

Intensive Care and the Trauma Victim

Anders Oldner

**Professor/Consultant Intensivist
Karolinska Univ. Hospital/ Institutet
Stockholm Sweden**



How important is the ICU in the trauma chain?

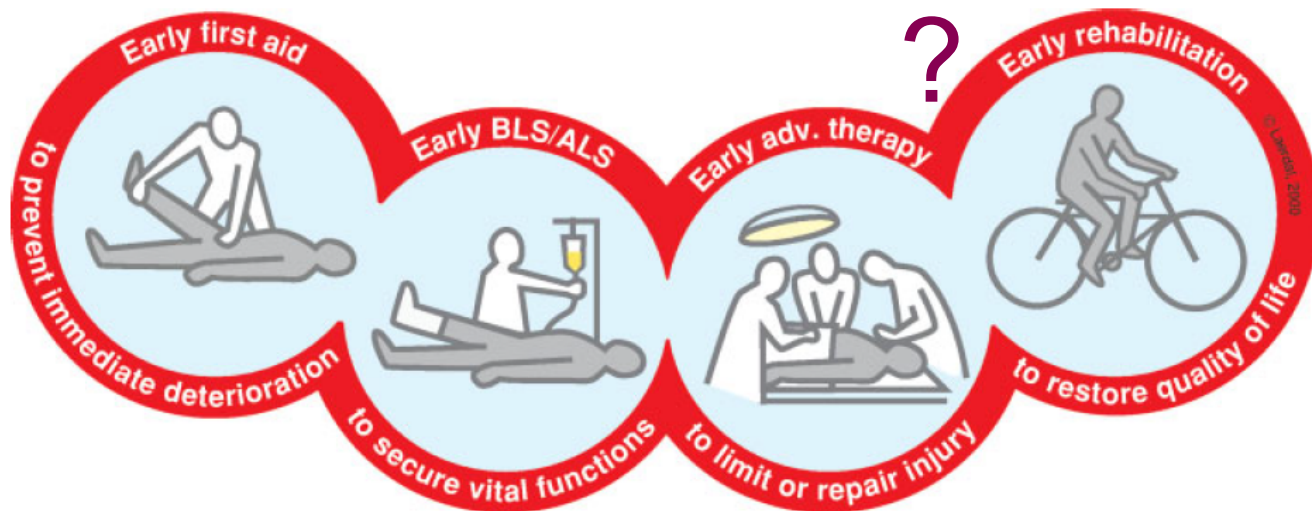
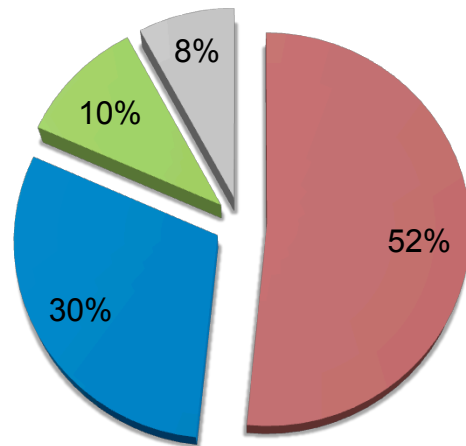


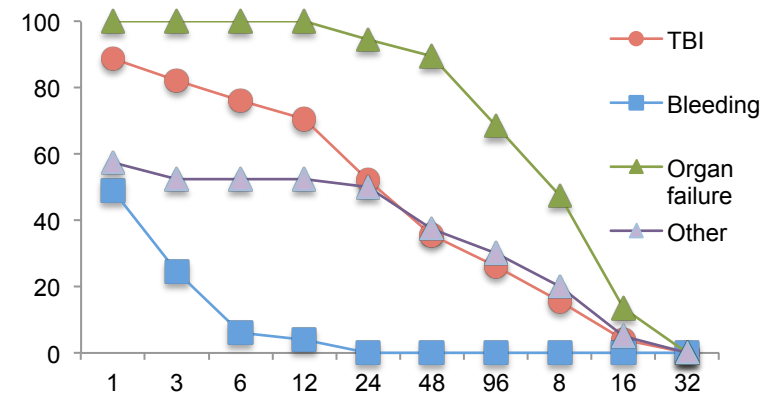
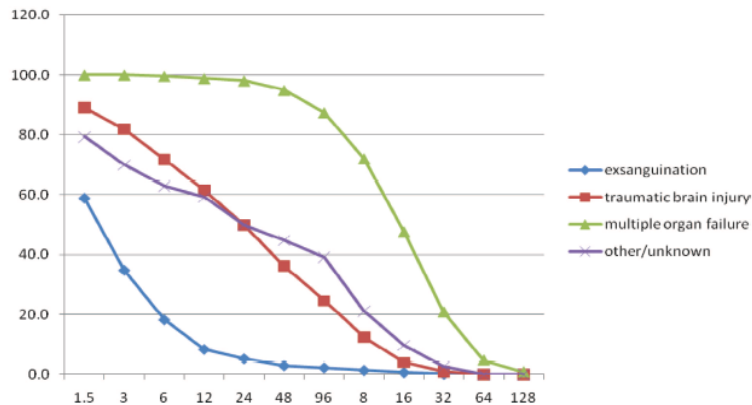
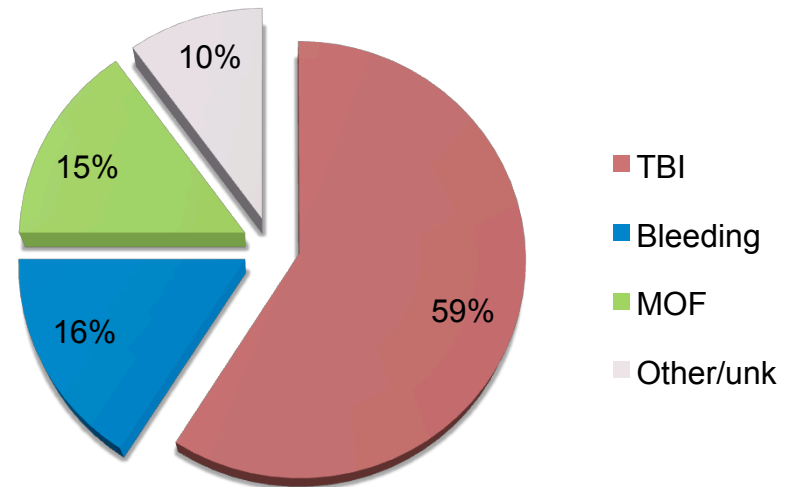
Fig. 1 The trauma chain of survival. First displayed at the *TraumaCare2002* conference in Stavanger, Norway, and reproduced with permission from Laerdal Medical, Stavanger, Norway. BLS, basic life support; ALS, advanced life support.

Causes of short-term death

Maryland US



Karolinska



Dutton et al. J Trauma 2010.

Ghorbani P et al. Scand J Trauma 2014.

Distribution of death after severe injury



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Quadrimodal distribution of death after trauma suggests that critical injury is a potentially terminal disease☆☆☆★

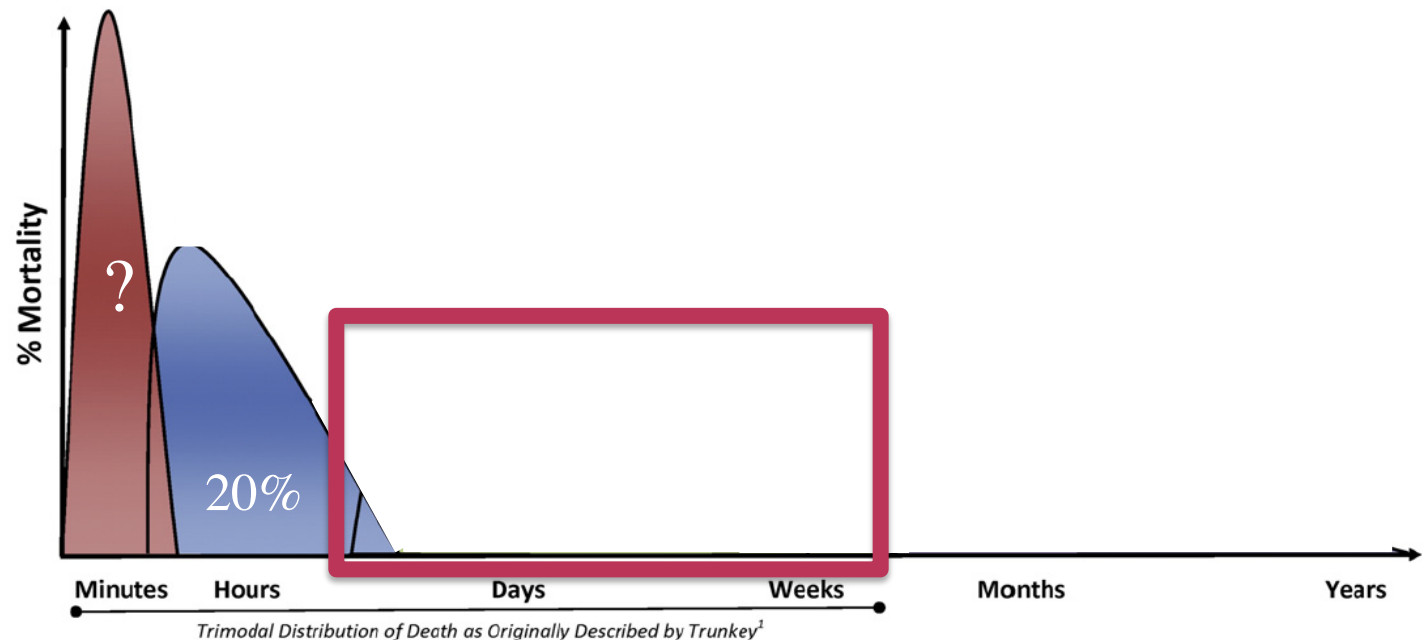


Heena P. Santry, MD, MS^{a,b,*}, Charles M. Psinos, MD^a, Christopher J. Wilbert, MD^c, Julie M. Flahive, MS^a, Aimee R. Kroll-Desrosiers, MS^b, Timothy A. Emhoff, MD^a, Catarina I. Kiefe, MD, PHD^b

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Trends in causes of trauma death -effects of improved resuscitation



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Injury, Int. J. Care Injured 40 (2009) 907–911



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Injury

journal homepage: www.elsevier.com/locate/injury



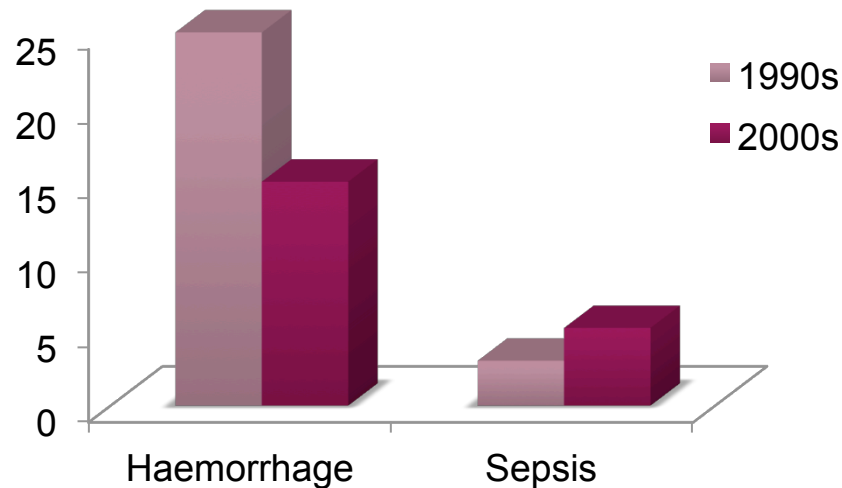
Review

Patterns of mortality and causes of death in polytrauma patients—Has anything changed?

