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Postersession V

Abstract 42

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Overskrift Near-infrared spectroscopy determined brain and muscle oxygenation during head-up tilt induced central hypovolemia

Introduction
It remains debated why blood pressure decreases during hemorrhage. Near-infrared spectroscopy (NIRS) is used for non-invasive assessment of tissue oxygenation and may be a useful monitoring modality in anaesthesia and intensive care. This study examined the effect of central hypovolemia induced by head-up tilt (HUT) on NIRS-determined regional brain (ScO2) and muscle (SmO2) oxygenation.

Methods
20 healthy male volunteers (age 19-38 yrs.) were subjected to passive 50° HUT for 1 hour or until presyncope. ScO2 (N=20) and SmO2 (N=17) were determined using an INVOS-5100c monitor and middle cerebral artery mean blood flow velocity (MCAvmean, N=18) was obtained by transcranial Doppler. Mean arterial pressure (MAP) and heart rate (HR) were measured using an arterial catheter and stroke volume (SV), cardiac output (CO), and total peripheral resistance (TPR) were derived using Modelflow® technology. In addition, skin blood flow (SkBF) and oxygenation (SskinO2) were monitored using laser Doppler and white light spectroscopy, respectively.

Results
MAP increased upon HUT (89 (84-94) to 96 (90-101) mmHg; mean and 95% CI), but then gradually declined to a nadir of 80 (74-85) mmHg. SV declined throughout tilt (94 (87-101) to 71 (64-78) ml), while HR increased (65 (57-72) to 89 (82-96) bpm), keeping CO unchanged (6.2 (5.7-6.8) l/min). ScO2 gradually decreased from 78 (75-80) to 72 (70-75)% and MCAvmean from 51 (48-54) to 36 (33-39) cm/s during tilt, and SmO2 declined from 73 (67-80) to 62 (56-68)% upon tilt and remained low. Presyncopal symptoms appeared in 17 subjects after 11 (median; range 2-34) min accompanied by a decrease in MAP (to 59 (54-65) mmHg), SV (to 65 (58-73) ml), and CO (to 5.6 (5.0-6.3) l/min) while HR remained elevated. During presyncope, ScO2 decreased further to 68 (65-71) and MCAvmean to 32 (29-36) cm/s, while SmO2 recovered to 70 (63-76)%. SkBF and SskinO2 were initially unchanged but decreased towards the end of tilt and were lowest during presyncope (SkBF from 99 (72-125) to 71 (45-97) PU; S skinO2 from 66 (61-72) to 53 (47-58)%). All variables returned to baseline values upon return to the supine position, except SkBF, which remained low 10 min after tilt-down.

Discussion
ScO2 and MCAvmean decreased during HUT, indicating diminished CBF despite a rise in MAP. The abrupt decrease in ScO2 and MCAvmean during presyncope is likely explained by a decrease in MAP below the threshold for cerebral autoregulation. Conversely, SmO2 decreases immediately upon HUT, likely due to muscle vasoconstriction, but recovers during presyncope, suggesting muscle vasodilation.

Conclusion
Changes in ScO2 mirror those of MCAvmean during HUT. The increase in SmO2 during presyncope suggests sympathetic withdrawal resulting in muscle vasodilation that may account for the decrease in MAP.

Abstract 17

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Overskrift A technique for continuous bedside monitoring of global cerebral energy state

Introduction:
In critical care when cerebral energy metabolism might be jeopardized (e.g. after cardiac standstill, open heart surgery, multi-trauma etc.) it may be useful to monitor the global cerebral energy state. In the present experimental study of global cerebral ischemia induced by hemorrhagic shock, we investigate whether the lactate/pyruvate (LP) ratio obtained from microdialysis of cerebral venous blood may be used as a surrogate marker of global cerebral energy state.

Methods
The study was approved by the National Committee on animal Research Ethics. Six female pigs were anesthetized and vital parameters were recorded. Microdialysis catheters were placed in the left parietal lobe, the superior sagittal sinus and femoral artery. Hemorrhagic shock was achieved by bleeding the animals to a mean arterial pressure (MAP) of approximately 35 mmHg, and kept at a MAP of about 30-40 mmHg for 90 minutes. The animals were resuscitated with autologous whole blood followed by 3 hours of observation.

