PLACING BACK PATIENTS TO MECHANICAL VENTILATION: NEW PREDICTORS OF EXTUBATION OUTCOME

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INTRODUCTION. The minute ventilation recovery time appears as a new predictor of extubation outcome based on preliminary data, as an easy to measure parameter at the bedside. Our objective was to confirm, in patients who successfully tolerated an spontaneous breathing trial (SBT), whether Minute Ventilation Recovery Time after placing them back to mechanical ventilation (MV) helps to predict extubation outcome.

METHODS. One year prospective study of all patients approaching an SBT from MV > 48 hours. Exclusion criteria were tracheostomy, self-extubation, or neuromuscular disease. Basal respiratory parameters were measured within the 6 hours previous to the SBT under stable Pressure Support Ventilation of 14 ± 2 and PEEP of 5 ± 4. SBT consisted in 30-120 minutes of spontaneous ventilation with supplementary oxygen on a T-tube. After SBT, patients were placed back on their previous PSV setting with a continuous recording of RR, Vt and minute ventilation to evaluate the time needed to return to baseline Minute Ventilation. Statistical analysis was done by multivariate analysis and receiver-operating-curves (ROC).

RESULTS. We studied 93 patients who successfully passed an SBT. Reintubation rate was 19.5%. Patients who failed extubation were older (62±12 vs. 55±15, p<0.05), but comparable in all the other variables. After successful SBT, the time to recover baseline minute ventilation was longer in Failed-Extubation patients (14±5/7 vs. 5±4/5, p = 0.001), and its area under the ROC curve for extubation outcome was 0.729 (CT: 95%: 0.56-0.89) (see figure).

CONCLUSION. The minute ventilation recovery time after placing back to mechanical ventilation patients who tolerate an SBT is a useful adjunct to predict the extubation outcome.

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263

RECOVERY AND QUALITY OF LIFE AFTER ARDS - FIRST RESULTS FROM A PROSPECTIVE CROSS-SECTIONAL STUDY

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INTRODUCTION. Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are marked by high mortality and persistent functional disability. Ventilation with high tidal volume has been shown to be in part responsible for the lethal outcome, however, severe restrictions in oxygenation and ventilation may not always allow lung protective ventilation. Extracorporeal membrane oxygenation (ECMO) may be used to avoid such injurious ventilation, thereby improving long-term outcome. The aim of the study was to investigate the influence of ECMO on quality of life and lung function in patients with ALI and ARDS.

METHODS. Patients who were admitted to the Marburg ECMO center between 1990 and 2001 were seat a package containing the SF-36 and the St.Geroge's Respiratory Questionnaire (SGRQ). Details regarding diagnosis and treatment were taken from the medical charts. Data analyses made use of Chi-square tests, t-tests and Spearman-rank correlations.

RESULTS. N = 71 patients (44 female) were included. Median age at treatment was 27 (16 – 69), median PaO2/FIO2 was 72 (56 – 277) and median time since treatment was 10 years (2 – 15). Primary diagnoses were trauma (n=22), pneumonia (n=27), sepsis (n=13), aspiration (n=5), and other (n=4). 34 patients were treated with ECMO. Contrasting our sample with SF-36 norm reference data of the German population revealed considerable impairments (> 10 score points) regarding physical, social and emotional functioning. Baseline variables that affected SF-36 scores were age at treatment (higher age resulted in lower physical functioning, role functioning and performance) and length of hospital stay (longer stay resulted in lower physical and emotional functioning). There were no significant differences between ECMO and non-ECMO patients regarding the eight SF-36 scores (all p > 0.10). Similar results were obtained regarding the SGRQ, except for one item that tpped into high physical burden (walking uphill): 55 % ECMO, but only 25% non-ECMO patients reported problems (p = 0.015).

CONCLUSION. ALI and ARDS result in persistent functional disability when compared to the general population. The potential benefit of ECMO in avoiding ventilator-associated lung injury does not result in an improved long-term outcome. Whether this is the result of differences in severity or etiology of lung failure or injurious ventilation despite ECMO has to be determined.

264

THE MORTALITY OF ACUTE RESPIRATORY DISTRESS SYNDROME IS HIGHER IN THE NON-METROPOLITAN AREAS

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INTRODUCTION. The mortality for acute respiratory distress syndrome (ARDS) is over 40%. Whether or not patients form non-metropolitan areas have a similar mortality is not known. We performed this study to determine ARDS mortality among patients from non-metropolitan areas.

METHODS. We used the Illinois Healthcare Cost Containment Council Database for the year 2001. Using the ICD-9 CM (International Classification of Diseases, 9th Revision, Clinical Modification) code for ARDS, all patients in the state of Illinois, USA with the diagnosis of ARDS were studied. The geographical area of the state was divided into Chicago metropolitan statistical area (CMSA), other metropolitan statistical areas (OMSA) and non-metropolitan (rural) areas (NMSA). Data was analyzed based upon these geographical areas and the patients’ age, gender, type of health insurance and mortality.

RESULTS. The state’s population was 12,419,293 and 3999 had ARDS. The incidence was 32.2/100,000. The CMSA, with 2282/3999 (57.1%) had the largest number of patients. This was significantly higher than the OMSA’s 885/3999 (22.1%) and NMSA’s 696/3999 (17.4%) (P<0.01). One hundred thirty six (3.4%) patients were from unknown areas. There were 1282/2282 (56.5%) in the CMSA, 488/885 (55.1%) in the OMSA, and 426/696 (61.2%) in the NMSA who were 65 years of age or older. The increase in older patients in the NMSA was statistically significant (P<0.05). With respect to health insurance, 1136/2282 (49.8%) from the CMSA, 475/885 (53.7%) from the OMSA and 426/696 (61.6%) from the NMSA were covered by the US government (medicare for patients > 65 years of age). The larger number of medicare patients in the NMSA was also statistically significant (P<0.05). The overall mortality was 942/3999 (23.6%). Its distribution was 518/2202 (22.7%) in the CMSA, 205/885 (23.2%) in the OMSA and 168/696 (24.7%) in the NMSA. The NMSA mortality was significantly higher (P<0.05). A total of 1737/3999 (43.4%) were 64 years or younger and 226/3999 (55.6%) were 65 years and older. Among patients 64 and younger, 286/1737 (16.5%) died. Among those 65 and older, 606/2262 (29.0%) died. The mortality rate for the older age group was significantly higher (P<0.01).

CONCLUSION. ARDS patients from non-metropolitan areas have higher mortality than those from large metropolitan areas and so are patients older than 65 years of age.

265

QUALITY OF LIFE AND MORPHO-FUNCTIONAL ABNORMALITIES IN 6 MONTH SURVIVORS OF THE ARDS

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INTRODUCTION. ARDS survivors have decreased quality of life after hospital discharge, nevertheless, there are no data that relate these test results to pulmonary function or CT scan images.

METHODS. Prospective multicentric study in 3 ICUs (1998-2003). Quality of life (Nottingham Health Systems Research, University of Illinois College of Medicine-Rockford, Rockford, United States

RESULTS. n=38 (50%). Age 47±16 yr-old. When ARDS was diagnosed they presented: LIS 18th Annual Congress – Amsterdam, Netherlands – 25–28 September 2005 S71 0.015). Similar results were obtained regarding the SGRQ, except for one item that tpped into high physical burden (walking uphill): 55 % ECMO, but only 25% non-ECMO patients reported problems (p = 0.015).

CONCLUSION. ALI and ARDS result in persistent functional disability when compared to the general population. The potential benefit of ECMO in avoiding ventilator-associated lung injury does not result in an improved long-term outcome. Whether this is the result of differences in severity or etiology of lung failure or injurious ventilation despite ECMO has to be determined.

Grant acknowledgement. Red Gira (G03/063) y Respir (RTIC 03/11), Instituto Carlos III, Ministerio de Sanidad
Comparing heated humidifiers (HH) to heat and moisture exchangers (HME), the lung lies among the most frequently affected organs during sepsis. New data indicated that a ventilator care bundle was implemented within a 6-bed ICU in 2003. The care bundle was defined as: 1) high-flow humidification, 2) limitation of sedation, 3) periodic cessation of sedation, and 4) elevation of the patients’ chest to 30 degrees to the horizontal. Significant problems exist in implementing research findings into clinical practice. It has been suggested that care bundles encourage the implementation of evidence-based practice. All these effects have the potential to affect NIV efficiency and rate of intubation. METHODS. We conducted a multicenter randomized controlled trial to test the hypothesis that the use of HME during NIV with ICU ventilators for patients with acute respiratory failure would increase the intubation rate (primary end point). After stratification by center and by type of respiratory failure (hypoxic or hypercapnic patients) eligible patients were randomized to either HH or HME. RESULTS. 247 patients were included in the study in 15 centers from November 2002 to December 2003. 128 patients were allocated to the HH group and 119 to the HME group. Patients were comparable for mean age 67.0 ± 12 vs 66.14, mean SAPS II 37.15 ± 37.15, for comorbidities, and for indication for NIV. The intubation rate was however similar: 30.6% in the HH group and 37.6% in the HME group (p = 0.31), with no differences in the subgroup analyses. At three hours, PaCO2 tended to be lower in the HME group. Patients died due to hypercapnic patients in the HH group (66 vs 72 mm Hg, P = 0.08). No differences were found for NIV duration, ICU and hospital LOS or ICU mortality (HME 14.1% vs HH 21.5%, P = 0.18). CONCLUSION. In spite of strong physiological data favoring HH in comparison with HME during NIV, no differences in intubation rate and outcome were found in this study. The physiologic effects observed in short term studies may be counterbalanced by other important factors in the clinical settings, or may play a role only in marginal cases.

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270 LEPTIN EXERTS A PROTECTIVE ROLE IN SEPSIS IN VIVO AND MODULATES UNCOUPLING PROTEIN EXPRESSION

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INTRODUCTION. Bioenergetic failure is implicated in the pathogenesis of sepsis-induced multiple organ failure. The adipokine leptin plays a key role in the regulation of energy expenditure, mediated in part via mitochondrial uncoupling proteins (UCPs). UCPs shift electron transfer away from oxidative phosphorylation, thus decreasing mitochondrial efficiency, and may also protect against superoxide injury. Circulating leptin levels rise in acute sepsis, but later fall due to nutrient deficiency. Our aims were to investigate how both deficiency and exogenous replacement of leptin affect UCP expression in sepsis in vivo.

METHODS. We used a fluid-resuscitated mouse model of facetectomy. Mice comprised 4 groups: (i) ad libitum fed septic, (ii) fed controls, (iii) fasted 48 h prior to sepsis and treated with i.p. saline, and (iv) fasted septic treated with i.p. leptin. At 24 h post-sepsis, mice were sacrificed, and blood, liver and skeletal muscle (SKM) collected. UCP-2 (liver, SKM) and -3 (SKM) mRNA was measured by real-time PCR, and serum leptin by enzyme immunoassay. Statistical analyses used Student’s t-test.

RESULTS. Leptin was higher in fed septic mice compared with controls (200±63 vs 70±19 pg/ml; p<0.05). Fasting induced hypo leptinaemia (44±2 µg/ml). Leptin treatment of fasted septic restored leptin levels to at least those observed in fed septic (46±25±18 pg/ml). Fasting increased sepsis-related mortality at 24 h compared with fed septic (78% vs 28%). Leptin treatment reduced fasting septic mortality to 28%. SKM UCP-2 and -3 expression increased in fed septic compared with controls (5±23 and 16±7% increase, respectively). In contrast, fasting septic showed a decrease in SKM UCP-2 (3±0.7-fold decrease vs fed septic; p<0.05) and -3 (16±6±36-fold decrease vs fed septic; p<0.05), which was abrogated by leptin treatment. In contrast, liver UCP2 increased 3000-fold in fasted septic compared with fed septic (p<0.001), this increase was abolished by leptin treatment.

CONCLUSION. In our sepsis model, nutrient deficiency results in hypo leptinaemia, reduced SKM UCP expression and increased sepsis-induced lethality. Leptin treatment prevents this increased mortality, and up-regulates SKM UCP expression. These data contrast with that found in liver, suggesting a tissue-specific differential regulation of UCP expression by leptin. Dysregulated UCP expression related to hypo leptinaemia may contribute to bioenergetic failure and organ dysfunction in sepsis. This warrants further study.

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272 HEMODYNAMIC OVERLOAD MODULATES THE INNATE IMMUNE SYSTEM AND PRIMES FOR LPS HYPERRESPONSIVENESS

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INTRODUCTION. It has been shown that hemodynamic overload (HO) results in a transient increase of proinflammatory cytokine expression, which returns to baseline levels within 3d while myocardial responsiveness to a second external stimulus increases dramatically (1). As the molecular mechanisms remain elusive, we tested the hypothesis that HO modulates the innate immune system by changing the expression of relevant receptors and investigated the corresponding signalling cascade including the activation of NFκB.

METHODS. Sustained HO was produced in C57BL6 mice for 3d by transverse aortic constriction (TAC) and sham-operation procedure (SOP) was used as control. Following 3d of TAC or SOP and 10min of LPS respectively PBS stimulation NFκB activation was determined by electro mobility shift assay.

RESULTS. Following 3d of TAC or SOP and 6h of LPS respectively PBS stimulation the expression of CD14 and TLR4 were tested by western blot and the expression of relevant cytokines were determined with RNase protection assay and ELISA. NFκB activation and CD14 expression increased significantly in the TAC+LPS group compared to the TAC+PBS group. The cytokine gene and protein expression increased significantly in the 3d TAC + 6h LPS group compared to the 3d SOP + 6h LPS group. The expression and activation of all investigated proteins and mRNA levels in the 3d TAC+PBS and 3d SOP+PBS groups remained on baseline levels at all time points. HO increased the expression of CD14, thus primes innate immune mechanisms and results in NFκB mediated LPS hyper-responsiveness.

CONCLUSION. The present data demonstrate that myocardial injury respectively hemodynamic overloading determines myoccardial reactivity to LPS by modulating parts of the innate immune system of the adult mammalian heart.

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271 CATECHOLAMINES DO NOT INTERFERE WITH ENDOTOXIN-INDUCED ALTERATIONS IN HEPATIC MITOCHONDRIAL FUNCTION

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INTRODUCTION. Endotoxin (E) impairs the mitochondrial respiration. In isolated muscle mitochondria these abnormalities are reversed by dopamine and dobutamine.1 Catecholamines can enhance enzyme activities in native hepatic mitochondria. On the other hand, dopamine decreases hepato-splanchnic VO2 in septic patients despite increase in DO2. We assessed the effects of E and catecholamines in isolated hepatic mitochondria.

