmHg if mechanically ventilated). (2C)
- ◆ Use a fluid challenge technique while associated with a hemodynamic improvement. (1D)
- ◆ Give fluid challenges of 1000 mL of crystalloids or 300–500 mL of colloids over 30 minutes. More rapid and larger volumes may be required in sepsis-induced tissue hypoperfusion. (1D)
- ◆ Rate of fluid administration should be reduced if cardiac filling pressures increase without concurrent hemodynamic improvement. (1D)

Vasopressors

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

Inotropic therapy

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

Fluid therapy

- Fluid-resuscitate using crystalloids or colloids. (1B)
- Target a CVP of ≥ 8mmHg (≥12mmHg if mechanically ventilated). (1C)
- Use a fluid challenge technique while associated with a hemodynamic improvement. (1D)
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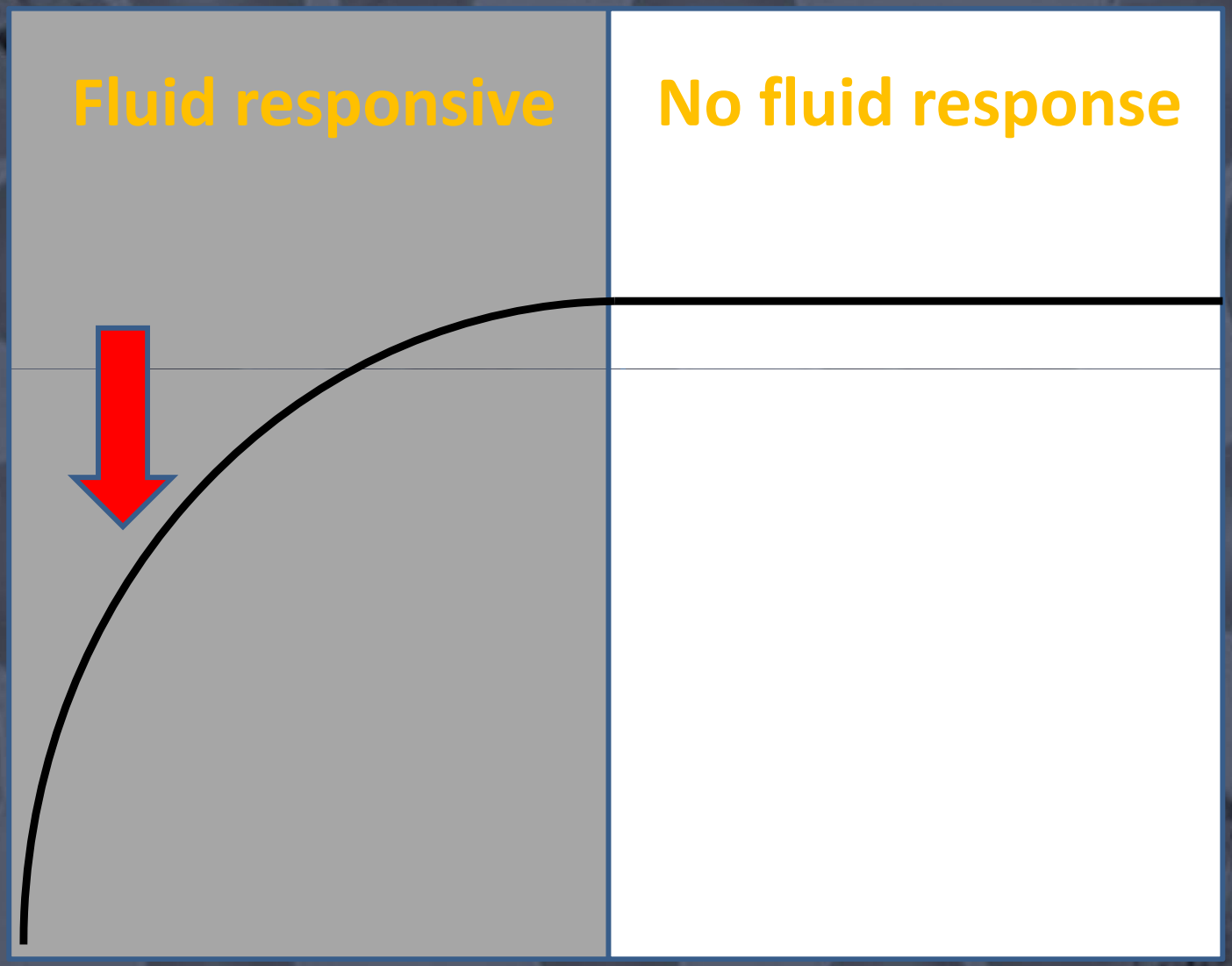
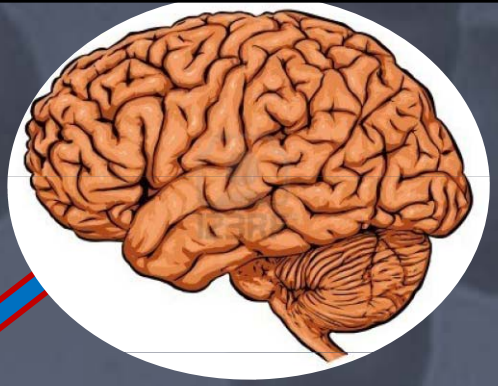
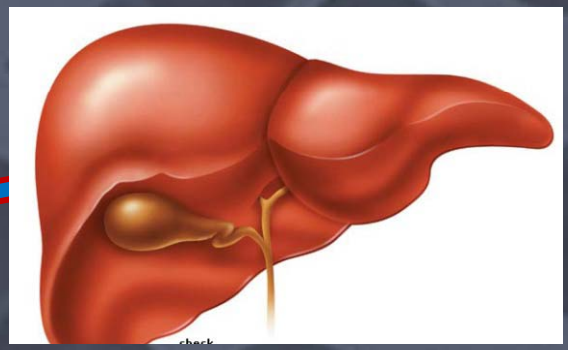
Starling curve

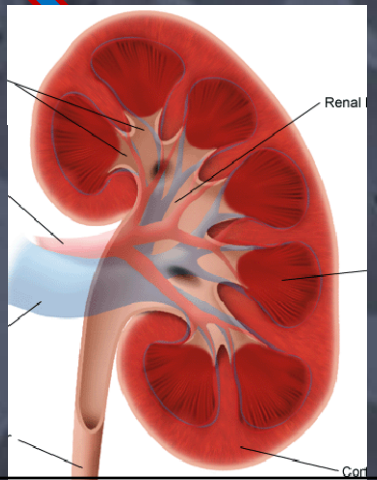


Systemic circulation

Microcirculation







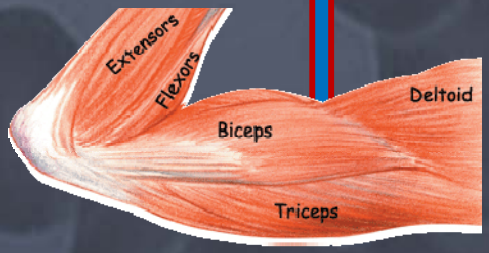
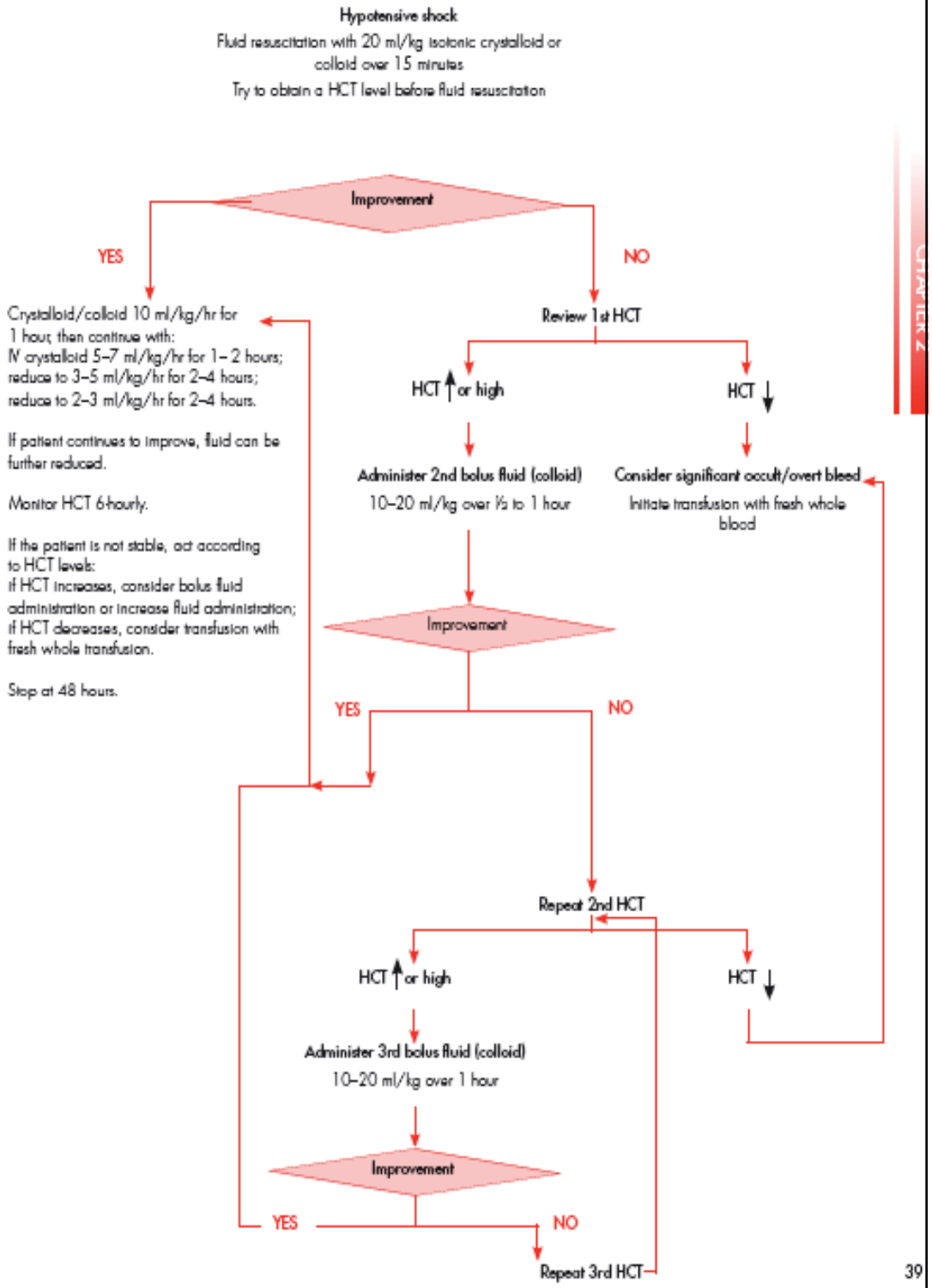
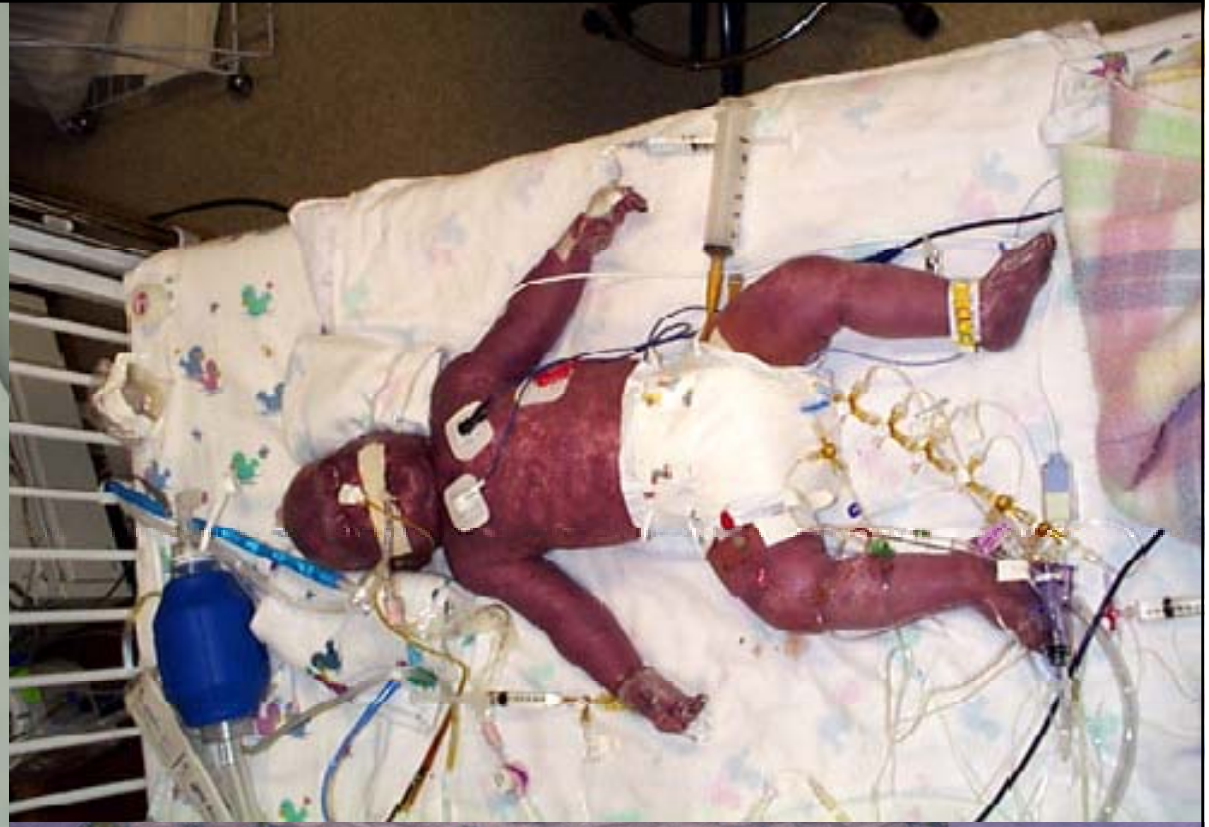
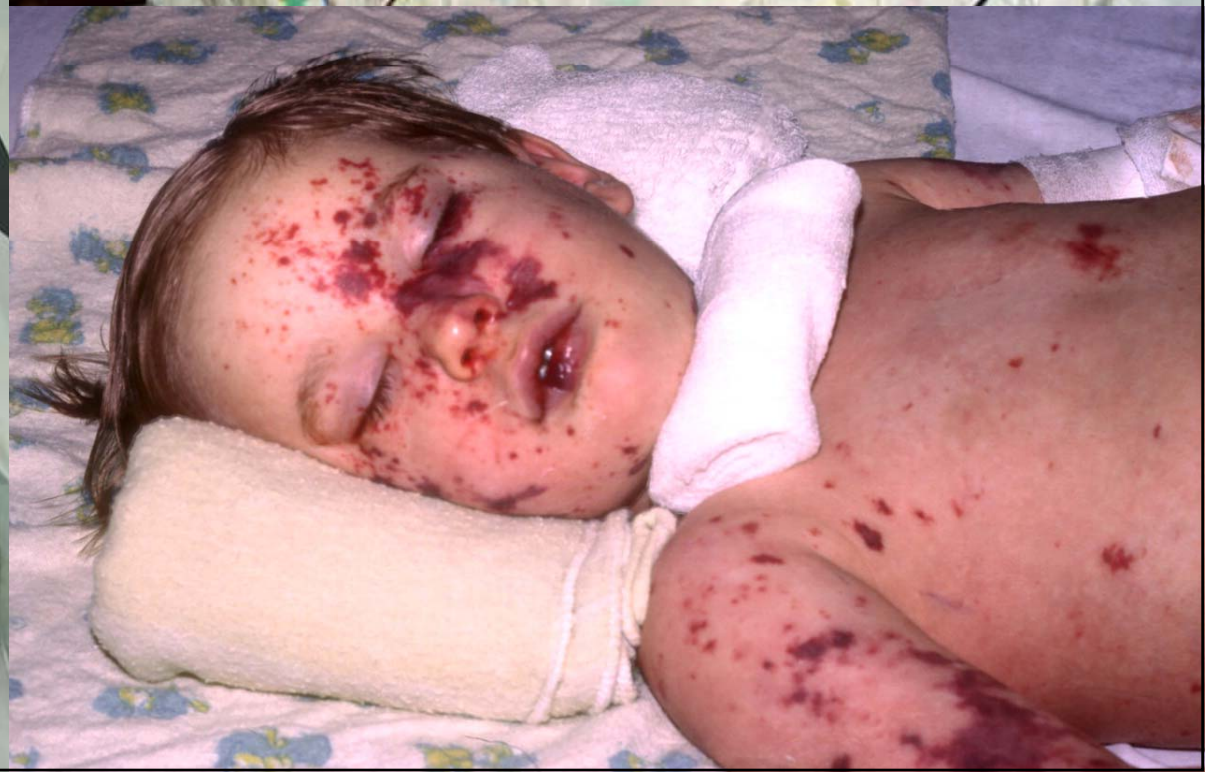
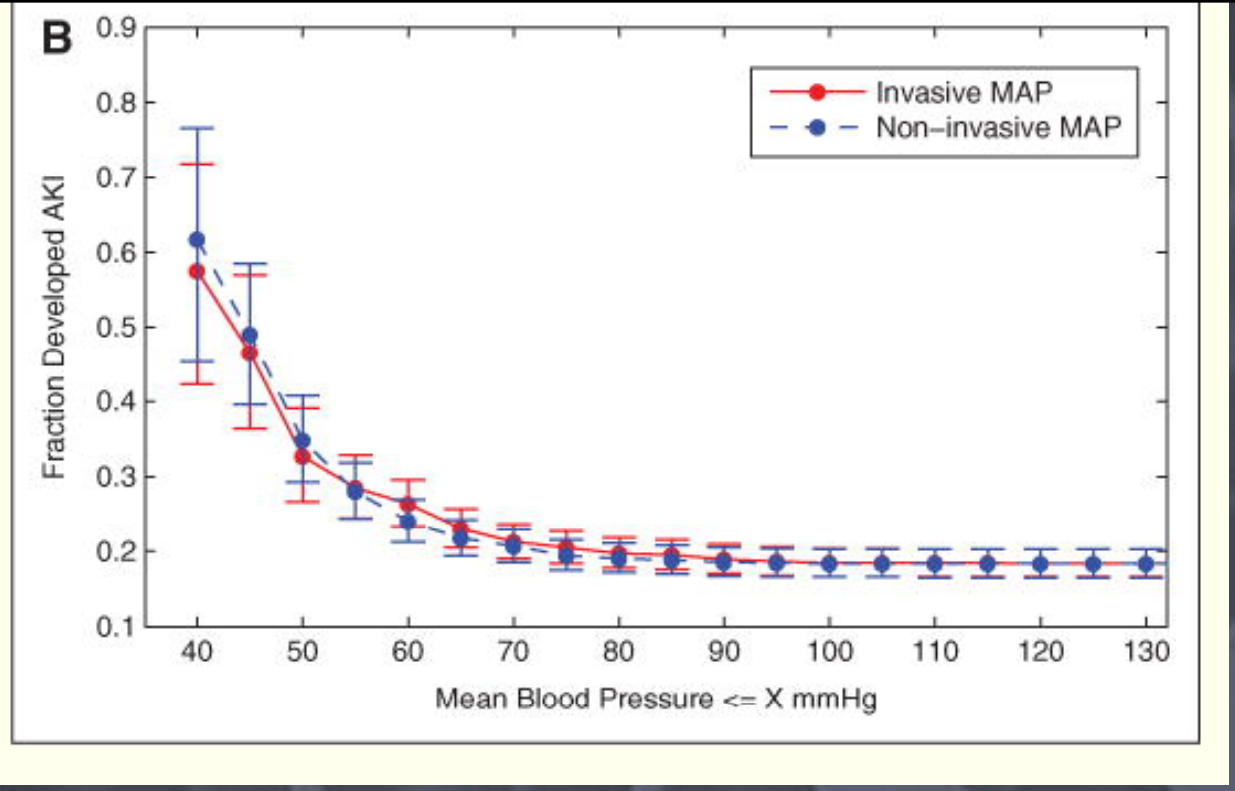


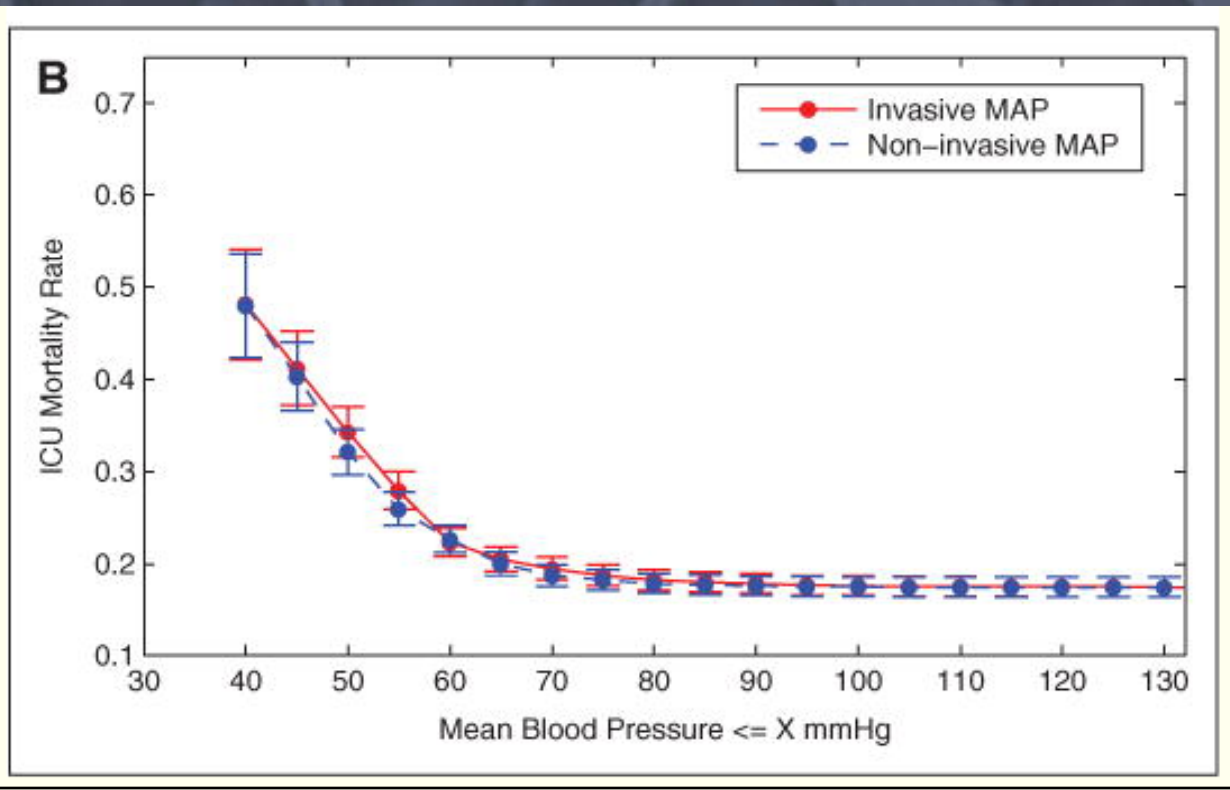
Figure 2.3 Algorithm for fluid management in hypotensive shock