Roman Pfeifer^{a,*}, Ivan S. Tarkin^a, Brett Rocos^b, Hans-Christoph Pape^a

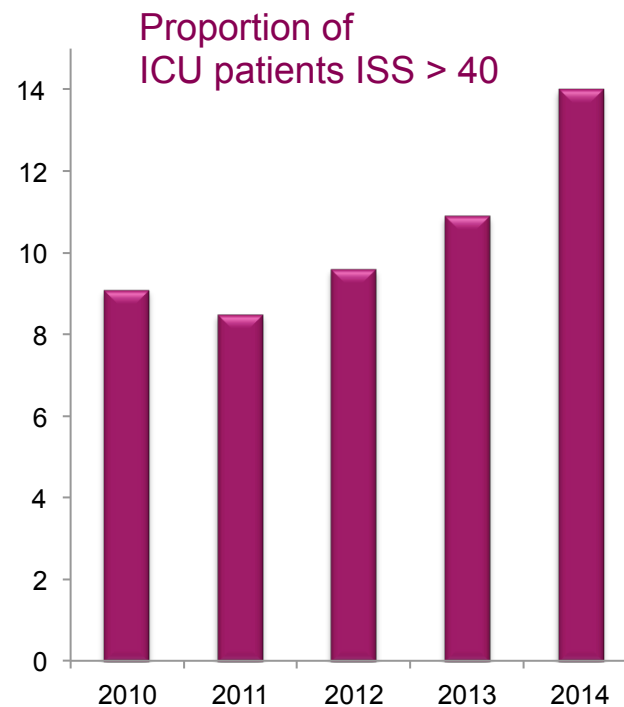
^a Department of Orthopaedic Surgery, University of Pittsburgh Medical Center, Kaufmann Medical Building, Suite 1010, 3471 Fifth Avenue, Pittsburgh, PA 15213, USA

^b Department of Trauma and Orthopaedics, Bristol Royal Infirmary University Hospitals, Bristol, UK

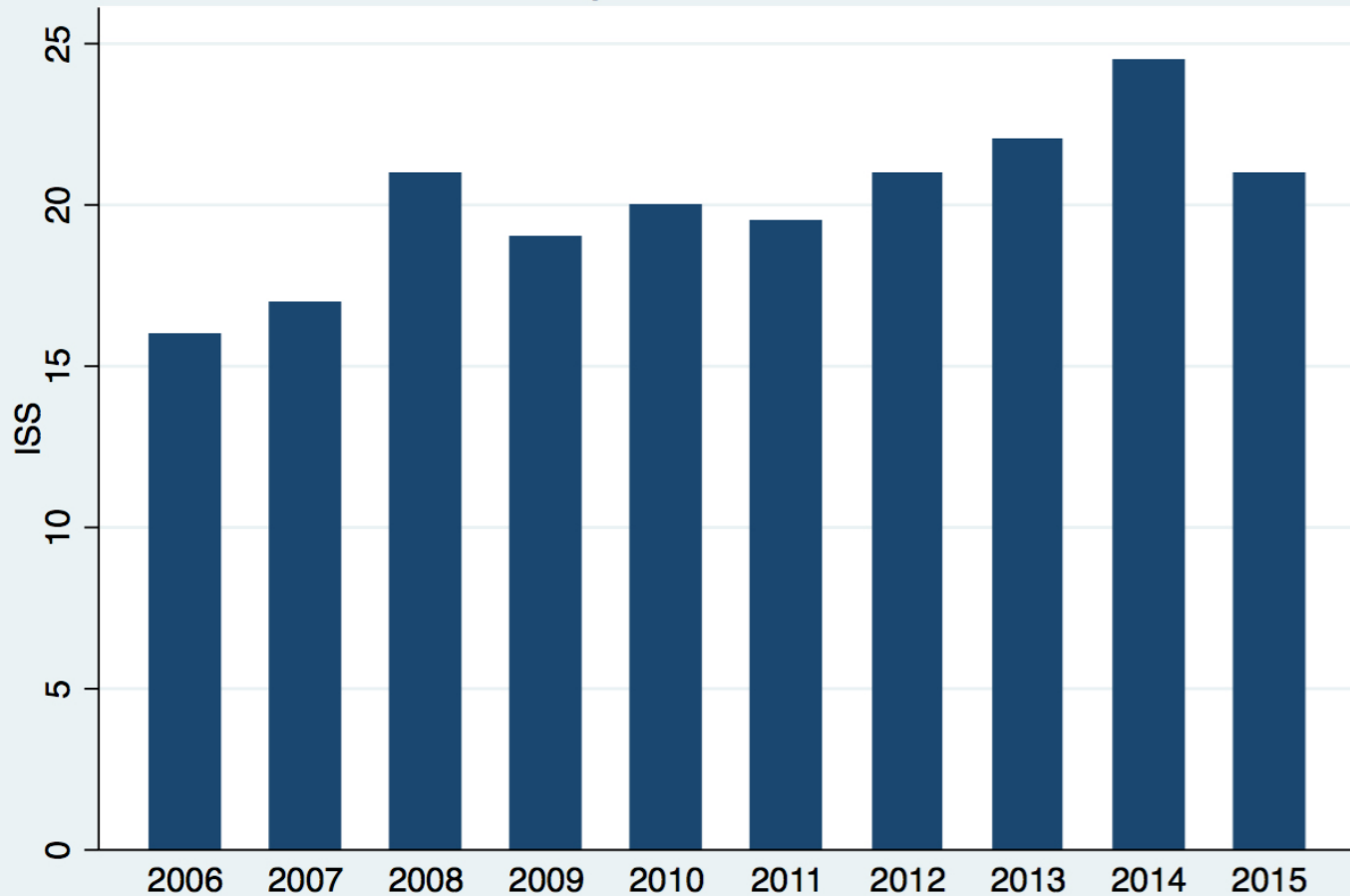


Injury severity in the ICU - trends

-Improved early trauma care leads to higher ISS in the ICU



Median ISS for trauma patients admitted to ICU 2006-2015





The relative importance of the post-resuscitation phase is increasing

Medical challenges transferred to the ICU

- Damage control surgery/resuscitation
- Conservative surgical management
- Severely injured survive to ICU admittance
- Increased burden of age and comorbidity

Traumapatienten på IVA faser

- **Ankomst**
- **Tidig fas 0-48 h**
 - Aggressiv behandling av störda vitalfunktioner
 - Diagnostik och ev. behandling av dolda skador
 - Kompletterande diagnostik och behandling av kända skador
- **Sen fas > 48 h**
 - Sedvanliga diagnoser
 - Sepsis
 - MOF
 - ARDS

Ankomst

- Upprätta en primär **HANDLÄGGNINGSPLAN** med kir/ort/neurokir
 - diskutera brytpunkter
- **Bedöm patientens status**
- **Etablera adekvat MONITORERING**
 - invasiv tryckmätning
 - överväg eko/PAC/annan CO mätning
 - Temp
 - Buktryck
 - ICP
 - Följ neurologi
- **TA ÖVER OCH DRIV VIDARE HANDLÄGGNING**

Cirkulationssvikt på IVA i tidig fas



The conjoint effect of reduced crystalloid administration and decreased damage-control laparotomy use in the development of abdominal compartment syndrome

Bellal Joseph, MD, Bardiya Zangbar, MD, Viraj Pandit, MD, Gary Vercruysse, MD, Hassan Aziz, MD, Narong Kulvatunyou, MD, Julie Wynne, MD, Terence O'Keeffe, MB, ChB, Andrew Tang, MD, Randall S. Friesse, MD, and Peter Rhee, MD, Tucson, Arizona



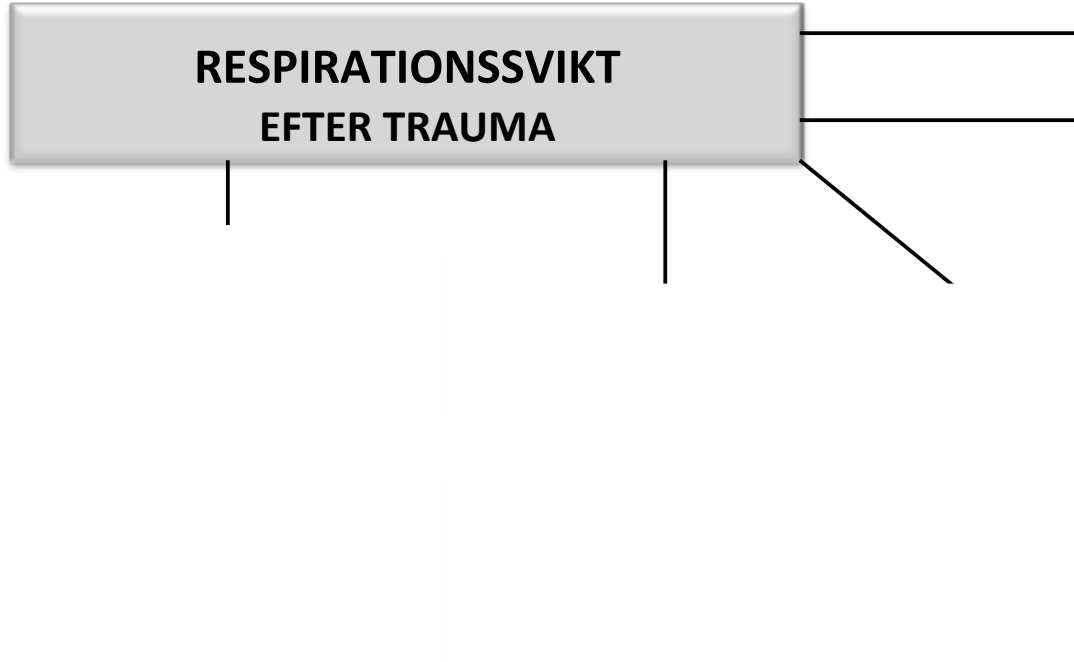
TABLE 3. Multivariate and Univariate Analysis of Patients Who Developed ACS