METHODS. Liver biopsies were taken from 6 anesthetized pigs, mitochondria isolated and divided into eight samples/pig. Lipopolysaccharide (100 µg/ml) (E) or placebo (P; isolation buffer) was added to four of the samples, each. After one hour, each E- and P-sample was incubated with dopamine, dobutamine (100 µM), norepinephrine (60 µM) or P for one hour. Mitochondrial ADP-dependent (state 3), ADP-independent (state 4) respiration and their ratio (RCR) were determined for the complex I, II and IV of the mitochondrial respiratory chain.

RESULTS. State 3 and 4 are in nanomol/min/mg protein. Data are expressed as mean (SD) MANOVA, effects: endotoxin: p<0.05. Catecholamine, drug: p=0.01; endotoxin-drug: p=0.08.

TABLE 1.

| Complex I | Complex II | Complex III | Complex IV |
|-----------|------------|-------------|------------|
| VO2 State | VO2 State 2 | RCR* | RCR |
| Placebo  E | 67 (15) | 29 (10) | 2.5 (0.9) | 3.2 (1.2) | 2.5 (0.8) |
| Placebo  P | 89 (14) | 20 (5) | 4.5 (0.6) | 3.9 (0.6) | 2.9 (0.8) |
| Dopamine E | 68 (56) | 24 (17) | 2.8 (1.0) | 3.4 (1.5) | 2.0 (0.5) |
| Dopamine P | 80 (42) | 23 (7) | 3.3 (1.0) | 4.1 (0.6) | 2.5 (0.3) |
| Dobutamine E | 78 (44) | 28 (9) | 2.6 (0.8) | 3.0 (1.1) | 2.3 (0.8) |
| Dobutamine P | 101 (33) | 27 (8) | 3.7 (0.6) | 3.9 (0.8) | 2.5 (0.5) |
| Noradrenaline E | 77 (39) | 34 (11) | 2.2 (0.9) | 3.0 (1.1) | 2.1 (0.5) |
| Noradrenaline P | 80 (20) | 24 (5) | 3.5 (1.2) | 4.2 (1.7) | 2.2 (0.6) |

CONCLUSION. Endothelin impaired the efficiency of hepatic mitochondrial respiration. Unlike in muscle mitochondria, catecholamines did not reverse this effect and even impaired the respiratory efficiency in native samples. Our findings suggest that catecholamines may have organ-specific effects on mitochondrial function.

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CT-SCAN EVIDENCE OF HYPERINFLATION DURING NIH PROTECTIVE STRATEGY VENTILATION IN ARDS PATIENTS

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INTRODUCTION. NIH mechanical ventilation protocol is the standard of care in ARDS. However individual characteristics of respiratory mechanics may expose the lung to some degree of mechanical stress. In the present study we tested the hypothesis that combination of morphological (CT scan) and functional (static PV curve) analysis may identify patients at risk of mechanical stress.

METHODS. 22 ARDS patients (NIH protective ventilatory strategy) were enrolled. Static PV curve at zEEP where obtained before CT. CT slides were achieved during end-inspiration and end-expiration hold and analyzed to detect total lung volume distribution.

RESULTS. In 10 patients the tidal increase in lung volume occurred with a 30-50 % increase of hyperinflated areas. In these patients Pplat during the NIH ventilation was higher than the UIP (fig.).

CONCLUSION. Combined evaluation of lung morphology on respiratory mechanics identify risk of mechanical stress in ARDS patients.

REGIONAL VENTILATION BY ELECTRICAL IMPEDANCE TOMOGRAPHY COMPARED TO CT IN EXPERIMENTAL LUNG INJURY

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INTRODUCTION. Electric impedance tomography (EIT) can be used as a non-invasive technique at bedside to gain information about the impedance distribution within a plane of electrodes placed around the thorax. A recent study [1] showed good agreement between regional relative tidal volume measured by EIT and X-ray computed tomography (CT) in patients with lung injury when measured in series. We hypothesized that in experimental lung injury also the time course of relative regional ventilation measured by EIT and CT shows good agreement when obtained simultaneously.

METHODS. 10 pigs were anesthetized and mechanically ventilated via a tracheostomy with the APRV mode. Lung injury was induced by acid aspiration or with oleic acid and increased abdominal pressure. After several hours the animals were transferred to the CT scanner. With volume controlled ventilation a low flow inflation maneuver was performed and registered with an EIT device (esf, Göttingen, Germany) and a dynamic CT scan in the plane of the electrodes with a resolution of about 15 Hz. Guided by the electrodes four quadrants were defined as regions of interest in the CT images, the relative distribution of air content was calculated from CT and EIT in four equivalent quadrants. Differences between the methods were assessed by Bland-Altman plots.

RESULTS. Differences between CT and EIT relative air contents were in an acceptable range for all quadrants with higher differences in the ventral quadrants (left bias 0.7%, 2xSD-interval 14.4%, right 0.8% and 12.3% respectively) having also higher air contents at the end of the maneuver than the dorsal quadrants, which show good agreement with lower scatter (2xSD 10.5% left, 6.4% right) but a slightly higher bias (3.9% left, 1.7% right) than the ventral half.

CONCLUSION. In an animal model of lung injury, simultaneous acquisitions of time courses of relative regional ventilation in four quadrants obtained by EIT and CT show acceptable to good agreement.

REFERENCE(S). 1. Victorino JA et al., Am J Respir Crit Care Med. 2004;169(7):791-800.
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A CT-SCAN ASSESSMENT OF EFFECT OF SURFACANT ON RE-AERATION OF THE LUNG IN PATIENTS WITH ARDS

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INTRODUCTION. Previous randomized multicenter trials failed to demonstrate a decrease in mortality of patients with Acute Respiratory Distress Syndrome or Acute Lung Injury (ARDS/ALI) treated by surfactant 1. However, the effect of surfactant on re-aeration of the lung has never been studied in supine (SP) and prone (PP) position, using two PEEP levels (0 and 10 cm of H2O). In each posture and positive end expiratory pressure (PEEP)-related changes in regional ventilation (V'A) were studied in supine (SP) and prone (PP) position. EIT measurements were performed in 20 regions distributed along the ventral-to-dorsal axis (Bins). Regional recruitment was computed as the difference of regional alveolar volume between 2 experimental conditions and global recruitment as the sum of regional derecruitment in ventral regions, probably by oedema redistribution. Finally, V'A/V A was less in dorsal compared to ventral regions.

METHODS. After oleic acid-induced lung injury, five mechanically-ventilated pigs were randomly assigned to surfactant 2. However, the effect of surfactant on re-aeration of the lung has never been studied in supine (SP) and prone (PP) position, using two PEEP levels (0 and 10 cm of H2O). In each posture and positive end expiratory pressure (PEEP)-related changes in regional ventilation (V'A) were studied in supine (SP) and prone (PP) position. EIT measurements were performed in 20 regions distributed along the ventral-to-dorsal axis (Bins). Regional recruitment was computed as the difference of regional alveolar volume between 2 experimental conditions and global recruitment as the sum of regional derecruitment in ventral regions, probably by oedema redistribution. Finally, V'A/V A was less in dorsal compared to ventral regions.

RESULTS. Differences between CT and EIT relative air contents were in an acceptable range for all quadrants with higher differences in the ventral quadrants (left bias 0.7%, 2xSD-interval 14.4%, right 0.8% and 12.3% respectively) having also higher air contents at the end of the maneuver than the dorsal quadrants, which show good agreement with lower scatter (2xSD 10.5% left, 6.4% right) but a slightly higher bias (3.9% left, 1.7% right) than the ventral half.

CONCLUSION. In an animal model of lung injury, simultaneous acquisitions of time courses of relative regional ventilation in four quadrants obtained by EIT and CT show acceptable to good agreement.

REFERENCE(S). 1. Victorino JA et al., Am J Respir Crit Care Med. 2004;169(7):791-800.
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EFFECTS OF POSTURE AND PEEP ON REGIONAL RECRUITMENT AND VENTILATION ASSESSED WITH PET IMAGING

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INTRODUCTION. Prone positioning (PP) is frequently performed in ARDS patients as a rescue therapy to improve arterial oxygenation. However, mechanisms by which PP improves oxygenation remain partially understood, but seem unrelated to significant gravity-dependent perfusion redistribution. Therefore, this study aims to evaluate with positron emission tomography (PET), posture and positive end expiratory pressure (PEEP)-related changes in regional ventilation (V'A) during experimental lung injury.

METHODS. After oleic acid-induced lung injury, five mechanically-ventilated pigs were randomly assigned to surfactant 1. However, the effect of surfactant on re-aeration of the lung has never been studied in supine (SP) and prone (PP) position. EIT measurements were performed in 20 regions distributed along the ventral-to-dorsal axis (Bins). Regional recruitment was computed as the difference of regional alveolar volume between 2 experimental conditions and global recruitment as the sum of regional derecruitment in ventral regions, probably by oedema redistribution. Finally, V'A/V A was less in dorsal compared to ventral regions.

RESULTS. Differences between CT and EIT relative air contents were in an acceptable range for all quadrants with higher differences in the ventral quadrants (left bias 0.7%, 2xSD-interval 14.4%, right 0.8% and 12.3% respectively) having also higher air contents at the end of the maneuver than the dorsal quadrants, which show good agreement with lower scatter (2xSD 10.5% left, 6.4% right) but a slightly higher bias (3.9% left, 1.7% right) than the ventral half.

CONCLUSION. In an animal model of lung injury, simultaneous acquisitions of time courses of relative regional ventilation in four quadrants obtained by EIT and CT show acceptable to good agreement.

REFERENCE(S). 1. Victorino JA et al., Am J Respir Crit Care Med. 2004;169(7):791-800.
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278
CT-PULMONARY ANGIOGRAPHIC OBSTRUCTION INDEX & BLOOD GASES 2 WEEKS AFTER ACUTE PULMONARY EMBOLISM
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INTRODUCTION. To assess the changes in blood gas values and in Computed Tomographic pulmonary artery obstruction index (CTPAOI) at 2 weeks follow up after the initial diagnosis of pulmonary embolism (PE).

METHODS. Acute pulmonary embolism (APE) was identified with spiral CT pulmonary angiography (CTPA) in 43 patients. Seventeen patients underwent a repeat CTPA at 2 weeks follow-up after the initial diagnosis of anticoagulant therapy. The CTPAOI and the blood gas values, including PaO2, PaCO2, SaO2 and Pa-aO2 were obtained at the time of the initial and the follow-up CTPA. The CTPAOIs between the initial and the follow-up CT scan were analyzed with the aid of the Wilcoxon rank test (p<0.05).

RESULTS. The initial CTPAOI (mean SD, 53.7±25.6%) vs CTPAOI at 15 days (23.0±20.7%, p<0.05) and initial blood gas measurements (PaO2: 63.8±15.7 mmHg, PaCO2: 32.5±8.7 mmHg, SaO2: 92.0±10.7% and Pa-aO2: 45.7±19.6) vs the values at 15 days (PaO2: 76.8±9.9 mmHg, PaCO2: 37.4±3.8 mmHg, SaO2: 95.3±1.8% and Pa-aO2: 26.4±8) were statistically significant (p<0.005). Furthermore, we found a high positive correlation between the initial CTPAOI and the CTPAOI 15 days later in our patients (r=0.8, p<0.005).

CONCLUSION. We conclude that both the CTPAOI and the blood gas values are significantly improved at the 15 days follow-up study. The CTPAOI at 15 days can be strongly predicted by the initial percentage of obstruction.

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279
DIFFERENT EFFECT OF PEEP-INDUCED LUNG PROTECTION IN TWO MODELS OF ACUTE LUNG INJURY
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INTRODUCTION. High vascular flow can increase lung damage in a ventilator-induced lung injury (VILI) model. Positive end-expiratory pressure (PEEP) might attenuate lung damage but its influence on the “vascular site” of VILI remains poorly understood. We hypothesized that PEEP might protect the lung by decreasing trans-alveolar-capillary pressure gradient during graded VILI low and high vascular flow with or without added oleic acid (OA) in the perfusate.

METHODS. Two series of experiments were performed. First, 15 sets of isolated rabbit lungs were randomized into 3 groups (n=5): low vascular flow/low PEEP (LFLP), high vascular flow/low PEEP (HLFP), and high vascular flow/high PEEP (HHP). Second, the same protocol was applied in another 15 sets of isolated rabbit lungs with 0.1 ml of OA added to the perfusate solution. All lungs were ventilated with peak airway pressure of 20 cmH2O during 30 minutes. Weight gain, changes in flow across lungs and in pulmonary vascular resistance, and extent of hemorrhage (scored by histology) were compared with ANOVA.

RESULTS. See Table 1. Data are expressed as mean±SD.

| TABLE 1. |
| --- | --- | --- | --- | --- | --- | --- | --- |
| LFLP | LFLP | HLFP | HLFP | HHFP | HHFP |
| oleic acid | oleic acid | oleic acid | oleic acid | oleic acid | oleic acid |
| Weight gain/g lung | 0±0.0 | 0±0.0 | 7.5±2.4 | 8±3.6 | 0±0.6 | 4±0.2 |
| Hemorrhage 0 to 10 | 1±0.1 | 3±0.1 | 7.0±0.8 | 6±1±0.6 | 3±0.2 | 6±1.5 |

*p<0.05 versus LFLP; **p<0.05 versus HHFP

CONCLUSION. Under these experimental conditions, PEEP attenuates lung injury in high vascular flow-induced VILI. The protective effect of PEEP is lost in second-hist preconditioned lungs that result in a more severe lung insult.

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281
LOD SCORE ALLOWS EARLY IDENTIFICATION OF PATIENTS WITH CARDIOGENIC SHOCK AT HIGH RISK OF DEATH
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INTRODUCTION. Cardiogenic shock in ICU still carries a high rate of mortality. We aimed to identify early prognostic factors associated with high risk of death in patients with cardiogenic shock.