Results
The LP ratio obtained from the intracerebral and intravenous catheters immediately increased during the period of hemorrhagic shock while

the LP ratio in arterial blood remained close to normal levels. At the end of the experiment median LP ratio (interquartile range) obtained from the intracerebral, intravenous, and intra-arterial microdialysis catheters were 846 (243-1990), 309 (103-488), and 27 (21-31), respectively. There was a significant difference in the LP ratio obtained from the intravenous location and the intra-arterial location (P<0.001).

Discussion:
After induction of hemorrhagic shock the intracerebral LP ratio rapidly increased to a very high level. The increase was due to a marked increase in lactate concentration simultaneously with a pronounced decrease in pyruvate. This metabolic pattern is characteristic of ischemia. In the superior sagittal sinus the LP ratio exhibited a similar though less pronounced pattern. In the femoral artery a modest increase in the LP ratio and a moderate increase in pyruvate level were obtained and remained close to the upper reference level (≤30) of normal cerebral tissue.

Conclusions:
A low MAP is recommended for patients in hemorrhagic shock until the bleeding is surgically controlled. This experimental study documents that during protracted pronounced hemorrhagic shock cerebral energy metabolism was severely compromised and exhibited a biochemical pattern typical of ischemia and cellular degradation. From intravenous microdialysis in the sagittal sinus, it is possible to achieve semi-quantitative information of intracerebral redox state. Accordingly, it might be possible to monitor global cerebral energy state continuously with a strictly extracerebral technique. Interestingly the study also showed that after reinfusion of blood other parts of the body recovered evaluated by microdialysis but the brain showed signs of damage, making the brain the limiting organ in hemorrhagic shock.

Abstract 23

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Overskrift Central Venous Injection Ports In Oncology Patients - Early And Late Complications.

Introduction:
Central venous injections ports (CVIP) are used in oncology to administer chemotherapy, blood products, symptomatic care and for diagnostic procedures. The aim of this study was to determine the type and rate of complications in patients who received a CVIP in our department.

Method:
The medical records of 100 consecutive oncology patients, who received a CVIP between January 1 2013 and June 13 2013, were studied retrospectively with a follow up period of one year. All patients signed an informed consent for the study of their medical records.
The age, sex, BMI, comorbidities, diagnosis as well as sites of metastases, leukocyte, and platelet counts at the time of insertion were recorded.
Also recorded were complications at the time of insertion, identity of the doctor performing the procedure, any late complications, results from x-ray controls, and date of possible CVIP removal. If there were any signs of infection, cultures were taken from the catheter or insertion site.

Results:
43 patients died within the first year.
17 intraoperative complications were registered: 2 pneumothoraces, 4 punctures of the artery, 8 technical problems at insertion and 3 wrongfully placed catheters or ports. 34 late complications were registered: 22 occlusions of the catheter, 10 infections, 1 hematoma, and 1 thrombosis of the vena cava. 18 of the 22 occluded catheters were sent to X-ray control. 11 CVIPs were removed within the first year due to complications.
One physician implanted 52 of the 100 ports. He had a significantly lower rate of intraoperative complications (X2, P=0.04) compared to the other group, consisting of 9 doctors, but had the same rate of late complications.
The median BMI was 26.1 kg/cm2, and patients with a BMI ≥ 25 kg/cm2 (58% of the patients), compared to patients with a BMI <25 kg/cm2, had a significantly higher rate of late complications (X2, P=0.003).

Discussion/Conclusion:
All CVIPs were inserted by experienced specialists in anesthesiology, and we found that the physician with the most insertions had the fewest immediate complications. The nature and occurrence of complications at the time of insertion were similar to other studies but the incidence of late malfunctions was high as was the incidence of infections, especially in overweight patients [1,2,3]. This calls for further evaluation of patients and details of the procedures, and a more extensive study. The high incidence of infections (0.4/1000 catheter days) may be explained by the limited duration of the study period. Further studies should include the use of ultrasound to locate the vein and possibly changed injection/implantation routines to reduce the infection rate.