	Univariate			Multivariate		
	OR	95% CI	p	OR	95% CI	p
Age	1.03	1.01–1.05	0.01	1.02	0.9–1.06	0.1
Sex, male	2.2	0.5–9.7	0.2	8.8	0.8–92	0.07
Systolic blood pressure	1.01	0.9–1.02	0.84	—	—	—
Heart rate	1.01	0.9–1.03	0.16	1.008	0.9–1.03	0.5
Temperature	1.2	0.8–1.7	0.2	1.11	0.7–1.7	0.6
Mechanism of injury, blunt	8.19	1.8–35	0.005	5.7	0.6–55	0.1
ISS	1.06	1.03–1.09	0.001	1.03	0.9–1.09	0.2
Base deficit	1.03	0.9–1.17	0.03	1.04	0.9–1.1	0.1
Crystalloids	1.09	1.04–1.1	0.001	1.07	1.01–1.1	0.02
Blood products	1.07	1.02–1.16	0.045	1.03	0.8–1.1	0.9
DCL	1.2	0.4–3.7	0.7	—	—	—



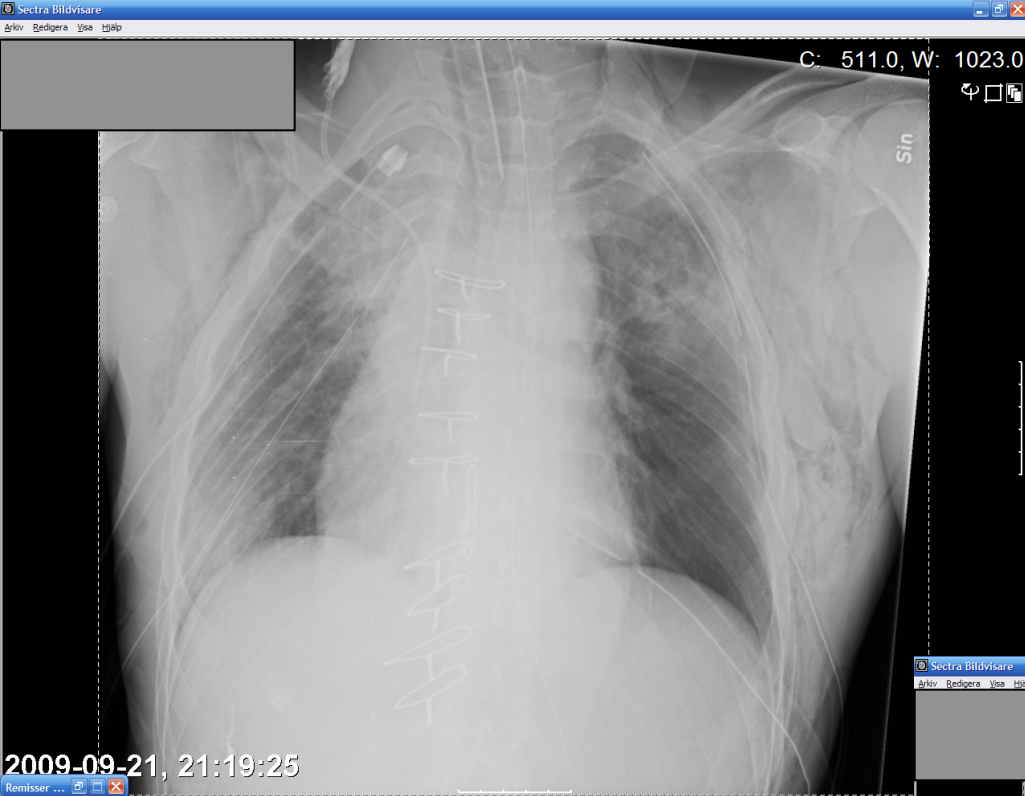
42. In hospital settings do not use crystalloids for patients with active bleeding (see NICE's guideline on intravenous fluid therapy in adults in hospital for advice on tetrastarches in adults).

Lungsvikt i tidig fas efter trauma

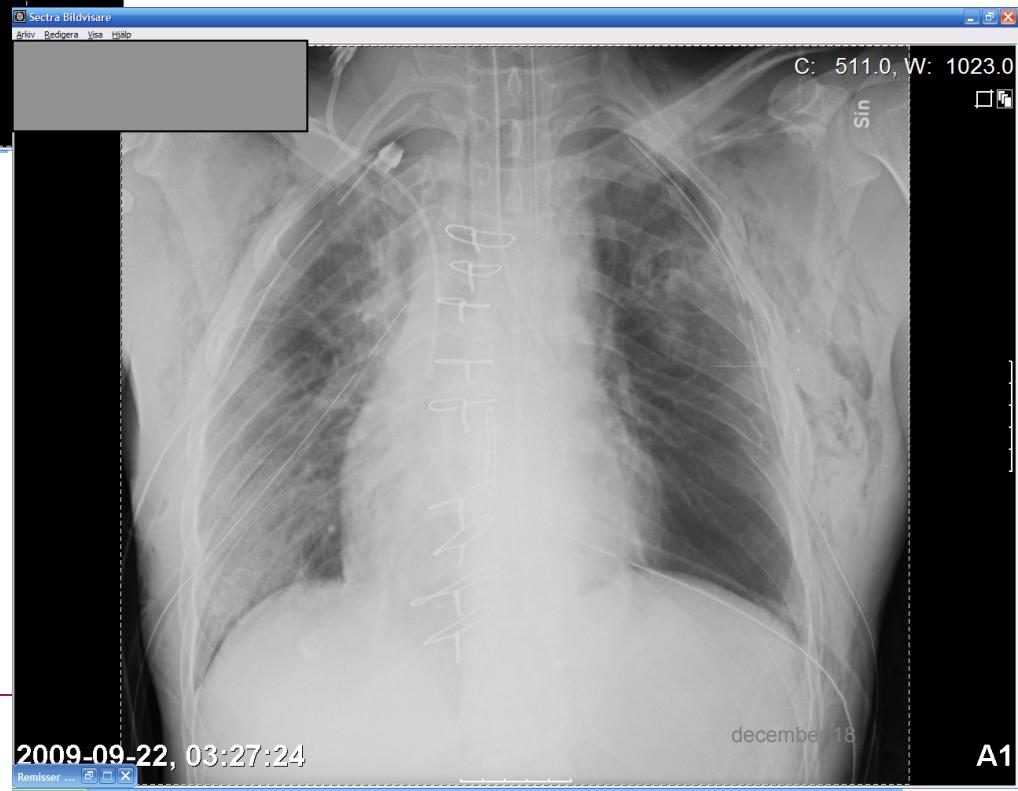


NIV – non-invasive ventilation, IV – invasive ventilation, TRALI – transfusion-related acute lung injury, TACO – transfusion-associated cardiac overload





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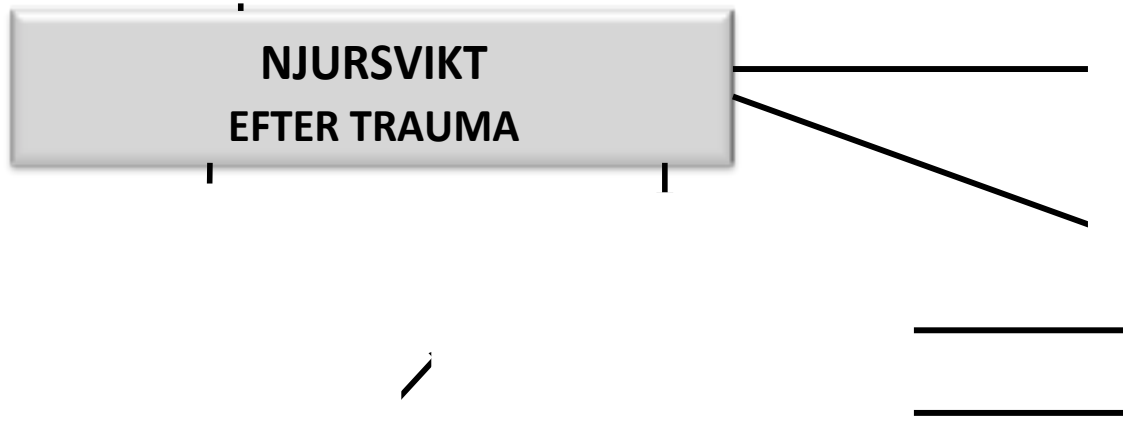




Njursvikt i tidig fas



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Acute kidney injury following severe trauma: Risk factors and long-term outcome

Mikael Eriksson, MD, Olof Brattström, MD, PhD, Johan Mårtensson, MD, PhD, Emma Larsson, MD, PhD, and Anders Oldner, MD, PhD, Stockholm, Sweden

Starches associated with AKI also in trauma patients

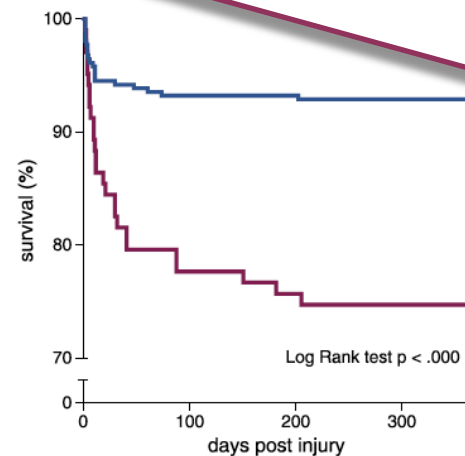


Figure 1. One-year postinjury survival. Kaplan-Meier curves displaying 1-year postinjury survival for AKI (n = 103, red line) and non-AKI patients (n = 310, blue line).

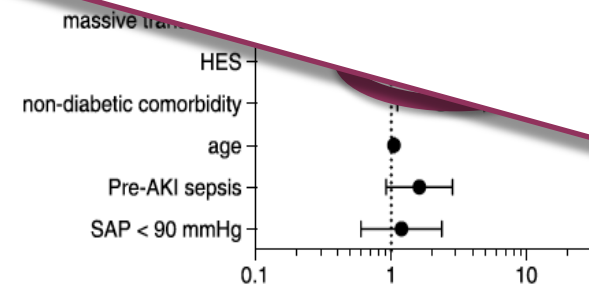


Figure 2. Multivariable model for AKI risk. Odds ratio and 95% confidence interval. Admission refers to the admission to the trauma unit.