METHODS. A retrospective study was conducted in an 11-bed medical ICU in a tertiary university hospital. We reviewed all patients admitted for cardiogenic shock (including for acute myocardial infarction) from January 2002 to February 2005, excluding post-operative cardiogenic shock and infectious endocarditis. 47 patients were included in the study. Seven physiology score, as SAPS II, and organ dysfunction scores as OSF and LOD (both at H0 and H48) were assessed. Survival rate, demographic data, use of catecholamines (number of days), initial left ventricular ejection fraction (LVEF), and biological markers were also issued from the medical charts.

RESULTS. Mean age was 66.5±11.3 years-old. Respectively means of SAPS II, OSF at H0 and H48, and LOD at H0 and H48 were 56.8±17.4, 2.7±1 and 2.7±1.1, and 9.4±4.4 and 8.7±4.8. Mean LVEF was 52±11.8%. Mortality rate at 36 days was 61.7% (29 patients). Persistence of shock (p<0.001), use of epinephrine (p=0.004), higher LOD score at H0 (p=0.0013) and H48 (p=0.0011), higher OSF score at H48 (p=0.0001), higher lactates at H0 (p=0.0017) and H48 (p=0.0008), and higher white blood cells count (p=0.0034) were significantly associated with a fatal outcome. Interestingly, a LOD score at H48 >7 identified patients who subsequently died, with a sensitivity at 86.2%, a specificity at 83.5%, a positive predictive value at 89.2%, and a negative predictive value at 78.9%. Moreover, survival rates at 36 days were significantly better in patients with LOD score at H48 ≥7 than in those with a LOD score <7 (45.9% versus 5.7%; p<0.001).

CONCLUSION. 1) Risk factors associated with a fatal outcome in patients with cardiogenic shock seem mainly related to acute physiological disturbances, and not to initial cardiologic presentation. 2) A LOD score >7 at 48 hours of hospitalization could allow an early identification, with acceptable positive and negative predictive values, of patients with cardiogenic shock at high risk of death. Alternative and early therapeutic interventions, such as percutaneous cardiopulmonary support, could be then assessed in these “high-risk” targeted patients. However, a prospective assessment is mandatory to confirm these preliminary data.

Grant acknowledgement. ESICM, ASDI, SPIC, MERCS, MSD Portugal & iMDSof.
Acute Renal failure (ARF) is a life-threatening condition with significant mortality rates. It is crucial to predict excessive bleeding after cardiac surgery to improve patient outcomes. During six months of 2003, EPEC has been used for outcome prediction assessment.

To determine the effectiveness of different artificial intelligence methods in mortality prediction and compare their effectiveness with conventional prognostic scoring systems, we retrospectively analyzed a cohort of all patients admitted to two major ICUs in the UK from 2002 till 2004. 448 ARF patients were selected with a Cr >150 umol/L, then classified by RIFLE criteria to F=112/448 and Fc=115/448. Epidemiological data, survival, mortality, and morbidity scores were compared. Regression analysis was performed to predict independent risk factors for death.

RESULTS. Demographics showed no significant difference apart from age and APACHE II (p=0.032 and 0.038 respectively). MR in F group was significantly higher than Fc group (45%, 25%, p<0.0001). In the F group deterioration in MAP, HR, pH, ventilatory parameters and GCS was more severe than Fc group (p=0.018, 0.003, 0.000, 0.007 and 0.190 respectively) RIFLE-F criteria for death prediction were found to have the highest significant Odds Ratio (OR) (OR: 0.337, CI:0.1910 0.596, p=0.000) but no significant change in OR for the cause of ARF.

CONCLUSION. RIFLE-F (ARF) patients show worse prognosis and outcome compared to RIFLE-Fc patients in ICU. The RIFLE-F criteria were found to be more predictive of mortality in ARF patients in ICU.

A RISK MODEL FOR PREDICTING EXCESSIVE BLEEDING IN ICU

INTRODUCTION. The ability to predict excessive bleeding after cardiac surgery could improve patients’ management in intensive care unit (ICU). We developed a risk model able to predict the excessive bleeding in our postoperative ICU.

METHODS. We analysed 2297 patients underwent cardiac surgery from January 2001 to May 2004. Coronary surgery was performed on 1,175 patients. 352 were valvular surgical patients. Combined operations were 590. More than 80 periprotective risk variables were assessed. Excessive bleeding was defined as re-exploration and/or blood loss of more than 800 ml within 12 hours postoperatively. A bleeding risk score (BRS) was constructed using the independent risk factors’ logistic regression coefficient values. The predictive model was validated on 246 patients underwent cardiac surgery from June 2004 to December 2004. Logistic regression and receiver operating characteristic (ROC) curves were applied. SPSS software was used.

RESULTS. Emergency operation and urgent operation were done in 45 (1.9%) and 136 (5.9%) patients, respectively. Excessive bleeding was observed in 181 (7.9%) patients, and 973 (42.3%) subjects required transfusions. Twelve predictors of excessive bleeding were found: body surface area, age >70, preoperative hypertension on medication, preoperative creatinine, preoperative albumin, preoperative use of anti-aggregants or heparin or warfarin, cardiopulmonary bypass (CPB) and aortic clamp times, congestive heart failure, lowest temperature during CPB, emergent/gent surge operation. The BRS ranged from 0 to 14. Low and medium risk BRS resulted under 5 points (low risk = 0 to 2, medium risk = 3 to 5). Patients with a BRS higher than 6 points showed an incidence of bleeding of 95%. ROC curve for BRS applied to the validation group was 0.75 (95% CI from 0.640 – 0.850, p<0.01).

CONCLUSION. Our study identified 12 variables able to predict patients at risk of bleeding. These parameters have been included in the BRS, which seemed an useful tool to classify patients at risk of bleeding. The capability to identify patients with high BRS (>6 points) may allow physicians to use strategies reducing the postoperative bleeding. That could reduce the ICU-stay and improve the postoperative outcome.

A FUZZY-BIO HYBRID APPROACH TO ARTIFICIAL INTELLIGENCE IN MORTALITY PREDICTION

INTRODUCTION. To determine the effectiveness of different artificial intelligence methods in mortality prediction and compare their effectiveness with conventional prognostic scoring systems, we retrospectively analyzed a cohort of all patients admitted to two major ICUs in the UK from 2002 till 2004. 448 ARF patients were selected with a Cr >150 umol/L, then classified by RIFLE criteria to F=112/448 and Fc=115/448. Epidemiological data, survival, mortality, and morbidity scores were compared. Regression analysis was performed to predict independent risk factors for death.

RESULTS. Demographics showed no significant difference apart from age and APACHE II (p=0.032 and 0.038 respectively). MR in F group was significantly higher than Fc group (45%, 25%, p<0.0001). In the F group deterioration in MAP, HR, pH, ventilatory parameters and GCS was more severe than Fc group (p=0.018, 0.003, 0.000, 0.007 and 0.190 respectively) RIFLE-F criteria for death prediction were found to have the highest significant Odds Ratio (OR) (OR: 0.337, CI:0.1910 0.596, p=0.000) but no significant change in OR for the cause of ARF.

CONCLUSION. RIFLE-F (ARF) patients show worse prognosis and outcome compared to RIFLE-Fc patients in ICU. The RIFLE-F criteria were found to be more predictive of mortality in ARF patients in ICU.
**Oral Presentations**

**Ventilator-associated pneumonia 286-291**

**286 HERPES SIMPLEX VIRUS PNEUMONIA IN MECHANICALLY VENTILATED PATIENTS: A PROSPECTIVE STUDY**

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**INTRODUCTION.** Herpes Simplex Virus (HSV) was recently detected in the lower respiratory tract (LRT) of a large proportion of ICU patients, but its clinical importance in such situations remains unclear (Brounselle et al., Lancet 2003). It is not known whether the isolation of HSV from LRT samples corresponds to a true HSV pneumonia or to a bronchial contamination from mouth and/or throat. We did a prospective cohort study to determine the prevalence of and risk factors for HSV pneumonia in ICU patients undergoing prolonged mechanical ventilation (MV).

**METHODS.** 88 consecutive non-immunocompromised patients who were receiving MV for >5 days and were clinically suspected of having ventilator-associated pneumonia were studied using bronchoscopic BAL. HSV pneumonia was diagnosed when all the following criteria were met: 1) new and persistent pulmonary infiltrate on chest radiograph associated with at least 1 of the following: temperature >38°C, leukocytosis >10,000/mm3 and purulent tracheal secretions, 2) presence of HSV in the BAL fluid as determined by VERO cells cultures and/or PCR, and 3) presence of specific nuclear inclusions in cells collected by BAL, as determined by cytological examination.

**RESULTS.** HSV was detected by culture and/or PCR in the LRT of 54 (61%) of 88 patient, whereas HSV pneumonia was diagnosed in only 23 (26%). Mean duration of MV before HSV pneumonia diagnosis was 14 ± 7 days in these individuals. There were no differences between patients with and without HSV pneumonia with regards to age, SAPS II, reason for and duration of MV, ICU mortality and length of stay. However, patients with HSV pneumonia had more frequently HSV skin or oral lesions (57% vs. 18%, p<0.001), as well as HSV in the throat (87% vs. 43%, p<0.001) and in LRT (100% vs. 48%, p<0.001) than patients without HSV pneumonia.

**CONCLUSION.** Our data suggest that HSV pneumonia is frequent among patients ventilated for more than 5 days and is associated with HSV reactivation or infection of the mouth and/or throat. However, it is not yet known whether it is of clinical relevance.

**Grant acknowledgement.** This study was partially supported by a grant from the Société de Réanimation de Langue Française.

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**287 TRACHEAL ELEMENT SUPPLEMENTS ARE ASSOCIATED WITH FEWER NOSOCOMIAL PNEUMONIA AFTER MAJOR BURNS**

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**INTRODUCTION.** Nosocomial infections and particularly pneumonia, remain a leading cause of morbidity and mortality after major burns. A previous trial in 20 patients providing selenium, copper and zinc supplements for 8 days showed a reduction in pneumonia: the present analysis aimed at assessing the same aspects in a larger group of critically ill burned patients.

**METHODS.** Aggregation of 2 consecutive prospective randomised placebo controlled supplementation trials delivering Cu 59 µmol, Se 4.8 µmol (370 mg), Zn 574 µmol IV per day (group TE) or vehicle (group V) for 8 to 21 days depending on surface burned. Infectious complications were considered to have positive SC (SC+) if at least one specimen (pharyngeal, cutaneous or rectal) revealed Ab, Pa or MRSA, within the week preceding the diagnosis of the VAP. For SC, sensitivity, specificity, ppv and npv were calculated.

**RESULTS.** 303 patients were admitted during the study-period, 9 patients were excluded from analysis as they had SCs after the diagnosis of VAP. 289 VAP were diagnosed in 21 patients (14.4%, 20.66/1000 days of mechanical ventilation). Among them, 17 were caused by Ab, Pa or MRSA. 7/17 had SCs for the same pathogens as those found in VAP (sensitivity for SC: 87.5%). 60 SC+ patients had no VAP while 226 patients had neither a VAP nor a SC+ (specificity for SC: 99%). PPV and NPP for SC were 10% and 99% respectively. A patient with VAP had 4.16 times more chances to have a SC+ than a patient without VAP (LR=4.16).

**CONCLUSION.** SC could reliably predict VAP-pathogens. Naturally, VAP diagnosis cannot be based on SC; however, ICU-physicians may be helped in empirical antibiotic prescription for VAP by systematic surveillance of MDR-B carriage.

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**288 VALIDATION OF SCREENING FOR MULTI-DRUG RESISTANT BACTERIA AS PREDICTOR OF PATHOGENS IN VAP**

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**INTRODUCTION.** VAP is the leading nosocomial infection in our ICU. Surveillance cultures (SC) for detection of multi-drug-resistant bacteria (MDR-B) have been used as predictors of microbial flora in VAP.

**METHODS.** In a 1-year prospective study we collected at admission and then weekly pharyngeal, cutaneous and rectal swabs (SC) from every patient admitted in the ICU in order to detect carriage of A.baumannii (Ab), P.aeruginosa (Pa) and Mettillin-Resistant-Statylococcus-Aureus (MRSA). Diagnosis of VAP was based on quantitative culture of protective-telescopic-catheter (PTC) performed blindly whenever clinical suspicion for VAP (positive culture if PTC>105cfu/ml). Patients were considered to have positive SC (SC+) if at least one specimen (pharyngeal, cutaneous or rectal) revealed Ab, Pa or MRSAs, within the week preceding the diagnosis of the VAP. For SC, sensitivity, specificity, ppv and npv were calculated.

**RESULTS.** 303 patients were admitted during the study-period, 9 patients were excluded from analysis as they had SCs after the diagnosis of VAP. 289 VAP were diagnosed in 21 patients (14.4%, 20.66/1000 days of mechanical ventilation). Among them, 17 were caused by Ab, Pa or MRSA. 7/17 had SCs for the same pathogens as those found in VAP (sensitivity for SC: 87.5%). 60 SC+ patients had no VAP while 226 patients had neither a VAP nor a SC+ (specificity for SC: 99%). PPV and NPP for SC were 10% and 99% respectively. A patient with VAP had 4.16 times more chances to have a SC+ than a patient without VAP (LR=4.16).

**CONCLUSION.** SC could reliably predict VAP-pathogens. Naturally, VAP diagnosis cannot be based on SC; however, ICU-physicians may be helped in empirical antibiotic prescription for VAP by systematic surveillance of MDR-B carriage.

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**289 EFFICACY OF HIGH DOSE OF AMPICILLINE-SULBACTAM IN MULTIRESISTANT ACINETOBACTER NOSOCOMIAL PNEUMONIA**

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**INTRODUCTION.** Acinetobacter baumanni is a common cause of late onset ventilator associated pneumonia (VAP). We examined the microbiologic and clinical efficacy of the administration of two dose regimen of A/S in mechanically ventilated patients with VAP caused by multiresistant Acinetobacter baumannii.

**METHODS.** Eleven patients (mean age:70 ± 10) with nosocomial pneumonia according to the criteria of CDC, caused by multiresistant Acinetobacter baumannii (quantitative cultures of a BAL specimen) were treated with A/S. Seven of them received 27gr A/S (9g sulbactam, group A) and four of them 56gr (12g sulbactam, group B). Follow up BAL and clinical evaluation of all patients was performed four days after the initiation of therapy. Clinical success was defined by a lessening of the signs and symptoms of Acinetobacter VAP, while microbiologic success was defined as suppression of Acinetobacter organisms to ≤10,000 cfu/ml (BAL culture).