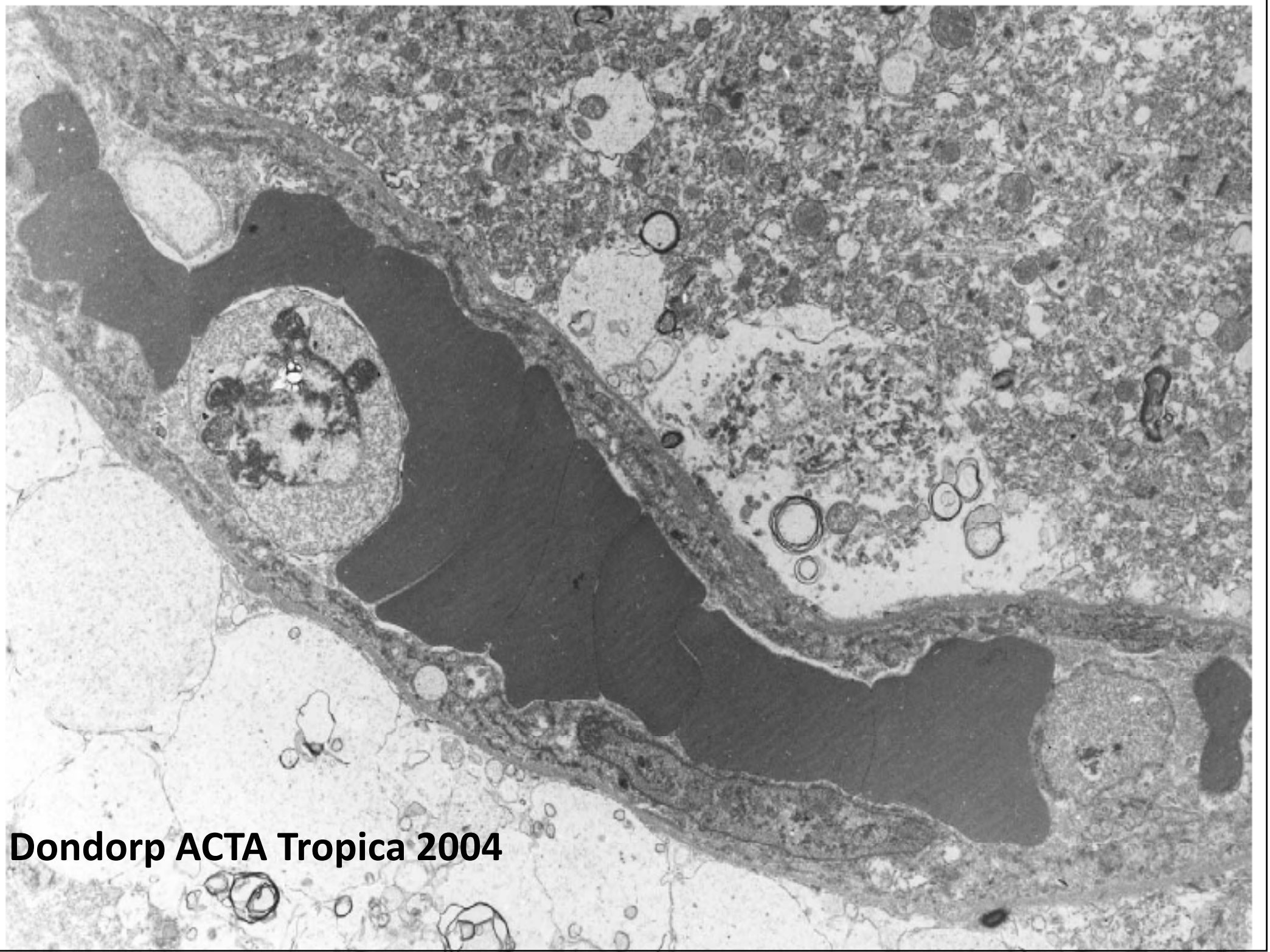








Lehman
CCM 2013


Dondorp ACTA Tropica 2004

Direct In Vivo Assessment of Microcirculatory Dysfunction in Severe Falciparum Malaria

A. M. Dondorp,[1,2,4] C. Ince,[1] P. Charunwatthana,[2] J. Hanson,[2] A. van Kuijen,[1] M. A. Faiz,[5] M. R. Rahman,[6] M. Hasan,[6] E. Bin Yunus,[6] A. Ghose,[5] R. Ruangveerayut,[3] D. Limmathurotsakul,[2] K. Mathura,[1] N. J. White,[2,4] and N. P. J. Day[2,4]

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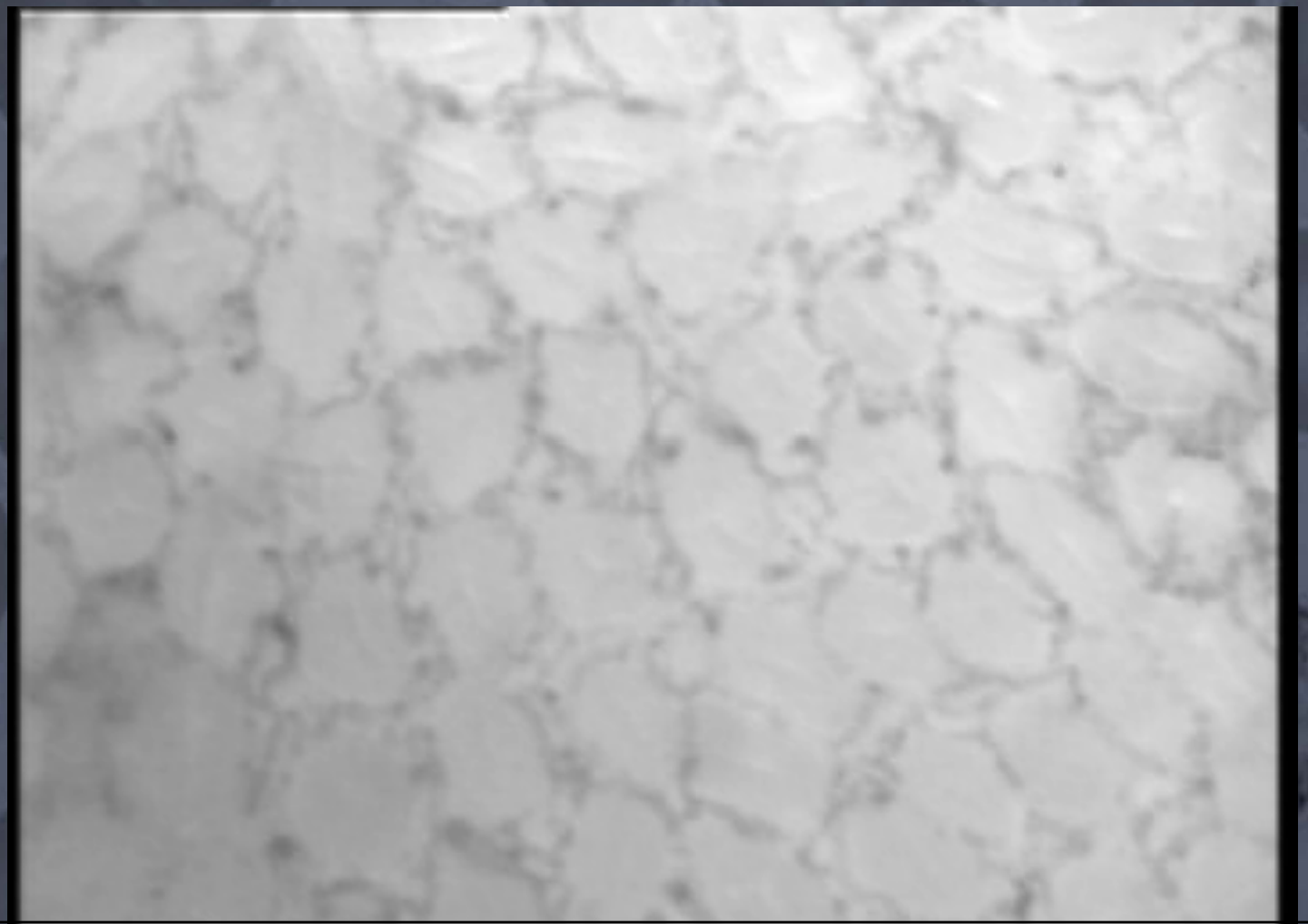

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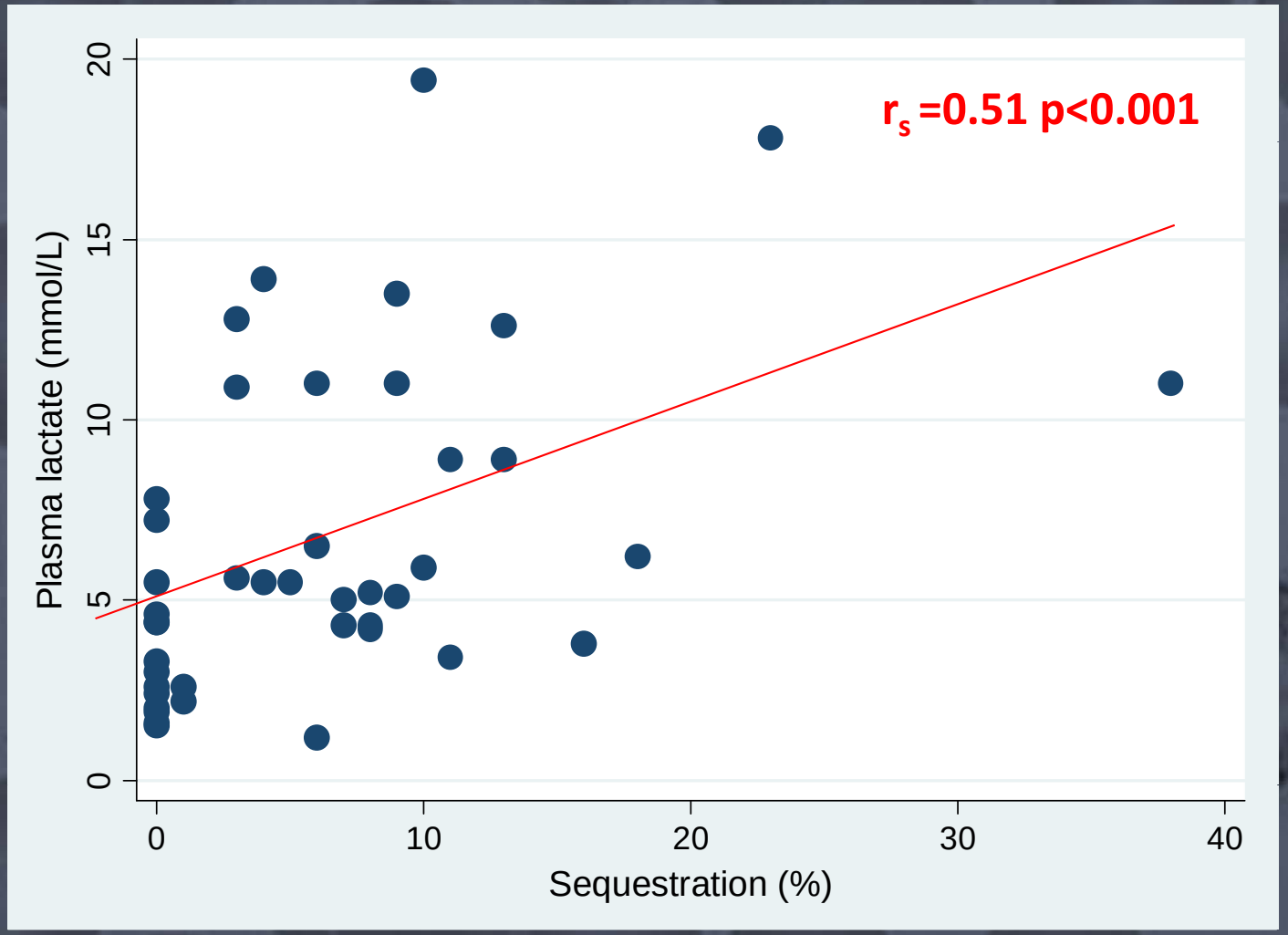

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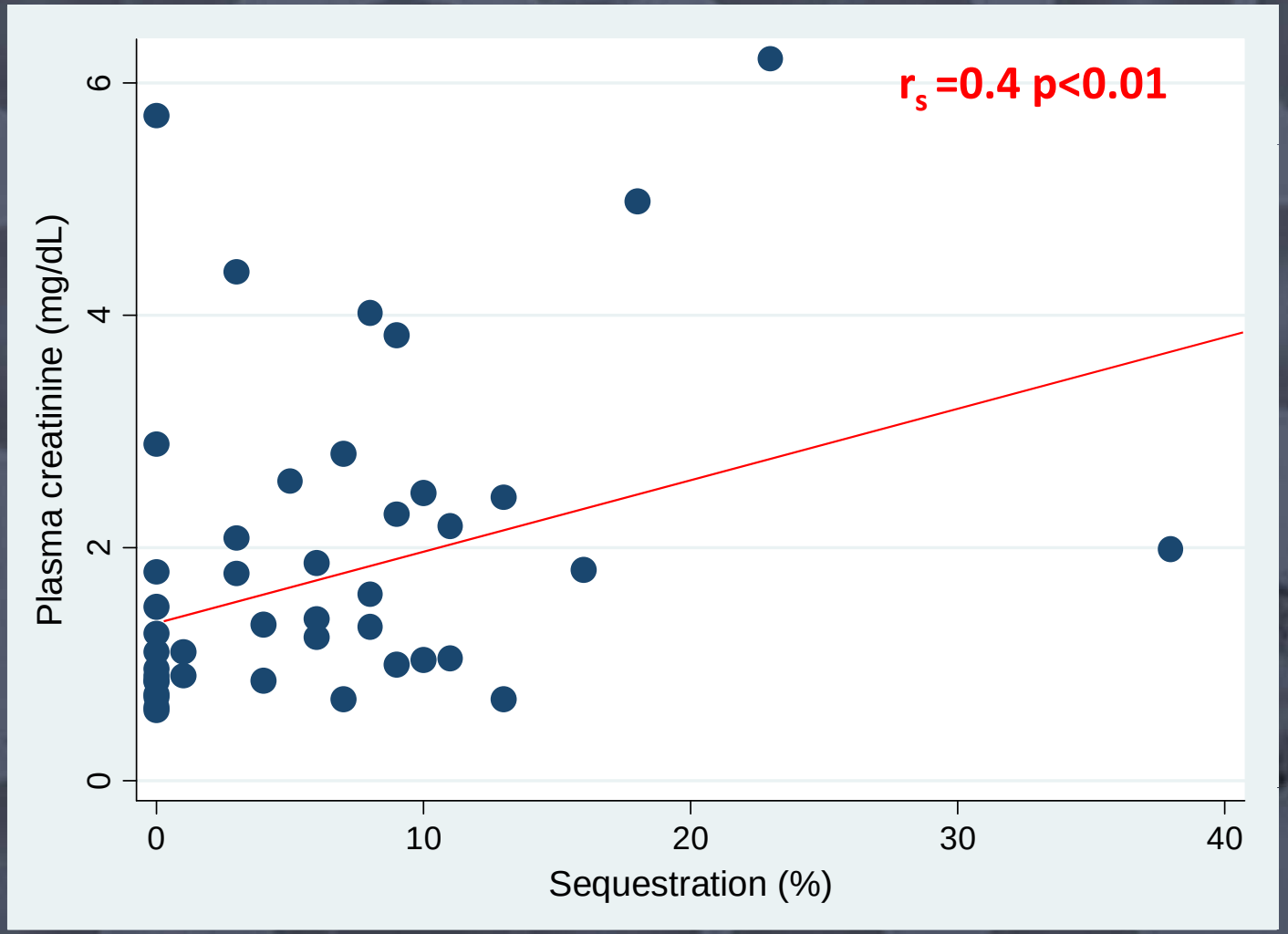
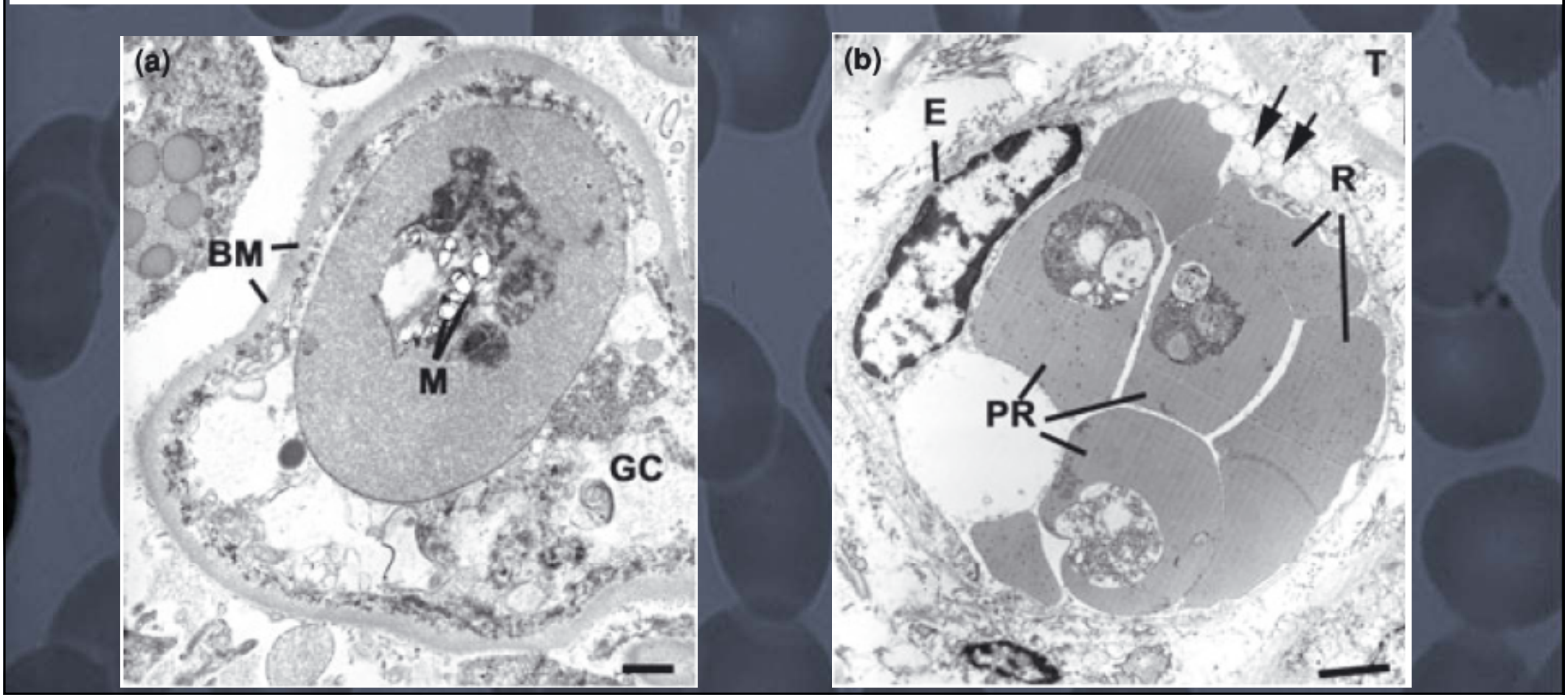


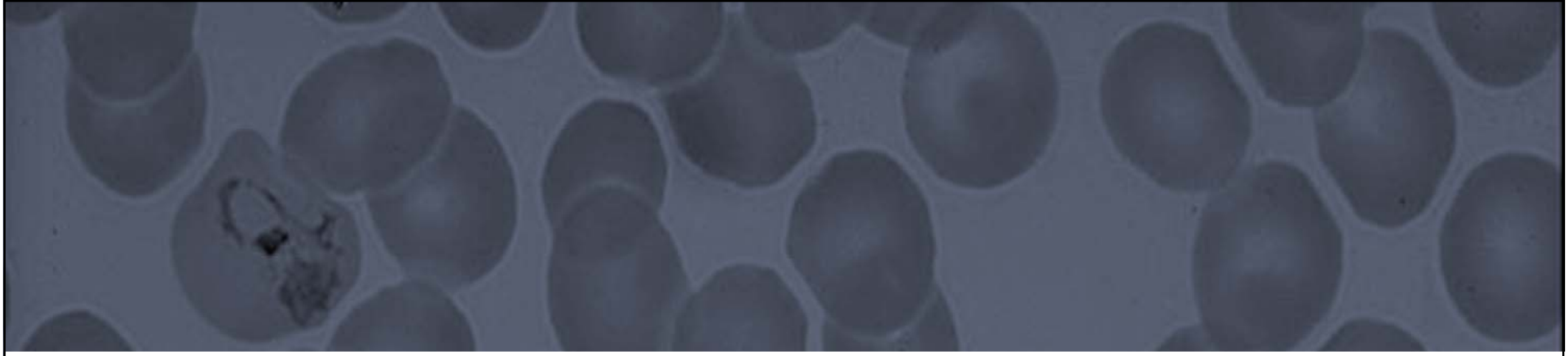
Tropical Medicine and International Health doi:10.1111/j.1365-3156.2007.01881.x

VOLUME 12 NO 9 PP 1037–1050 SEPTEMBER 2007

A quantitative ultrastructural study of renal pathology in fatal *Plasmodium falciparum* malaria

Sudarat Nguansangiam[1,2], Nicholas P. J. Day[3,4], Tran Tinh Hien[5], Nguyen Thi Hoang Mai[5], Urai Chaisri[1], Mario Riganti[1], Arjen M. Dondorp[3], Sue J. Lee[3], Nguyen Hoan Phu[5], Gareth D. H. Turner[3,6], Nicholas J. White[3,4], David J. P. Ferguson[6] and Emsri Pongponratn[1]