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TABLE 1. Early and Late complications

Complications - Intraoperative	n	Complications - Late	n
Arterial puncture	4	Occlusion	22 (3)
Technical problems		Clinical signs of Infection	
Multiple venous punctures	4	Staph. Aureus	4 (2)
Peel of sheet complications	3	E. Coli	1 (1)
Guide-wire complications	1	Staph. Aureus + GBS	1 (1)
		E. Cloacae	1 (1)
		Coag. Neg. Staph.	1 (1)
		No growth	1 (1)
		Not tested	1 (0)
Pneumothorax	2	Hematoma	1 (1)
Improper placement of catheter	2	Thrombosis (v.cava)	1 (0)
Improper placement of port	1		
Total	17	Total	34 (11)

Staph. Aureus= staphylococcus aureus
GBS=Group B hemolytic streptococcus
Coag. Neg. Staph= Coagulase negative staphylococcus.
Numbers in parenthesis indicate the number of catheters removed.

Abstract 37

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Overskrift Prediction of Outcome After Emergency High-risk Intraabdominal Surgery Using the Surgical Apgar Score

Introduction
With current literature quoting mortality rates up to 45 percent, emergency high-risk abdominal surgery has, compared with elective surgery, significantly greater risk of death and major complications. The Surgical Apgar Score (SAS) is predictive of outcome in elective surgery, but has never been exclusively validated in an emergency setting.

Method
A consecutive prospective single center cohort study of 355 adults undergoing emergency high risk abdominal surgery between June 2013 and May 2014. Post-operative major complications were defined according to the Clavien-Dindo Scale as well as NSQIP guidelines, SAS was calculated postoperatively. Cochran-Armitage test for trend was used to evaluate the incidence of both outcomes. Area Under the Curve (AUC) was used to demonstrate the scores discriminatory power. Data regarding ASA score as well as perioperative characteristics was retrieved from the Danish Anesthesia Database. The primary outcome measure was 30 day mortality.

Results
The overall incidence of major complications was 33,0 %, overall death rate 18,8 %. Risk of major complications, death and ICU admission increased significantly with decreasing Surgical Apgar Scores (all P<0,001). The score's c-statistics was 0,64.

Discussion
Any standardized scoring system can only fulfill an adjunctive role in perioperative decision-making. This study indicates that the SAS is a significant postoperative predictor of perioperative morbidity for patients undergoing emergency high risk intraabdominal surgery. SAS has proven to be an uncomplicated, objective tool that can easily be applied to identify patients at higher risk of poor outcome. However, the score does show a weak discriminatory power. In addition, strong correlation between SAS and risk of death was found only in the most critical group. This seems to suggest that, while predictive, the SAS cannot stand alone in an emergency setting.

Conclusion
We have demonstrated the Surgical Apgar Score to be significantly predictive but weakly discriminative for major complications and death among adults undergoing emergency high risk abdominal surgery.

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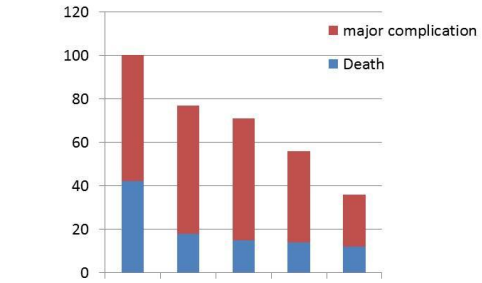

Score	0-2	3-4	5-6	7-8	9-10
No. of patients	19	61	127	107	41
Death No. (%)	8(42)	11(18)	19(15)	15(14)	5(12)
Relative risk	3,5	1,5	1,2	1,1	1
(95% CI)	[1,3-9,2]	[0,6-3,9]	[0,5-3,1]	[0,4-3,0]	[reference]
Major complications	11(58)	36(59)	71(56)	45(42)	10(24)
Relative risk	2,8	2,4	2,3	2	1
(95% CI)	[1,2-5,0]	[1,4-4,3]	[1,3-4,0]	[1,2-3,8]	[reference]
ICU admissions (%)	11 (58)	20 (33)	36 (28)	19 (18)	3 (7,3)
Relative risk	7,9	4,5	3,9	2,4	1
(95% CI)	[2,5-25,1]	[1,4-14,1]	[1,3-11,9]	[0,8-7,8]	(reference)

Figure 1. 30-day major complications, deaths and ICU admissions among 355 emergency high-risk abdominal surgery patients in relation to Surgical Apgar Score. Major complications, death rates as well as ICU admissions are shown according to the 10-point Surgical Apgar Score from the operation. Patients in the highest scores (9-10) served as reference group. Risk of major complications, death and ICU admissions increased significantly with decreasing scores (Cochran-Armitage trend test, P<0,001).