**RESULTS.** Follow up BAL revealed microbiologic success in culture specimens of five patients from group A (71%) and all patients from group B (100%), but the difference was not statistically significant. Clinical improvement followed microbiologic success in four patients from group A (57%) and three patients from group B (75%), difference which was not statistically significant. Three of the remaining patients showed positive blood culture with Acinetobacter baumanii, while two of them had a subsequent infection caused by a different pathogenic organism.

**CONCLUSION.** Preliminary results demonstrate that high-dose of A/S is a well tolerated effective treatment for VAP caused by multiring resistant Acinetobacter. Dose regimen of 36g Ampicillin-Sulbactam seemed to be more effective than 27g, but the difference was not significant, because of the limited number of patients. Positive blood cultures influence the efficacy of the treatment. Further data are needed to determine the role of A/S in the treatment of VAP.

**REFERENCE(S).** GC Wood, SD Hanes, MA Croce et al. Comparison of ampicillin-sulbactame and Imipenem-Cilastatin for the treatment of Acinetobacter ventilator associated pneumonia. Clinical Infectious Diseases 2002, 34:1425-30
**Oral Presentations**

**Trauma 292-297**

**292**

**PROTECTIVE EFFECT OF THE PARP-INHIBITOR 5-AIQ ON RAT LIVER MICROCIRCULATION AFTER HEMORRHAGIC SHOCK**

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**INTRODUCTION.** Hemorrhagic shock (HS) is a severe pathological condition and is associated with high mortality. It is known that reperfusion of ischemic tissue causes damage of the DNA, which leads to the activation of Poly-(ADP-Ribose)-Polymerase (PARP). 1 PARP repairs damaged DNA in energy-consuming steps, which might lead to cellular energy-depletion and cell death. In our experiments we inhibited the enzyme PARP with the PARP-Inhibitor 5-AIQ in HS prior to reperfusion and investigated the impact of PARP-inhibition on the microcirculation of the rat liver.

**METHODS.** Briefly, a HS was induced to a mean arterial pressure of 40 mmHg for one hour (2). Five minutes prior to reperfusion the animals in the treatment group received the water-soluble PARP-inhibitor 5-AIQ (3mg/kg) intravenously. Intravital fluorescence microscopy was performed at the baseline, the end of 1 hour and 5 hours after reperfusion. We observed changes in microcirculation, microcirculation and liver function. Statistical analysis: SigmaStat 3.0, ANOVA, groups n=5, p<0.05 significant

**RESULTS.** Animals treated with the PARP-Inhibitor 5-AIQ showed a significant reduced leucocyte stasis in liver sinusoids, less adherent leucocytes in post-sinusoidal venules, improved sinusoidal perfusion, reduced tissue hypoxia and a restored bile excretion.

**TABLE 1.** Results after 5 hours reperfusion

| shunt | HS | HS + 5-AIQ |
|-------|----|----------|
| MAP (mmHg) | 106±2 | 86±2.3 | 118±1.4* |
| adherent leucocytes (n/100µm²) | 8±2.6 | 6±3.7 | 8±3.6* |
| leukocyte stasis (n/100µm²) | 17±4.9 | 62±14.6 | 51±5.0* |
| sinusoidal perfusion (%) | 97±6.5 | 79±1.9 | 90±3.1* |
| NADH (arbitrary units) | 88±6.4 | 115±2.4 | 93±2.8* |
| bile (µg/g liver tissue) | 1.8±0.1 | 1.0±0.2 | 1.6±0.1* |

(*HS vs HS + 5-AIQ)

**CONCLUSION.** Our findings show a protective effect of the PARP-inhibitor 5-AIQ on the microcirculation and function of the liver given to rats in HS prior to reperfusion.

**REFERENCE(S).** 1) Chiaugni A et al. Science 2002; 2) Hozzelt et al. Hepatology 2001

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**293**

**NORADRENALIN VS. FLUID RESUSCITATION IN OVINE TRAUMATIC BRAIN INJURY AND SYSTEMIC INFLAMMATION**

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**INTRODUCTION.** Systemic inflammation (SIRS) frequently develops after major trauma. In traumatic brain injury (TBI), SIRS induces cerebrovascular dysregulation and hyperperfusion as well as arterial hypotension (1). We hypothesized that fluid resuscitation would aggravate cerebral hyperperfusion and brain ischemia compared to vasopressor treatment.

**METHODS.** In anesthetized and mechanically ventilated sheep (n=12) TBI was induced by a non-operative model. Animals treated with the vasopressor Noradrenalin (NA) and substituted by HES to achieve an identical hematocrit. Regional cerebral blood flows (rCBF) were measured using fluorescent microspheres.

**RESULTS.** TBI induced a marked increase in ICP in both groups. Subsequent endotoxin infusion was associated with a further drop in CPP and an increase in intrathal carotid blood flow (CBF) at 180. Both HES and noradrenalin infusion increased CBF between 10th and 13th (p<0.05). While sana venous oxygen saturation (SvO2) remained unchanged in the HES group, it increased in the NA group (p<0.05). The trend towards an increase in PbrO2 in the NA group was not statistically significant. These changes corresponded to higher CBF in all investigated brain regions in the NA group at 13th. ICP further increased in the HES group between 10th and 13th. This trend, however, reached statistical significance only when percentage changes were analyzed. CPP, arterial hematocrit, and PbrO2 were identical among groups.

**CONCLUSION.** We conclude that CPP-management with noradrenalin is associated with an increased oxygen supply to the injured brain in this model. The lack of an increase in SvO2 and PbrO2 despite an increase in ICBF after HES infusion may be explained by brain edema and decreased microvascular perfusion.

**REFERENCE(S).** 1. Stubbe HD et al. (2004) Cerebral vascular and metabolic response to sustained systemic inflammation in ovine traumatic brain injury. J Cereb Blood Flow Metab 24:1400-1408

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MICRODIALYSIS ENDOTHELIN-1 CONCENTRATIONS PREDICT VASOSPASM IN SUBARACHNOID HEMORRHAGE PATIENTS

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INTRODUCTION. Endothelin-1 (ET-1) seems to be involved in the pathogenesis of cerebral vasospasm after subarachnoid hemorrhage but measures of ET-1 in cerebrospinal fluid (CSF) of are not sensitive to predict vasospasm representing the average value of cerebral circulation. Cerebral microdialysis (MD) is a technique able to detect molecule concentrations in a small perivascular area. We performed a prospective observational clinical study to test the hypothesis that MD ET-1 concentrations should be sensitive predictor for vasospasm.

METHODS. Subarachnoid hemorrhage patients at high risk for vasospasm were included: they received surgery within 48 hours from the bleeding. MD probe was placed in the area at risk for vasospasm. Samples were hourly collected to measure lactate, piruvate (L/P) and glutamate levels; ET-1 levels in CSF and MD fluids were measured from admission until day 7. Two angiographies (on day 1 and 7) were performed to detect degree and extent of vasospasm, Transcranial Doppler and neurological evaluation were daily performed. Patients were classified for presence of vasospasm in 3 groups: absence of vasospasm (NV), presence of vasospasm (CV) and acute neurological deterioration (AND).

RESULTS. 18 patients were enrolled, 9 males, mean age 60±11, 13 with an aneurysm in the anterior circulation, mean Fisher scale 4±0.5, mean WENs 4±1. Seven patients were classified as CV (39%), 3 as NV (17%) and 8 as AND (44%). On admission ET-1 levels were similar among groups but MD levels were higher (p<0.005) than CSF values in CV and AND groups. On day 5 MD levels were significantly higher in the CV group (6.8±3.1 pg/ml) compared to day 1 (3.7±0.8, p<0.05) while remained stable in the other groups. Glutamate levels were higher (p<0.05) in the CV group on day 1 (27±20) in patients who developed the most severe vasospasm (p<0.05); L/P ratio was significantly higher from the admission in both CV (67±46) and AND (52±29) groups compared to the other group (p<0.05).

CONCLUSION. MD ET-1 levels were higher than CSF on admission in CV and AND groups and markedly increased on day 5 in patients who had vasospasm on day 7. Glutamate levels and L/P ratio confirmed the occurrence of ischemia. MD ET-1 concentrations were early predictors confirming their involvement in the pathogenesis of vasospasm.

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CYCLOSPORIN A IN SEVERE HUMAN TRAUMATIC BRAIN INJURY (TBI): EFFECT ON HEMODYNAMICS

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INTRODUCTION. Cyclosporin A (CsA) has been proposed for the use as neuroprotectant after severe TBI. The hemodynamic effect of the drug, when used as immunosuppressant, has been described and related to a multifactorial mechanism. The aim of this study was to evaluate the hemodynamic effect of CsA in a population of severe TBI patients.

METHODS. 50 adult severe TBI patients have been enrolled (37 patients at MCV Hospital in Richmond, 13 patients at the University of Florida) in a randomized, placebo controlled study.37 patients received, within 12 hours of the injury, 5 mg/kg of CsA diluted in 250 ml of 5% dextrose over 24 hours. Placebo was given to 13 patients. For statistical analysis the ANOVA test was used.

RESULTS. Over the studied period, mean arterial pressure (MAP)and cerebral perfusion pressure (CPP) were significantly higher (p<0.01) in patients receiving CsA. MAP in the CSA group, even if higher, was within the physiologic range during all the monitoring period.

CONCLUSION. The early administration of CsA after severe TBI is associated with an increased MAP and CPP. A potentially helpful hemodynamic effect of CsA may be proposed as part of its neuroprotective effect, especially in those situations, characterized by reduced CBF; in which defending CPP and restoring MAP are main objective of the treatment.

REFERENCE(S). Gardiner SM et al: Br J Pharmacol 2004;141:634-643

EFFECTS OF RECOMBINANT ACTIVATED FACTOR VII ON PERIINAL EDEMA IN ACUTE INTRACEREBRAL HEMORRHAGE

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INTRODUCTION. Up to 50% of patients who suffer acute Intracerebral hemorrhage (ICH) die and the majority of survivors have significant morbidity. Two factors that may contribute to secondary injury after ICH are hematoma growth and cerebral edema. The presence of thrombin has been implicated as an important factor in the development of edema. We recently performed a prospective randomized controlled trial of recombinant activated factor VII (rFVIIa) to determine if it could limit hematoma growth. Of concern was that the ‘thrombin burst’ generated by rFVIIa could exacerbate edema. We now report on an analysis to determine if rFVIIa worsens edema volume in acute ICH.

METHODS. Patients with spontaneous ICH confirmed by CT scan within 3 hours of symptom onset were randomized to placebo or rFVIIa (40, 80, or 160 µg/kg) within 1 hour of the baseline scan. Hematoma volume was determined by computerized scans performed at presentation and 72 hours after onset. Edema volume was determined on the 72-hour scan. Edema/hematoma volume ratios were compared across groups.

RESULTS. 399 patients (placebo, N=96; 40 µg/kg, N=108; 80 µg/kg, N=92; 160 µg/kg, N=103) were included in the analysis. Groups were well matched in terms of age, time to treatment and baseline hematoma volume, GCS, NISS and blood pressure. rFVIIa significantly reduced hemorrhage growth relative to placebo (p<0.001). While the absolute edema volume was lower for the 40, 80 and 160 doses relative to placebo (31±25; 29±26; 28±22; 37±29 ml), the ratio of edema/hematoma volume did not differ between groups (1.8±0.9, 2.0±1.2, 2.3±3.5, 2.1±2.3 for placebo; 40, 80 and 160µg/kg respectively, p=0.46).

CONCLUSION. Treatment with rFVIIa did not result in exacerbation of cerebral edema over the first 72 hours following ICH.

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EFFECT OF PARENTERAL ALANYL-Glutamate on Interstitial Glutamate in the Brain of Head Trauma Patients

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INTRODUCTION. Intravenous glutamine supplementation has been shown to decrease morbidity and mortality in ICU patients with multiple organ failure. However, in head trauma patients concerns about the extra glutamine leading to increased glutamate concentration in the brain have been raised, as glutamate is an excitatory neurotransmitter. The aim of the present study was to elucidate whether exogenous intravenous glutamine supplementations to head trauma patients increases interstitial free glutamate concentration in the brain close to the injured area.

METHODS. Fifteen head trauma patients treated in the neurosurgical ICU were included. Patients were blindly randomised to receive glutamine and placebo in a cross-over design during two consecutive 24 h periods. A 50 µg/kg/h of a 5% glutamine solution was infused over 24 hours.

RESULTS. The head trauma patients had low plasma glutamine concentrations at baseline, 425±171 µmol/L, increasing to 648±208 µmol/L at the end of glutamine infusion. No change was seen during the placebo period (454±186 vs. 428±166 µmol/L). Plasma glutamate concentrations, on the other hand, were normal 78±46 µmol/L and unaltered following glutamine infusion 83±38 µmol/L, or after the placebo period (82±57 vs. 83±51 µmol/L). Interstitial glutamine and glutamate concentrations in the brain did not change over time in either the glutamine or the placebo period.

CONCLUSION. Intravenous glutamine supplementations to head trauma patients were not associated with an increase in the interstitial glutamate concentration in the brain close to the injured area.

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300

ADRENALEN FUNCTION IN SEPSIS: THE RETROSPECTIVE CORTICUS COHORT STUDY

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INTRODUCTION. The prevalence of adrenal insufficiency (AI) in septic shock (SS) is still debated. The retrospective part of CORTICUS aimed at testing cut-offs for the definition of AI by investigating baseline and cosyntropin stimulated cortisol (F) levels in relation to mortality from SS.

METHODS. This was a retrospective multicenter study of 477 SS who had undergone a cosyntropin stimulation test on onset of sepsis, from 20 ICUs. The main outcome measure was in-hospital mortality.

RESULTS. As compared to survivors, non-survivors had higher baseline F levels (29.5±63.9 vs 24.3±16.5 µg/dl, p=0.03), similar peak F values (37.6±40.2 vs 35.2±22.9 µg/dl, p=0.42), lower Dmax (6.4±22.6 vs 10.9±12.9 µg/dl, p=0.006). In 267 SS who did not receive steroids, 3 had basal F <=3µg/dl and died. When SS had either baseline F <15µg/dl or any Dmax or >=15µg/dl and a Dmax<9µg/dl the likelihood ratio of dying was 1.26 (95%CI: 1.11 – 1.44). Similarly, SS who had Dmax<9µg/dl and any basal F had a likelihood ratio of dying of 1.38 (95%CI: 1.18 – 1.61). Patients with basal F <=3µg/dl and any Dmax or >=15µg/dl and a Dmax<9µg/dl had a longer duration of shock and shorter survival time.