Post injury CRRT

- Ischemia/reperfusion
- Pro-inflammation
- Oedema – fluid overload
- Rhabdomyolysis

Intensive Care Med (1999) 25: 805-813
© Springer-Verlag 1999

ORIGINAL

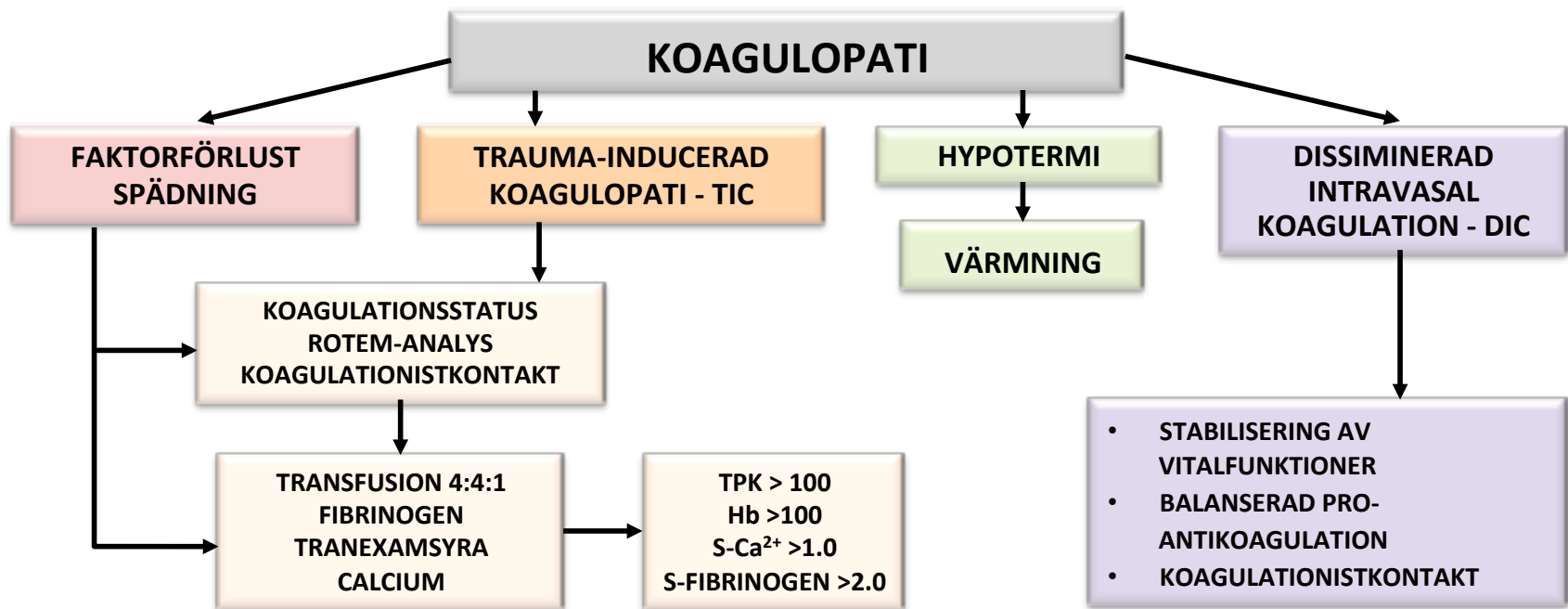
Outcome in post-traumatic acute renal failure when continuous renal replacement therapy is applied early vs. late

L.G. Gettings
H.N. Reynolds
T. Scalea



Consider early CRRT in oliguric patients

Koagulopati i tidig fas



Traumapatienten på IVA

Medicinskt panorama sen fas > 48 h
– ”sedvanliga diagnoser”

- SEPSIS
- MOF
- ARDS
- VAP/PNEUMONI

Diagnoser senare IVA-fas

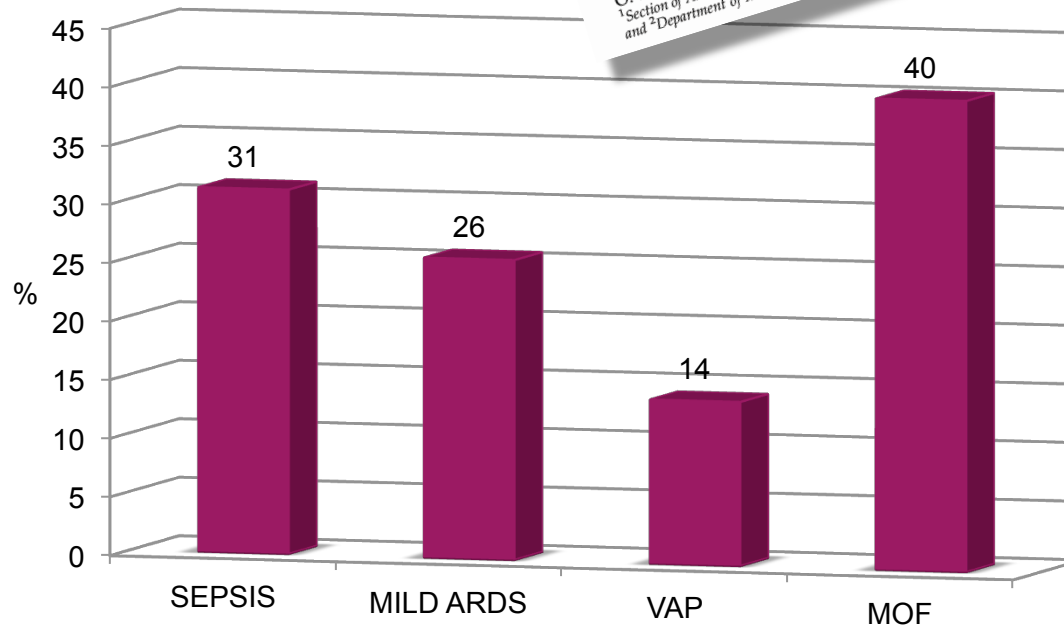
High incidence of post-injury pneumonia in intensive care-treated trauma patients

P. HYLLIENMARK^{1,2}, O. BRATTSTRÖM^{1,2}, E. LARSSON^{1,2}, C.-R. MARTLING^{1,2}, J. PETERSSON^{1,2} and A. OLDNER^{1,2}
¹Section of Anesthesiology and Intensive Care Medicine, Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden and ²Department of Anaesthesiology, Surgical Services and Intensive Care, Karolinska University Hospital, Stockholm, Sweden

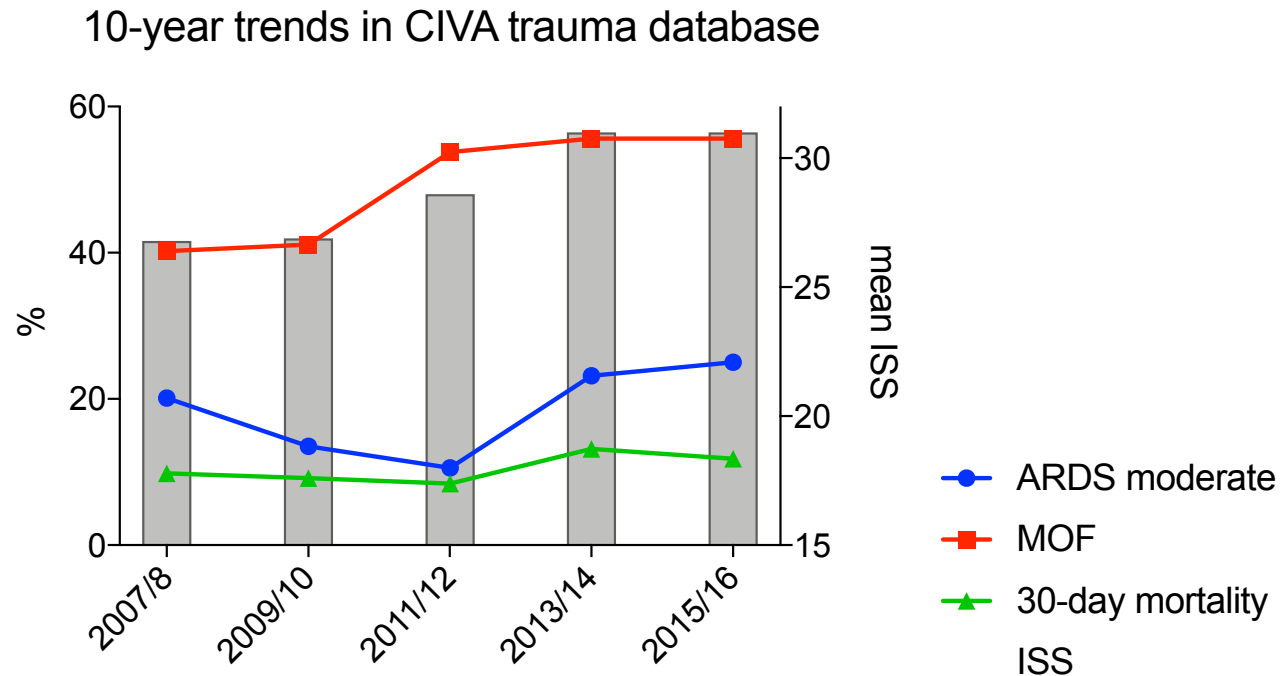
Acta Anaesthesiol Scand 2010; 54: 1007-1017
 Printed in Singapore. All rights reserved

Early predictors of morbidity and mortality in trauma patients treated in the intensive care unit

O. BRATTSTRÖM¹, F. GRANATH², P. ROSSI¹ and A. OLDNER¹
¹Section of Anesthesiology and Intensive Care Medicine, Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden and ²Department of Medicine, Clinical Epidemiology Unit, Karolinska University Hospital, Stockholm, Sweden