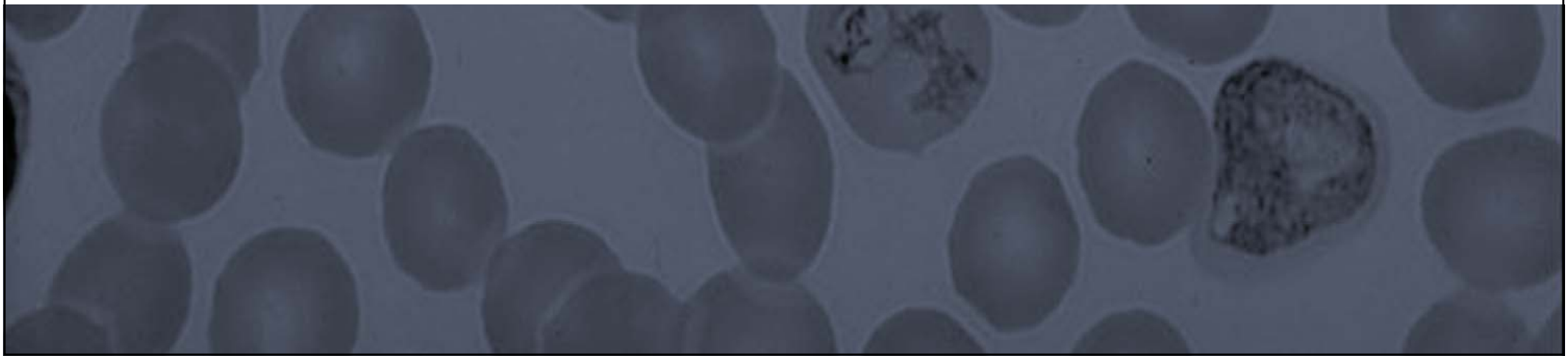


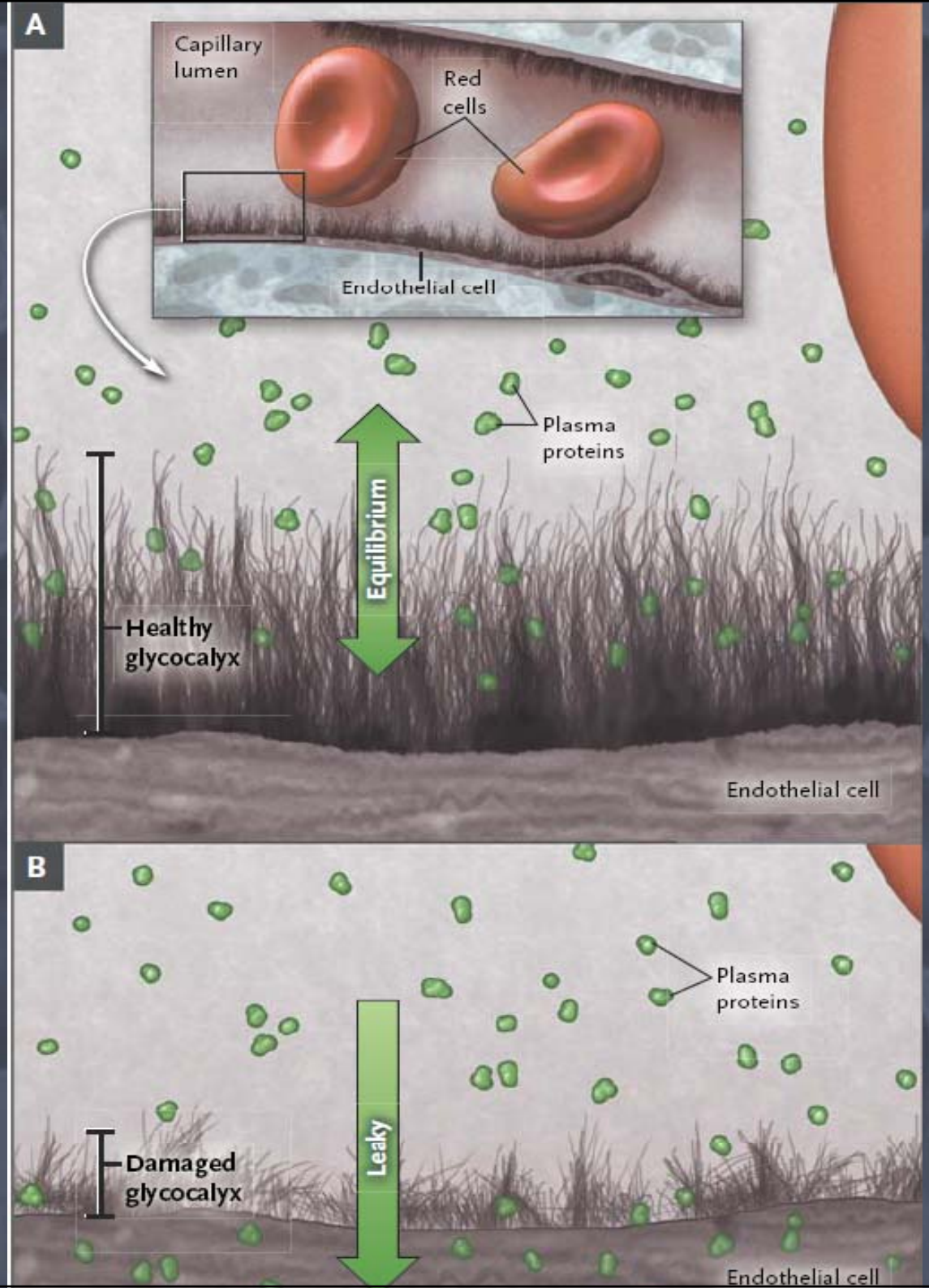


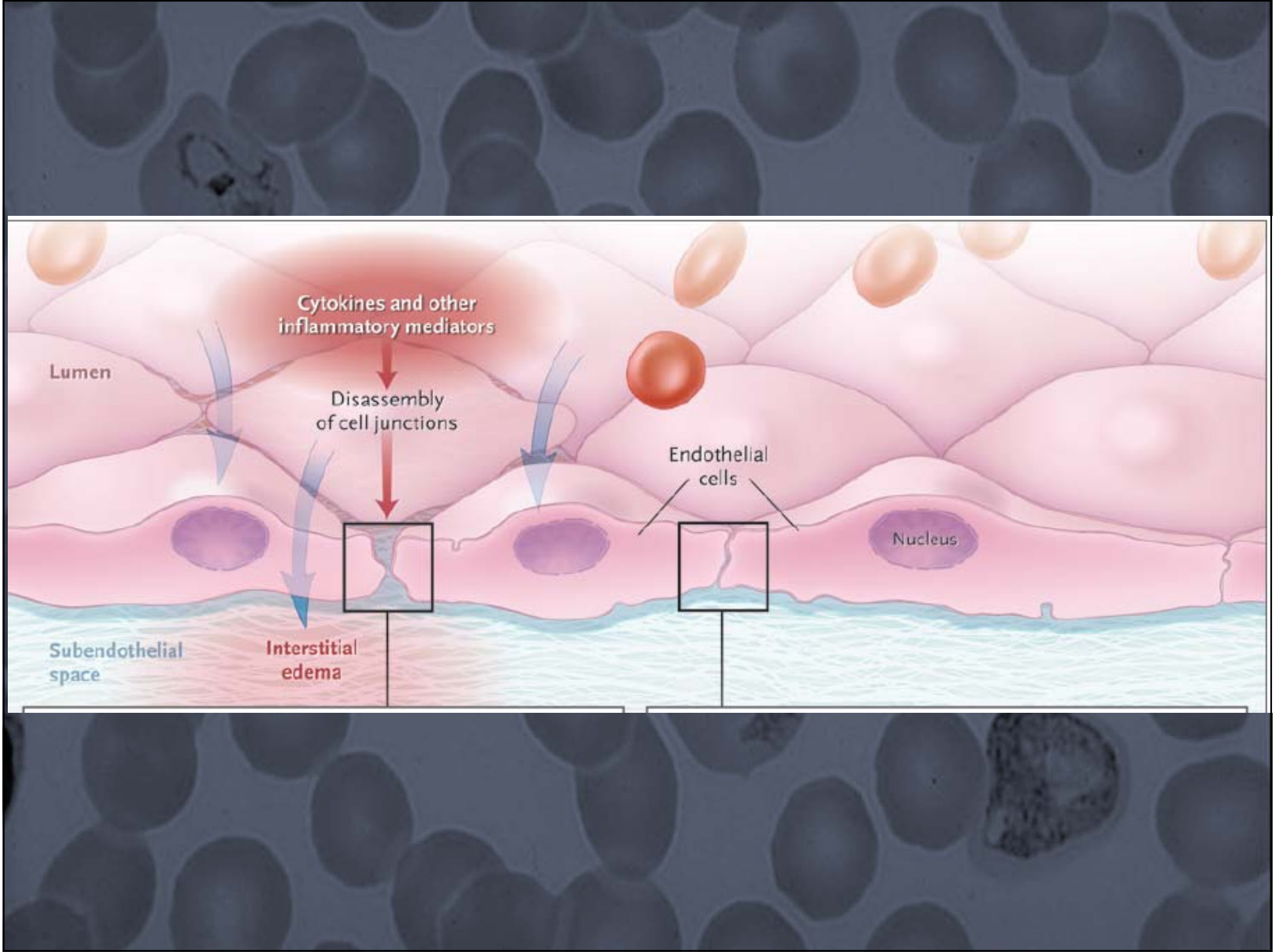
Measures of Capillary Permeability in Acute Falciparum Malaria: Relation to Severity of Infection and Treatment

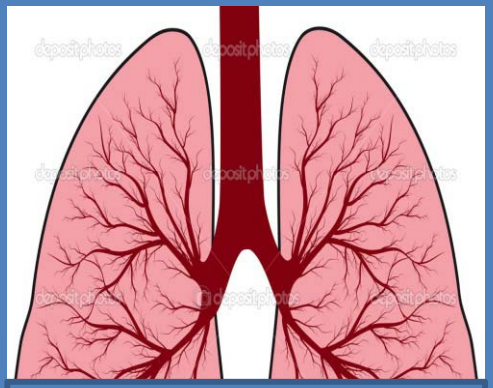
T. M. E. Davis, Y. Suputtamongkol, J. L. Spencer, S. Ford, N. Chienkul, W. E. Schulenburg, and N. J. White

From the Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; the Department of Medicine, Paholpolpayuhasena Hospital, Kanchanaburi, Thailand; the Tropical Medicine Unit, Nuffield Department of Clinical Medicine, University of Oxford, John Radcliffe Hospital, Headington, Oxford, United Kingdom; and the Western Ophthalmic Hospital, London, United Kingdom




A
Capillary lumen
Red cells
Endothelial cell
Plasma proteins
Equilibrium
Healthy glycocalyx
Endothelial cell
B
Plasma proteins
Leaky
Damaged glycocalyx
Endothelial cell


Cytokines and other inflammatory mediators
Lumen
Disassembly of cell junctions
Endothelial cells
Nucleus
Subendothelial space
Interstitial edema



PULMONARY EDEMA IN CEREBRAL MALARIA PATIENTS IN THAILAND

Boonrut Aursudkij[1], Polrat Wilairatana[2], Suparp Vannaphan[2], Douglas S Walsh[3], Victor R Gordeux[4], Sornchai Looareesuwan[2]

[1]Division of Pulmonary Medicine, Ramathibodi Hospital, Faculty of Medicine, Mahidol University, Bangkok, Thailand; [2]Division of Critical Care for Tropical Diseases, Hospital for Tropical Diseases, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; [3]Department of Immunology and Medicine, United States Army Medical Component, Armed Forces Research Institute of Medical Sciences (AFRIMS), Bangkok, Thailand; [4]The George Washington University Medical Center, 2150 Pennsylvania Avenue NW, Washington DC, USA

Anaesth Intens Care 1996; **24**; 217-223

Ordinary Papers

Predictors of Mortality in Severe Malaria: a Two-Year Experience in a Non-Endemic Area

L. BLUMBERG*, R. P. LEE , J. LIPMAN , S. BEARDS§
South African Institute of Medical Research and University of the Witwatersrand Hospital, South Africa

A PRACTICAL HANDBOOK

Third Edition

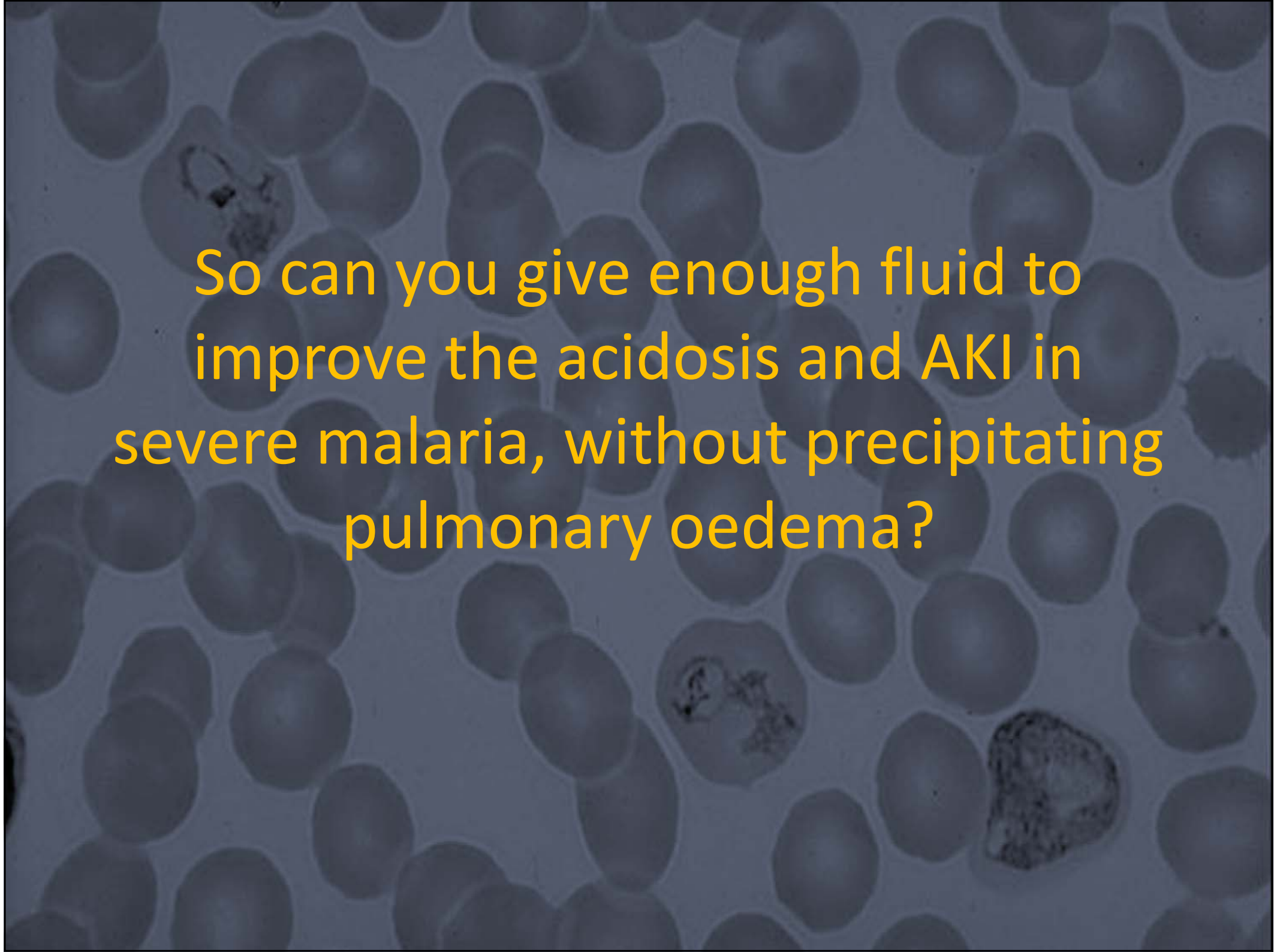
MANAGEMENT OF SEVERE MALARIA

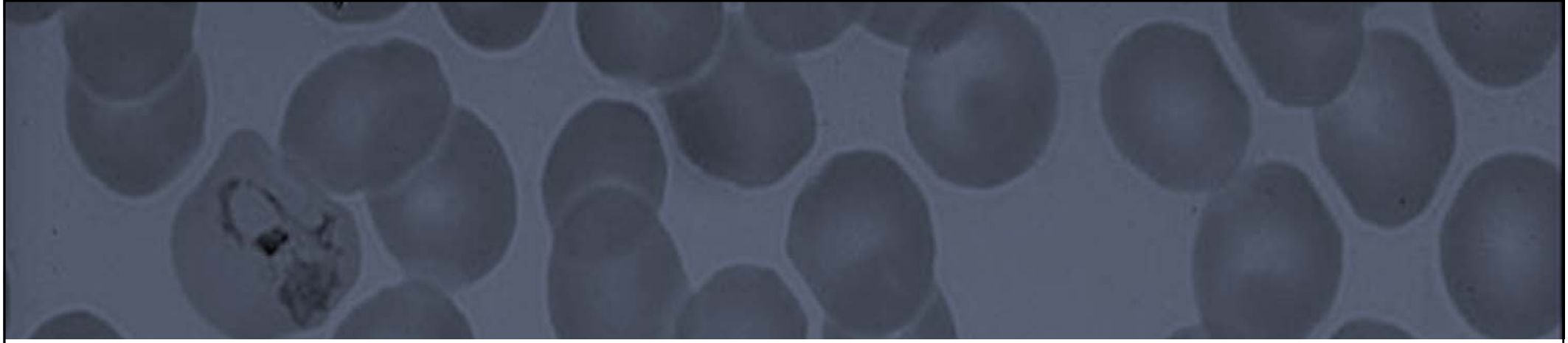
World Health Organization

Management

If there is evidence of dehydration:

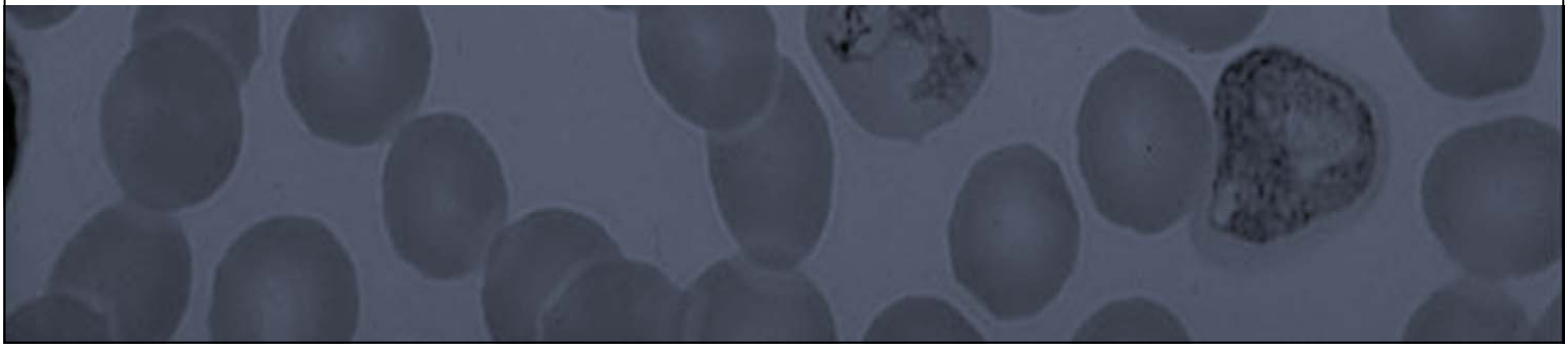
- Give only isotonic fluid (0.9% saline) by slow intravenous infusion to restore the circulating volume, but avoid circulatory overload, which may rapidly precipitate fatal pulmonary oedema.


So can you give enough fluid to improve the acidosis and AKI in severe malaria, without precipitating pulmonary oedema?



Fluid Resuscitation of Adults With Severe Falciparum Malaria: Effects on Acid-Base Status, Renal Function, and Extravascular Lung Water

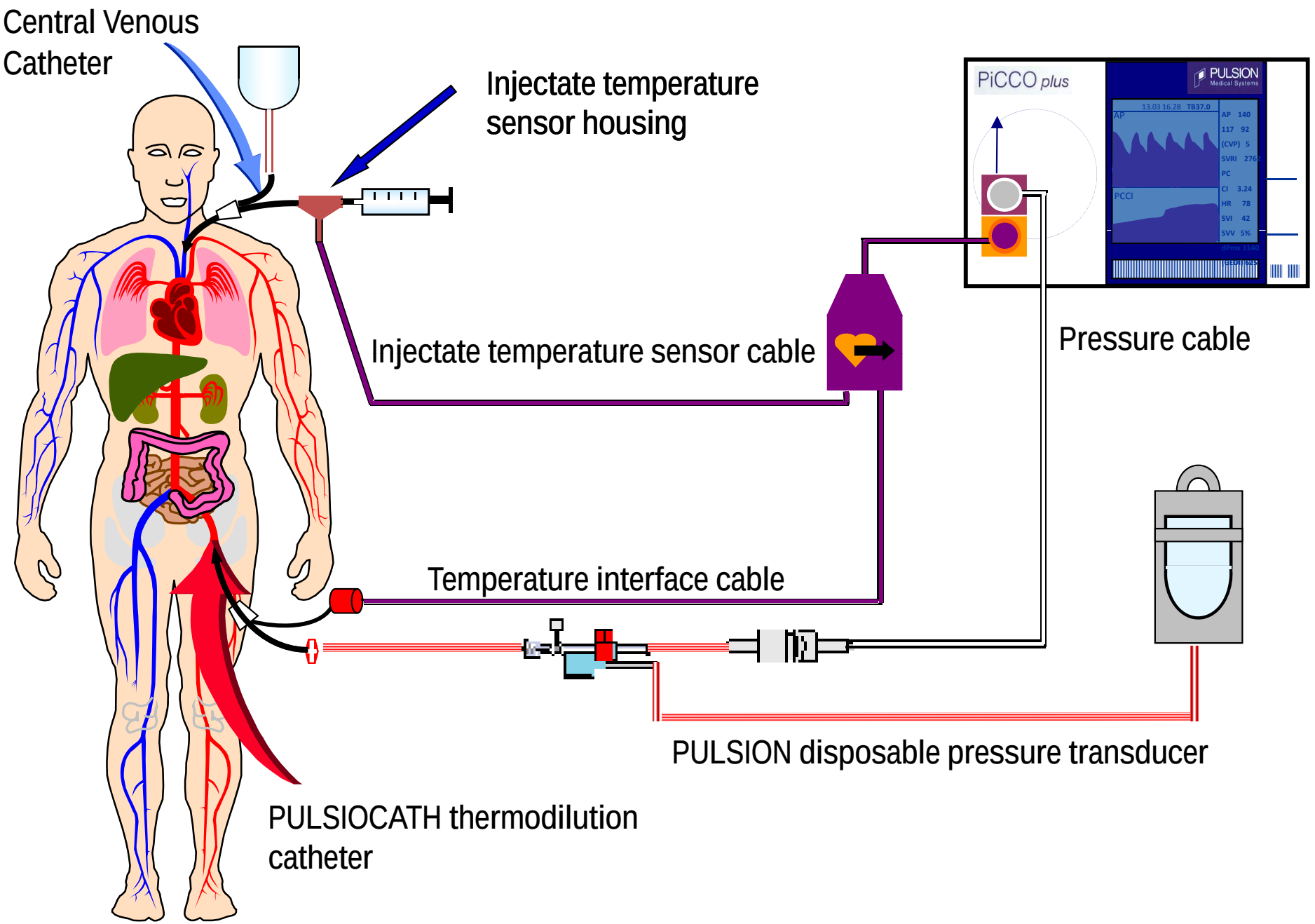
Josh P. Hanson, MBBS[1]; Sophia W.K. Lam, MBBS[1]; Sanjib Mohanty, MD[2]; Shamshul Alam, MD[3]; Rajyabardhan Pattnaik, MBBS[2]; Kishore C. Mahanta, MD[2]; Mahatab Uddin Hasan, MD[3]; Prakaykaew Charunwatthana, MD[1]; Saroj K. Mishra, MD[2]; Nicholas P.J. Day, MD[1,4]; Nicholas J. White, MD[1,4]; Arjen M. Dondorp, MD[1,4]



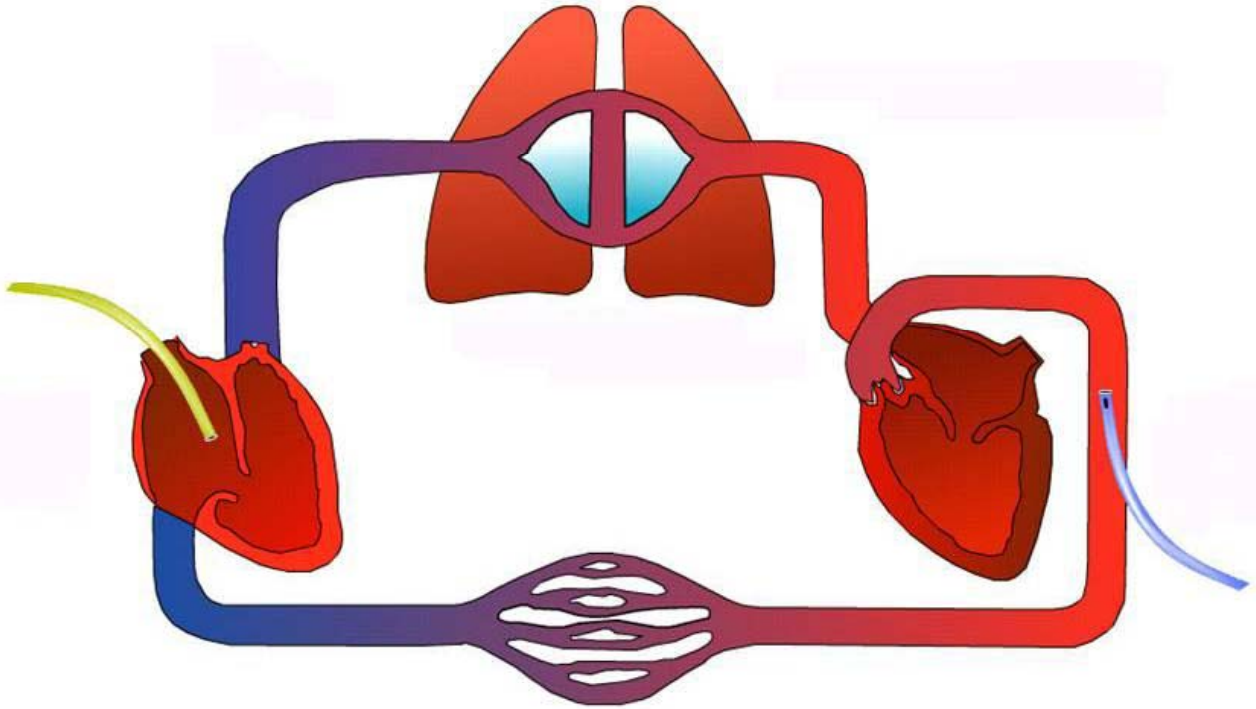
In this study

- ICU patients
- Severe acidosis (base deficit >6mEq/L)
- Acute Kidney Injury (BUN >60mg/dl)
- Received a median of 3360 mL of N saline in the 1st 6 hours & 5900 mL in the 1st 24 hours guided by invasive measures of volume status
- .

