

## Oral Presentations

### Acute respiratory failure (I) – 1-5

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#### FUNCTIONAL MAGNETIC NERVE STIMULATION OF THE ABDOMINAL MUSCLES IN INTUBATED PATIENTS.

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**INTRODUCTION.** Functional Magnetic Nerve Stimulation (FMS) of the abdominal muscles has previously been described in awake volunteers. The expiratory flows generated with FMS of the abdominal muscles have been comparable to expiratory flows generated during a voluntary cough[1-3]. This technique of abdominal muscle stimulation has been considered for application in the critical care patient, but there are no published studies of this technique having been applied in sedated intubated subjects. The aim of our study is to measure the expiratory flows achieved in an anaesthetised group. In a voluntary cough temporary glottic closure probably augments the expiratory flows achieved, therefore we also observed the effect on expiratory flows of the addition of a pneumatic occlusion valve.

**METHODS.** 5 subjects were taken who were to have elective surgery. Following induction of anaesthesia without paralysis, two air filled balloon catheters were placed in the oesophagus and stomach and these recorded oesophageal and gastric pressure. Flow was recorded using a heated screen pneumotachograph. With the subject in the supine position a 190mm (OD) round coil was placed over the back with the coil centred over the spinous process of T11. A 0.5 second, 25Hz stimulus was delivered using a super rapid magnetic nerve stimulator set at 60% intensity. This intensity level had been tolerable to awake volunteers in previous work in our department. The effect of temporary glottic closure on expiratory flows was observed by activating a pneumatic occlusion valve for 210msec at the start of stimulation.

**RESULTS.** Peak gastric and oesophageal pressures were 18cmH2O (SD 4.0) and 9.9cmH2O (SD 4.1) respectively. Peak expiratory flows were 59 l/min (SD 20). The addition of the occlusion valve significantly increased both Pes (15.4cmH2O SD3.6)(p<0.01) and the peak expiratory flows (91 l/min SD 34 (p<0.01). Pga remained unchanged 18cmH2O (SD 4.3).

**CONCLUSION.** Magnetic nerve stimulation of the abdominal muscles generates expiratory flows in the anaesthetized supine subject. However, peak expiratory flows generated were lower than during a voluntary cough. The addition of a pneumatic occlusion valve increased the expiratory flows generated.

**REFERENCES.** 1. Lin, VW, Hsieh, C, Hsiao, IN, Canfield, J, ., Apr;84(4):1144-50. Functional magnetic stimulation of expiratory muscles: a noninvasive and new method for restoring cough. J Appl Physiol 1998; 84: 44-50. 2. Polkey, MI, Luo, Y, Guleria, R, Hamnegard, CH, Green, M, Moxham, J. Functional magnetic stimulation of the abdominal muscles in humans. Am J Respir Crit Care Med 1999; 160: 513-22. 3. Kyroussis, D, Polkey, MI, Mills, GH, Hughes, PD, Moxham, HD, Green, M. Simulation of cough in man by magnetic nerve stimulation of the thoracic nerve roots. Am J Respir Crit Care Med 1997; 156: 1696-9.

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#### RELATIONSHIP BETWEEN EXTRA VASCULAR LUNG WATER AND PAO<sub>2</sub>/FIO<sub>2</sub> RATIO

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**INTRODUCTION.** Extra vascular lung water (EVLW) is a useful parameter that can be measured both with COLD system (double indicator technique) and with PiCCO system (single indicator technique). Even if some studies have been made on its correlation with pulmonary oedema, few papers have been published on its relationship with PaO<sub>2</sub>/FIO<sub>2</sub> ratio.

**METHODS.** Two sets of patients were considered. In the first data set 15 patients with refractory septic shock treated with methylene blue were considered. In the second data set 9 patients with acute respiratory failure were considered. All patients were monitored both with a Swan-Ganz catheter and COLD system, that is a fiberoptic catheter in femoral artery. PCWP and CVP were monitored with the Swan-Ganz catheter and EVLWI and intrathoracic blood volume (ITBV) with double indicator technique (COLD system, Pulsion). Data obtained were divided following PaO<sub>2</sub>/FIO<sub>2</sub> ratio higher or lower than 200 and for each parameter in each data set mean and standard deviation was calculated. PCWP, CVP and EVLW when PaO<sub>2</sub>/FIO<sub>2</sub> ratio < 200 were compared to PCWP, CVP and EVLW when PaO<sub>2</sub>/FIO<sub>2</sub> ratio ≥ 200. T-test was used as statistical analysis. P<0.05 was considered significant.