Organ failure, mortality and ISS over a decade at CIVA Karolinska



Patients ICU-admitted > 24 hrs

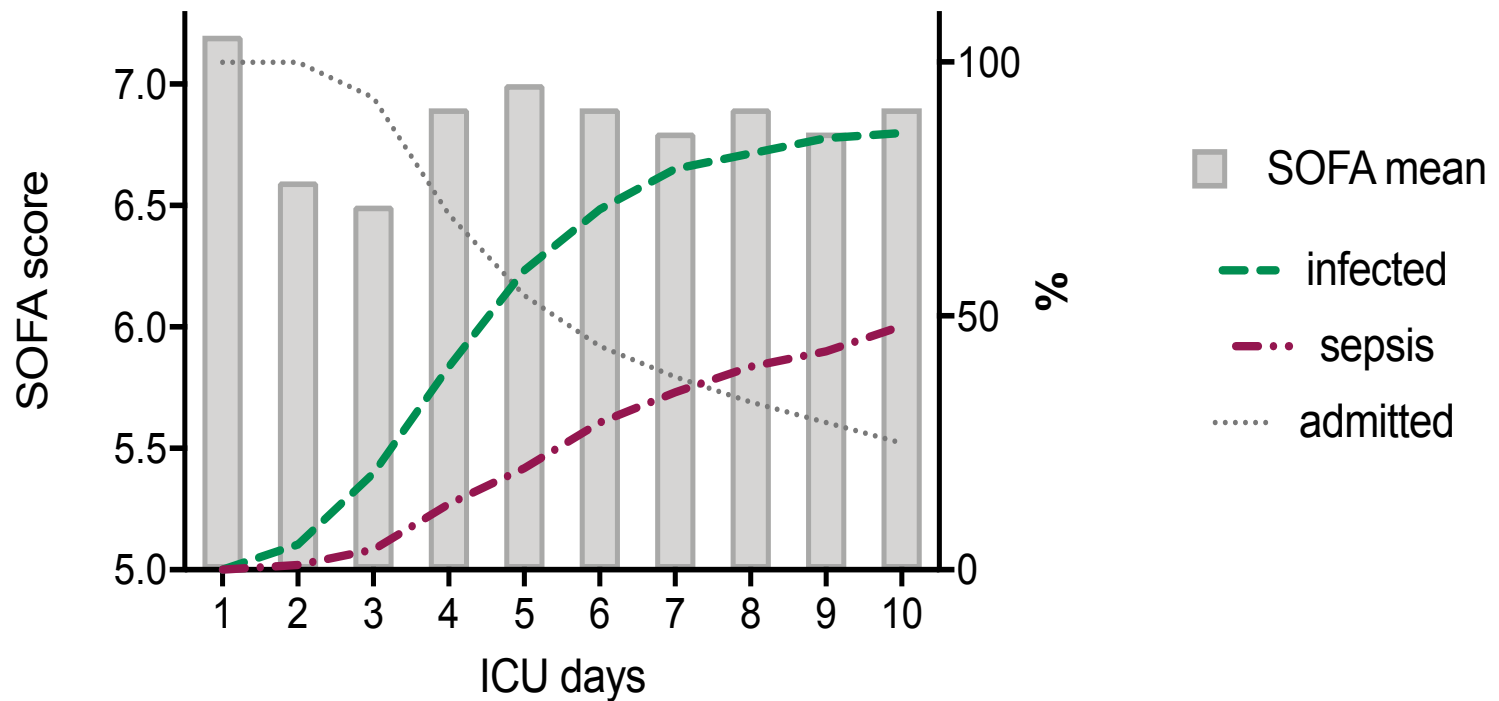
POST-INJURY SEPSIS

-a significant challenge



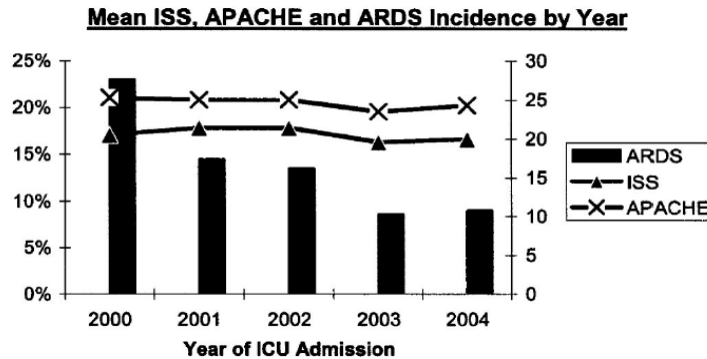
- No reduction in incidence
(Wafaisade et al. Crit Care Med. 2011)
- Incidence of up to 40% reported in severely injured ICU patients
(Shalhub et al. J Trauma. 2009)
- > 10 fold increase in mortality
(Osborn et al. CCM. 2004)
- Sepsis and MOF cause > 10% of trauma deaths
(Pfeifer et al. Injury 2009)
- A mean ICU LOS of 27 days for survivors with post-injury sepsis
(Bohmer et al. Crit Care. 2014)

Post trauma sepsis at the Karolinska



722 ICU treated trauma victims

Traumarelaterad ARDS



Martin et al. J Trauma. 2005.

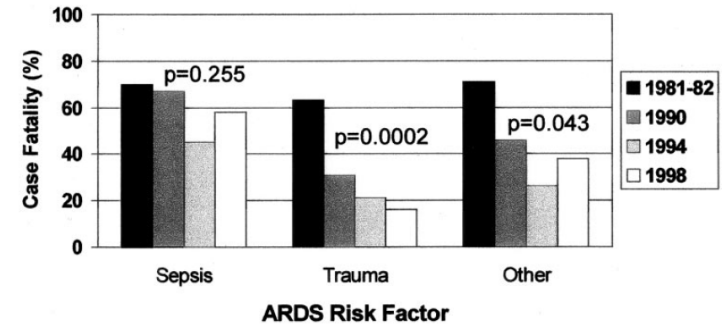
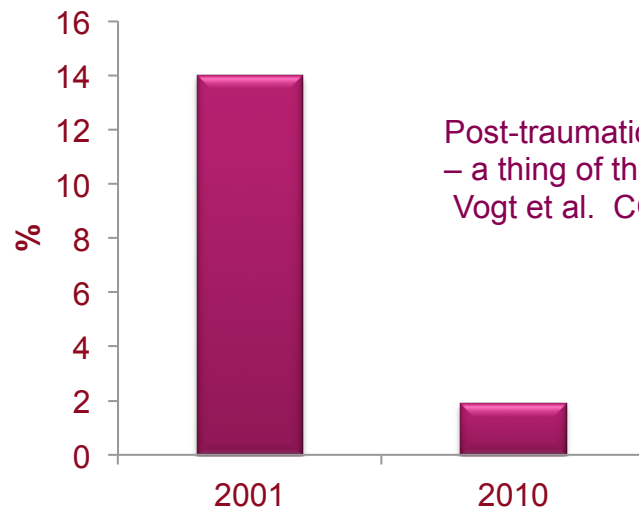


FIGURE 3. ARDS case fatality in all four cohorts stratified by risk factor, showing significant decrease in patients whose risk factor for ARDS is trauma or "other" (p = 0.255 for sepsis, p = 0.0002 for trauma, p = 0.043 for other; Cochrane-Armitage test for trend).

Stapleton et al. Chest 2005



Post-traumatic ards
– a thing of the past?
Vogt et al. CCM. 2012

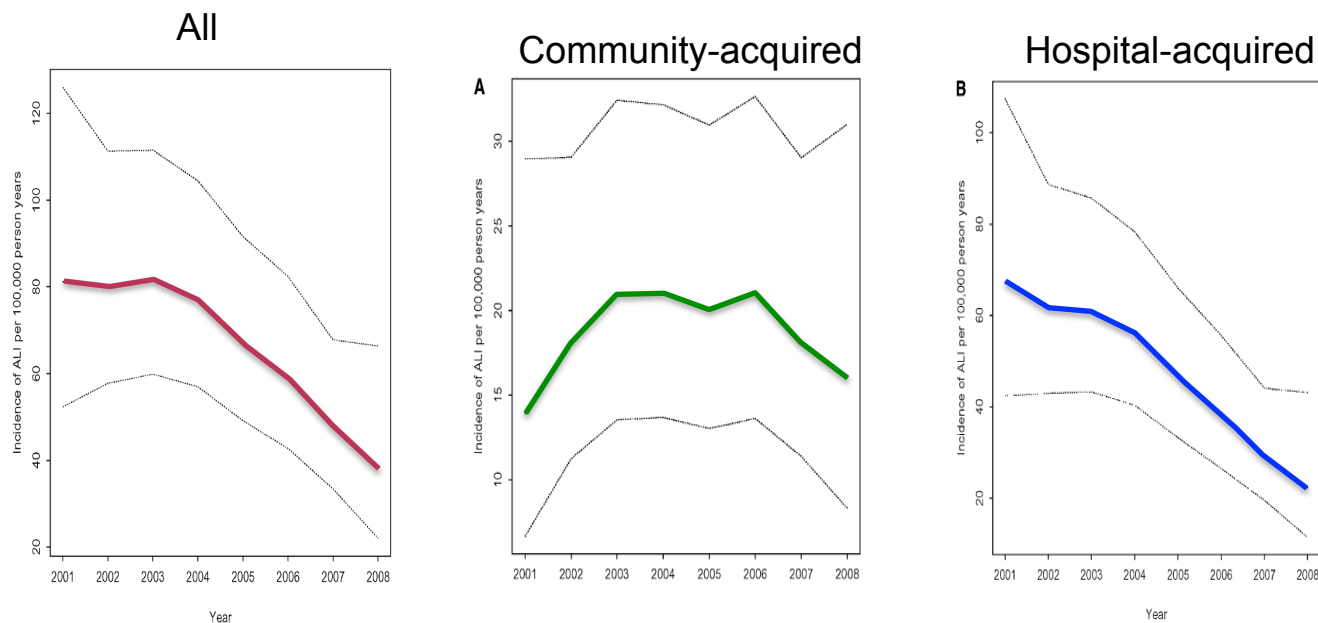
Eight-Year Trend of Acute Respiratory Distress Syndrome

A Population-based Study in Olmsted County, Minnesota

Guangxi Li^{1,2}, Michael Malinchoc^{1,3}, Rodrigo Cartin-Ceba¹, Chakradhar V. Venkata¹, Daryl J. Kor^{1,4}, Steve G. Peters¹, Rolf D. Hubmayr¹, and Ognjen Gajic¹

¹Division of Pulmonary and Critical Care Medicine, Mayo Epidemiology and Translational Research in Intensive Care, ³Division of Biomedical Informatics and Biostatistics, and ⁴Division of Critical Care Medicine, Department of Anesthesiology, Mayo Clinic, Rochester, Minnesota; and

²Division of Pulmonary Medicine, Guang An Men Hospital, China Academy of Chinese Medical Science, Beijing, China

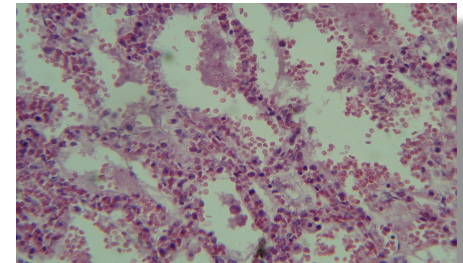


Li et al. Am J Respir Crit Care Med. 2011

ARDS

Partly iatrogenic and thus avoidable

- "Less is more"
 - Smaller tidal volumes
 - Less fluids
 - Targeted transfusion policies
 - "a lot to a few"
- Timing of surgical interventions
- Early control of fluid balance
 - CRRT



Multiple Organ Failure

The solution of one problem unfolds a new

A chain is only as strong as its weakest link. When links are strengthened where the chain has broken previously, new weak spots appear simply because the chain holds to test them. The obvious weak link in the severely wounded in this war (W.W. II) was the kidney.