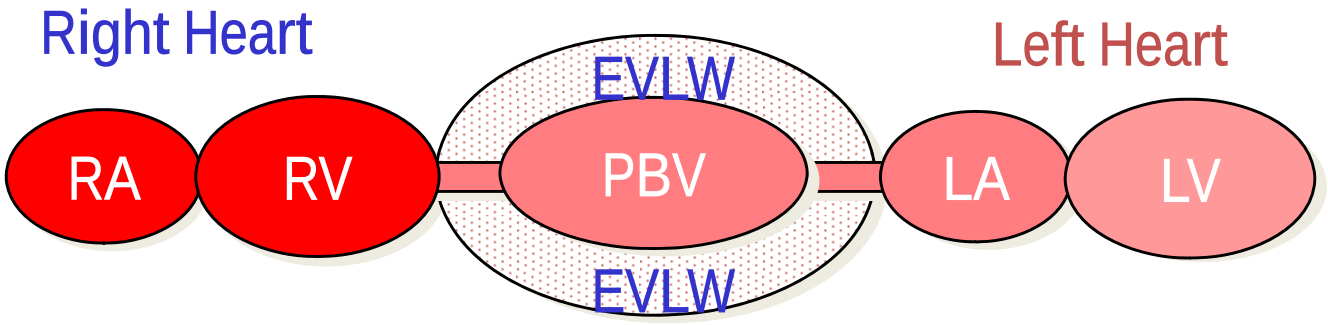
PiCCO*plus* setup

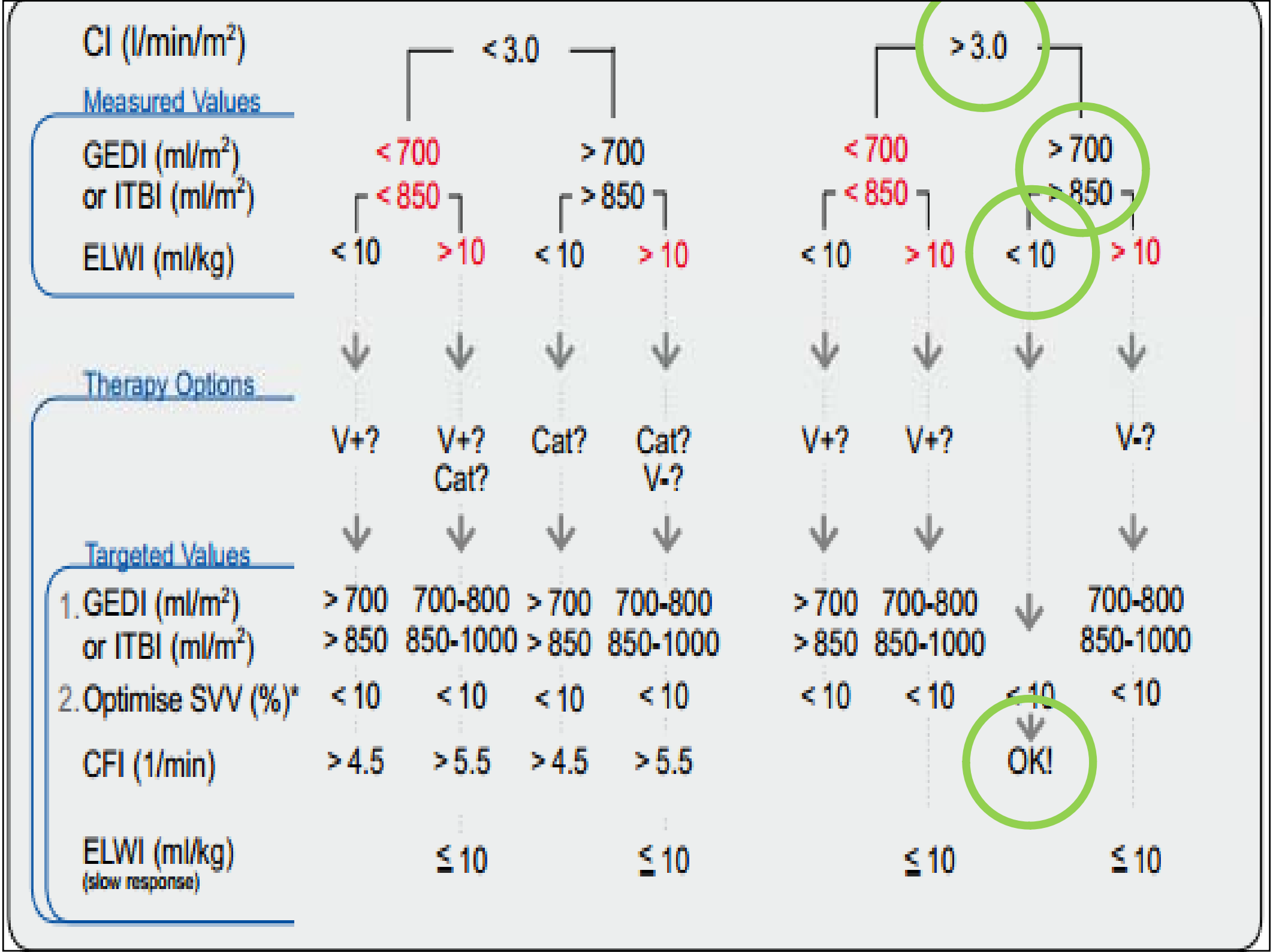


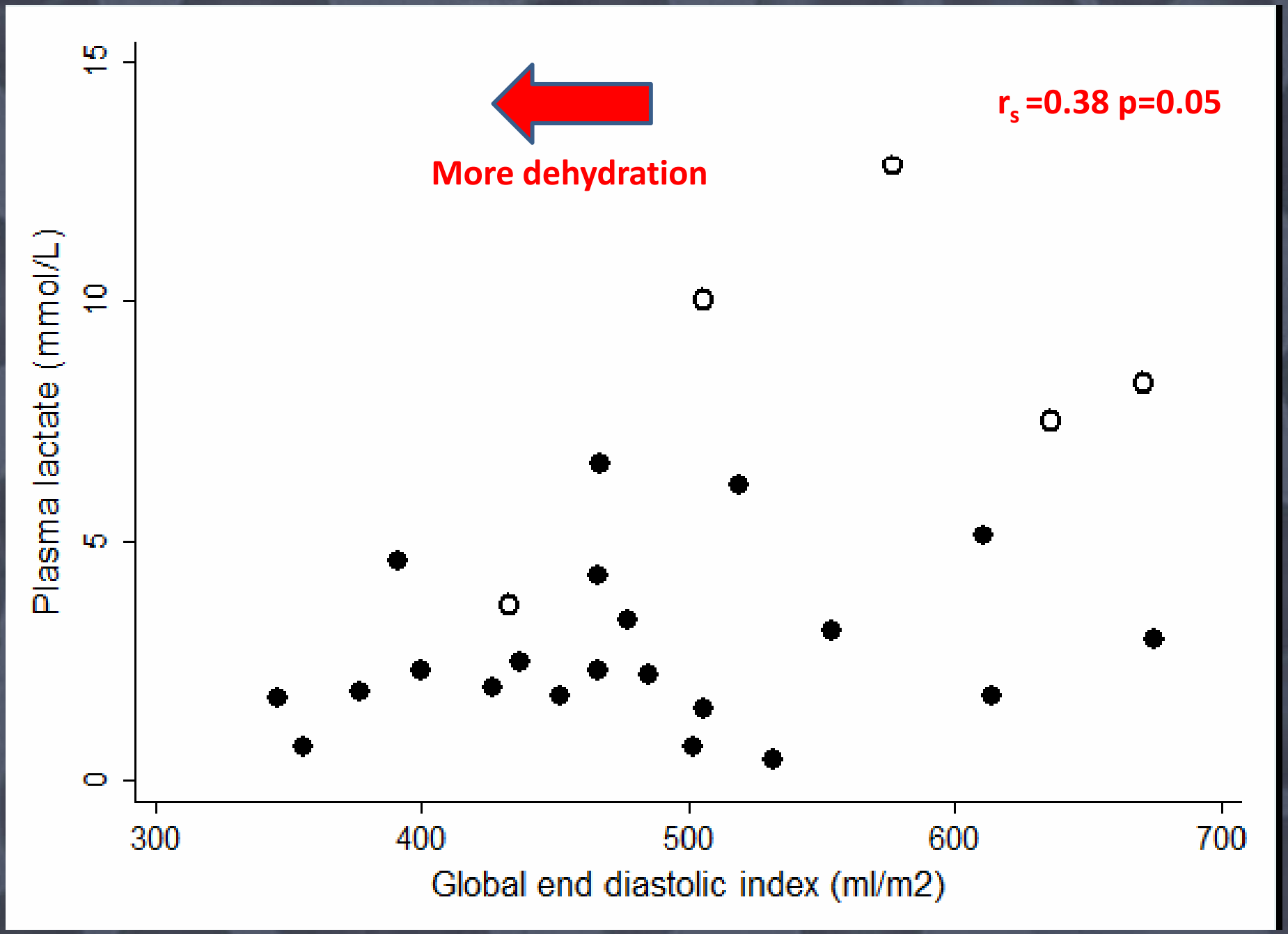
Bolus Injection

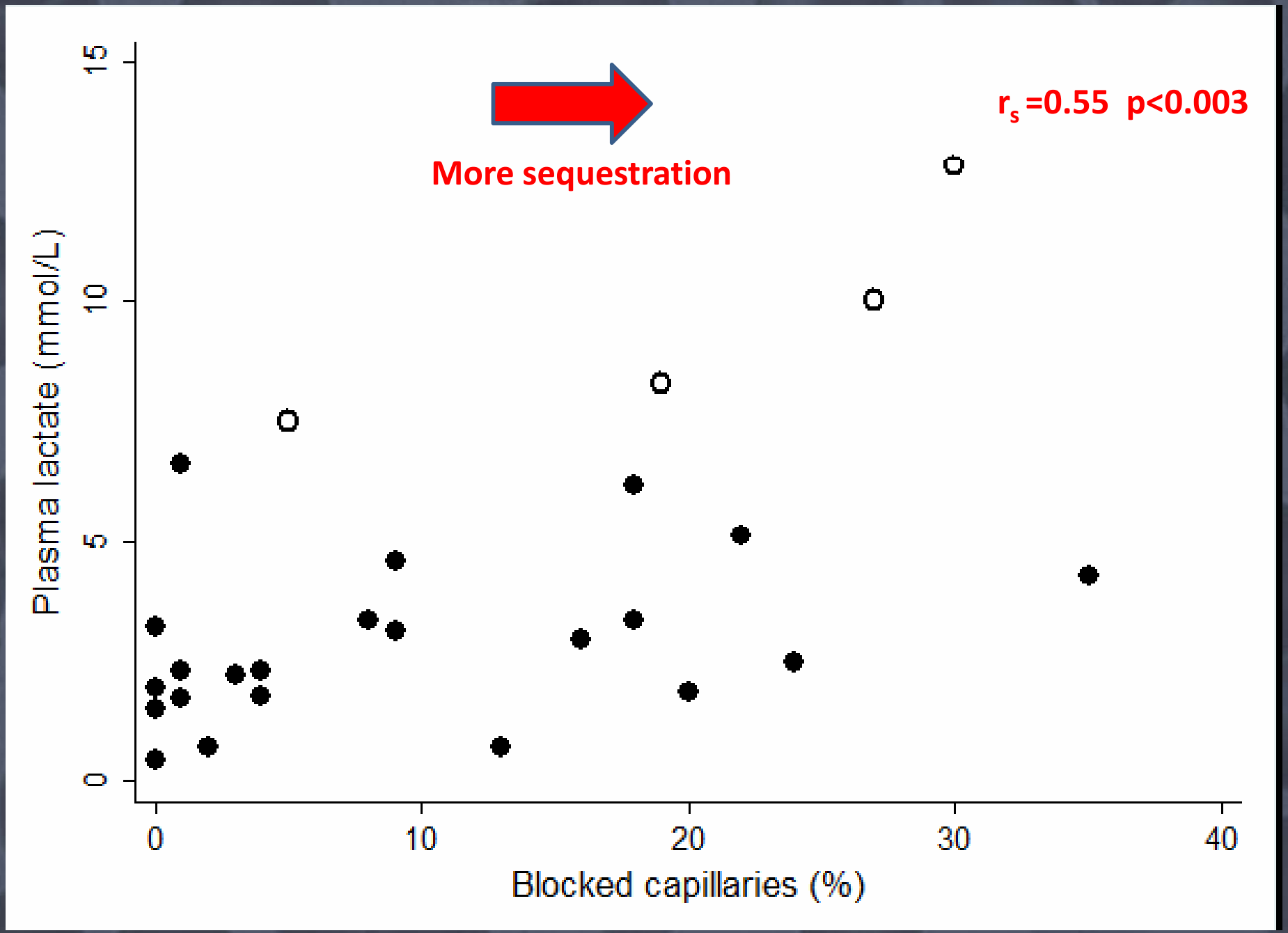


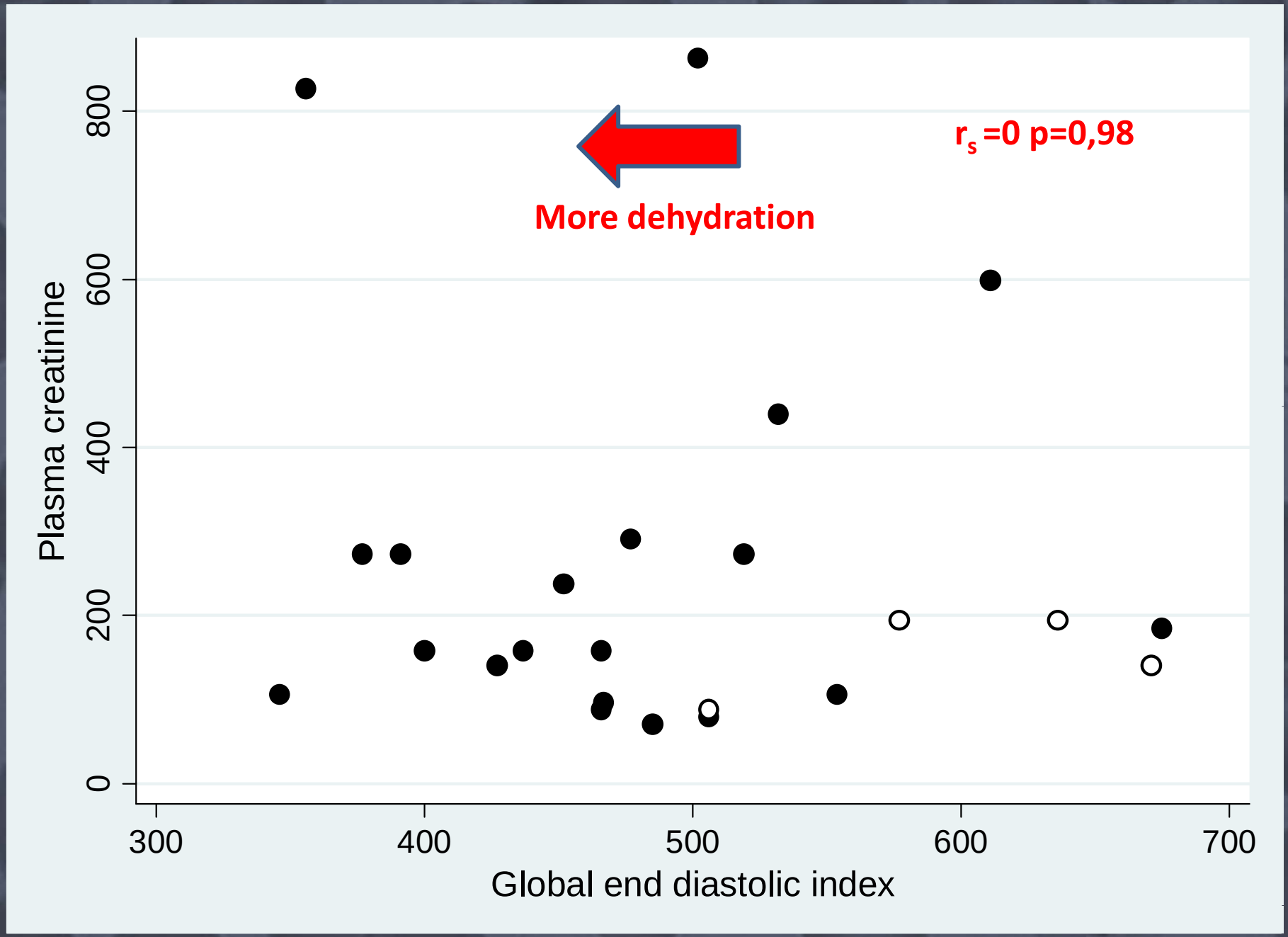
PiCCO Catheter e.g. in femoral artery

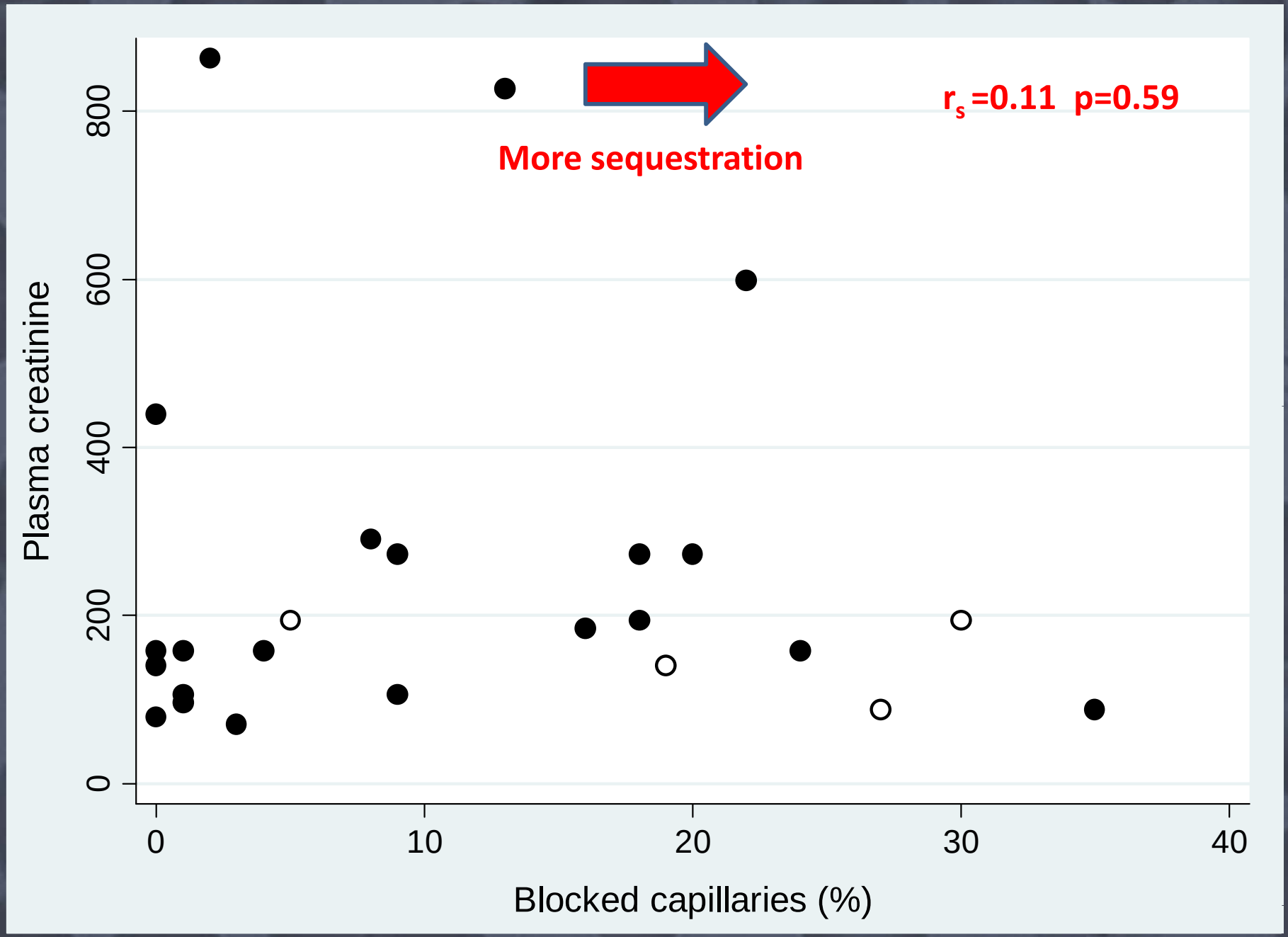



CI (l/min/m²)
< 3.0
> 3.0
Measured Values
GEDI (ml/m²)
or ITBI (ml/m²)
ELWI (ml/kg)
< 700
> 700
< 850
> 850
< 10
> 10
Therapy Options
V+?
V+?
Cat?
Cat?
V-?
Cat?
V+?
V+?
V-?
Targeted Values
1. GEDI (ml/m²)
or ITBI (ml/m²)
> 700
> 850
700-800
850-1000
2. Optimise SVV (%)*
< 10
CFI (1/min)
> 4.5
> 5.5
OK!
ELWI (ml/kg)
(slow response)
≤ 10