CONCLUSION. In SS, absolute AI may be defined by basal F <=3µg/dl, and relative AI is defined by basal F between 3 and 15µg/dl and any Dmax or >=15µg/dl and Dmax<9µg/dl.

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302
DISCREPANCIES BETWEEN METABOLIC NEEDS (INDIRECT CALORIMETRY) AND NUTRITIONAL SUPPORT ADMINISTERED
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INTRODUCTION. Nutritional support is an important therapeutic intervention in critically ill patients. However, it is often considered a second order treatment, compared to other therapies. ICU physicians focus on supporting emergencies from other systems and start nutritional support late or underestimate patients’ metabolic needs. We conducted a prospective study to evaluate the real metabolic needs of ICU patients and to detect discrepancies between the measured metabolic needs of the patients and the prescribed nutritional support.

METHODS. 37 consecutive patients with a mean age of 52 years and an APACHE score of 18±9, admitted with an expected ICU stay longer than 4 days, were included in this study. Starting the third day after admission, the metabolic needs of each patient were measured by indirect calorimetry every day for a period of one week. The caring physician was informed of the daily metabolic needs of each patient. We recorded the day nutrition was initiated, the differences between the metabolic needs measured by indirect calorimetry, the nutritional support prescribed by the physician in charge and the total amount of calories the patient received daily. The reasons for temporary interruption were also noted. Paired t-test with Bonferroni correction was used for statistical analysis.

RESULTS. Despite daily information of the physician in charge concerning the metabolic needs of each patient, nutrition was started the 7±6 post admission day. The metabolic needs measured by indirect calorimetry were 1826±407 Kcal/day and the nutritional support prescribed was 1327±55 kcal/day. The amount of calories the patient received was 1020±650 Kcal/day (p<0.05). The reasons for temporary daily nutrition interruption in order of frequency were: diarrhea, vomiting, transport to the Radiology Department, no restitution of the nutrition after the every 4 hours tolerance test, interrupation 4 hours before tracheotomy and abdominal distension without vomiting.

CONCLUSION. Our study demonstrates that nutritional support is surprisingly not a first order therapy in the mind of the ICU physicians. Very often it starts late and the prescribed amount of calories is less than the real metabolic needs of the patient. Even worse, the amount of calories administered is less than the prescribed. Most of the reasons for temporary interruption are unjustified.

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303
EARLY INTRODUCTION OF PROKINETICS DURING ENTERAL NUTRITION IN ICU PATIENTS
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INTRODUCTION. During enteral nutrition (EN) in critically ill patients, upper digestive intolerance is frequent. It can be screened for by monitoring gastric aspirate volume (GAV). However, the GAV cut-off requiring administration of prokinetics to allow a better compromise between feeding goals achievement and pneumonia is not known.

METHODS. Multicentre prospective randomised study comparing early (GAV 100 ml) and classical (GAV 500 ml) strategies for administration of erythromycin as a prokinetic agent during nasogastric tube enteral feeding in critically ill patients. Feeding goal was 30 kcal/kg theoretical weight. When GAV exceeded group cut-off or when vomiting occurred patient was given erythromycin 200 mg IV. Pneumonia was diagnosed on clinical, biological and radiological suspicion criteria and a positive quantitative distal bronchial sample culture. The Ethics Committee approved the study.

RESULTS. 400 patients (men 58%, age 61±16 y, SAPS II 49±19) under mechanical ventilation and started on EN via a nasogastric tube (NGT) were enrolled. 5618 EN days were surveyed (median per patient 10 d). The two groups were comparable on inclusion. Mean daily caloric order via NGT did not differ between groups (27±6 kcal/kg) nor mean daily administered/ordered ratio (86±17 % vs 84±17 %). In the early group, less patients had GAV over 500 ml (16% vs 31%, p=0.003), max GAV was lower (257±216 ml vs 356±271 ml, p<0.001), mean GAV over first 10 days was lower (p=0.007). The proportion of patients with vomiting was similar (30% vs 35%). In the early group, more patients received erythromycin as a prokinetic (67% vs 48%, p=0.001), and total dose of erythromycin as a prokinetic was higher (923±1404 mg vs 571±1213 mg, p=0.008). One patient experienced an episode of non sustained ventricular tachycardia after an erythromycin infusion (1/229, 0.44%, 95CI [0.01-2.48]). Groups did not differ for frequency of ventilator associated pneumonia (23% vs 27%), length of ICU stay (23 ± 24 j) and hospital mortality (43% vs 39%).

CONCLUSION. Early administration of erythromycin lowered GAV during EN in critically ill patients under mechanical ventilation. However this strategy did not allow to increase caloric intake or to decrease the frequency of pneumonia.

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Oral Presentations
Cardiac intensive care and inflammation 304-308

304
SYSTEMIC AND MYOCARDIAL MANIFESTATIONS OF THE INFLAMMATORY RESPONSE TO CPB AND THE HEAT SHOCK RESPONSE

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INTRODUCTION. Experimental evidence suggests that the heat shock response to CPB may be protective, limiting the inflammatory response and myocardial injury. Little is known about the correlation between the heat shock response to CPB and the inflammatory response in human patients. Lactate acidosis, particularly occurring early, is associated with an adverse outcome and increased mortality.

METHODS. Blood samples and atrial biopsies were taken before and after CPB. Whole blood stimulation with lipopolysaccharide was performed on samples pre and post cardiopulmonary bypass, and measured for cytokines TNFα and IL-10 production. RT-PCR was performed for HSP72 mRNA and TNFα mRNA. Lactate measurement was performed regularly during CPB and the first 24hrs in ICU.

RESULTS. There was suppression of responsiveness to ex-vivo LPS stimulation of whole blood. (Mean IL-10 production pre CPB was 2172 ± 1270 pg/ml and post CPB was 282 ± 351 pg/ml p<0.001; Mean TNFα production pre CPB was 29.26 ± 8.010 pg/ml and post CPB mean was 2.559 ± 1.782 pg/ml p<0.001.) There was no difference in relation to the degree of suppression of either IL-10 or TNFα production after CPB between the three groups 'early acidosis', 'late acidosis' and 'never acidosis'. However lower levels of both cytokines were produced pre CPB in the group who subsequently went on to develop early acidosis. (Mean IL-10 production 'Early' =1295pg/ml, 'Late' =2156pg/ml, 'Never' =3067pg/ml (P=0.01); Mean TNFα production 'Early' =1295pg/ml, 'Late' =2156pg/ml, 'Never' =3067pg/ml (P=0.03).) No correlation was found between HSP72 mRNA expression and EUROscore, age, total bypass time, cross clamp time or minimum temperature on CPB. Early acidosis was associated with a lesser increase in HSP72 in the myocardium. When the patients who developed an early acidosis are compared to the rest of the group the mean relative increase in myocardial HSP72 RNA is by a factor of 1.2 ±0.18 versus 2.6 ± 1.0 (P = 0.046).

CONCLUSION. This data suggests that lower preop immune responsiveness predicts subsequent inflammatory response and extent of heat shock response, and that early acidosis is associated with less cardiac induction of HSP70 and TNFα.

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305
HYPEROXIC MECHANICAL VENTILATION LIMITS CARDIAC REPERRFUSION INJURY THROUGH MITOKATP CHANNEL OPENING

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INTRODUCTION. Spontaneously breathing rats exposed to pure oxygen for 1 hour are protected against myocardial reperfusion injury, during mechanical ventilation, in rat subjected to acute infarction. In addition we investigated whether mitochondrial ATP-sensitive K+ channels (mitoKATP) are involved in the protective mechanism.

METHODS. Mechanically ventilated rats (Vt=7ml/Kg, RR=30 breaths/min) were exposed to normoxia (FgO2 =0.3) or hyperoxia (FgO2 =1.0) for 30 minutes. Their hearts (n=6 each group) were surgically removed immediately afterward, buffered-perfused in a Langendorff apparatus, and subjected to 30 minutes of global ischemia followed by 120 minutes of reperfusion. Infarct size was assessed by tetrazolium staining and expressed as a % of the risk area. In an additional group of hyperoxic rats (n=6), the mitoKATP channel blocker 5-hydroxydecanoate (5-HD, 200μM) was infused immediately before global ischemia.

RESULTS. Exposure to a brief period of hyperoxia during mechanical ventilation reduced infarct size compared to normoxia (31±7% vs 52±8% p<0.05). However, the treatment with 5-HD abolished the protective effect of hyperoxia (infarct size = 48±5%, p<NS versus normoxia; p<0.05 vs hyperoxia).

CONCLUSION. In this ischemia-reperfusion rat model, preconditioning with a brief period of hyperoxic mechanical ventilation limits infarct size. Our data suggest that mitoKATP channel opening is necessary for hyperoxic cardioprotection.

306
PROCLACTITONIN KINETIC IN PEDIATRIC PATIENTS WITH SEVERE SIRS AFTER OPEN HEART SURGERY

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INTRODUCTION. Procalcitonin (PCT) is associated with systemic inflammatory response (SIRS) during cardiac surgery (1). SIRS with accompanying organ failure has been classified as severe SIRS (2). We conducted this study to evaluate the PCT and C-RP kinetics in pediatric patients with SIRS and severe SIRS after open heart surgery.

METHODS. This prospective observational study was conducted on 36 patients with SIRS (n=19) and severe SIRS (n=17). Plasma PCT and C-RP was measured before the operation, at the end of the operation, 1, 2, 3, 4 days after surgery, concomitant SOFA scores were recorded. Organ failure was diagnosed according to Duke’s criteria. Mann Whitney U test was used to compare the groups.

RESULTS. PCT levels of severe SIRS (median value 29 ng/mL) were significantly higher than SIRS group (median value 3 ng/mL) during the postoperative period and peaked on day 1. C-RP were similar among the groups except for the higher post-CPB values of severe SIRS group (median 2 vs 0.3 μg/dL; p=0.01). Patients with SOFA scores >5 had higher PCT levels compared to those who had levels <5 (p=0.05). Six patients among the severe SIRS group infected after postoperative day 5.

CONCLUSION. PCT significantly increased after surgery in severe SIRS group compared to SIRS in the absence of an infection. Early postoperative C-RP values predicted organ failure before it took place, whereas PCT did not. Peak PCT was found to be correlated with prolonged cross-clamp and CPB times, mortality and severity of organ failure, whereas C-RP was not. A double peak PCT curve was observed in 6 infected severe SIRS patients postoperatively.

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REDUCED INCIDENCE OF MORTALITY WITH STATINS AFTER CORONARY SURGERY

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INTRODUCTION. Preoperative statin therapy has recently been shown to convey a survival benefit in patients undergoing major non cardiac vascular surgery. The aim of this study was to search the effects of preoperative use of statins after coronary artery bypass graft surgery (CABG).

METHODS. A retrospective study of consecutive patients (n=883) undergoing isolated CABG between 1999-2003 was performed. Patients were classified into 2 groups: statins (n=490) and without statins (n=393). Hospital mortality was determined in relation to preoperative risk factors.

RESULTS. Preoperative demographic and risks factors are presented in table 1. Mortality and morbidity tended to be lower among treated patients (table 2). Multivariate logistic regression analysis demonstrated that preoperative statins therapy was independently associated with less mortality (RR=4.8; p=0.0025).

| Statins | Without Statins | p     |
|---------|-----------------|-------|
| Age (years) | 64.5              | 67.7   | ns    |
| Renal failure (%) | 1.4               | 4.6    | 0.004 |
| Diabetes (%) | 25.2              | 32.8   | 0.025 |
| LVEF (%) | 60.2              | 59.2   | ns    |
| EURScore | 2.4               | 6.7    | 0.004 |

CONCLUSION. Preoperative statin therapy may reduce the risk of hospital mortality and morbidity after CABG.

310

b-BLOCKER TREATMENT, HEART RATE VARIABILITY AND SURVIVAL OF INTENSIVE CARE PATIENTS

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INTRODUCTION. The multiple organ dysfunction syndrome (MODS) is the endstage of initial trigger events, such as acute coronary syndrome or sepsis. The mortality is high – up to 60%. We have recently shown that a decrease in heart rate variability ([HRV], parasympathetic parameter lnVLF) can identify a subgroup with a worse prognosis. Parasympathetic stimulation can depress inflammation and might thus improve survival. The aim of the present study was to detect whether b-blockers as indirect parasympathetic modulators have a positive impact on prognosis.

METHODS. We retrospectively analysed the data of 120 consecutively admitted ICU patients with MODS. HRV was measured according to the international standards using a 24-hours-ECG. All patients were checked for b-blocker treatment and followed up for 28-day-survival. We calculated a cutpoint (maximum of sensitivity x specificity in ROC analysis) for the HRV parameter lnVLF which predicted 28-days-survival best. The APACHE II score (API) was calculated to characterize the severity of illness; a MODS was defined as an API of 20 or more points.

RESULTS. The demographic data of the patients were as follows: age 59.8±13 y, weight 76.5±14.9, height 170.4±10.0 cm. APACHE II score 26.9±7.6. 56 of the 120 included patients received b-blockers during the ICU stay. Patients with b-blockers had a significantly higher HRV at admission than patients without b-blockers (3.4 vs. 4.5 bit/sec, p=0.0001). Dividing the cohort into four subgroups we found that patients with b-blocker treatment and a high HRV on admission had the best survival compared with 1) patients with low HRV and b-blocker-treatment (log rank [LR] of Kaplan-Meier-Analysis=3.9, p=0.047), 2) patients with high HRV but without b-blockers (LR=4.8, p=0.03) and 3) patients with low HRV and without b-blockers (LR=13.4, p=0.0003).

CONCLUSION. b-blocker treatment could improve survival in MODS patients. This favorable effect might be mediated by a restoration of blunted HRV which could yield depression of the overwhelming inflammation seen in MODS.

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311

THERAPEUTIC APPLICATION OF MARS IN CHRONIC SEVERE HEPATITIS PATIENTS COMPLICATED WITH MULTI ORGAN FAILURE

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INTRODUCTION. The aim of this study is to evaluate the therapeutic effectiveness of Molecular Adsorbents Recirculating System (MARS) in patients of chronic severe hepatitis complicated with multi organ failure.