EDWARD D. CHURCHILL¹

IMPROVED OUTCOME



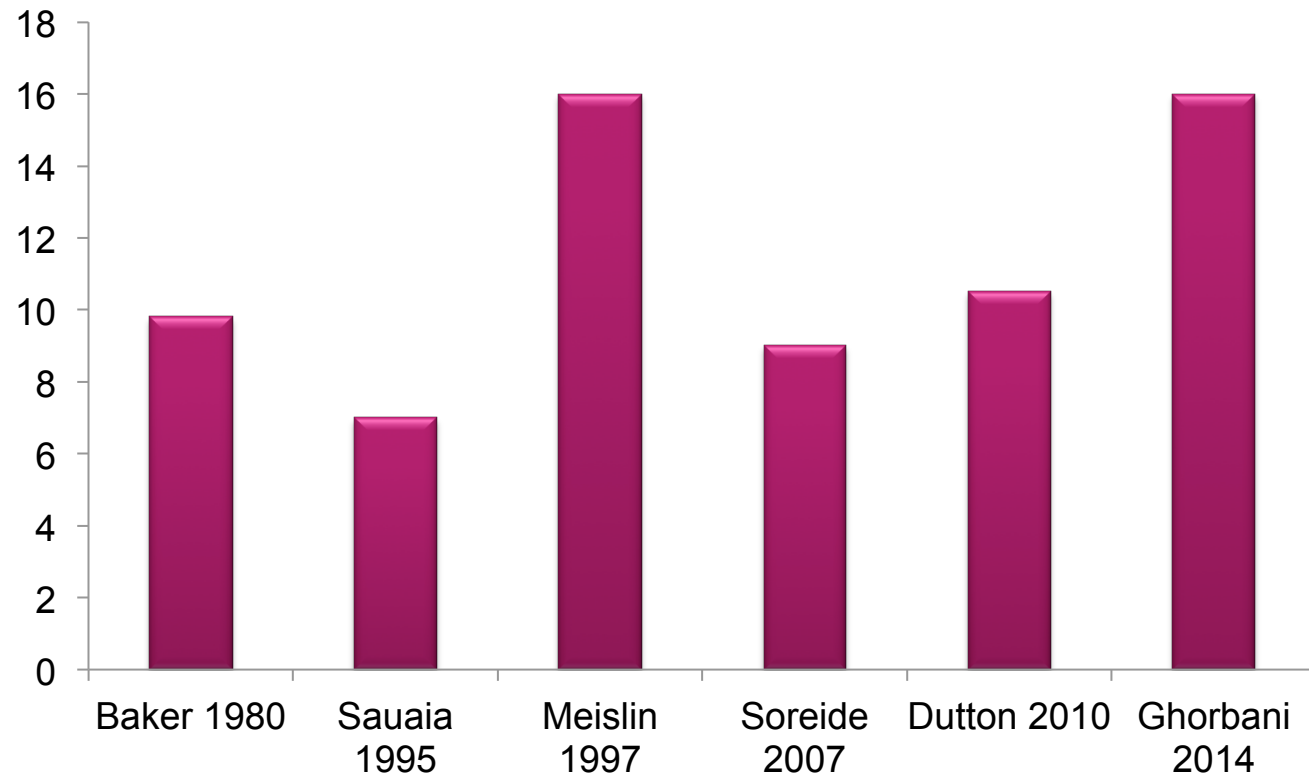
Early WW II - cardiovascular collapse – shock

Late WW II & KOREAN WAR – transfusions – AKI

VIETNAM WAR – crystalloid treatment – ARDS

1970s – Multiple organ failure - MOF

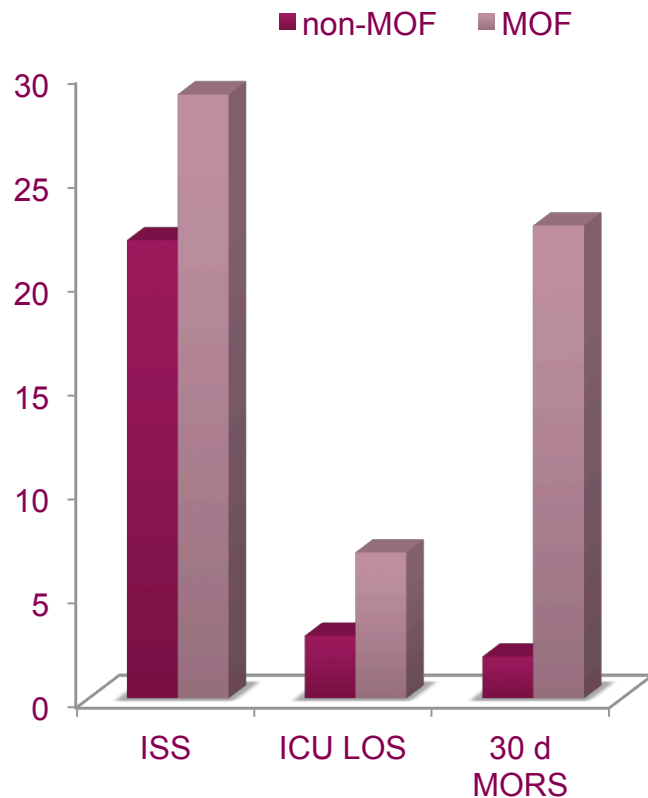
Proportion of MOF/sepsis as cause of death



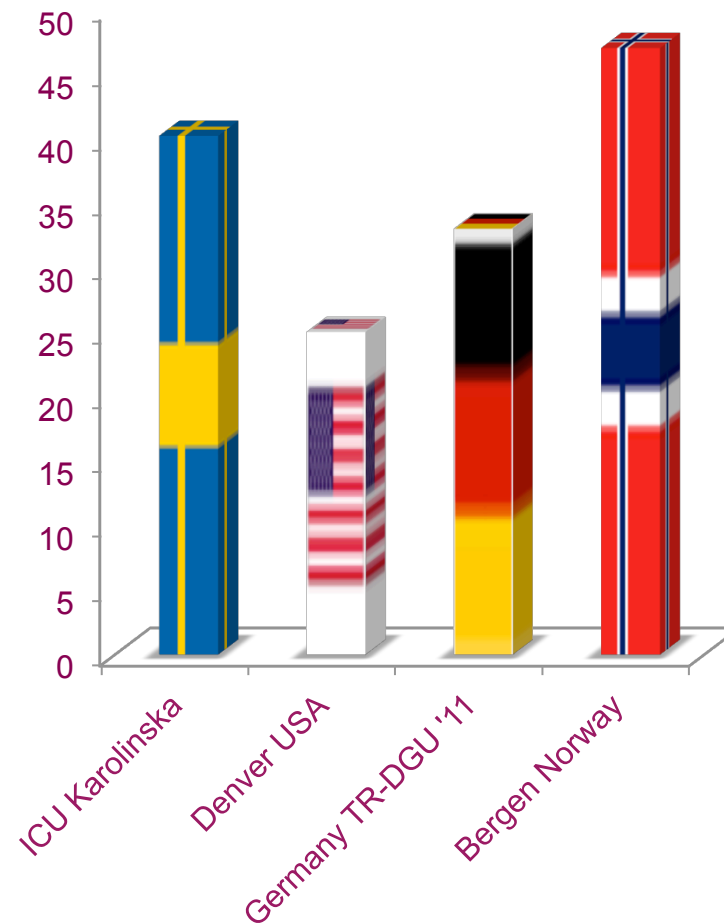
Multipel organsvikt – effekt och incidens



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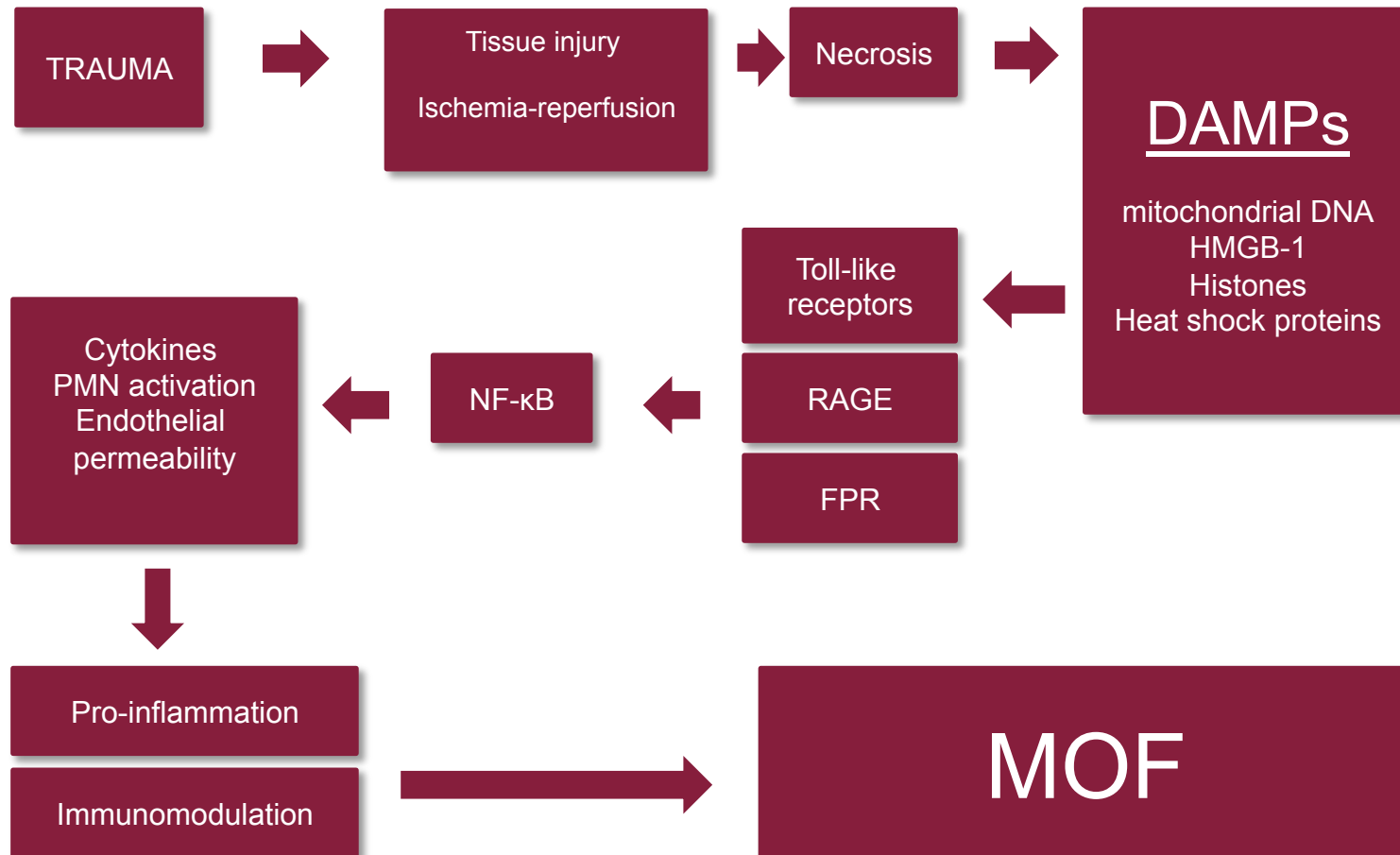


posttraumatisk MOF incidens



Damage-associated molecular patterns DAMPs

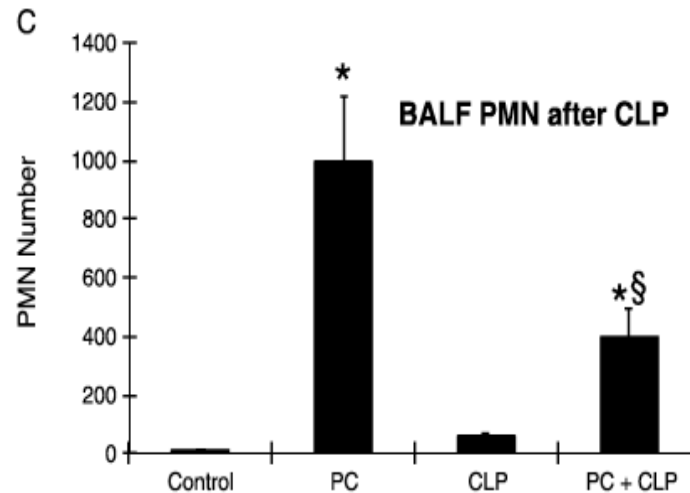
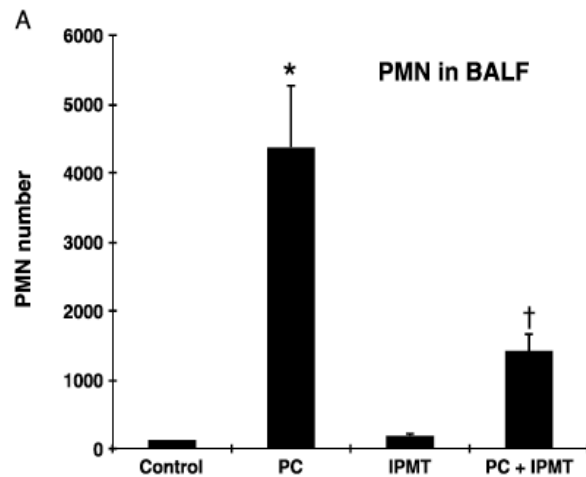
- en länk till multipel organsvikt