More dehydration
r_s =0.38 p=0.05
Plasma lactate (mmol/L)
0
5
10
15
300
400
500
600
700
Global end diastolic index (ml/m2)


More sequestration
r_s =0.55 p<0.003
Plasma lactate (mmol/L)
0
5
10
15
0
10
20
30
40
Blocked capillaries (%)


Plasma creatinine
0
200
400
600
800
300
400
500
600
700
Global end diastolic index
More dehydration
r_s =0 p=0,98


r_s =0.11 p=0.59
More sequestration
Plasma creatinine
0
200
400
600
800
0
10
20
30
40
Blocked capillaries (%)

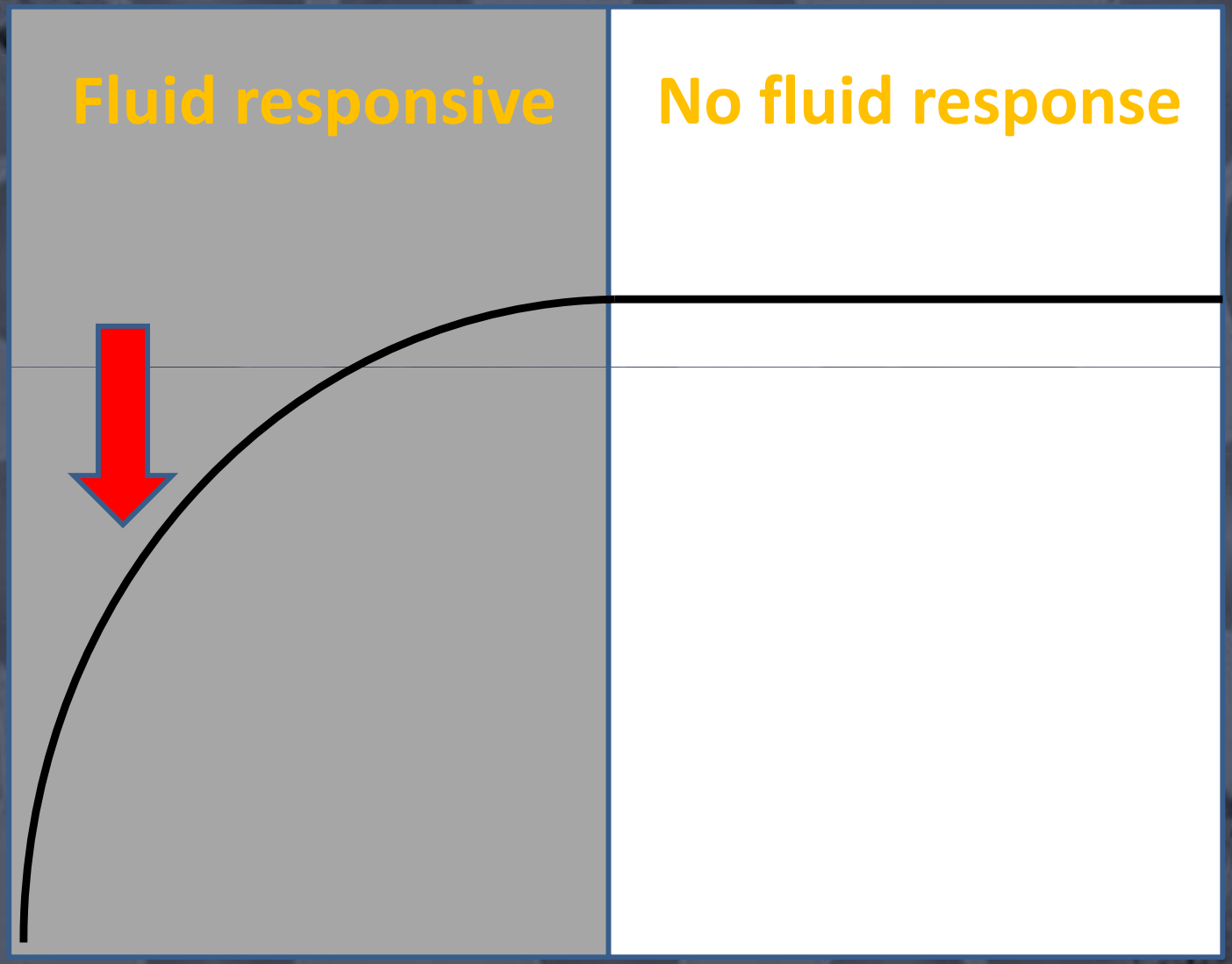
AKI in the study

	Median (IQR) blocked capillaries on admission
AKI during hospitalisation	30% (7-36)
No AKI during hospitalisation	6% (1-18)

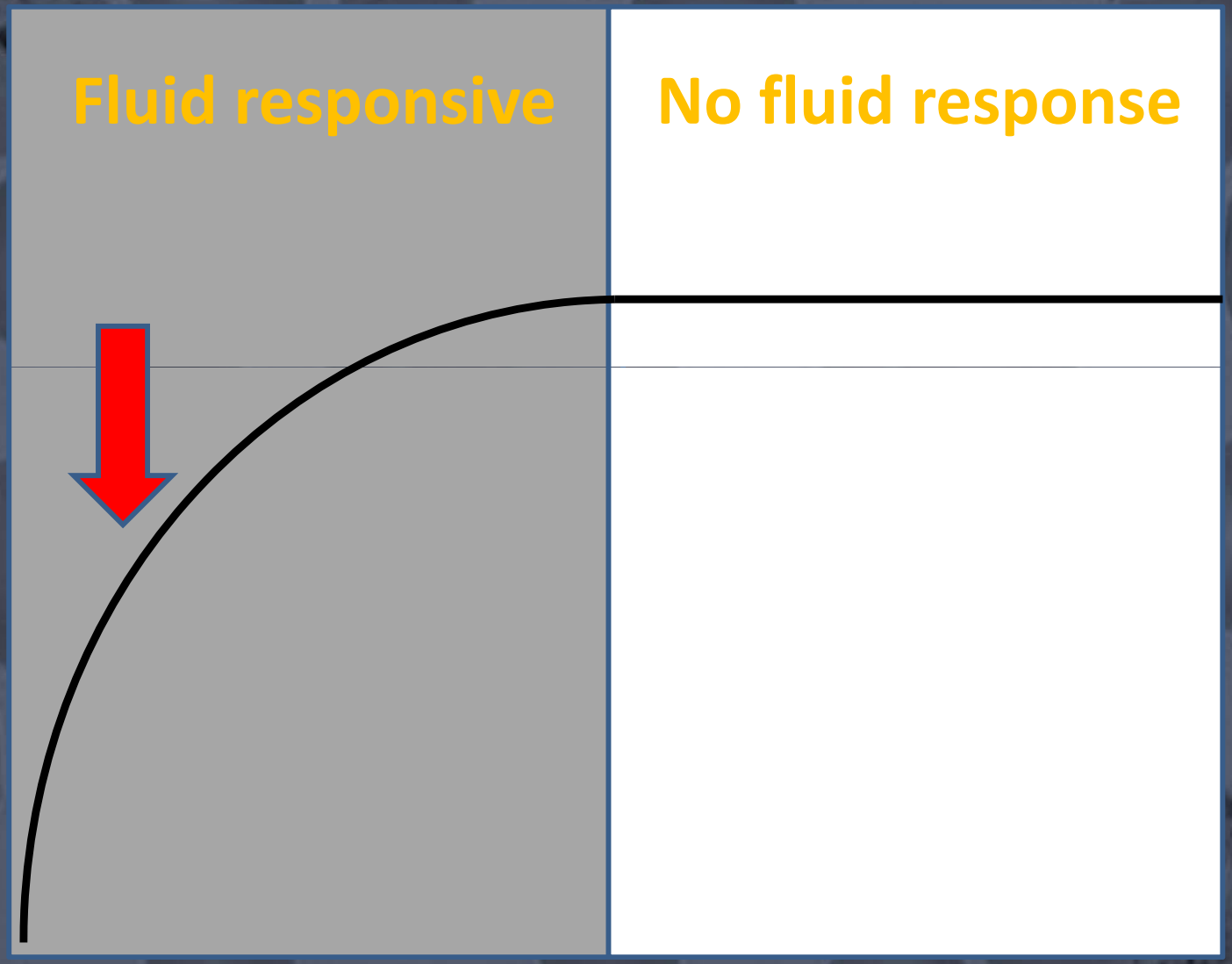
Fluid responsiveness in severe malaria

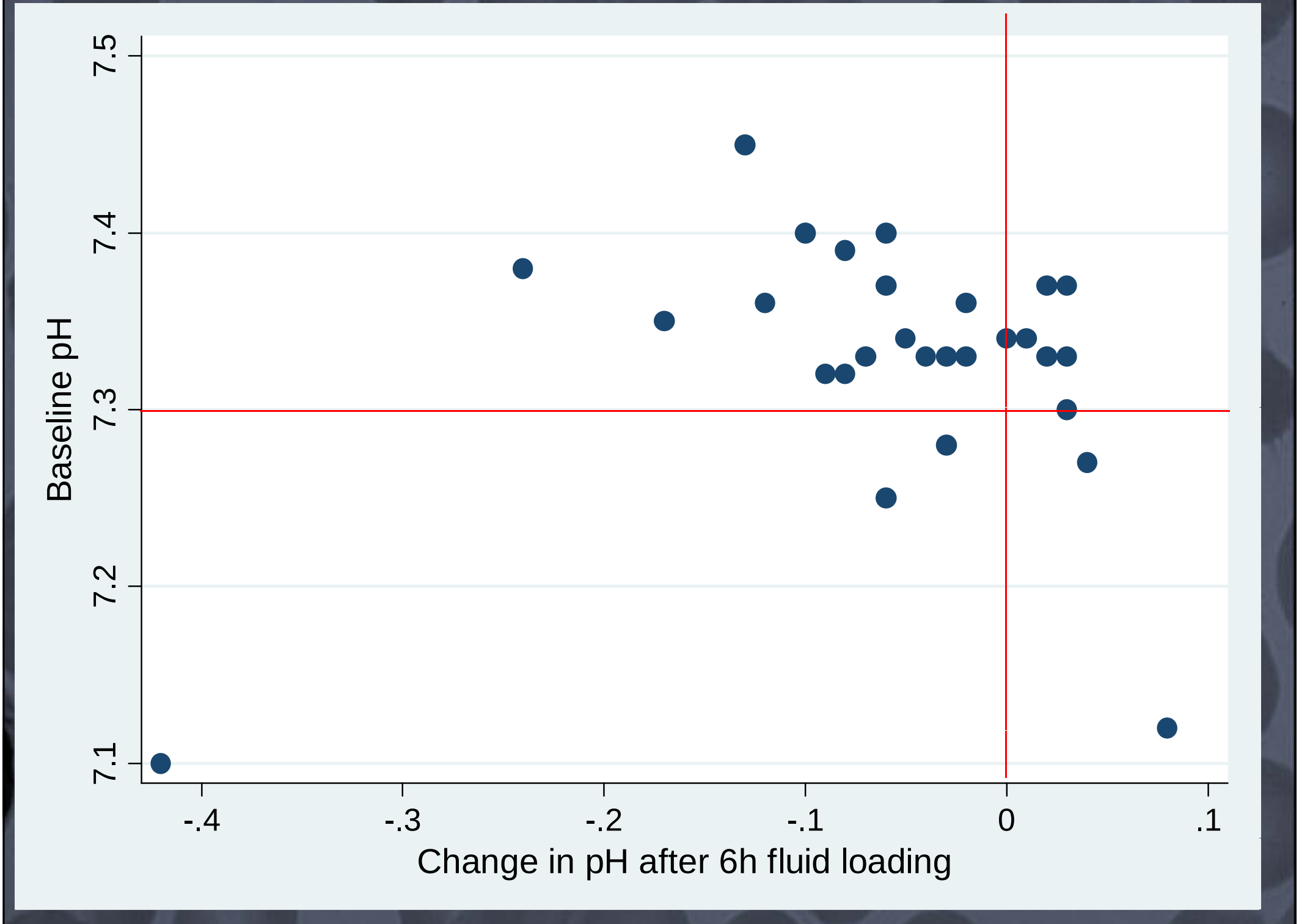
- 26 patients received 81 fluid boluses of >500ml
- The patient was fluid responsive on 23 (28%) of these occasions

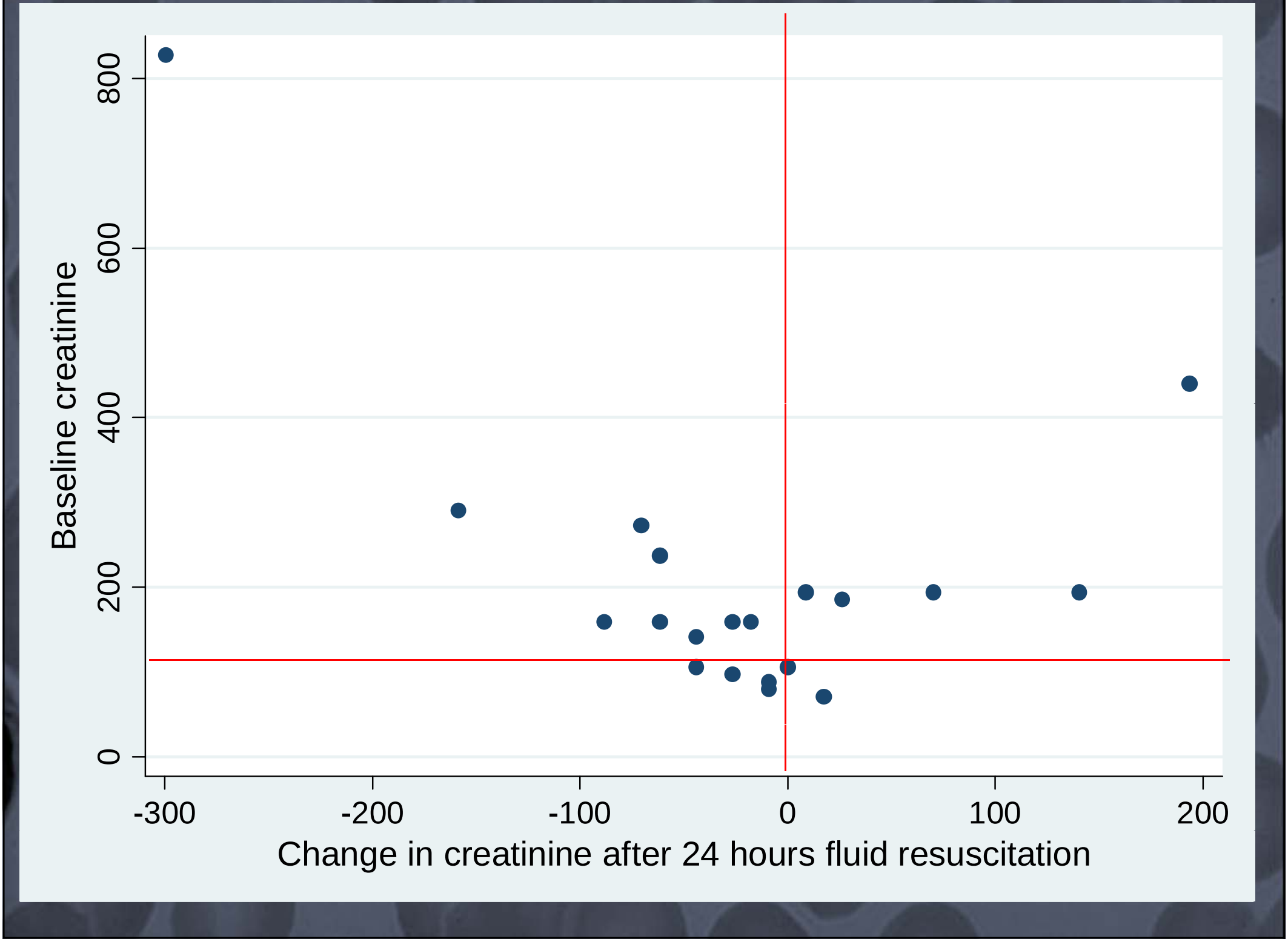
Starling curve



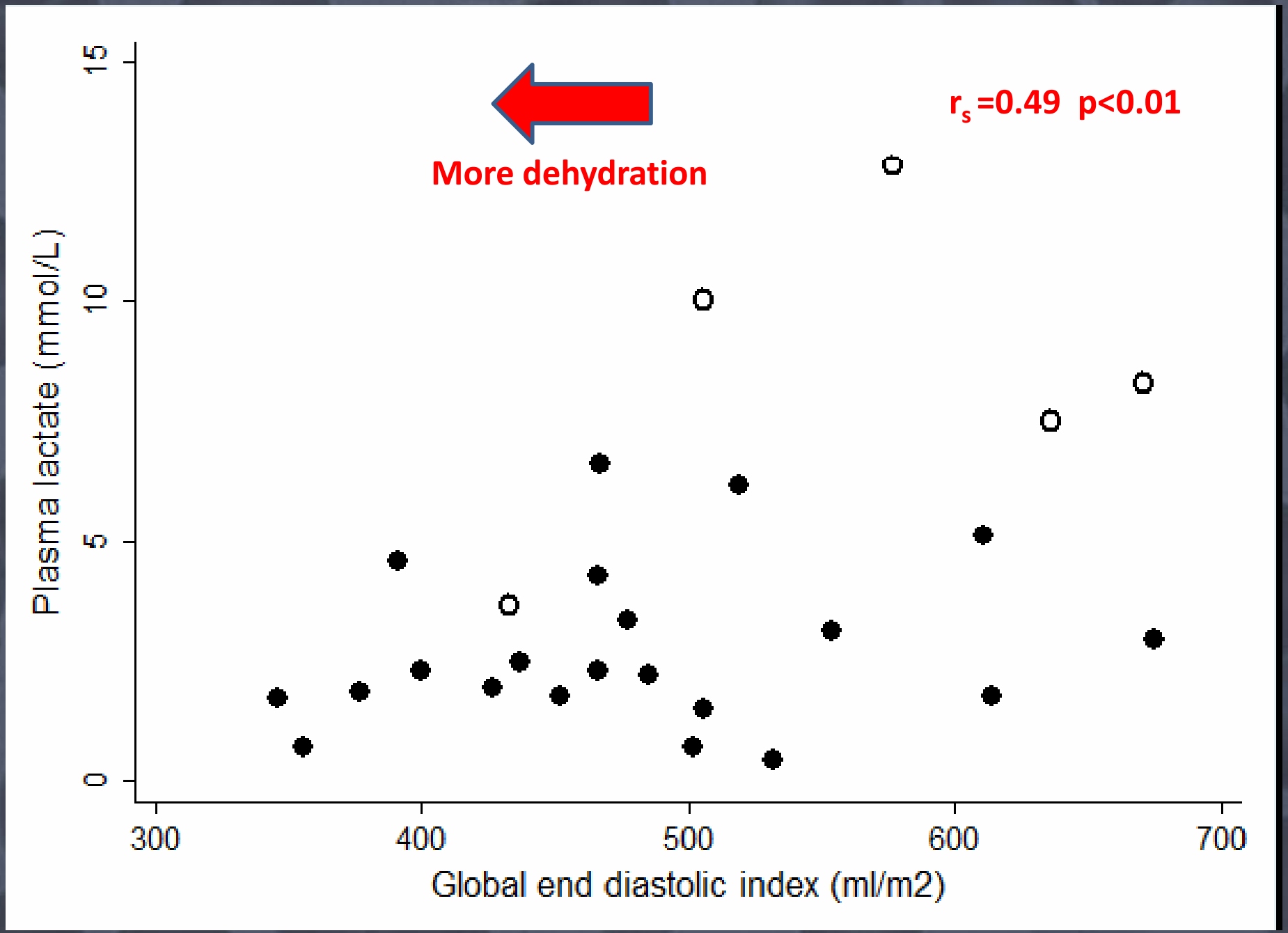
Starling curve



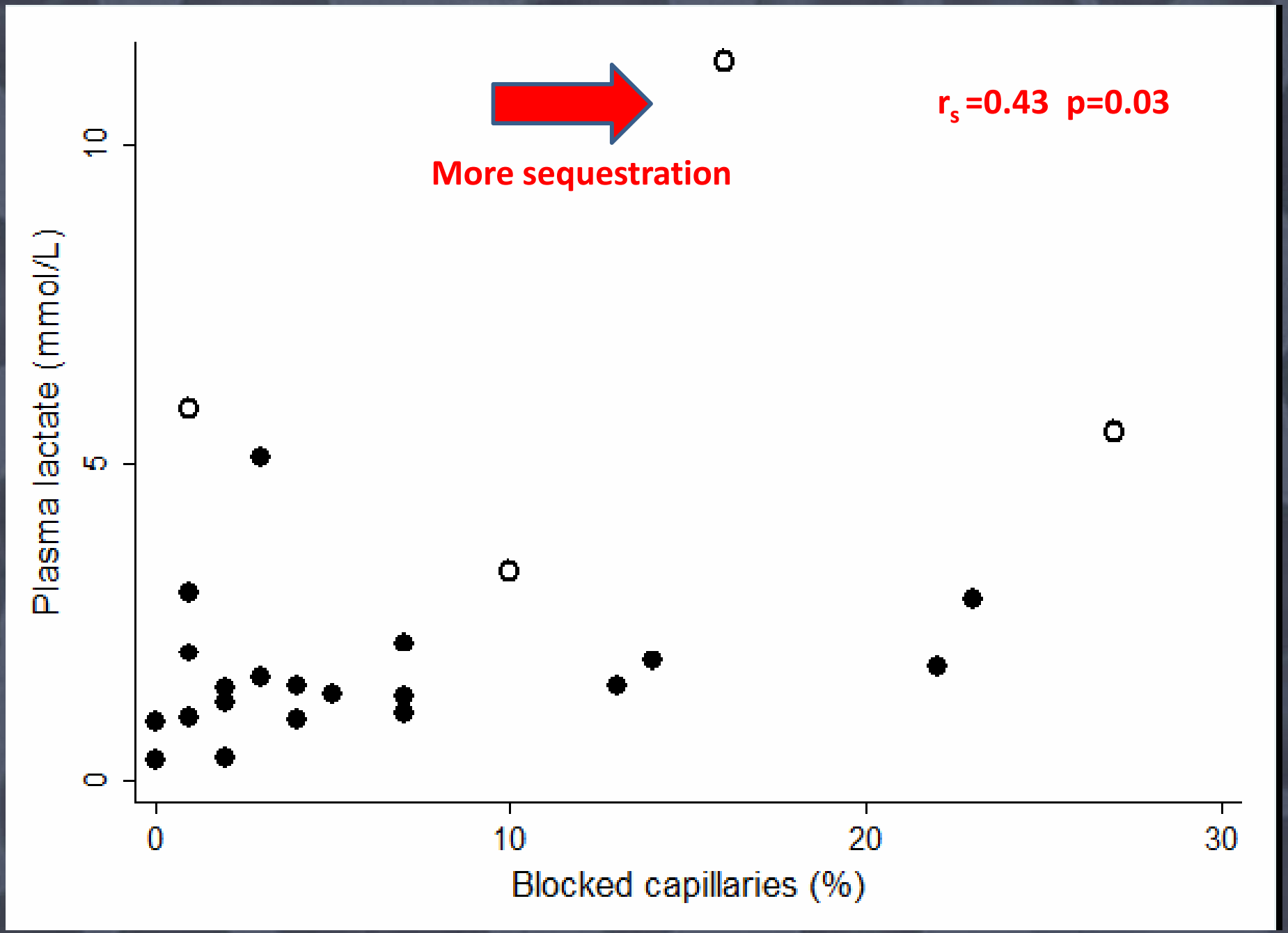

Baseline pH
7.5
7.4
7.3
7.2
7.1
-.4
-.3
-.2
-.1
0
.1
Change in pH after 6h fluid loading