METHODS. The present study randomized 82 patients of chronic severe hepatitis complicated with multi organ failure into MARS therapy group of 40 patients and rests of 42 patients of the control group respectively, 110 sessions of MARS treatments were performed with average of 2.75 sessions per patient, all were evaluated clinically by Model for End-stage Liver Disease(MELD) and liver function, hemogram, ammonia level, coagulopathy, BUN and Creatinine levels before and after treatments.

RESULTS. MARS therapy resulted in remarkable improvement of prognosis assessment model of MELD(27.1±2.81 to 19.5±3.66, p<0.01) and finally benefited the improved survival in the MARS group(19/40, 47.5% vs 10/42, 23.8% of control group, p<0.05), clinically presented in significant improvement of hemodynamic and respiratory function by selective elimination of accumulated metabolic toxins and management of electrolyte, fluid and acid base balance with nicer safe record.

CONCLUSION. MARS therapy can be applied safely as preferable liver support for liver failure patients in therapeutic management for complications and multi organ failure.

308

Oral Presentations

Treatment of sepsis: A never-ending challenge (II)

309

ENDOTOXIN ADSORPTION THERAPY (PMX-DHP) FOR SEPTIC MULTIPLE ORGAN FAILURE PATIENTS (SOFA SCORE ≥10)

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INTRODUCTION. Efficacy and application of PMX-DHP were examined in septic shock patients with a SOFA score ≥10. The patients were divided into two groups (survival and non-survival) according to the outcome 28 days after PMX-DHP. The changes in respiration (PaO2/FiO2), circulation (SAP, MAP, HR), and a variety of inflammatory mediators before and after PMX-DHP were compared between the two groups.

METHODS. The subjects were sepsis patients with a SOFA score ≥10 and multiple organ failure, who received PMX-DHP for 2 hours in the ICU. PaO2/FiO2, SAP, MAP, HR, blood analysis (WBC, platelets) and inflammatory mediators (endotoxin, TNF-α, IL-6, IL-1ra, PAI-1, procollactin) were measured before and after PMX-DHP.

RESULTS. The APACHE II score was 27.8±3.7 and 32.4±8.4, respectively, in the survival and non-survival groups. The number of impaired organs was at least 3 in all cases. A significant increase in blood pressure was observed after PMX-DHP in both groups (p=0.031) (survival group: 99±27 to 118±27 mmHg, non-survival group: 95±24 to 109±27 mmHg). Endotoxin decreased from 16.5±24.9 to 9.8±11.0 pg/ml in the survival group and from 24.6±56.4 to 12.5±25.9 pg/ml in the non-survival group, with a significant difference in the survival group (p=0.05). The median IL-6 level decreased from 663 to 58±4 pg/ml in the survival group and from 7580 to 494±956 pg/ml in the non-survival group, but with no significant difference. There was no significant change in TNF-α, while a significant decrease in the median value of IL-1ra was observed, from 15,600 to 10,850 pg/ml in the survival group, and from 30,700 to 28,800 pg/ml in the non-survival group. The median value of PAI-1 changed from 175 to 136 ng/ml in the survival group and from 562 to 310 ng/ml in the non-survival group, with a significant decrease (p=0.031) in the survival group. Procollactin significantly decreased from 87±136 to 67±96 ng/ml in the survival group, whereas it rather increased from 87±136 to 362±165 ng/ml in the non-survival group.

CONCLUSION. The efficacy of PMX-DHP was examined in patients with sepsis with a SOFA score ≥10 and multiple organ failure. The mortality rate was 52%. Hemodynamics improved in both the survival and non-survival groups, and procollactin significantly decreased in the survival group. Further analyses using a larger number of cases are required for evaluation of the efficacy of PMX-DHP.
SELENIUM SUBSTITUTION IN SEVERE SEPSIS AS USEFUL ADDITIVE? PRELIMINARY RESULTS OF THE SIC STUDY

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INTRODUCTION. Despite large studies in the past the mortality rate of patients with severe sepsis remained high. Many trace elements have low blood levels. The substitution of selenium was studied in pilot studies with considerable results (1). We had performed a prospective, randomised, double-blind, placebo controlled, multicenter trial in patients with severe sepsis to evaluate the effectiveness of selenium substitution on 28 day mortality.

METHODS. Inclusion criteria: age more than 18year, APACHE III score at least 70, SIRS and sepsis criteria fulfilled, inclusion within 24h after exclusion. Diagnosis criteria: missing informed consent, necrotising pancreatitis, DNR-code, after cardiopulmonary resuscitation. Interventional protocol: 1000µg selenium as short time infusion followed by 1000µg selenium every 24h as continuous infusion during day 2-14 (Se+ patients). All patients including the control patients (Se-) received a baseline selenium substitution of 32µg per day and best supportive care including adequate antibiotics. The primary efficacy criterion was 28day mortality. Chi-square test and Kaplan Meier analysis were performed.

RESULTS. The intention to treat group consisted of 238 patients. The patient groups were comparable regarding sex, age or severity (APACHE III and LOD score). In the Se+ group 46 out of 116 patients (39.7%) died compared to 61 out of 122 patients (50.0%) in the Se- group, OR 0.66 (0.39-1.1). In the Kaplan-Meier analysis this difference did not reach significance (P=0.098). There was no difference in surgical or internal patients. The largest mortality difference was found at day 14 with 27.6% and 38.6% mortality in Se+ and Se- patients (P=0.073), respectively. No significant adverse event occurred due to selenium substitution.

CONCLUSION. The result of the SIC study did not reach statistically significant level, however, confirmed the previous pilot studies. The selenium substitution might therefore be a very promising additive in patients with severe sepsis and should be studied in further larger trials.

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316  GASTROINTESTINAL MANIFESTATIONS IN SEVERE SCORPION ENVENOMATION

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INTRODUCTION. Scorpion envenomation is common in tropical and subtropical regions. In Tunisia, almost 40,000-45,000 stings are recorded per year. Around thousand of them have systemic manifestations requiring hospitalisation and about 10 patients eventually die. Cardiogenic shock and pulmonary edema, are the leading causes of death after scorpion envenomation. However, severe envenomation may be accompanied by gastrointestinal manifestations and metabolic acidosis. The aim of the present study was to study the type and incidence of gastrointestinal manifestations secondary to scorpion envenomation and their prognostic significance.

METHODS. Retrospective chart review of a 13 year period (1990 – 2002)in a Medical Intensive Care Unit of a university hospital in Sfax, Tunisia. We included All patients admitted to our ICU for scorpion envenomation.

RESULTS. During the study period, 951 patients were admitted for scorpion envenomation and 72 (7.6%) died. Ages ranged from 0.5 to 90 years with a mean of 14.7 ± 17.7 years. Gastrointestinal symptoms were recorded in 708 patients (73.6 %); nausea in 24 (2.5%), vomiting in 667 (72.2%) and diarrhea in 41 patients (4.3 %). In the univariate analysis, the presence of diarrhea was associated with a fatal outcome (p < 0.05). Diarrhea also correlated with other indicators of severe envenomation and poor prognosis: respiratory failure (p=0.01), neurological failure (p=0.0001), liver failure (p=0.001) and low blood pressure requiring catecholamine vasopressor support (p=0.025). The multivariate analysis showed that young age (age less than 5 years) was the independent factor of severity, but diarrhea was not correlated with poor outcome. Moreover, digestive disorders were more frequent in children and in this age group diarrhea appears to associate with poor outcome. In addition, among a subset of patients for whom data were available, fatal cases demonstrated significantly higher mean values of aspartate amino-transferase (ASAT), alanine amino-transferase (ALAT), and total bilirubin on admission.

CONCLUSION. In Tunisia Gastrointestinal symptoms are often observed in severe scorpion envenomations. There were more observed in children. The presence of diarrhea and elevation of liver enzymes appear to predict a fatal outcome. Diarrhea may serve as an early clinical indicator of dangerous form with cardio-respiratory and/or neurological failure.

317  RECOMBINANT FACTOR VIIa FOR ACUTE INTRACEREBRAL HEMORRHAGE: IMPACT OF TIMING OF TREATMENT

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INTRODUCTION. Recombinant activated factor VII (rFVIIa, NovoSeven®) administered within four hours of intracerebral hemorrhage (ICH) onset significantly reduces hematoma growth, mortality, and severe disability at 90 days. We performed this analysis to evaluate the impact of timing of treatment on the efficacy of rFVIIa for ICH.

METHODS. Patients with spontaneous ICH (N=399) scanned within 3 hours of onset were randomized to receive placebo or rFVIIa (60, 80, or 160 µg/kg) within 1 hour of the baseline CT. Poor outcome (90 days) was defined as a modified Rankin Scale (mRS) score of 4 to 6 (indicating death or moderate-to-severe disability) at 90 days. CT lesion volumes were analyzed with generalized linear mixed models, and dichotomized clinical endpoints with multiple logistic regression.

RESULTS. Mean baseline ICH volume (all subjects) was 24 ± 26 ml. The increase in ICH volume between baseline and 24 hours was 8.7 ml in placebo versus 4.2 ml with rFVIIa (P=0.009). There was an interaction between treatment and onset-to-treatment (OTT) time (P=0.02), indicating that the efficacy of rFVIIa depended on how quickly the patient was treated: for each 30 minute reduction in OTT time, the mean reduction in ICH growth versus placebo increased by 3.6 ml (Figure). However, shorter OTT time was not associated with a reduction in the odds or poor outcome (adjusted odds ratio 0.98 per 30 minute decrease in OTT, P=0.88) after controlling for treatment assignment, age, gender, Glasgow Coma Scale score, baseline ICH volume, hemorrhage location, and IVH.

CONCLUSION. Early treatment of ICH patients with rFVIIa is associated with a greater reduction in bleeding relative to placebo. However, the clinical benefit of rFVIIa within the 0 to 4 hour time window is not dependent on OTT time.

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Grant acknowledgement. This study was supported by Novo Nordisk.

318  WORKLOAD AND OUTCOME WITH A CENTERALIZED TRANSFER SERVICE FOR CRITICALLY-ILL ADULTS

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INTRODUCTION. Since October 2000, a centralized service has facilitated the interhospital transfer (IHT) of over 1400 critically-ill adult patients using a modified standard emergency ambulance and mobile intensive care unit (ICU) equipment. Since quality of escort is an important factor in the transport of all potentially unstable patients (1,2), all IHTs are performed by an experienced ICU team (1 doctor and 1 nurse in addition roles). The aim of this project was to assess the quality and use of the service.

METHODS. The transferring team prospectively recorded information regarding the indications for, and conduct of, all IHTs performed during the year 03/04 to 02/05. IHTs prospectively collected data including admission APACHE II score and ICU (and hospital) outcomes. All data were entered on a centrally-held database (Microsoft Access).

RESULTS. In 12 months, 335 IHTs occurred between 17 hospitals. No deaths occurred during transfer and 99% of patients received mechanical ventilation. Most IHTs (n=244, 73%) occurred outside normal working hours and 232 IHTs (69%) occurred due to lack of an ICU or an available ICU bed at the referring hospital. Median admission APACHE II score was 18 (range 3-42). ICU survival was 79% (n=265 of 335). Four patients still remain in hospital and 37 patients died in hospital after ICU discharge. The remaining 224 patients (67% of those transferred) survived to hospital discharge. The workload was performed by 20 doctors and 25 nurses (median 15 and 14 transfers each respectively).

CONCLUSION. A centralized service, using a standard ambulance with appropriate escort and equipment can provide safe IHT for critically-ill adults. With such a service, large numbers of IHTs were performed by a small number of ICU staff using the same equipment on all occasions. The inability to provide ICU care was the commonest reason for IHT.

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Oral Presentations

319  ASSESSMENT OF RENAL FUNCTION IN CRITICALLY ILL PATIENTS

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INTRODUCTION. Renal function is most often evaluated by serum creatinine (Cr) measurement. Alternatives are the Cockroft-Gault (CG) and the original and simplified Modified Diet in Renal Disease equations (MDRD resp. MDRDs), or measurement of creatinine clearance (Ccr). Finally, serum levels of cystatin C (CystC) or beta-trace protein (Btrace), novel markers of renal function, may be an alternative. We evaluated methods for assessment of renal function and compared these to the inulin clearance (Cinu), as the standard for assessment of glomerular filtration rate (GFR).

METHODS. The study was performed at the 22 beds ICU of an academic medical centre. A 24 hour urinary Ccr (Ccr24) was measured, and during this period also the Cinu and an exactly timed 1-hr urinary Ccr (Ccr1) were measured. In addition to Cr levels, we also measured CystC and Btrace. Finally, renal function was assessed by the CG equation for Ccr, the MDRD and MDRDs equations for GFR, and the CystC based equation for GFR (Cyst-c).

RESULTS. At present, 21 patients are included in the study. Mean age was 57±19 (Q38-70) yrs, 16 were male (76%), and mean APACHE II score was 19 (14-24). Compared to GFR measured by Cinu (53±16-89) µl/min per 1.73m2, renal function was overestimated by all methods for clearance, except Cyst-c: Cinu=97±28±140), Ccr24=96±23±141), CCr84±44±160), MDRD=258±117±366), MDRDs=15±12±192±92; for all p<0.01, except for Cyst-c, p=0.08. Both measured Ccr’s, and also Cyst-c had a good correlation with Cinu (correlation coefficient (r) with Ccr=0.84, r for Ccr24=0.86, r for Cyst-c=0.78, all p<0.01). MDRD, MDRDs and CG had a weak but significant correlation with Cinu (r=0.62 and p<0.01 for all 3 equations). After logarithmic transformation, also CystC and Btrace had a good correlation with Cinu (r for CystC =0.72, and r for Btrace=0.75, both p<0.01). The correlation between Cr at start, end, and during the 24-hr study period was weak (r between p>0.60, worst at the end of the 24-hr study period, r=0.57, both p<0.01).

CONCLUSION. Serum CystC and Btrace were better markers for renal function than Cr. Also, Cyst-c, Ccr1, and Ccr24 correlated well with Cinu. Because, Ccr1 and Ccr24 are labour intensive, and overestimate GFR due to tubular excretion of creatinine, CystC seems a promising alternative. The CG and MDRD equations were not useful in ICU patients.
Acute renal failure (ARF) is associated with an excess risk of hospital mortality. We present a series of patients requiring RRT during a 10-year period where the incidence of ARF and number of patients treated with RRT were evaluated and updated. Patients included were ARF requiring RRT but had chronic renal failure were excluded. Data were extracted for the 127298 admissions to the 22 ICUs participating to the database since 1993.