DAMPs cause of post trauma infections

Mitochondrial damage-associated molecular patterns released by abdominal trauma suppress pulmonary immune responses

Cong Zhao, MD, Kiyoshi Itagaki, PhD, Alok Gupta, MD, Stephen Odom, MD, Nicola Sandler, MBBS,
and Carl J. Hauser, MD, Boston, Massachusetts



RESEARCH

EDUCATION & OUTREACH

PUBLIC & PATIENT INVOLVEMENT

STAFF

LONDON TRAUMA SYSTEM

RESEARCH

Bleeding and Coagulation >>

Brain and Spinal Cord Injury >>

Organ Failure & Protection >>

National Studies: ORDIT >>

What is ORDIT?

ORDIT Study Sites

England & Wales: Study Protocol and Procedures

England & Wales: REC Information

England & Wales: Consent

England & Wales: Data Collection for CCUs

Scotland: Study Protocol and Procedures

Scotland: REC Information

Scotland: Data Collection for CCUs

ORDIT: Organ **Dysfunction** in **Trauma** - A national point prevalence study

Background

Multiple organ dysfunction syndrome (MODS) is an exaggerated systemic inflammatory response following major tissue trauma. Recent reports suggest that the incidence of MODS has reduced, yet it remains a resource-intensive, morbid sequelae following serious injury. Despite advances in initial trauma management early fulminant MODS has the greatest association with mortality. Previous evidence suggests that the onset of MODS has a multimodal distribution with a peak incidence present within the first 24-72 hours following injury. However a phenotype of persistent inflammation-immunosuppression catabolism syndrome (PICS) has recently been described, characterised by a prolonged, late resolving MODS lasting more than seven days post injury. In the era of haemostatic resuscitation, damage control surgery and trauma networks the incidence, pattern and severity of MODS following major trauma in the UK have not been evaluated. The national trauma system is perfectly positioned to prospectively capture the current epidemiology and outcomes of MODS for injured patients admitted to UK Major Trauma Centres.

ORDIT Aims

- Identify the prevalence of MODS in patients admitted to UK critical care units following major traumatic injury.
- Investigate the severity and temporal variation of MODS in this cohort of patients.
- Examine the incidence and mode of mortality associated with MODS following major traumatic injury.
- Evaluate the relationship between MODS and other clinical outcomes, length of stay and longer-term quality of life.

TRAUMA ORGAN PROTECTION USING **ARTESUNATE** (TOP-ART)

Trial registration number: ISRCTN15731357

Artesunate is a drug that has been in use for many years as the treatment of choice for severe malaria. It has very few adverse effects and can even be used safely by patients with kidney failure or liver dysfunction.

Using experimental (rat) models of severe bleeding, we have discovered that the intravenous injection of small doses of Artesunate (1 to 4.8 mg/kg) upon resuscitation reduces organ failure after trauma haemorrhage. The drug appears to enhance the protection of organs by reducing the body's excessive inflammatory response to injury and blood loss, and by activating well-known cell-survival pathways.

Having made this exciting discovery in the laboratory, C4TS now want to translate these findings to patients by conducting a Phase 2a clinical trial.

The aim of this trial, 'Trauma Organ Protection using ARTesunate' (TOP-ART), is to compare safety and benefit of Artesunate administration in addition to standard treatment in severely-injured bleeding trauma patients.

Study Design

TOP-ART will be conducted as a single centre study at the Royal London Hospital Major Trauma Centre. We will recruit 105 adult trauma patients who will be randomised to receive either:

- Low dose intravenous Artesunate (35 patients)
- High dose intravenous Artesunate (35 patients)
- Placebo (35 patients)

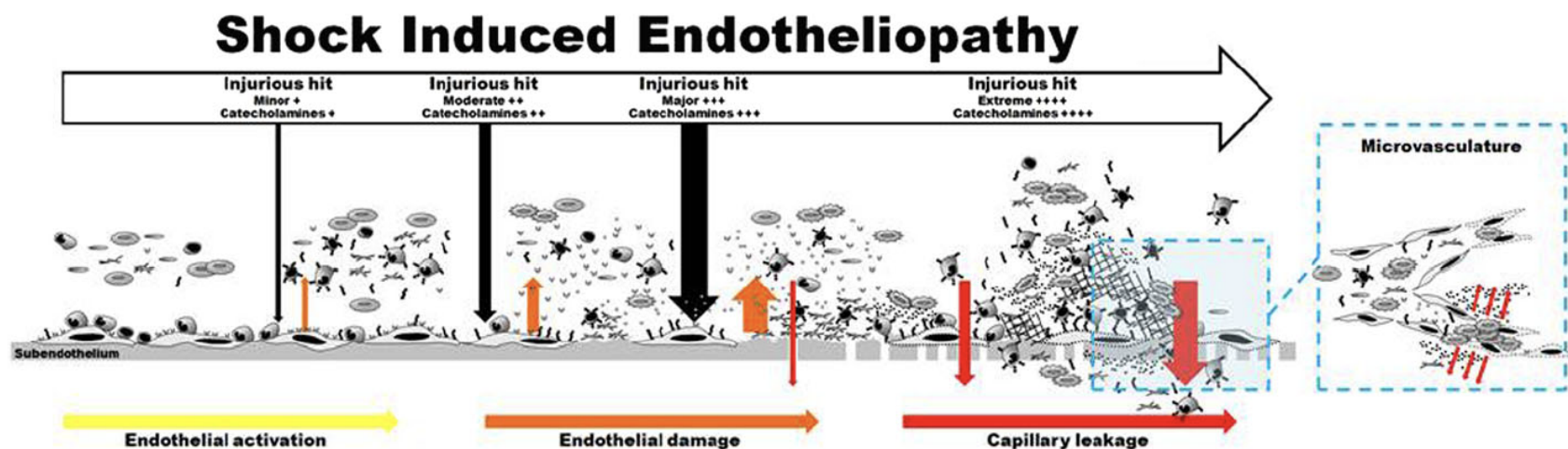
The trial will enrol eligible patients over a 24-month period (starting early 2016) and determine patient outcomes in-hospital for up to 28 days and mortality at 90 days.

A therapeutic agent that reduces the incidence and severity of multiple organ failure could have a major global impact on trauma patient outcomes and their requirements for healthcare utilisation.



Shock induced endotheliopathy (SHINE) in acute critical illness - a unifying pathophysiologic mechanism

PärIngemar Johansson^{1,2,3*}, Jakob Stensballe^{1,4} and SisseRye Ostrowski¹



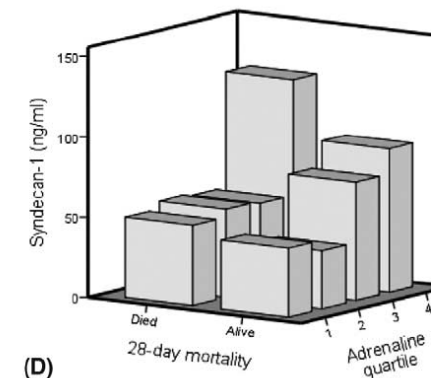
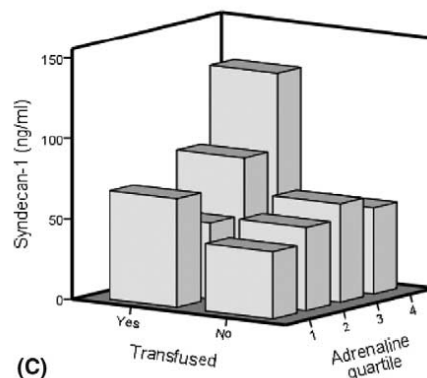
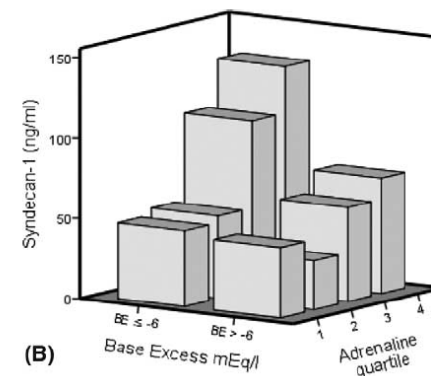
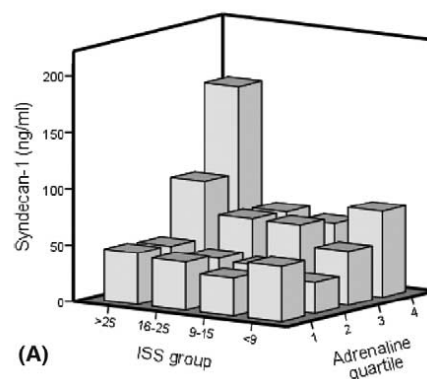
OPEN

Traumatic Endotheliopathy: A Prospective Observational Study of 424 Severely Injured Patients

Pär I. Johansson, MD, DMSc, MPA,*† Hanne H. Henriksen, BSc,* Jakob Stensballe, MD, PhD,*†
Mikkel Gybel-Brask, MD,* Jessica C. Cardenas, PhD,† Lisa A. Baer, BSc,† Bryan A. Cotton, MD, MPH,†
John B. Holcomb, MD,† Charles E. Wade, PhD,† and Sisse R. Ostrowski, MD, PhD, DMSc*

Copenhagen
426 trauma patients

- Endothelial damage (syndecan-1) and adrenaline more associated with mortality than ISS or BE
- Beta blockers?