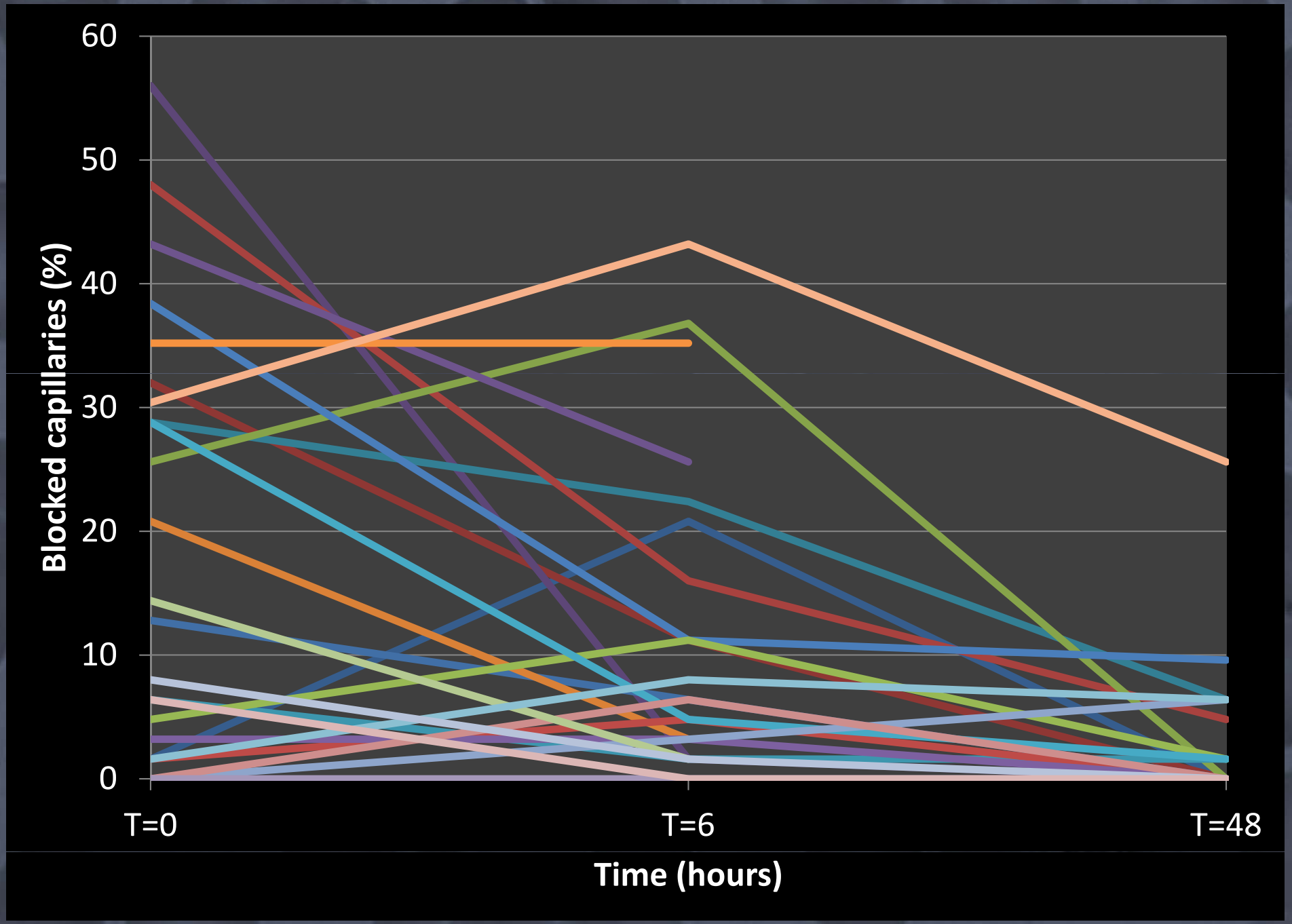

Baseline creatinine
0
200
400
600
800
-300
-200
-100
0
100
200
Change in creatinine after 24 hours fluid resuscitation

Post resuscitation



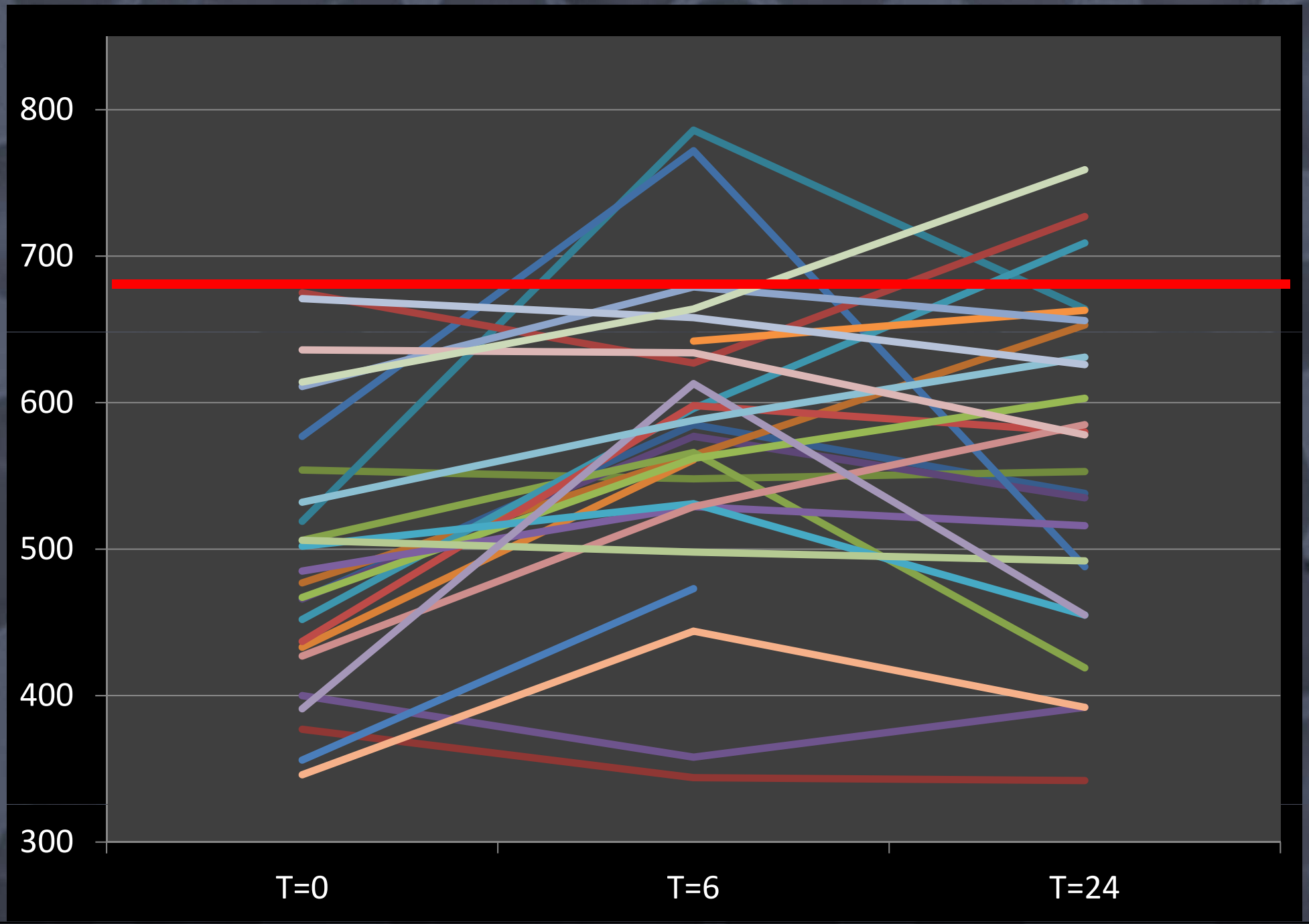
Post resuscitation

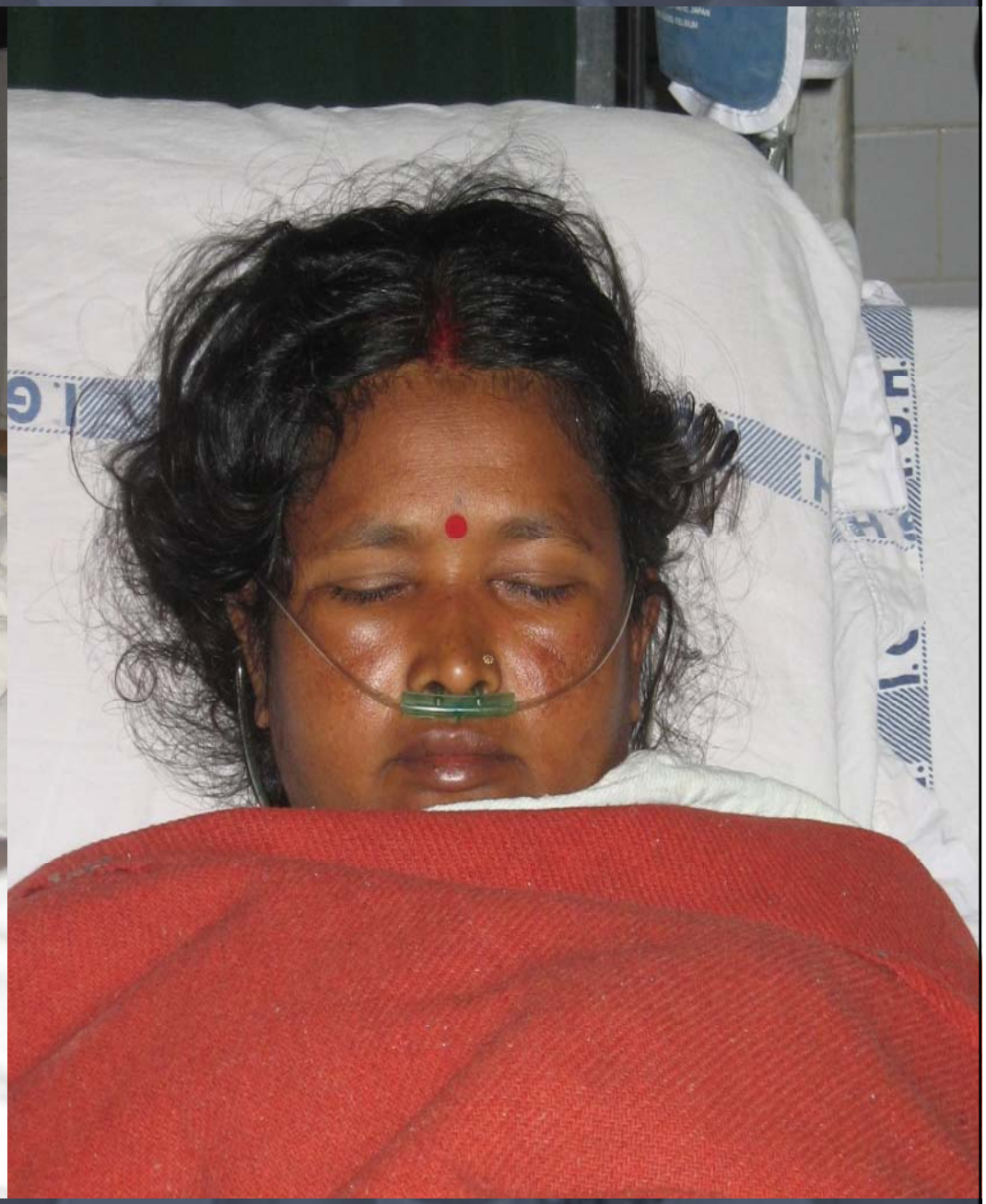


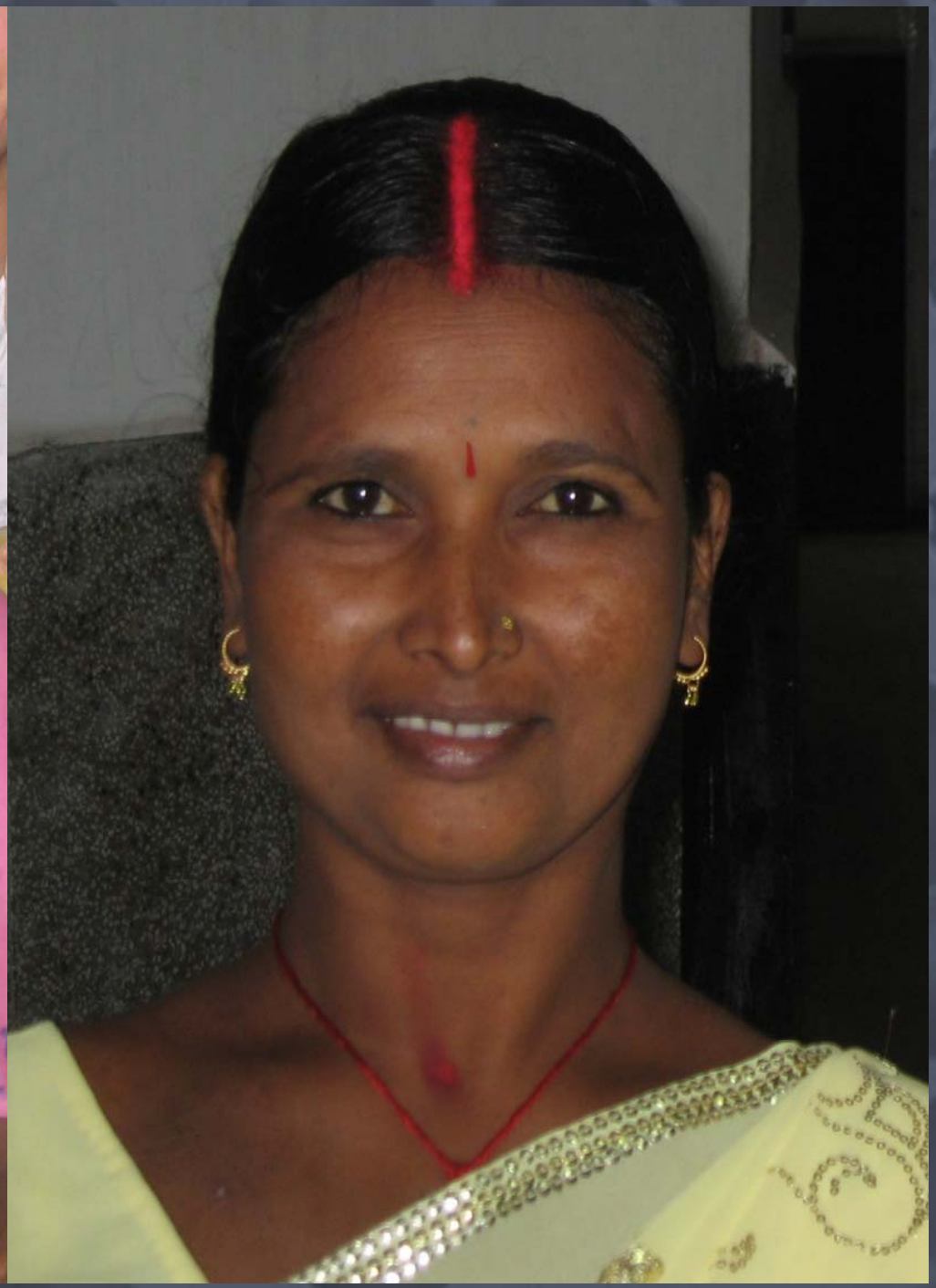

60
50
40
30
20
10
0
Blocked capillaries (%)
T=0
T=6
T=48
Time (hours)

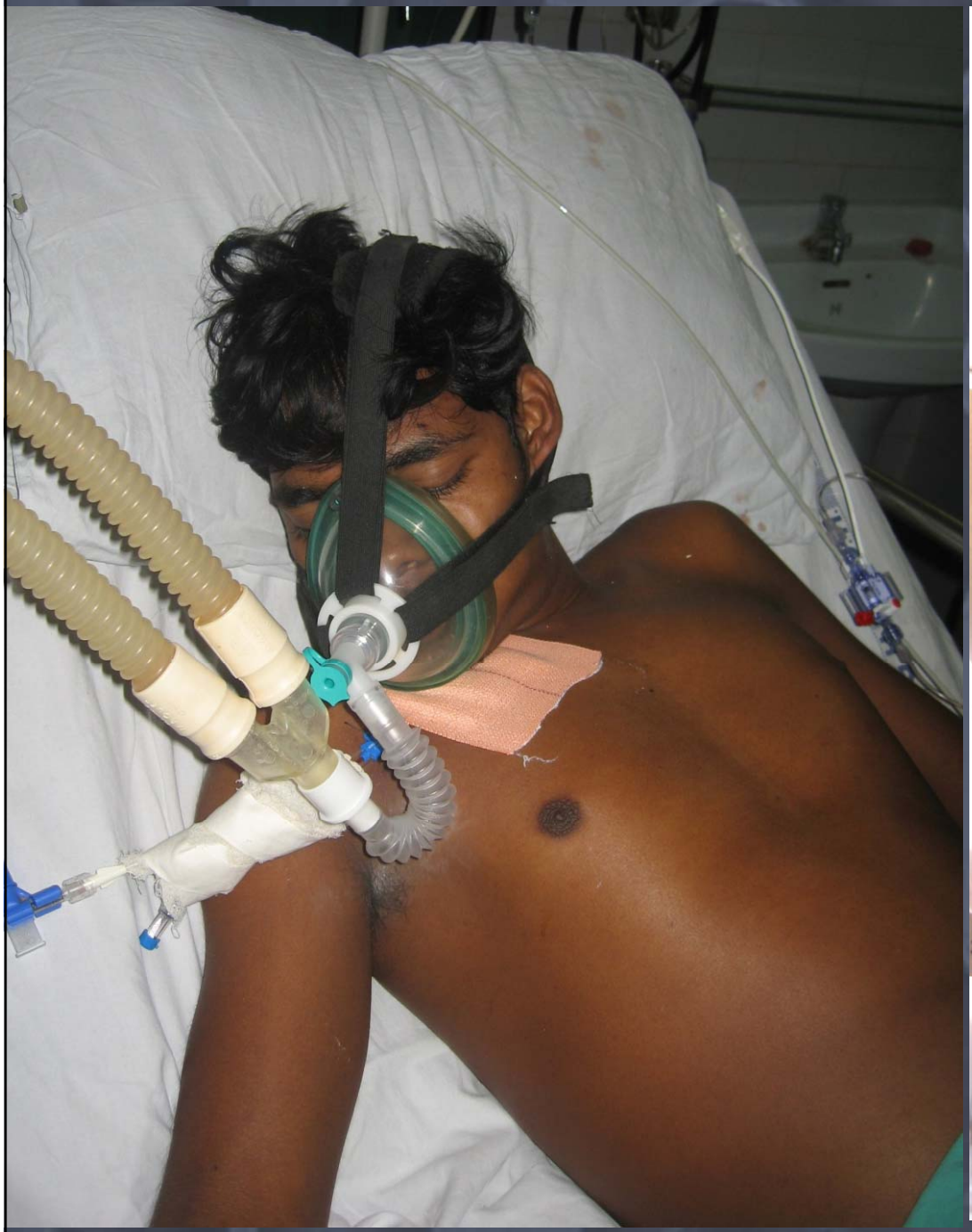
Median (range) 3360 (1035-7070) over the first 6h

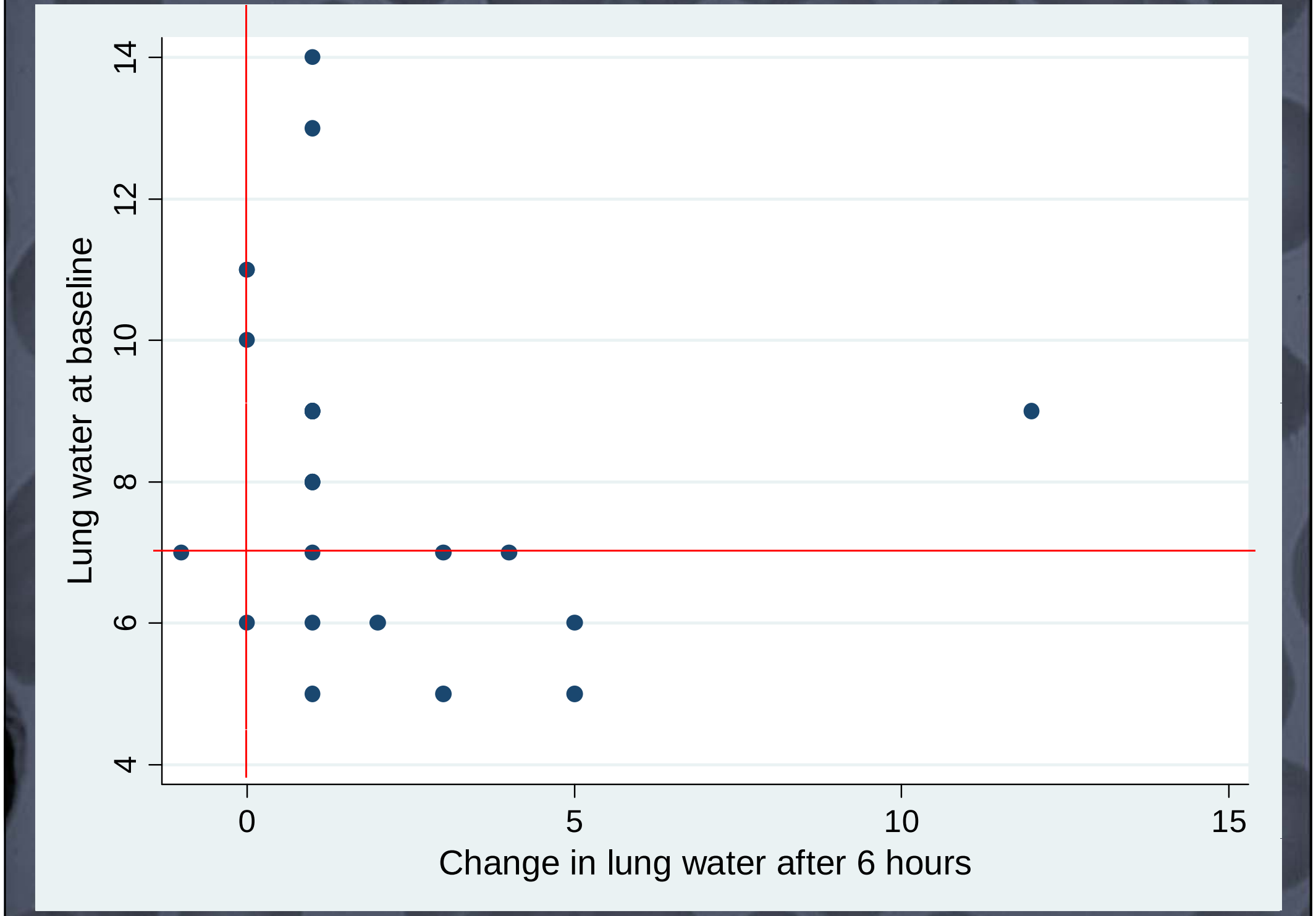
Median (range) 5900 (1985-13720) over the first 24h