**RESULTS.** In the first data set EVLWI was significantly higher when PaO<sub>2</sub>/FIO<sub>2</sub> < 200 (p<0.01), while no differences were found for PCWP and CVP. Also in the second data set EVLWI was extremely higher when PaO<sub>2</sub>/FIO<sub>2</sub> < 200 (p=0.0006), while no significant changes were found for PCWP and CVP.

**CONCLUSION.** Only EVLWI can accurately reflect different respiratory clinical setting and can be useful to monitor patients with respiratory failure. PaO<sub>2</sub>/FIO<sub>2</sub> ratio lower than 200 can be due to pulmonary oedema. A high EVLWI can confirm this hypothesis and allow prompt diuretic therapy.

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#### OVERINFLATION IN ACUTE LUNG INJURY: COMPARISON OF DYNAMIC CT WITH DYNAMIC RESPIRATORY MECHANICS

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**INTRODUCTION.** Overinflation by inappropriate ventilatory strategies can exacerbate Acute Lung Injury(ALI). A proposed method of estimating overinflation uses a volume-dependent single compartment model of the equation of motion; Pao=(E1+E2V)V+Rrs.V'+Po with overinflation assessed as the contribution of volume-dependent elastance to total elastance (%E2), derived as (100E2VT)/(E1+E2VT) (1). We have previously found that pressure-controlled ventilation with an inverse ratio (PC 2:1) was associated with higher %E2 than pressure-controlled ventilation at an I:E ratio of 1:2 (PC 1:2), or volume-controlled ventilation using a constant flow with an I:E ratio of 1:2 (VC 1:2)(2). We compared the volume-dependent single compartmental model with dynamic CT of 5 patients with ALI.

**METHODS.** 5 ventilated patients with ALI had dynamic CT performed at 2 levels (sub-carinal and above the diaphragmatic cupola) of sufficient duration to record dynamic images of at least 1 respiratory cycle. This was performed after random application for 30 min each of VC at 1:2, PC at 1:2 and PC at 2:1 with a constant total PEEP and tidal volume (VT). In addition, flow and airway pressure were measured with 60s of data being collected at a sampling frequency of 100Hz. Multilinear regression (MLR) analysis of the complete breath averaged data using a volume-dependent single-compartment model was used to calculate the %E2. End-expiratory and end-inspiratory CT images were identified by volumetric analysis. Image analysis was performed using the region of interest function, total area of each lung and mean density were determined by including all pixels with density values between -1000 and +100 Hounsfield units (HU). We calculated hyperinflation as the fraction of CT numbers within -1000 HU and -900 HU. Parameters were tested with repeated measures ANOVA.

**RESULTS.** Data are mean±SEM; ns=not significant.\*Contrast p=.005 with PC2:1 versus PC1:2, VC 1:2.

| Mode  | PC 1:2   | VC 1:2   | PC 2:1   | P-value |
|---|----------|----------|----------|---------|
| %E2   | 7.3±12.3 | 15.2±7.2 | 24.9±4.3 | .017    |
| PEEPtotal (cm H2O)                            | 11.5±1.7 | 11.5±1.7 | 11.5±1.7 | ns      |
| VT (ml)                                       | 502±31.7 | 502±31.7 | 502±31.7 | ns      |
| <i>Hyperinflated pixels (end-inspiration)</i> |          |          |          |         |
| L base  | 196±38   | 194±31   | 221±42   | ns      |
| R base  | 223±43   | 231±37   | 225±44   | ns      |
| L carina                                      | 154±29   | 181±37   | 213±33*  | .019    |
| R carina                                      | 174±41   | 160±29   | 160±15   | ns      |

**CONCLUSION.** Both MLR and dynamic CT data suggest a greater degree of alveolar overinflation with PC 2:1 compared with either PC 1:2 or VC 1:2.