- Frågeställning
 - Är pre-traumatisk β -blockad skyddande vid allvarligt multitrauma?
- Design
 - Kohortstudie



- Patienter från Traumaregister Karolinska 2006-2015
 - Ålder ≥ 50 år, ISS 16-74
- Via personnummer kopplade till nationella register
 - LISA (utbildning)
 - Patientregistret (komorbiditet)
 - Läkemedelsregistret
- Justering för confounders med logistisk regression

Resultat

■ β -blockerade

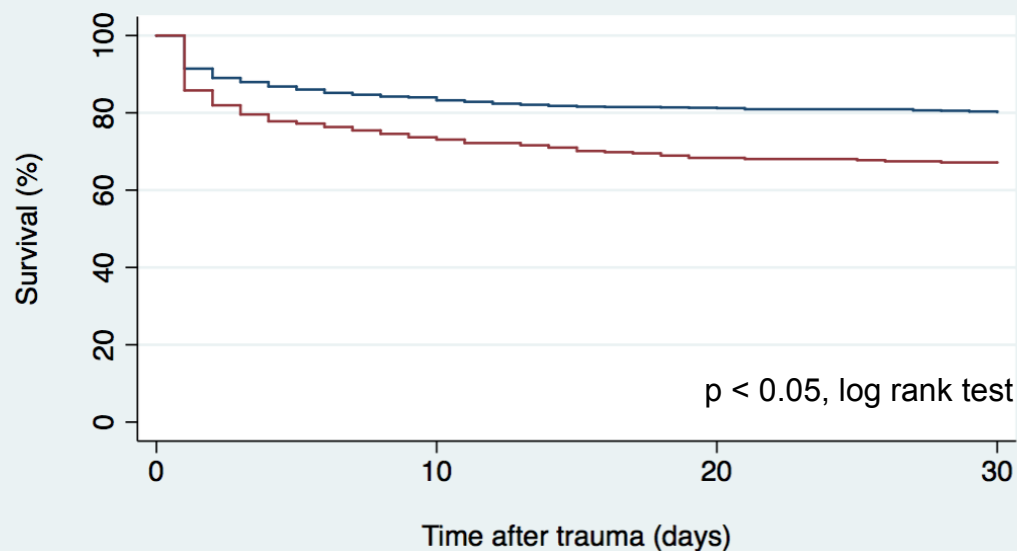
→ Äldre, mer somatisk komorbiditet

→ Samma skadegrad

→ Ingen skillnad i blodtryck eller chock

	β -blocker (-)	β -blocker (+)	p-value
Count (%)	1038 (75.4)	338 (24.6)	
Age, median (IQR)	63.5 (56-73)	71.5 (63-82)	< 0.001
Male, count (%)	733 (70.6)	223 (66.0)	0.108
Education level, count (%)			
Low	240 (25.1)	88 (30.6)	0.175
Medium	444 (46.3)	125 (43.4)	
High	274 (28.6)	75 (26.0)	
CCI categories, count (%)			
CCI 0	693 (66.8)	118 (34.9)	< 0.001
CCI 1	168 (16.2)	88 (26.0)	
CCI >1	177 (17.1)	32 (39.1)	
Ischemic heart disease, count (%)	27 (2.6)	96 (28.4)	< 0.001
Congestive heart failure, count (%)	28 (2.7)	60 (17.8)	< 0.001
Hypertension, count (%)	118 (11.4)	141 (41.7)	< 0.001
Diabetes mellitus	69 (6.6)	62 (18.3)	< 0.001
Anticoagulation therapy	31 (3.0)	65 (19.2)	< 0.001
Psychiatric comorbidity, count (%)	142 (13.7)	39 (11.5)	0.312
Substance abuse, count (%)	172 (16.6)	48 (14.2)	0.302
ISS, median (IQR)	24 (17-27)	25 (17-26)	0.911
Blunt trauma, count (%)	1020 (98.3)	331 (97.9)	0.689
Severe head injury, count (%)	651 (62.7)	216 (63.9)	0.694
Severe thoracic injury, count (%)	400 (38.5)	132 (39.1)	0.865
Severe abdominal injury, count (%)	89 (8.6)	28 (8.3)	0.868
SAP*, median (IQR)	144 (120-164)	150 (120-170)	0.073
SAP* < 90 mm Hg, count (%)	83 (8.0)	32 (9.5)	0.396
ICU admittance, count (%)	602 (58.0)	190 (56.2)	0.565

Resultat – 30-dagars mortalitet



23.0 % mortalitet (totalt)

Resultat – 30-dagars mortalitet

Table 3. Associations between pre-injury β -blocker use and 30-day mortality, unadjusted and adjusted OR (95 % CI).

	OR (95 % CI)	p-value	z	coefficient
Unadjusted	1.99 (1.51-2.61)	< 0.001	4.92	0.687
Restricted model*	1.35 (0.96-1.90)	0.085	1.72	0.300
Full model**	1.09 (0.70-1.70)	0.703	0.38	0.086
Full model, missing data analysed with MI***	1.09 (0.73-1.61)	0.675	0.42	0.084

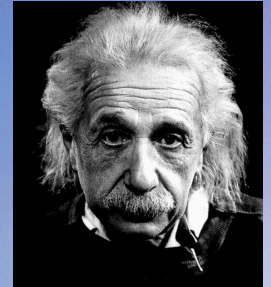
- *Justerad för ålder, kön, skadegrad, svår skallskada och chock
- ** Även justerad för utbildning, ischemisk hjärt-sjd, hjärtsvikt, HT, DM och antikoagulantia
- *** Som modell 2, multiple imputations av saknade data

- β -blockad kan ses som en markör för ökad risk för död hos den svårt skadade patienten
- Ingen skyddande, eller skadlig, effekt av β -blockad *per se* verkar föreligga

Sammanfattning

- Intensivvården en viktig del i traumavårdkedjan
- En gradvis förskjutning av den medicinska utmaningen till IVA
- Posttraumatisk organdysfunktion står för en betydande del av traumarelaterad mortalitet och morbiditet
- Sannolikt föreligger en del “preventable death” i intensivvårdsfasen
- Förbättring av framtidens utfall vid trauma kommer sannolikt att ske i intensivvårdsfasen

"I never think of the future - it comes soon enough."



THANK YOU!



Ongoing trials on fluid therapy

The CLASSIC trial

Conservative vs. Liberal Approach to Fluid Therapy of Septic Shock in Intensive Care (CLASSIC)

By the Scandinavian Critical Care Trials Group

ClinicalTrials.gov Identifier:
NCT02079402

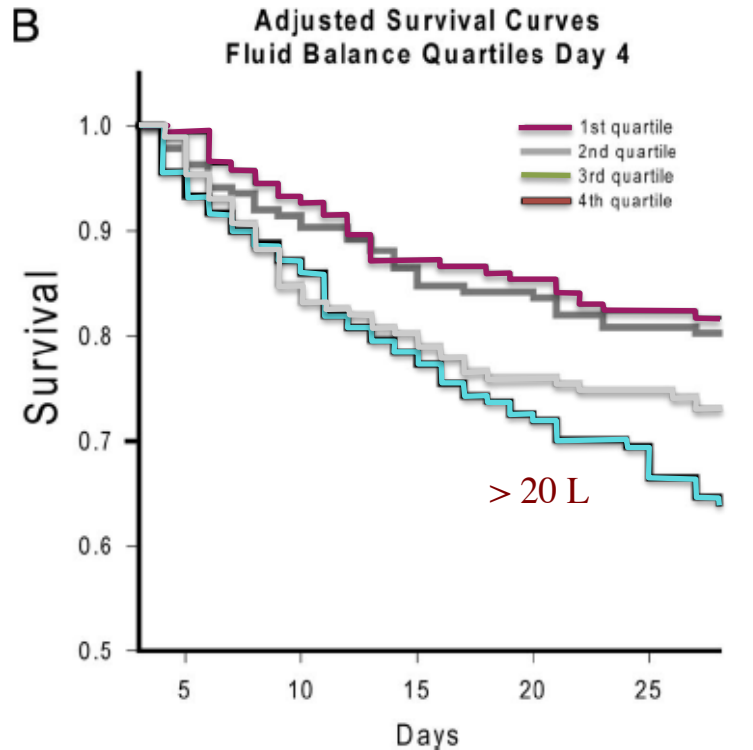
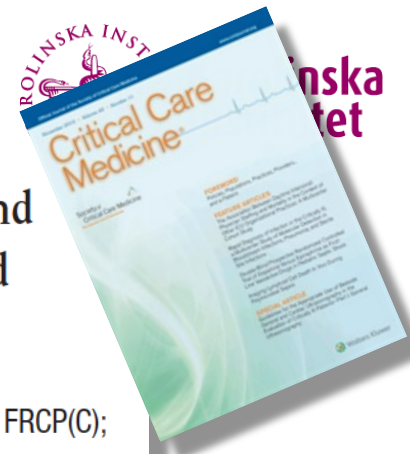


Fluids might be bad, but....

Fluid resuscitation in septic shock: A positive fluid balance and elevated central venous pressure are associated with increased mortality*

John H. Boyd, MD, FRCP(C); Jason Forbes, MD; Taka-aki Nakada, MD, PhD; Keith R. Walley, MD, FRCP(C); James A. Russell, MD, FRCP(C)

Crit Care Med 2011 Vol. 39, No. 2



- Retrospective studies
- Sometimes with huge fluid loads

RCTs on fluid strategies



Karolinska
Institutet

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

The FACTT trial

- Shorter time on mechanical ventilation with conservative fluid management
- No difference in mortality at 60 days

Liberal vs. conservative fluid strategy



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The ACOS study

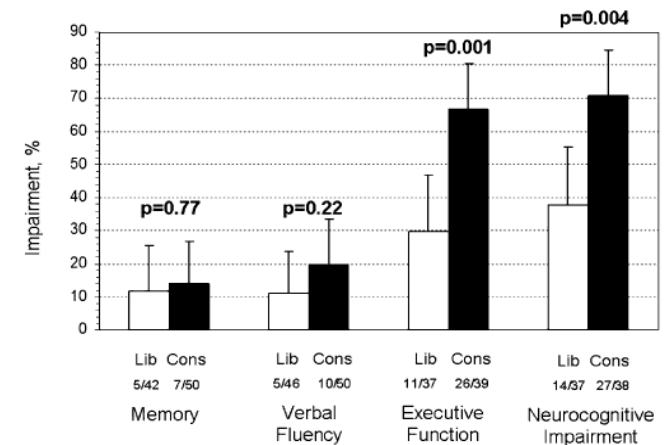
The Adult Respiratory Distress Syndrome Cognitive Outcomes Study

Long-Term Neuropsychological Function in Survivors of Acute Lung Injury

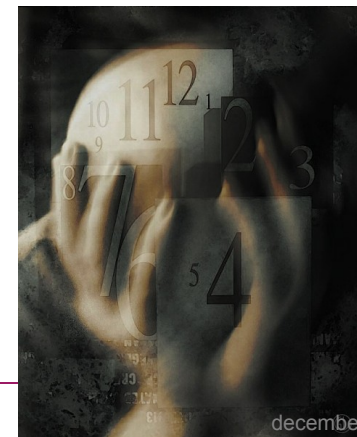
Mark E. Mikkelsen^{1,2*}, Jason D. Christie^{1,2*}, Paul N. Lanken¹, Rosette C. Biester^{3,4}, B. Taylor Thompson⁵,
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- Conservative fluid therapy in ALI resulted in increased cognitive impairment



december 18

Is conservative always better?