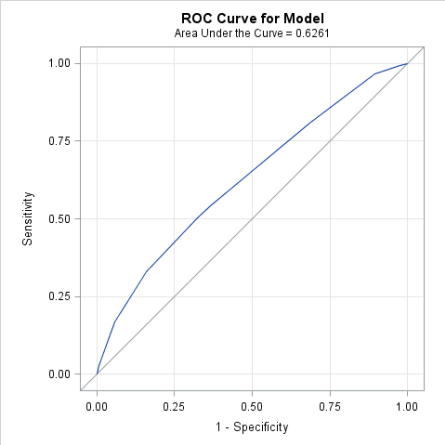

Figure 2: Receiver Operating Characteristics (ROC) curve with Area Under the Curve (AUC) for prediction of postoperative major complications or death. The score achieved c-statistics of 0,63 for predicting major complications or death.

Abstract E

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Overskrift Stress ulcer prophylaxis in the intensive care unit. Protocol for a randomized trial examining benefits and harms of pantoprazole - the SUP-ICU trial

Background
In patients in the intensive care unit (ICU) clinically important gastrointestinal (GI) bleeding is rare but acid suppressants are frequently used [1, 2]. Evidence on stress ulcer prophylaxis (SUP) is of low quantity and quality [3], and studies have shown that proton pump inhibitors (PPI) may increase the risk of a number of serious adverse events [4, 5]. Taken together high-quality research is needed to describe benefits vs. harms of SUP, because millions of ICU patients are likely exposed every year.

Objectives
To assess the benefits and harms of SUP with PPI in adult, critically ill patients in the ICU.

Design
An investigator-initiated, pragmatic, international, multicentre, randomized, blinded, parallel-group trial of SUP with PPI versus placebo. Inclusion and exclusion criteria: Inclusion criteria: Adult patients acutely admitted to the ICU with one or more of the following conditions: shock, renal replacement therapy, mechanical ventilation expected to last > 24 hours, any kind of coagulopathy, treatment with anticoagulant drugs or liver disease. Exclusion criteria: contraindications to PPI, daily treatment with PPI and/or histamine-2-receptor antagonist, GI bleeding of any origin or known peptic ulcer during current hospital admission, organ transplant, withdrawal from active therapy or brain death, positive urine human chorionic gonadotropin (hCG) or plasma hCG or consent according to national regulations not obtainable.

Intervention: Experimental intervention is intravenous pantoprazole 40 mg daily during ICU stay. Control intervention is matching placebo (saline).

Outcomes
Primary outcome: Mortality 90 days after randomization. Secondary outcomes: proportion of patients with clinically important GI bleeding, pneumonia, Clostridium difficile infection or myocardial ischemia, proportion of patients with clinically important GI bleeding, proportion of patients with pneumonia or clostridium difficile infections, 1-year mortality, days alive without organ support in the 90-day period, serious adverse reactions and a health economic analysis.
Trial size: 2 x 1675 patients are required to show a 20% relative risk reduction or increase (5% absolute risk reduction or increase) in the primary outcome measure, assuming a baseline 90-day mortality of 25% (α=0.05 (two-sided), and β=0.1).
Trial conduct: The trial will be coordinated by the Centre for Research in Intensive Care – CRIC – and patients will be enrolled at 50 ICUs in 7 countries in a 2-year period.
The first patient is expected to be enrolled in August 2015.

Conclusions
The SUP-ICU trial will provide high-quality data on the benefits and harms of SUP with pantoprazole in acutely ill ICU patients at risk of GI bleeding.

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Abstract 7

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Overskrift Prognostic factors for reoperative surgery following perforated peptic ulcer. A Danish nationwide cohort study

Introduction
Perforated peptic ulcer (PPU) is an emergency with 30-day mortality up to 30%(1). Surgery and sepsis treatment are keystones in PPU management. Risk factors for mortality have been identified but knowledge of prognostic factors for reoperation is sparse. Appropriate identification of patients at increased risk of reoperation is essential to adequately plan the perioperative continuum of care. We aimed to identify prognostic factors for reoperation after PPU.