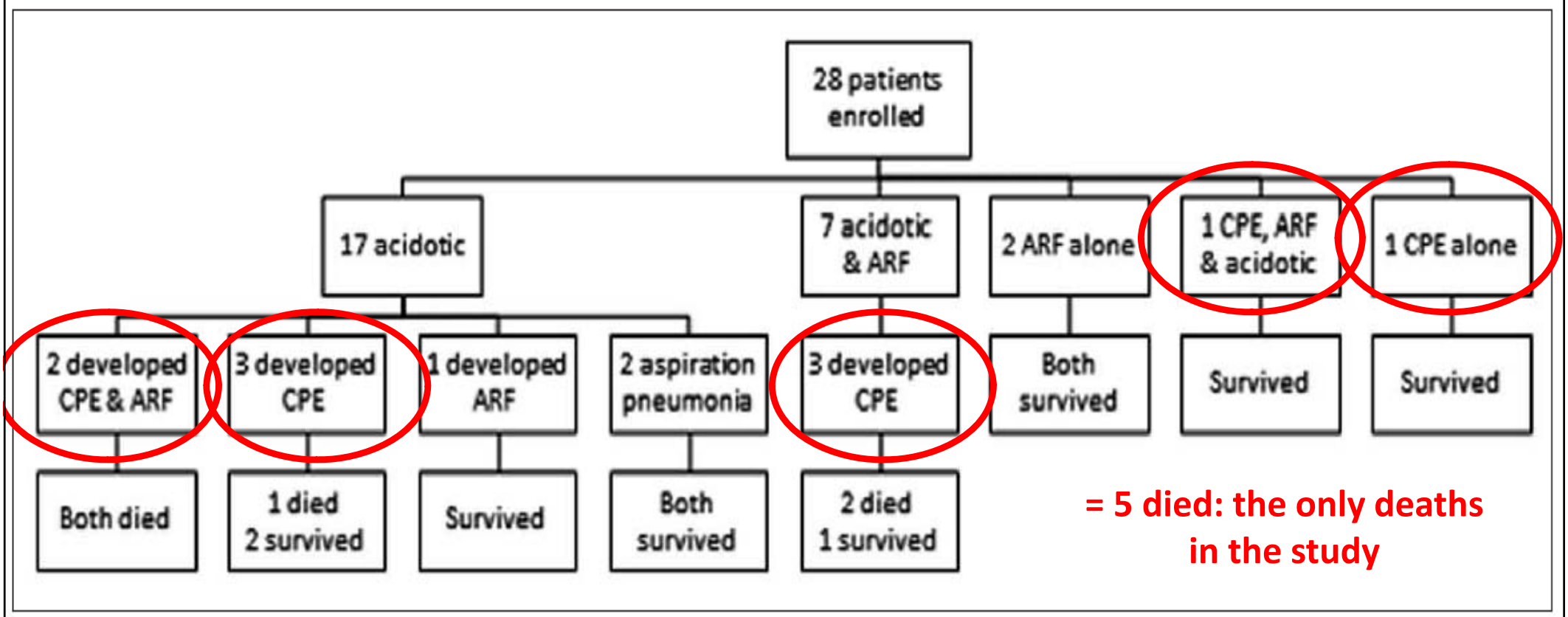






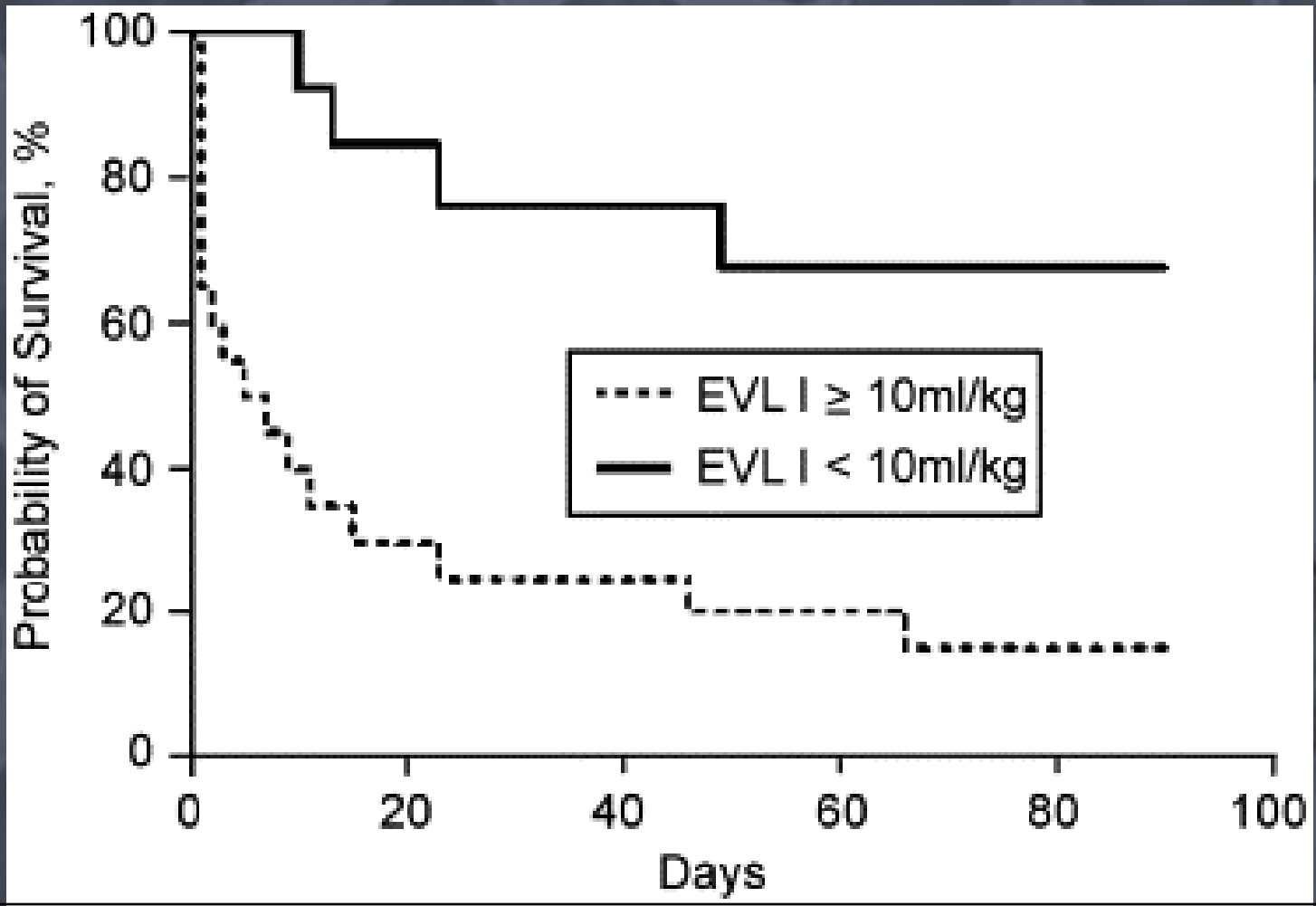


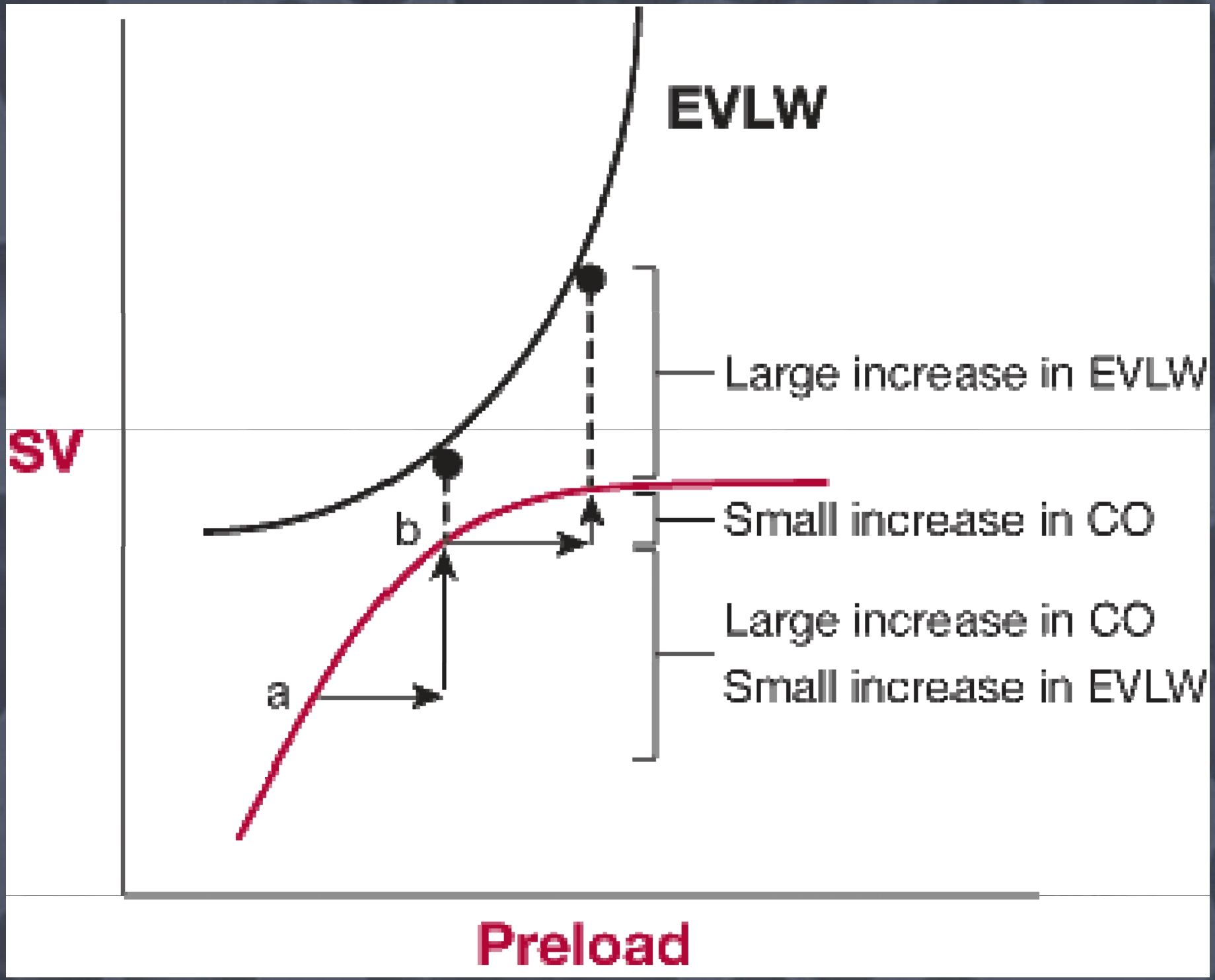

Lung water at baseline
14
12
10
8
6
4
0
5
10
15
Change in lung water after 6 hours


28 patients enrolled
17 acidotic
7 acidotic & ARF
2 ARF alone
1 CPE, ARF & acidotic
1 CPE alone
2 developed CPE & ARF
3 developed CPE
1 developed ARF
2 aspiration pneumonia
3 developed CPE
Both survived
Survived
Survived
Both died
1 died 2 survived
Survived
Both survived
2 died 1 survived
= 5 died: the only deaths in the study

Impact of extravascular lung water index on outcomes of severe sepsis patients in a medical intensive care unit

Fu-Tsai Chung[a,1], Shu-Min Lin[a,1], Shinn-Yn Lin[b,c,d], Horng-Chyuan Lin[a,*]




EVLW
SV
Large increase in EVLW
Small increase in CO
Large increase in CO
Small increase in EVLW
b
a
Preload

Sepsis in Eurc
study*

Jean-Louis Vincent, MI
V. Marco Ranieri, MD;
Jean Carlet, MD, PhD;
Acutely Ill Patients Inve

clinical investigations in critical care

High Tidal Volume and Positive Fluid Balance Are Associated With Worse Outcome in Acute Lung Injury*

Research

Open Access

Pulmonary artery catheter versus pulse contour analysis: a prospective epidemiological study

Shigehiko Uchino[1], Rinaldo Bellomo[2], Hiroshi Morimatsu[3], Makoto Sugihara[4], Craig French[5],

An observational study fluid balance and patient outcomes in the randomized evaluation of normal vs. augmented level of replacement therapy trial*

The RENAL Replacement Therapy Study Investigators

Objective: To examine associations between mean daily fluid balance during intensive care unit study enrollment and clinical outcomes in patients enrolled in the Randomized Evaluation of Normal vs. Augmented Level (RENAL) replacement therapy study.

was −1941 vs. +1755 mL ($p = .0003$). A negative mean daily fluid balance during study treatment was independently associated with a decreased risk of death at 90 days (odds ratio 0.318; 95% confidence interval 0.24−0.43; $p < .000.1$) and with increased survival time ($p < .0001$). In addition, a negative mean

Micek et al. Critical Care 2013, 17:R246
http://ccforum.com/content/17/5/R246

CRITICAL CARE

RESEARCH Open Access

Fluid balance and cardiac function in septic shock as predictors of hospital mortality

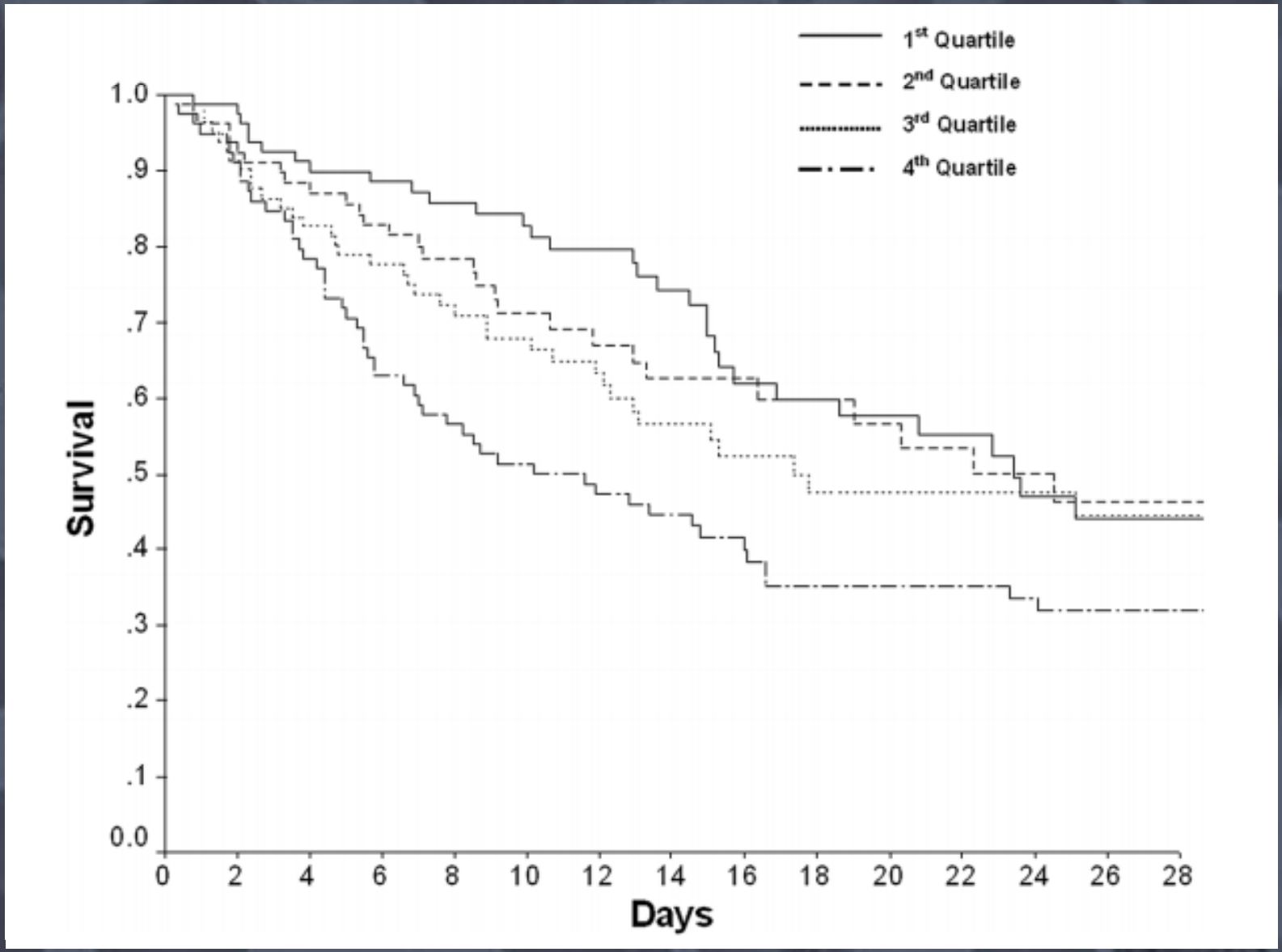
Scott T Micek[1], Colleen McEvoy[2], Matthew McKenzie[1], Nicholas Hampton[3], Joshua A Doherty[4] and Marin H Kollef[2*]

Abstract

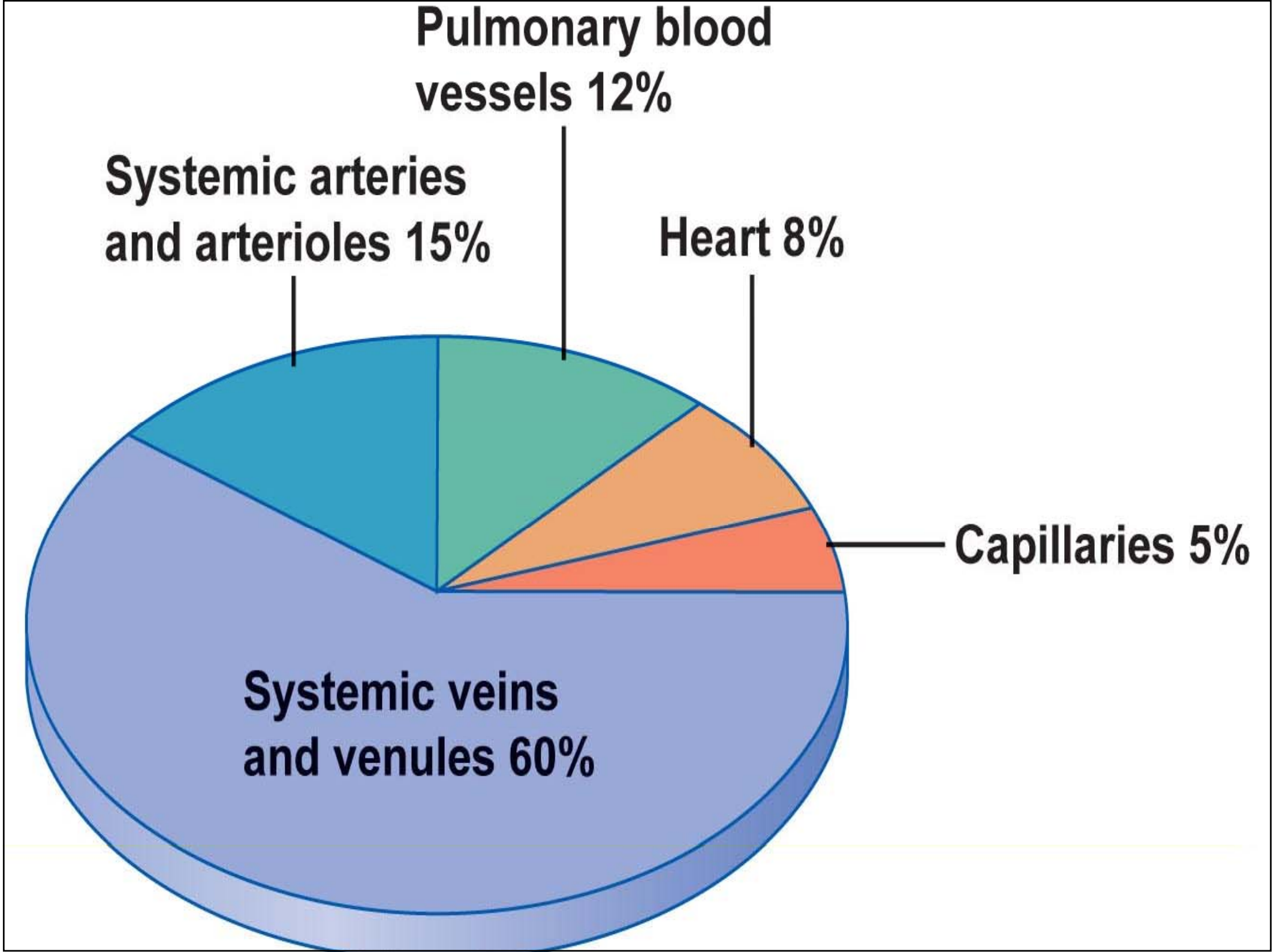
Introduction: Septic shock is a major cause of morbidity and mortality throughout the world. Unfortunately, the optimal fluid management of septic shock is unknown and currently is empirical.

Methods: A retrospective analysis was performed at Barnes-Jewish Hospital (St. Louis, Missouri). Consecutive patients (n = 325) hospitalized with septic shock who had echocardiographic examinations performed within 24 hours of shock onset were enrolled.