Results. Among the 21201 ARF admitted during the 10 years period to the 36 ICUs, 180 patients requiring RRT were included. Risk factors for ARF requiring RRT were age (OR 1.05, p<0.05), APACHE II at CRRT initiation (OR 1.14, p<0.05), number of organs failing at initiation (OR 1.98, p<0.05) and NRs (OR 11.54, p<0.001) were related to mortality. Selecting only patients for whom Ca supplementation is obligatory. We hypothesized that citrate CVVH results in an endocrine effect that can increase the filter lifespan by more than 100%. The continuous infusion is a better method to maintain a level of AT above 60 % and can increase more significantly the filter lifespan. Cost-effectiveness should be evaluated shortly.

Grant acknowledgement. LFB laboratory financial participation.

Hemodynamic improvement after initiation of high flow hemofiltration carries a good prognosis. We intend to demonstrate that early hemodynamic improvement after standard continuous renal replacement therapy (CRRT) is also related to survival.

RESULTS. 94 patients (mean 54±13.8 years, APACHE II on admission 20.9±6.1 and at CRRT initiation 22.1±5.7), organs failing at CRRT start 3.7±1.3, dose of clearance 2.45±0.5 L/h were included. 72.3% were unstable before treatment. Global mortality was 54.3% (57.7% stable vs 52.9% unstable, p<0.05), patients (44.7%) were classified as R and 55.3% as NRs. Excluding mortality no differences were detected between these groups in any of the variables studied: R51.9±12.6 years, APACHE II at CRRT initiation 21.6±4.9, organs failing 3.8±1.2, dose of CRRT 2.5±0.6 L/h and NRs 55.8±14.5 years, APACHE II at CRRT 22.5±6.3, organs failing 3.7±1.4, dose 2.35±1.5 L/h, Rs mortality was 28.6% vs 75% in NRs (p<0.001). Logistic regression analysis: (OR 1.05, p<0.05), APACHE II at CRRT initiation (OR 1.14, p<0.05), number of organs failing at initiation (OR 1.98, p<0.05) and NRs (OR 11.54, p<0.001) were related to mortality. Selecting only patients unstable (N 68), Rs mortality was 23.7% (9 out of 38) vs 97% (27 out of 30) in NRs. Logistic regression analysis: APACHE II at CRRT (OR 1.18, p<0.05) and NRs (OR 26.5, p<0.001) only variables related to mortality.

CONCLUSION. Early hemodynamic improvement after CRRT is closely related to survival and this relationship is even stronger when considering unstable patients. This response is a better predictor of survival than APACHE II or number of failing organs.
**Oral Presentations**

**Prophylaxis therapy and surveillance 324-328**

**324**

**PATIENT-BASED INFECTION SURVEILLANCE IN EUROPE: THE HELICS LEVEL 2 FIRST EXPERIENCE.**

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**INTRODUCTION.** Patient-based surveillance of nosocomial infections in the ICU is the level 2 component of HELICS (Hospitals in Europe Link for Infection Control through Surveillance). The ICU protocol was published Oct 2004 (http://helics.univ-lyon1.fr). The goal is to generate a harmonised database to improve knowledge about variability in incidence rates of nosocomial infections and to allow standardised benchmarking. Surveillance was done for blood stream infections, ventilator associated pneumonia, central venous catheter infection/colonisation and urinary tract infections. The aim of this investigation is to compare the level 2 data from 7 European countries.

**METHODS.** In 2004 data from 7 countries (Austria, Belgium, Spain, France, Luxembourg, Netherlands, Portugal) were transferred to the HELICS database in Brussels, checked for consistency and analysed.

**RESULTS.** A total of 83488 (832-42544) patients with a length of stay > 2 days was available for analysis. A total of 62289 patient days were analysed. Demographic characteristics are given in the Table.

**TABLE 1.**

| European mean rate | Minimum rate | Maximum rate |
|--------------------|--------------|--------------|
| Age (a)            | 66.9         | 22.5         |
| Gender ratio M:F    | 1.73         | 1.21         |
| LOS ICU            | 10.7         | 1.39         |
| SAPS II            | 35.9         | 42           |
| ICU mortality      | 15.1         | 22.2         |
| ICU acquired pneumonia | 16.9     | 4            |
| Catheter associated BSI | 3           | 2            |

**CONCLUSION.** In this first report from the patient-based infection surveillance according to the harmonised European HELICS standard a large variability between countries could be found that is partially explained by differences in case-mix. This new harmonised database will allow multi-national benchmarking in Europe.

Grant acknowledgement, ECDG SANCIO/F 4

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**325**

**IMPACT OF SDD ON BLOODSTREAM INFECTIONS: A SYSTEMATIC REVIEW OF RANDOMIZED TRIALS.**

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**INTRODUCTION.** Selective decontamination of the digestive tract (SDD) is an infection control procedure that uses parenteral and enteral non-absorbable antimicrobials, usually polymyxins, aminoglycosides and polynes. The aim is prevention and/or eradication of oropharyngeal and gut carriage to control endogenous infections. Nine meta-analyses of randomized controlled trials (RCTs) evaluated SDD in critically ill patients. SDD reduces lower airway infections and mortality. No meta-analysis that assesses the impact of SDD on bloodstream infections (BSIs) has been performed. A systematic review of SDD RCTs has been performed to assess whether the manoeuvre of SDD controls BSIs.

**METHODS.** A systematic review and meta-analysis of RCTs on SDD was undertaken. Data sources were Medline, Embase, Cochrane Register of Controlled Trials, previous meta-analyses, personal communications, and conference proceedings, without restriction of language or publication status. The main outcome measures were patients with bloodstream infection, and type of microorganism involved.

**RESULTS.** Fifty-five RCTs conducted between 1987 and 2005, comprising a total of 9,280 critically ill patients, were included in the review; 4,659 patients received SDD and 4,571 were controls. Of those trials, 28 studies including 4,280 patients (2,213 SDD, 2,067 control) reported data on patients with bloodstream infections. There were 235 patients with bloodstream infections in the SDD group (10.5%) and 296 patients in the control (14.3%). Thirteen studies, including 1,817 patients (893 SDD, 924 control), reported data on the type of microorganism causing bloodstream infection. SDD significantly reduced the number of patients with bloodstream infections (common Odds Ratio 0.69, 95% confidence interval 0.55 to 0.88), and patients with BSIs due to Gram-negative bacteria (OR 0.45, 95% CI 0.25 to 0.78). Gram positive BSI and fungemia were not significantly different among the two groups.

**CONCLUSION.** SDD reduces bloodstream infections, and, in particular, Gram-negative bloodstream infections, with no significant effect on infections due to Gram-positive microorganisms and fungi.

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**326**

**ENTERAL VANCOMYCIN CONTROLS EMRSA-15 WITH PANTON-VALENTELEUCOCIDIN GENE.**

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**INTRODUCTION.** MRSA rates have been consistently low in our paediatric intensive care unit (PICU) using a policy of enteral vancomycin with no secondary endogenous infections.

**METHODS.** 1. Describe an outbreak of carriage/infection due to a variant EMRSA-15 resistant to gentamicin and carrying the Panton-Valentineleukocidin (PVL) gene [outbreak strain]; 2. establish the pathogenicity of the outbreak strain.

**RESULTS.** 1. Summer 2004 the outbreak strain emerged which was distinct from the EMRSA-15 strains. 19 children were affected, they were younger [3 vs 10 months, p<0.01] and stayed longer [20 vs 9 days, p<0.01], compared with the 10 children positive for gentamicin-sensitive EMRSA-15. 63% had congenital heart disease. 14 children developed secondary carriage due to transmission [median 19 days IQR 1.5-34]; 11 had 23 infections [median 35 days IQR 18-67]. Half were wound infections [tachycardia, tachypnoea, central venous line]. There were 3 lower airway and 3 bloodstream infections. 5 infections were primary endogenous due to the outbreak strain present in the patient flora, and 18 [9 secondary endogenous, 9 exogenous] due to the strain being acquired. 4 children developed 6 EMRSA-15 infections (4 exogenous, 2 secondary endogenous). In August, when a patient acquired an infection each week, the incident team was convened and an infection control policy rigorously implemented. Acquired carriage/infection due to the outbreak strain ceased following this reinforcement. Transmission reduced and was abolished after four months. Endemicity of the outbreak strain did not ensue and remains so. 2. Despite similar efficacy in eradicating EMRSA-15 and the outbreak strain, the latter escaped infection control suggesting emergence of a new fitter clone that disseminated more quickly and easily amongst the same high risk patients. The new clone was intrinsically more pathogenic as half the carriers developed infections compared with 1 in 10 patients with gentamicin-sensitive EMRSA-15. No one with EMRSA-15 died, whilst the outbreak strain mortality was 22%. 1 patient died of necrotising pneumonia. 2 hypotheses: EMRSA-15 already carrying SCCmec acquired PVL, or a methicillin-resistant S aureus with PVL acquired SCCmec.

**CONCLUSION.** The presence of PVL and SCCmec in a genetic background of proven epidemicity such as EMRSA-15 could prove highly transmissible and cause serious disease in a hospital setting. Reinforcement of enteral vancomycin cleared the new more virulent clone.

Grant acknowledgement, Chris Stoutenbeek Foundation

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**327**

**COMBINATION OF MYCROGRAB® AND AMPHOTERICIN B IN CULTURE CONFIRMED CANDIDIASIS.**

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For the Mycograb Invasive Candidiasis Study Group.

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**INTRODUCTION.** Candida infections carry a high mortality. Monotherapy is associated with persistent candidemia in 12-17% and a candida-attributable mortality of 10-19% [1,2]. Combination studies using existing agents have failed to show improvements in clinical efficacy. The development of antibodies against HSP90, a molecular chaperone present in yeast cell wall is associated with recovery from fungal infections. Mycograb®, a human antibody against HSP90 enhances the immune response to candida infections and can be combined with Lipid Amphotericine-B (L-AM-B). Mycograb® shows synergy with L-AM-B in vitro and in animal models of invasive candidiasis. The current pivotal study was undertaken in adult hospitalised patients with culture-confirmed deep-seat candidiasis.

**METHODS.** This randomised prospective double-blind placebo controlled study looked at the efficacy and safety of a 5 day course of Mycograb® (1 mg/kg iv bid) combined with L-AM-B versus placebo (saline iv) combined with L-AM-B. Patients were stratified on the basis of their germ tube test result. Efficacy was assessed on the basis of clinical and mycological response at Day 10. Candida-attributable mortality (28 days after last dose of study drug) and speed of culture-confirmed resolution of the infection. The primary efficacy variable was overall response at Day 10 i.e. clinical and mycological resolution of the infection. There were 117 patients (from 12 Centres) in the modified ITT population.

**RESULTS.** A complete overall response was obtained in 48% (29/61) of the placebo group compared to 84% (47/56) of the Mycograb®-treated group (P < 0.001). The following secondary efficacy criteria were also met: clinical response (52% versus 86%, P < 0.001), mycological response (54% versus 89%, P < 0.001), Candida-attributable mortality (18% versus 4%, P = 0.03), and rate of culture-confirmed clearance of the infection, being over twice as fast in the Mycograb®-treated group (P = 0.001). Mycograb® was well-tolerated.

**CONCLUSION.** This is the first double blind, placebo controlled trial showing synergy between 2 antifungals in the treatment of invasive candidiasis. The combination of Mycograb® with L-AM-B produced a highly statistically significant improvement in outcome in patients with culture-confirmed invasive candidiasis and should therefore become the first choice treatment.

**REFERENCE(S).** 1. N Engl J Med 2002; 347:207, 2. Clin Infect Dis 2003:36:1212

Grant acknowledgement, Neutec Pharma, Manchester, UK

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ANTIFUNGAL PROPHYLAXIS WITH AZOLES IN HIGH-RISK, SURGICAL ICU PATIENTS: A META-ANALYSIS

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INTRODUCTION. The use of antifungal prophylaxis remains controversial in most populations including the surgical intensive care unit (SICU) patients. A meta-analysis of randomized controlled trials (RCTs) was performed in order to evaluate the safety and effectiveness of azoles, as antifungal prophylaxis in high-risk patients receiving treatment in SICU.

METHODS. Data were obtained from PubMed, Current Contents, Cochrane central register of controlled trials, and references from relevant articles. STUDY SELECTION: RCTs using azoles as antifungal prophylaxis versus placebo were included in the study. DATA EXTRACTION: Two independent reviewers extracted data concerning the development of fungal infections (superficial or invasive), reported adverse effects, and mortality.

RESULTS. Six RCTs were included in the main analysis. Publication bias and statistically significant heterogeneity was not observed among the analyzed studies. Patients receiving antifungal prophylaxis developed fewer episodes of either, candidaemia (OR=0.28, 95% CI 0.09-0.86), non-bloodstream invasive fungal infections (OR=0.26, 95% CI 0.12-0.53), and non-invasive (superficial) fungal infections (OR=0.22, 95% CI 0.11-0.43), respectively. Mortality was also lower among those who received azole prophylaxis in the main analysis (OR=0.74, 95% CI 0.52-1.05), and was reduced to a statistically significant level when RCTs with septic shock patients were included (OR=0.68, 95% CI 0.49-0.95). There was no significant difference in reported adverse effects (OR=1.28, 95% CI 0.82-1.98).

CONCLUSION. The prophylactic use of azoles in high-risk SICU patients is associated with lower rates of fungal infections and lower mortality. However, although not noted in the analyzed RCTs, the shift towards non-albicans species and development of resistance to azoles are of major concern.

LONG-TERM SURVIVAL FOR 22,978 ICU PATIENTS USING LINKED DATA

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INTRODUCTION. The value of intensive care to the community is dependent ultimately on long-term outcomes. Relevant long-term outcome data has been limited by issues related to design or methods – total duration of follow up, loss of subjects to follow up, small sample size and absence of information concerning severity of illness and pre-existing illness.

METHODS. A retrospective cohort study was conducted between 1987 and 2002 for all patients admitted to a 22-bed ICU. Two administrative databases (WA hospital morbidity and death data) were linked with the ICU clinical dataset that contains admission diagnosis, APACHE II, and daily organ failure and therapies using probabilistic data linkage. The linked dataset contains data on all hospitalisations for all patients from 1980 onwards, ICU clinical data and vital status. Survival from a patient’s first ICU admission was measured at hospital discharge and at 1, 3, 5, and 10 years, with differences between subgroups compared using univariate analysis.