Methods
We included patients operated for PPU in Denmark from 1 January 2003 to 31 December 2014 using the Danish Clinical Register of Emergency Surgery. We assessed potential predictors for reoperation and their association with in-hospital reoperative surgery by unadjusted and adjusted multivariable regression. We used the competing risks subdistribution hazards approach by Fine and Gray to account for mortality as a competing risk.

Results
4086 primary operations were identified (Table 1). 454 underwent reoperation. Male gender, in-hospital admission, increased BMI, increased ASA-score, shock at admission, and other chronic diseases were independent prognostic factors (Table 2). Use of steroids and high age displayed lower risk of reoperation.

Discussion
Of the identified predictors for reoperation, shock at admission, high ASA-score and chronic disease were also in previous studies related to mortality after PPU(2). In addition, we identified male gender, high BMI, and in-hospital admission as predictors. Surprisingly, use of steroids and high age showed a significantly decreased risk of reoperation, which stands in contrast to previous studies(3). This may be due to concealed symptoms in these patients, but further studies exploring possible causal links are needed.

Conclusion
Male gender, in-hospital admission, shock at admission, high BMI, ASA III-V, and chronic disease were associated with higher risk of reoperation after PPU in a large population-based study. Age above 70 years and use of steroids were related to lower risk of reoperation.

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Table 1: Baseline characteristics

Variable	Total, n (%) (N=4086)	No reoperation, n (%) (N=3632)	Reoperation, n (%) (N=454)	Missing, n (%)
Median BMI (IQR), kg/m^2		23.1 (20.5-26.0)	24.3 (21.5-28.4)	1029 (25.2)
ASA III-V	1941 (48.3)	1651 (46.2)	290 (64.9)	64 (1.6)
In-hospital admission	909 (30.5)	722 (28.5)	187 (41.6)	1107 (27.1)
Male gender	1839 (45.0)	1602 (44.1)	237 (52.2)	0 (0.0)
Shock at admission*	623 (21.0)	483 (19.2)	140 (30.8)	1114 (27.3)
Coexisting diseases				
Liver cirrhosis	200 (4.9)	162 (4.5)	38 (8.4)	0 (0.0)
COPD	583 (14.3)	501 (13.8)	82 (18.1)	0 (0.0)
Diabetes	310 (7.6)	268 (7.4)	42 (9.3)	0 (0.0)
Malignant disease or AIDS	257 (6.3)	226 (6.2)	31 (6.8)	0 (0.0)
Heart disease	1289 (31.5)	1135 (31.3)	154 (33.9)	0 (0.0)
Other chronic diseases	1204 (29.5)	1034 (28.5)	170 (37.4)	0 (0.0)
Smoker	1972 (54.7)	1735 (54.8)	237 (54.4)	483 (11.8)
Excess alcohol consumption**	654 (17.7)	555 (17.1)	99 (22.2)	393 (9.6)
Duodenal ulcer	1865 (48.3)	1664 (48.5)	201 (47.1)	227 (5.6)
Median age (IQR). years		71 (59-81)	70 (61-77)	0 (0.0)
Preadmission use of steroids	422 (10.9)	384 (11.3)	38 (8.5)	218 (5.3)
In-hospital mortality	926 (22.7)	775 (21.3)	151 (33.3)	0 (0.0)

* Systolic blood pressure <100 mmHg and heart rate > 100 bpm.
** Weekly alcohol intake below or above national recommendations: < 168 g per week for males and <84 g per week for females