Results: A total of 163 (50.2%) patients with septic shock died during hospitalization. Non-survivors had a significantly larger positive net fluid balance within the 24 hour window of septic shock onset (median (IQR): 4,374 ml (1,637 ml, 7,260 ml) vs. 2,959 ml (1,639.5 ml, 4,769.5 ml), $P = 0.004$). The greatest quartile of positive net

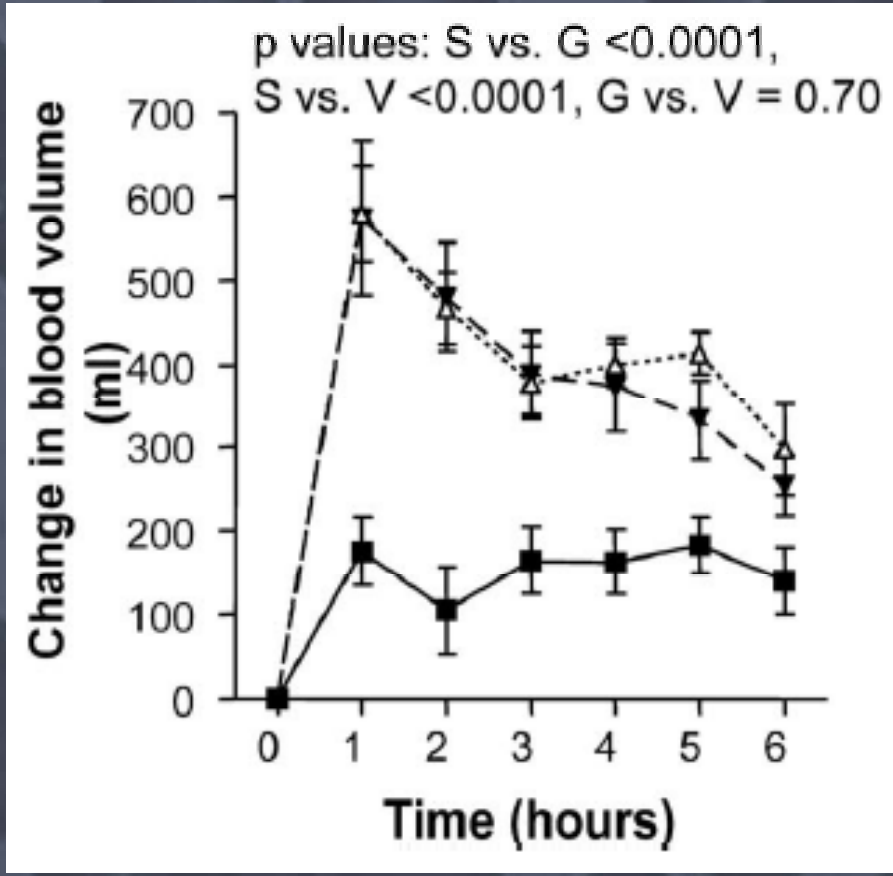


	Median (IQR) fluid load in first 24 hours
Survivors	2959 (1639- 4769)
Non-survivors	4374 (1637-7260)


Pulmonary blood vessels 12%
Systemic arteries and arterioles 15%
Heart 8%
Capillaries 5%
Systemic veins and venules 60%

Effect of volume loading with 1 liter intravenous infusions of 0.9% saline, 4% succinylated gelatine (Gelofusine) and 6% hydroxyethyl starch (Voluven) on blood volume and endocrine responses: A randomized, three-way crossover study in healthy volunteers

Dileep N. Lobo, DM, FRCS; Zeno Stanga, MD; Mark M. Aloysius, MRCS; Catherine Wicks, BMedSci, BM, BS; Quentin M. Nunes, MRCS; Katharine L. Ingram, FRCA; Lorenz Risch, MD, MPH; Simon P. Allison, MD, FRCP



CCM 2010

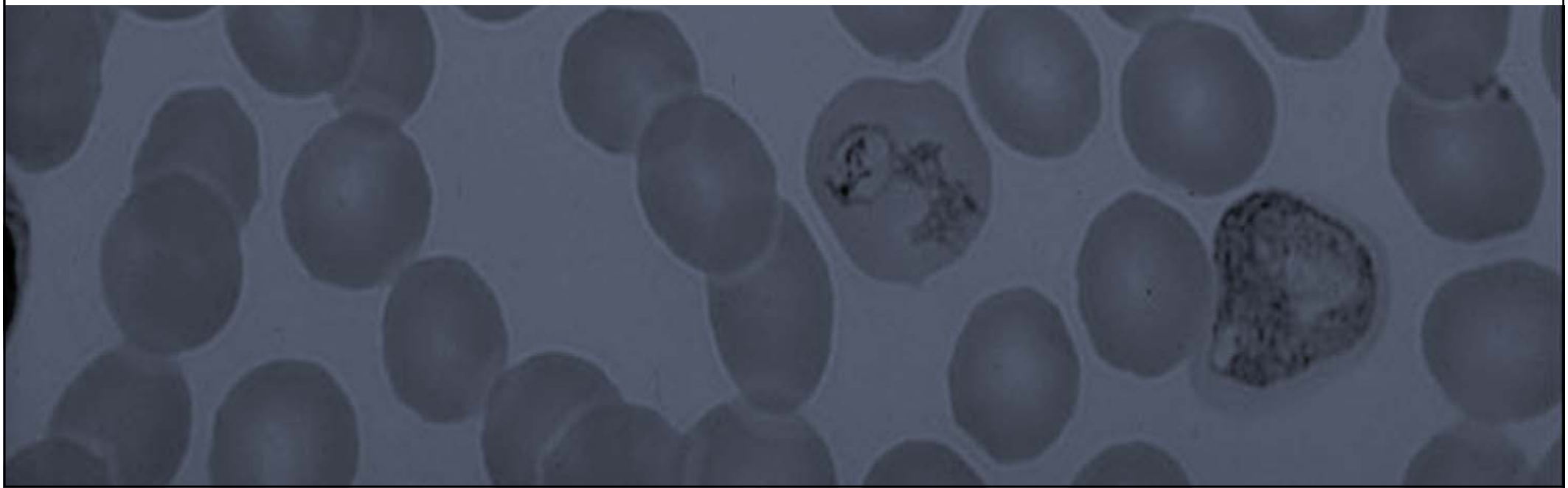
Jacob *et al. Critical Care* 2012, **16**:R86
http://ccforum.com/content/16/3/R86

CRITICAL CARE

RESEARCH Open Access

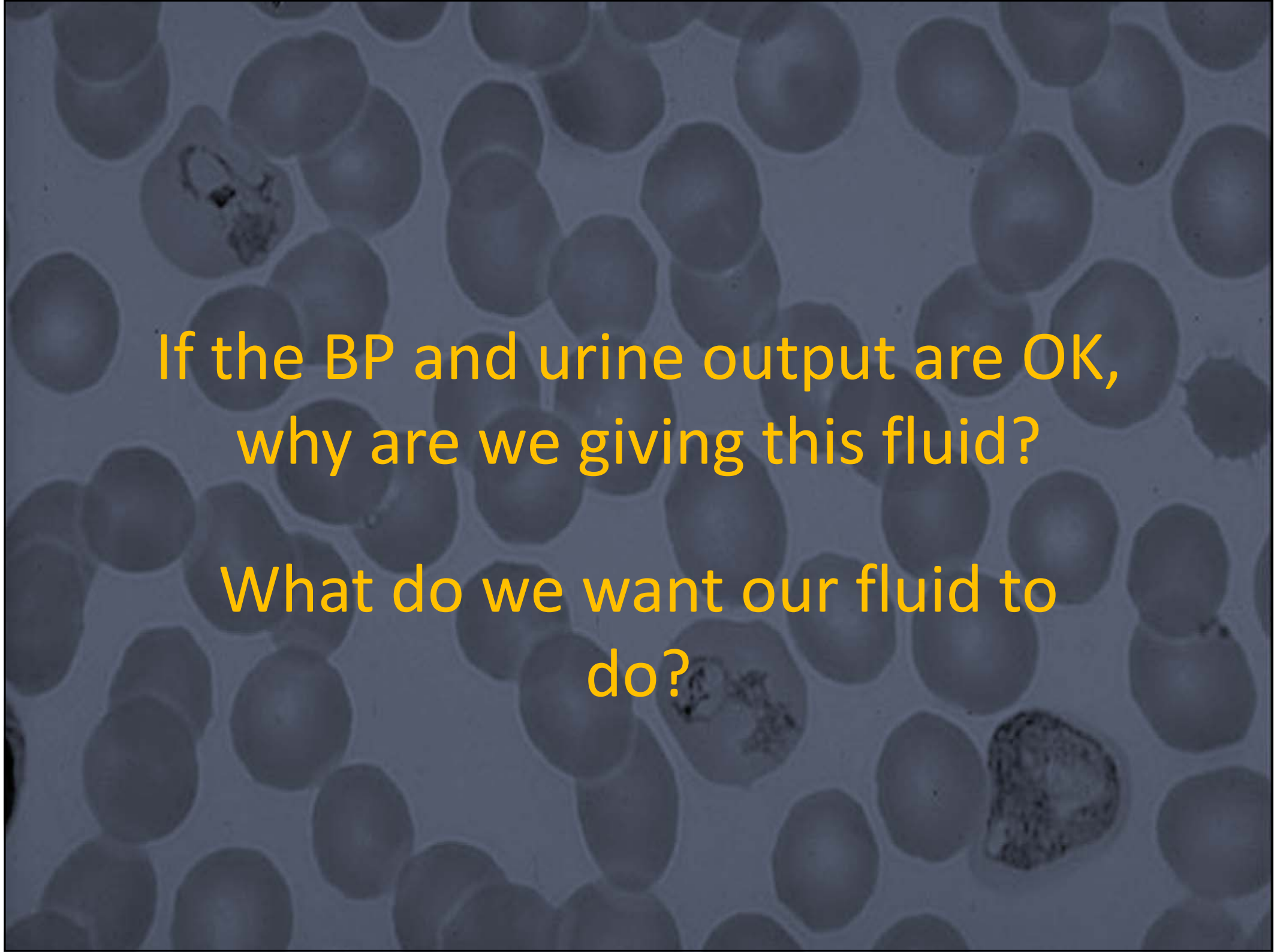
The intravascular volume effect of Ringer's lactate is below 20%: a prospective study in humans

Matthias Jacob[1*†], Daniel Chappell[1†], Klaus Hofmann-Kiefer[1], Tobias Helfen[1], Anna Schuelke[1], Barbara Jacob[1], Alexander Burges[2], Peter Conzen[1] and Markus Rehm[1]



Fluid resuscitation in severe malaria

- Is hypovolaemia strongly linked to acidosis?
- Does fluid loading improve acidosis?
- Is hypovolaemia strongly linked to AKI?
- Does fluid loading improve AKI?
- Is sequestration linked to acidosis?
- Is sequestration linked to AKI?
- Does fluid loading improve sequestration?
- Does the fluid go and stay where we want it to?
- Does fluid loading increase risk of complications?

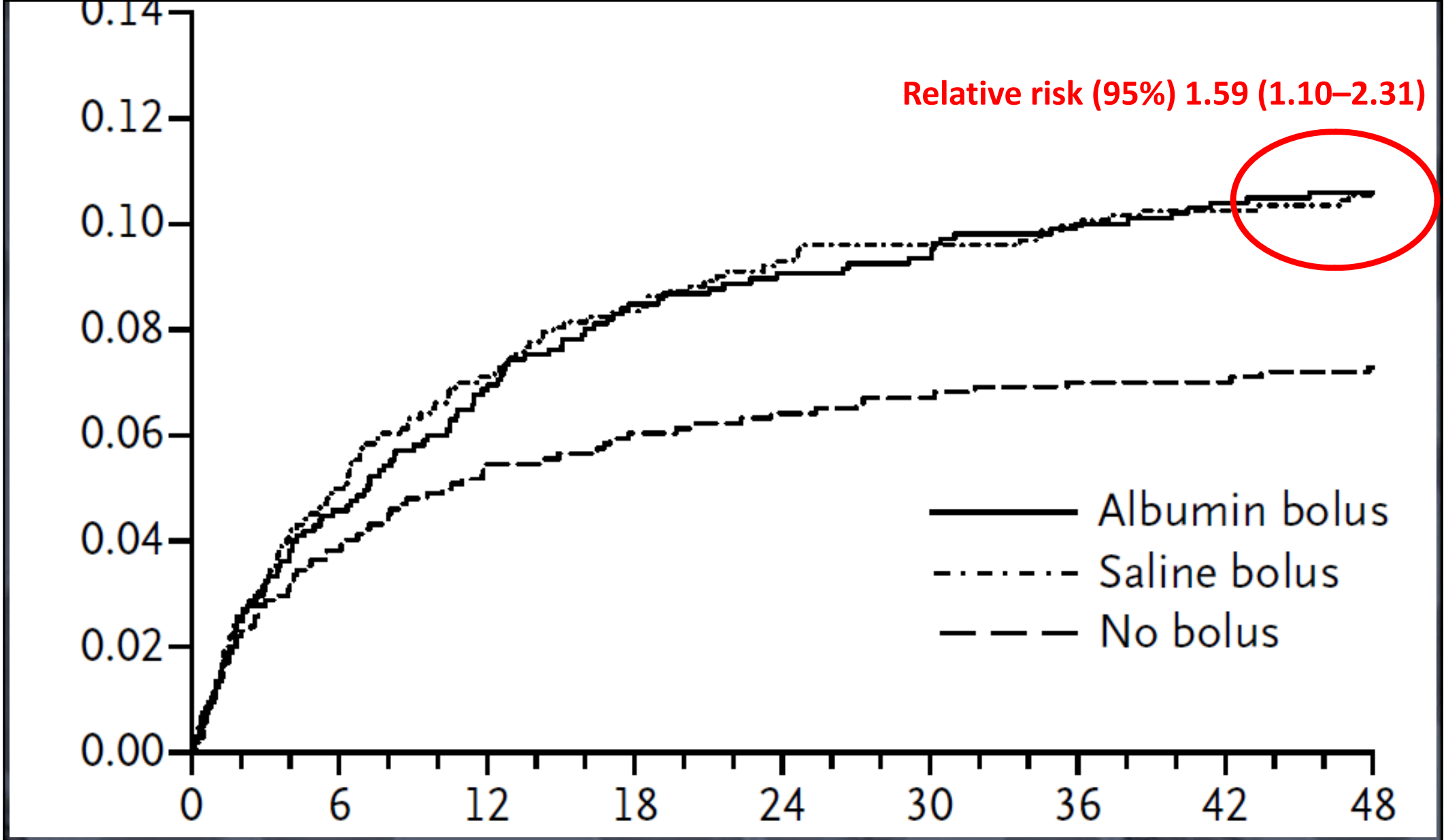

If the BP and urine output are OK, why are we giving this fluid?
What do we want our fluid to do?

The NEW ENGLAND JOURNAL of MEDICINE

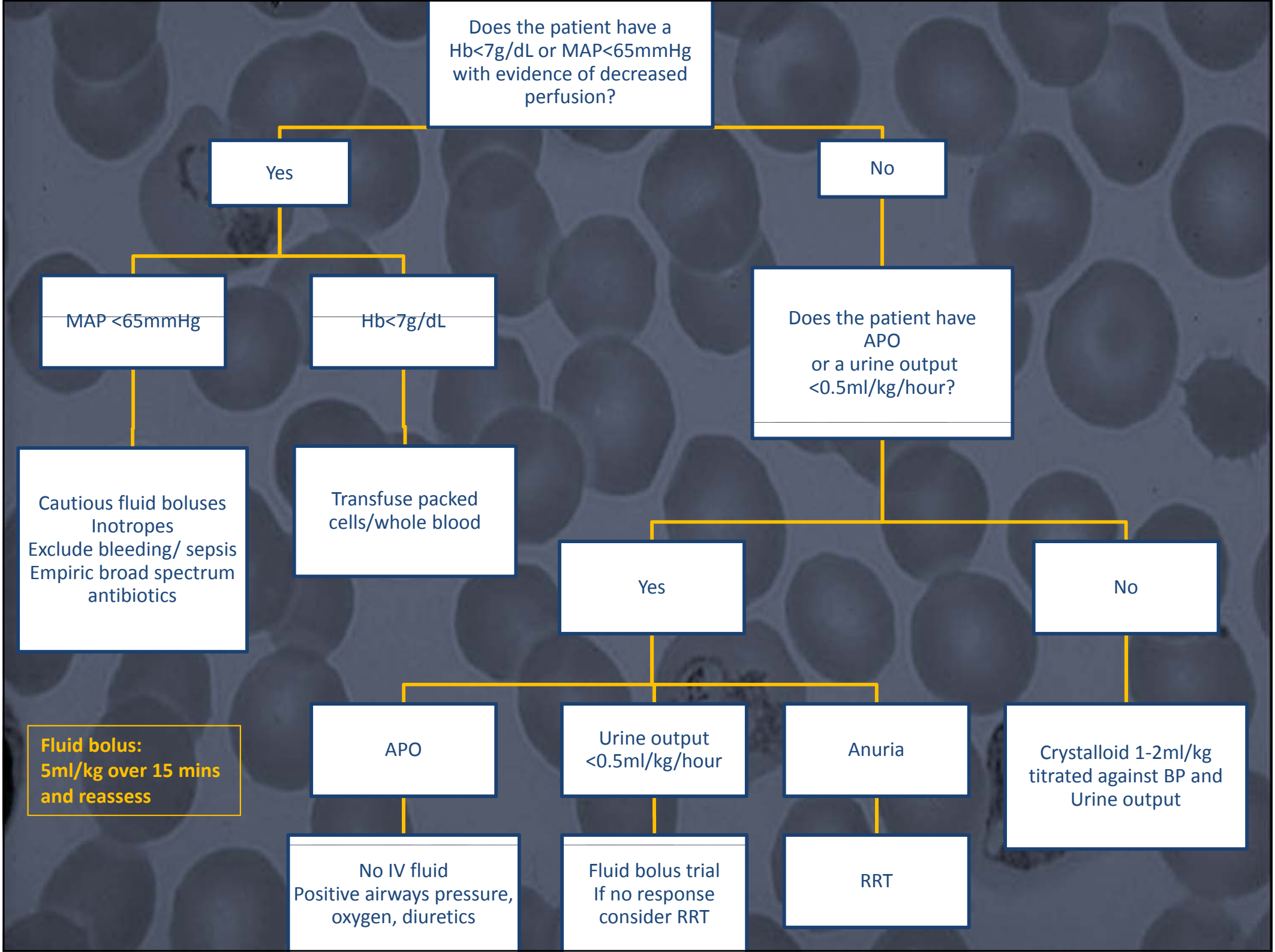
ESTABLISHED IN 1812 JUNE 30, 2011 VOL. 364 NO. 26

Mortality after Fluid Bolus in African Children with Severe Infection

Kathryn Maitland, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., Charles Engoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Richard Nyeko, M.B., Ch.B., M.Med., George Mtove, M.D., Hugh Reyburn, M.B., B.S., Trudie Lang, Ph.D., Bernadette Brent, M.B., B.S., Jennifer A. Evans, M.B., B.S., James K. Tibenderana, M.B., Ch.B., Ph.D., Jane Crawley, M.B., B.S., M.D., Elizabeth C. Russell, M.Sc., Michael Levin, F.Med.Sci., Ph.D., Abdel G. Babiker, Ph.D., and Diana M. Gibb, M.B., Ch.B., M.D., for the FEAST Trial Group*



Patients in the "no bolus" arm received a median (IQR) of 10.1 (10-25)ml/kg over the first 8 hours of their hospitalisation


Does the patient have a Hb<7g/dL or MAP<65mmHg with evidence of decreased perfusion?
Yes
No
MAP <65mmHg
Hb<7g/dL
Does the patient have APO or a urine output <0.5ml/kg/hour?
Cautious fluid boluses
Inotropes
Exclude bleeding/ sepsis
Empiric broad spectrum antibiotics
Transfuse packed cells/whole blood
Yes
No
Fluid bolus: 5ml/kg over 15 mins and reassess
APO
Urine output <0.5ml/kg/hour
Anuria
Crystalloid 1-2ml/kg titrated against BP and Urine output
No IV fluid
Positive airways pressure, oxygen, diuretics
Fluid bolus trial
If no response consider RRT
RRT

Acknowledgements

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- Prakaykaew Charunwatthana
- Kesinee Chotivanich
- Kamolrat Silamut
- Sue Lee
- Richard Maude
- Katherine Plewes
- Hugh Kingston
- Sanjib Mohanty
- Saroj K. Mishra
- M. A. Faiz
- Mahtab Uddin Hassan
- Shamshul Alam
- Ashraf Kabir
- Kishore Mahanta
- Radja Pattnaik
- Nick Anstey
- David Bihari


Any questions?

Severe falciparum malaria: An important cause of multiple organ failure in Indian intensive care unit patients

Anand Krishnan, MD; Dilip R. Karnad, MD

Objective: To study the incidence and severity of multiple organ dysfunction in severe falciparum malaria.

Design: Prospective, observational study.

Setting: Intensive care unit of a tertiary care university hospital.

Patients: Three hundred one consecutive patients with severe falciparum malaria admitted during the 30-month study period.

Interventions: Daily assessment of clinical and biochemical variables required for calculating the Sequential Organ Failure Assessment (SOFA) score.

Measurements and Main Results: Central nervous system failure was present in 121 patients (53 deaths). Renal failure occurred in 91 patients (48 deaths), and 33 required dialysis. Severe thrombocytopenia occurred in 114 patients (seven required platelet transfusion), and 19 patients had thrombocytopenia and disseminated intravascular coagulation; all required component therapy; 229 patients received blood transfusion for severe hemolytic anemia. Hepatic failure occurred in 77 patients (38 deaths). Respiratory failure developed in 79 patients and carried the worst outcome (70 deaths). It occurred later in the course of the illness (mean, 3.1 days; $p < .001$) compared with cerebral, renal, and coagulation failure (mean, 1.3–2.3 days). Regardless of the organ system involved, only 11 of 172 patients with one or no organ failure died (6.8%), whereas mortality rate increased to 48.8% in 129 patients with multiple organ failure. Other abnormalities associated with poor outcome included seizures in 54 patients (56% mortality rate), metabolic acidosis in 167 (40% mortality rate), hypoglycemia in 88 (39% mortality rate), and hemoglobinuria in 190 (33% mortality rate). Sixty patients had quinine toxicity requiring dosage reduction. Bacterial sepsis occurred in 39 patients (35 deaths) and accounted for 85% of deaths occurring after day 7. Twenty-three pregnant women had no significant difference in outcomes. Overall mortality rate was 24.6% (301 patients, 74 deaths).

Conclusions: Malaria is an important cause of multiple organ failure in India. Mortality rate is 6.4% when one or fewer organs fail but increases to 48.8% with failure of two or more organs. However, outcomes are better than for similar degrees of organ failure in sepsis. (Crit Care Med 2003; 31:2278–2284)

KEY WORDS: *Plasmodium falciparum*; cerebral malaria; acute renal failure; acute respiratory distress syndrome; hepatitis; multiple organ dysfunction syndrome; parasitic diseases; bacterial sepsis; tropical diseases