RESULTS. There were 22,978 patients comprising 26,021 admissions. The crude survival at hospital discharge was 89.2%, 84.7% at 1 year, but only 50.7% by 15 years. Crude survival was worse in females (p<0.001) until the 10 year follow up with little difference at 15 years (p=0.988). Age, APACHE II, ICU LOS, Charlson comorbidity index and any organ failure in ICU were all associated with survival at all the follow up time points (p<0.001). Survival was poorest for medical and non-elective surgical patients but the differences had narrowed by 15 years. Open heart surgery had the best survival until the 10 year follow up when trauma had better survival. Sepsis was associated with the worst long-term survival.

| Table 1. | Long-term survival at selected time points |
|---------|------------------------------------------|
|         | Hospital 1-year | 3-year | 5-year | 10-year | 15-year |
| Number  | 22978          | 22978  | 20504  | 18042   | 11258 |
| Crude Survival % | 89.2 | 84.7 | 80.1 | 75.7 | 62.8 |
|          |                |        |        |        |        |

CONCLUSION. This linked data set provides unique information about long-term survival after critical illness.

Grant acknowledgement. BUPA Foundation, TAW is a NHMRC Scholar

ONE-YEAR SURVIVAL OF ELDERLY PATIENTS FOLLOWING INTENSIVE CARE UNIT ADMISSION

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INTRODUCTION. Age is a predictor of longer-term mortality in critically ill patients [1]. We followed up 140 patients aged between 80 and 94 years sequentially admitted to our teaching hospital general intensive care unit (ICU) over one year to determine mortality over the subsequent 12 months.

METHODS. In this retrospective study, patients were identified from admission records and classified by age (5 groups: 80-84, n=89; 85-89, n=36; 90-94, n=15), sex, and source of referral. Data was gathered from hospital and general practitioner records. During sequential 30-day periods both inter-group and month-to-month variation in mortality was compared.

RESULTS. 140 patients (10.4% of all ICU admissions) entered the study. 39 were lost to follow up. 40 patients (39.6%) died in ICU. Amongst patients surviving to discharge 57.42% died during the first 30 days and 9.03% during the second 30 days. The average mortality in each 30-day time period for the subsequent 300 days fell to 3.9%. Overall one-year survival was 25.74%. Acute admissions from the emergency department and emergency surgical patients suffered a mortality of 72.7% and 83.3% respectively during the first 30 days and an average 30-day mortality rate of 3.1% and 7.8% respectively during days 31-360. Log rank analysis revealed a statistical significance (p=0.0017) between the survival of emergency compared to elective surgical patients. There was no significant difference in survival between emergency surgical, inpatient or emergency department admissions with no significant difference between the survival curves across the three age groups, or between sexes.

CONCLUSION. For elderly patients admitted to ICU as emergencies, there is a marked difference between short and long term survival and a plateau in mortality 30 days post-discharge. Elective surgical patients of the same age group show less reduction in serial month-to-month mortality rates. Age was not a predictor of 30-day or 1-year survival.

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Oral Presentations

Long-term outcomes (II) 329-333

329 WEIGHT LOSS AT 3 MONTHS IS COMMON AFTER LONG INTENSIVE CARE STAY AND ASSOCIATED WITH POOR APPETITE

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INTRODUCTION. Continued weight loss after intensive care (IC) is both a poor quality outcome and prognostic marker[1]. Recently published data suggests that up to 40% of IC patients were still 10kg underweight 7.8 months post discharge. Reasons for this were unclear[2]. This is the first prospective study which aims to specifically investigate the incidence and causes of gastrointestinal symptoms post prolonged IC.

METHODS. Between December 2002 to January 2004, all patients with IC stays of 4 days or longer, were invited to attend an outpatient follow up clinic 3 months after hospital discharge. In addition to basic demographic and SF-36 data, we recorded information related to gastrointestinal function: Weight, appetite, swallowing or taste disturbance, change in bowel habit, and symptoms of indigestion. Factors that might be significantly associated with continued weight loss, such as advanced age, severity of illness score and prolonged IC stay were also investigated.

RESULTS. A total of 542 patients stayed more than 4 days on intensive care. Mean age, APACHE II and length of stay were 61.4 years, 19.1 and 11 days respectively. Basic demographic data was similar in clinic attenders compared with non-attenders. By 3 months 336 patients were available for follow up. Complete follow up data was available for 84 (25%) patients. The incidence of GI disturbance is as follows: Persistent weight loss 33%, poor appetite 9.7%, taste disturbance 24.1%, dysphagia 9%, change in bowel habit 6.2%, indigestion 12.3% and trachoesophagus 61%. Factors significantly associated with failure to regain pre IC weight were poor appetite (p=0.0008) and age over 65 (p=0.018). Severity of illness, ITU length of stay or presence of trachoesophagus were not significantly associated.

CONCLUSION. 40% of patients fail to attain pre IC weight by 3 months. This may be due to poor appetite. We plan to further investigate appetite disturbance and its causes in patients after critical illness, as continued weight loss is an important clinical marker.

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LONG-TERM OUTCOMES AFTER SEVERE TRAUMA

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INTRODUCTION. Three months after injury life expectancy is similar to the normal population (1).

METHODS. Cohort study of all 208 severely traumatized patients (> 18 years) admitted to our general ICU from 1998-2001. Data concerning the ICU stay were retrieved from our ICU database. During March and April 2005 semi-structured telephone interviews were performed with 139 (60%) of the 161 patients still alive three to seven years after the injury. The interview included evaluation of HRQoL using the EQ-5D questionnaire (present status and prior to trauma), Glasgow Outcome Scale (recovery) and Karnofsky Index (functional status).

RESULTS. Mean age was 40 ± 17 years, mean SAPS II 31 and median Injury Severity Score 25. According to Glasgow Outcome Scale 84% experienced good or moderate recovery. Karnofsky Index below 60 (i.e. requiring significant help in daily life) were obtained by 13%. A total of 66% of full-time workers before the trauma were still employed. Results from the EQ-5D evaluation are shown in the table.

| Quality of life (EQ-5D) before and after (3 to 7 years) severe trauma (n=123) |
|------------------------|------------------|---------------|-------------------|---------------|
| Before                  | after            | before        | after            |
| Mobility                | Self-care        | Usual activity| Pain and discomfort| Anxiety and depression |
| No problem              | 119 (97%)        | 121 (98%)     | 120 (98%)        | 114 (93%)     |
| Major problem           | 0 (0%)           | 0 (0%)        | 0 (0%)           | 0 (0%)        |

CONCLUSION. Less than 10% of long-term survivors after severe trauma experience major problems as measured by the EQ-5D. Thirteen percent still need considerable assistance in daily life, while 84% had a good to moderate recovery.

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333 LONG TERM FUNCTIONAL AND COGNITIVE STATUS AND QUALITY OF LIFE IN VERY ELDERLY PATIENTS SURVIVING INTENSIVE CARE TREATMENT

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INTRODUCTION. Few studies were undertaken to investigate the long-term outcomes of very elderly patients surviving ICU. This may be partly due to the high risk of ICU or hospital mortality among these patients, often expressed as the short-term outcome of ICU treatment. However, mortality is not the only outcome of ICU treatment. We aimed to study the long term cognitive and functional outcomes and health-related quality of life in very elderly patients surviving ICU.

METHODS. In this retrospective observational cohort study we interviewed the survivors of a cohort of 578 patients aged 80 years and older, admitted, planned or non-planned, to a medical and surgical ICU during 1st of January 1997- 1st of December 2002 in a general tertiary university teaching hospital. Data were collected on preoperative conditions, demographic and social background, and present medical consumption. Cognitive screening was obtained by the IQCODE, activities of daily living by the Katz ADL Index. Health-related quality of living was measured by the Euroqol and the VAS score. All were validated quantitative measurement instruments. Patients and relatives were interviewed concerning their ICU experiences.

RESULTS. A total number of 578 patients were studied. ICU and hospital mortality for this cohort was 31.7 %, and 28.2 % died following hospital discharge. The 1-years survival of all patients was 37.9 %.

A total number of 204 survivors (mean follow-up of 44.2 months, sd 19.9 months) and 155 relatives were interviewed. Although independence in activity of daily living was decreased after ICU stay, 74.3 % of the patients who lived at home before ICU admission were still at home with or without assistance.

CONCLUSION. The most important findings of this study are the good long term functional outcome, cognitive status and health related quality of life among this cohort of very old patients. The largest part of the survivors remembered their ICU stay not as a negative part of their treatment.

335 INDOXYLANE GREEN PLASMA DISAPPEARANCE RATE IS MAINTAINED DURING WHOLE BODY HYPERTERMIA

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INTRODUCTION. To study feasibility and toxicity of induced whole body hyperthermia (WBH) for treatment of cancer patients we measured indocyanine green plasma disappearance rate (PDR) as a parameter for liver function.

METHODS. 35 treatments with whole body hyperthermia (body core temperature up to 42.2°C for 1 hour) in combination with hyperoxemia (paO2>250 mmHg), hyperglycemia (blood glucose>400 mg/dl) and cytostatic drugs were performed in 25 patients with disseminated malignancies. For guidance of volume therapy goal parameters were intraarterial blood volume index (ITBVI) of 800-1100 ml/m\(^2\), cardiac index > 3.5 l/min/m\(^2\), hemoglobin concentration > 10 g/dl, and mean arterial pressure (MAP) > 55 mm Hg. MAP was maintained using noradrenaline in all patients. Measurements included PDR, cardiac index, ITBVI, as well as blood lactate levels. All parameters were measured at three defined points: after induction of anesthesia at 37°C, 30 minutes after reaching the plateau phase at 42.2°C, and at 39°C during cooling phase. For statistical analyses a paired test according to Wilcoxon was used. Statistical significance was accepted for p<0.05. Data presented as mean ± standard error of the mean.

RESULTS. Under WBH CI increased significantly while PDR stayed within a normal range. PDR did not increase, and in contrast, CI and blood lactate levels increased significantly (see table).

| TABLE 1. Results |
|------------------|
| Temperature      | PDR [%/min] | CI [l/min/m\(^2\)] | Blood lactate [mmol] |
| 37°C             | 23.6±1.6   | 5.2±0.2           | 1.4±0.8             |
| 42.2°C           | 23.1±1.4   | 7.9±0.2           | 4.1±0.3             |
| 39°C             | 22.7±1.2   | 6.1±0.3           | 3.9±0.2             |

CONCLUSION. During WBH PDR as a marker for liver perfusion and liver excretion is maintained.

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**336**

**WEANING OFF NOREPIEORPHINE DELIVERY DURING SEPTIC SHOCK VIA FUZZY CONTROLLER**

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**INTRODUCTION.** The review of the current state of the art reveals that fuzzy logic has been used in a number of medical device application. The aim of this study is to demonstrate that a fuzzy controller of the norepinephrine infusion rate can reduce septic shock duration.

**METHODS.** A prospective, randomized study, approved by the “Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale”. Between the 6th and 24th hour after introduction of the vasopressor therapy, patients with septic shock and hemodynamic status controlled by norepinephrine (NOR) were included. The NOR infusion rate in the control group (SURV) was managed by the doctors of the intensive care unit, whereas the NOR delivery of the tested group was controlled by a fuzzy controller (CATECHO) depending on the mean arterial pressure (MAP) variations. The fuzzy-logic-based, automated drug delivery system was able to increase or reduce the norepinephrine infusion rate, every 7 minutes, after analysis of the variations in MAP. A MAP between 70 and 75 mmHg was the wanted set point. The mean criteria was the shock duration defined by the vasopressor support duration.

**RESULTS.** There was no significant difference between the 2 groups with regard to demographic data, severity scores at inclusion, fluid resuscitation and initial norepinephrine infusion rate.

**TABLE 1.**

| Survival (n=10) | Catecho (n=7) |
|----------------|--------------|
| Shock duration (min) | 54.1 ± 37.2 | 22.8 ± 11.7 p=0.04 |
| Mortality | 4/7 | 0/1 |
| Hospitalisation (day) | 23 ± 14 | 44 ± 47 p=0.685 |

**CONCLUSION.** These preliminary results show a decrease in shock duration in the CATECHO group. In such a situation fuzzy logic algorithms appear to be a novel approach to optimize catecholamine delivery. We need more results to evaluate the benefits of this promising new technique.

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**337**

**BIOCHEMICAL AND CLINICAL EFFICACY OF SINGLE PASS ALBUMIN DIALYSIS (SPAD) IN SEVERE LIVER DYSFUNCTION**

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**INTRODUCTION.** Albumin dialysis has been proposed as a method for the removal of protein bound toxins in liver dysfunction. SPAD employs standard haemodialfiltration with a solution of albumin which is then discarded. As opposed to other methods of albumin dialysis SPAD is simple to perform and does not require the purchase of specialised equipment. We have evaluated the clinical use of SPAD in patients with severe liver dysfunction.

**METHODS.** 25 patients with severe liver dysfunction requiring intensive care underwent 48 sessions of SPAD. Median SOFA score was 13 (range 6-21), mean serum total bilirubin was 466µmol/L, and mean serum creatinine was196µmol/L prior to treatment.

**RESULTS.** Mean arterial pressure, SOFA score, creatinine and lactate did not change over treatment. There were highly significant reductions in total and conjugated bilirubin and serum bile acids after 1 session of SPAD.

**TABLE 1.** Changes in serum bilirubin during SPAD therapy

| Pre SPAD treatment | Post SPAD treatment | p value |
|--------------------|---------------------|---------|
| Total bilirubin µmol/L | 466 ±237 | 355 ± 203 | <0.00001 |
| Conjugated bilirubin µmol/L | 434 ±206 | 293 ±154 | <0.00003 |
| Serum bile acids U/ml | 127.5 | 65.5 | 0.012 |

Data presented as mean ± S.D

**TABLE 2.** Clearance of Bilirubin and bile acids by SPAD

| Bile acids µl | Conjugated Bilirubin µmol/L |
|---------------|-----------------------------|
| Clearance (ml/min) | 15 (6.4-20.7) | 7.5 (3.3-10.65) |

CONCLUSION. SPAD is an easily applicable method of detoxification in severe liver disease and organ dysfunction.