Table 2: Regression analysis of risk factors for reoperation

Variables	Crude HR (95% CI)	P-value	Adjusted HR* (95% CI)	P-value
BMI, kg/m^2				
<18	1.00 (ref)		1.00 (ref)	
18-24.9	1.30 (0.89-1.90)	0.181	1.36 (0.92-2.02)	0.128
25-29.9	1.82 (1.21-2.75)	0.004	1.85 (1.21-2.81)	0.004
>30	2.06 (1.34-3.15)	0.001	1.98 (1.27-3.07)	0.003
ASA III-V	1.62 (1.33-1.97)	<0.001	1.58 (1.26-1.99)	<0.001
In-hospital admission	1.53 (1.26-1.86)	<0.001	1.43 (1.17-1.75)	<0.001
Male gender	1.52 (1.26-1.82)	<0.001	1.43 (1.19-1.77)	<0.001
Shock at admission**	1.55 (1.27-1.91)	<0.001	1.40 (1.13-1.73)	0.002
Coexisting diseases				
Liver cirrhosis	1.64 (1.17-2.29)	0.004	1.18 (0.81-1.71)	0.39
COPD	1.19 (0.94-1.51)	0.151	1.16 (0.90.1.48)	0.256
Diabetes	1.10 (0.81-1.51)	0.542	0.94 (0.68-1.29)	0.693
Malignant disease or AIDS	0.97 (0.67-1.40)	0.878	0.92 (0.62-1.37)	0.696
Heart disease	0.97 (0.80-1.17)	0.74	0.88 (0.71-1.09)	0.253
Other chronic diseases	1.34 (1.11-1.62)	0.003	1.24 (1.02-1.52)	0.031
Smoker	1.07 (0.89-1.29)	0.458	0.99 (0.80-1.21)	0.892
Excess alcohol consumption***	1.35 (1.08-1.69)	0.008	0.98 (0.75-1.28)	0.907
Duodenal ulcer	0.99 (0.82-1.20)	0.938	0.96 (0.80-1.17)	0.71
Age>70 years	0.69 (0.58-0.84)	<0.001	0.72 (0.58-0.89)	0.002
Preadmission use of steroids	0.69 (0.49-0.95)	0.025	0.59 (0.42-0.84)	0.004

*Competing risks subdistribution hazards approach by Fine and Gray
** Systolic blood pressure <100 mmHg and heart rate > 100 bpm.
*** Weekly alcohol intake below or above national recommendations: < 168 g per week for males and <84 g per week for females

Abstract 39

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Overskrift Therapeutic hypothermia after cardiac arrest in a real life setting

Introduction:
Therapeutic hypothermia has been the cornerstone in the treatment of unconscious survivors after cardiac arrest since the publication of two landmark studies in 2002, which concluded that induced hypothermia (32-34 °C) improves survival and neurologic outcome in patients with shockable rhythms and Out- of-Hospital Cardiac Arrest (OHCA)(1,2). However the evidence on whether therapeutic hypothermia also can improve the prognosis in patients with non-shockable rhythms or In-Hospital Cardiac Arrest (IHCA) is sparse. The aim of the present study was to assess the prevalence and prognosis of patients with non-shockable rhythms or IHCA after implementation of therapeutic hypothermia in a real life setting.

Methods:
During a 5-year period - from 2008 to 2013 - 72 consecutive unconscious patients admitted to the ICU at Holbaek Hospital after cardiac arrest and successful resuscitation were included. Patients were included regardless of initial cardiac rhythms and location of the cardiac arrest. All patients were cooled according to guidelines to a target temperature of 32-34 °C. Patients were stratified into groups of patients who fulfilled the criteria of the original randomized trials (shockable rhythms and OHCA) and patients who did not fulfil the criteria (non-shockable rhythms or IHCA). The primary outcome was survival with a favourable neurologic outcome within six months.

Results:
Almost 2/3 (63%) of the included patients had non-shockable rhythms or IHCA and did not fulfill the criteria of the original randomized studies upon which the current guidelines are based. Furthermore only 8.7 % of these patients survived with a favorable neurologic outcome (Figure 1). Nearly 1/3 (29%) of the included patients had an out of hospital cardiac arrest (OHCA) with an initial non-shockable rhythm. Despite successful resuscitation and subsequently treatment with hypothermia in the ICU, none (0%) of these patients survived with a favorable neurologic outcome (figure 2).

Conclusion:
In a real life setting the majority of patients (63%) receiving therapeutic hypothermia after resuscitation do not fulfill the criteria of the original studies upon which the current guidelines are based. Furthermore these patients have a poor outcome, indicating that not all patients may benefit from cooling. This may result in unnecessary and ethically questionable treatment among subgroups of patients treated with therapeutic hypothermia after cardiac arrest.

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Abstract 46

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Overskrift Copeptin as a predictor of mortality and renal failure in patients with severe sepsis – a prospective observational study

Introduction
Copeptin is a by-product of the synthesis of vasopressin and is released during hypovolemia, inflammation and stress among others. In line with this, copeptin has been proposed as a biomarker in the diagnosis and prognosis of severe sepsis and septic shock. We assessed the predictive value of copeptin for mortality and renal failure in terms of dialysis in patients presenting in the intensive care unit with severe sepsis.

Methods
Prospective observational multicentre substudy of the Scandinavian Starch for Severe Sepsis / Septic Shock (6S) trial, which randomised patients with severe sepsis in the intensive care unit to fluid resuscitation with hydroxyethyl starch vs. Ringer's acetate (NCT00962156). At five trial sites, copeptin was measured at baseline, and clinical data including mortality and use of dialysis within 90 days were retrieved from the trial database. Statistical analyses included correlation analyses, logistic regression and receiver operating characteristics (ROC) curves.

Results
247 of the 798 patients in the 6S trial were included in the present substudy (table 1). The median copeptin level was 76 pmol/l (IQR 39-162). The 214 (87%) patients with septic shock appeared to have higher copeptin levels than those without shock (81 pmol/l (IQR 39-181) vs. 57 pmol/l (IQR 39-79), P=0.045). However, copeptin was poorly correlated with disease severity as measured by SOFA score at baseline (Spearman correlation coefficient 0.19) and SAPS II (0.29) as well as with volume of resuscitation fluid in the 24 hours prior to inclusion (-0.05). In both unadjusted and adjusted logistic regression analyses copeptin was associated with both mortality and dialysis within 90 days (table 2).

ROC curve analysis revealed that copeptin was a poor predictor of mortality (area under curve (AUC) 0.63, 95%-confidence interval (CI) 0.56-0.70) and dialysis within 90 days (AUC 0.72, 95%-CI 0.64-0.80).

Discussion

In this study, copeptin did not correlate well with disease severity at time of measurement. However, copeptin was associated with clinical outcome in terms of mortality and use of dialysis, but the predictive values of copeptin for these outcomes were relatively low as illustrated with small areas under the ROC curves. This questions the usefulness of copeptin as a clinical tool. In line with our findings, several other promising biomarkers have previously failed to predict clinical outcome and course in patients with sepsis. Their sensitivity and specificity are probably hampered by the fact that often the exact onset of sepsis is unclear and that the systemic inflammation itself may affect levels of most biomarkers.

Conclusion

Single measurements of copeptin had a relatively low predictive value of 90-day mortality and dialysis in patients with severe sepsis.

Table 1 Demographics, baseline characteristics and outcomes of 247 patients with severe sepsis

Demographics and baseline variables	
N	247
Age, median (IQR)	66 (57-75)
Male, n (%)	135 (55)
Source of sepsis, n (%)	
Respiratory	142 (58)
Abdominal	81 (33)
Urogenital	20 (8)
Soft tissue	37 (15)
Other	27 (11)
SOFA score, median (IQR)	8 (6-9)
SAPS, median (IQR)	53 (40-65)
Septic shock, n (%)	214 (87)
Admitted to a university hospital, n (%)	181 (73)
Surgical reason for admission, n (%)	85 (34)
Randomised to HES (vs. Ringer's acetate), n (%)	122 (49)
Comorbidities, n (%)	
Hematologic cancer	44 (18)
Heart failure*	21 (9)
Stroke*	23 (9)
COLD*	26 (11)
Diabetes	19 (8)
Hypertension	77 (31)
Outcomes	
Mortality at 90 days, n (%)	135 (55)
Any dialysis within 90 days, n (%)	50 (20)

SOFA denotes Sepsis-related Organ Failure Assessment, SAPS Simplified Acute Physiology Score, HES Hydroxyethyl Starch, COLD Chronic Obstructive Lung Disease.

*Previous cause of hospital admission

Table 2 Association of copeptin with mortality and dialysis in 247 patients with severe sepsis

	Unadjusted		Adjusted	
Outcome	**OR**	**P-value**	**OR**	**P-value**
Mortality at 90 days	1.6 (1.2-2.0)	P < 0.001	1.5 (1.2-2.0)	P = 0.001
Dialysis within 90 days	2.3 (1.6-3.2)	P < 0.001	2.4 (1.6-3.5)	P < 0.001

The odds ratio (OR) refers to a 2.7-fold increase in copeptin levels.

Adjustments were made for gender, hydroxyethyl starch vs. Ringer's acetate, presence of septic shock or not, presence of hematologic cancer or not and Sepsis-related Organ Failure Assessment Score.