**REFERENCES.** 1. Kano S, et al. JAP 1994; 77:1185-1197. 2. Edibam CE et al. Am J Respir Crit Care Med 2001; 63:A767

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#### LOCAL VENTILATION PERFUSION RATIO DURING PARTIAL LIQUID VENTILATION MEASURED BY MAGNETIC RESONANCE

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**INTRODUCTION.** In order to analyse lung physiology we developed a method to estimate local ventilation perfusion ratio by the regional alveolar oxygen tension (pO<sub>2</sub>). As a <sup>19</sup>F-MRI technique made it possible to quantify local pO<sub>2</sub> of perfluorocarbon (1), we applied this method to study ventilation perfusion ratio during partial liquid ventilation.

**METHODS.** We studied 17 anaesthetized pigs (18 ± 1 kg weight). 7 pigs were lung healthy. In 10 pigs ARDS was induced by intravenous injection of oleic acid (0.15 ml/kg). All animals underwent partial liquid ventilation with perflubron (20 ml/kg) in supine position. Under steady state condition, we measured local lung pO<sub>2</sub> by <sup>19</sup>F-MRI (1) and sampled physiological parameters (e.g. analysis of arterial and mixed venous blood gases, inspiratory and expiratory gas fractions). We set up an equation balancing oxygen uptake by local ventilation on the one hand and oxygen delivery by local perfusion on the other hand. According to this, the local ventilation perfusion ratio (V'/Q') was equal to the local capillary change in blood oxygen content (DC<sub>kap</sub>O<sub>2</sub>) divided by the local change in respiratory oxygen fraction (DF<sub>res</sub>O<sub>2</sub>): V'/C=DC<sub>kap</sub>O<sub>2</sub>/DF<sub>res</sub>O<sub>2</sub>. After transformation to logarithmic scale, differences in V'/Q' were analysed by student's paired t-test.

**RESULTS.** In healthy pigs we found a mean ventral V'/Q' of 0.31 versus a mean dorsal V'/Q' of 0.07 (p=0.0004). In ARDS pigs ventral V'/Q' averaged 0.67 contrary to the dorsal V'/Q' of 0.09 (p=0.0005).

**CONCLUSION.** During partial liquid ventilation, ventilation perfusion ratio is unevenly distributed throughout the lung. In supine position, highest values are found ventral and lowest values dorsal. MRI measurements of local lung pO<sub>2</sub> provide an insight into this distribution of ventilation perfusion ratio.

**REFERENCES.** 1. Laukemper-Ostendorf S et al. <sup>19</sup>F-MRI of Perflubron for Measurement of Oxygen Partial Pressure in Porcine Lungs during Partial Liquid Ventilation. Magn Reson Med 47:82-89 (2002)

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VENTILATION-SYNCHRONOUS PAO<sub>2</sub> OSCILLATIONS IN A RABBIT MODEL OF LAVAGE ARDS

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**INTRODUCTION.** Dynamic Computed Tomography of ventilated ARDS lungs shows cyclic alveolar collapse and reopening [1,2], a phenomenon which is thought to contribute to ventilator-associated lung injury (VALI). By using a fast-responding intraarterial PO<sub>2</sub> probe, this study aimed to resolve and quantify the cyclic variation of venous admixture to arterial blood expected from this phenomenon.

**METHODS.** With IRB approval, six anesthetized NZW rabbits were ventilated in a pressure-constant mode with an FiO<sub>2</sub> of 1.0 (Servo 900C, Siemens) before and after induction of saline lavage ARDS. PO<sub>2</sub> was measured continuously by a fluorescent-quenching probe (Ocean Optics Inc., USA) placed in the brachiocephalic artery. Ventilator settings were varied in random order over 3 levels each of PEEP, respiratory rate (RR) and plateau pressure minus PEEP (deltaP). The dependence of the amplitude of PaO<sub>2</sub> oscillations on PEEP, RR, and deltaP was modeled by response surface methodology using a full second order model.

**RESULTS.** PaO<sub>2</sub> oscillations were detected in all animals at a frequency which corresponded closely to RR. Peak-to-peak amplitude varied from 9 ± 6 mmHg (mean ± SD) in healthy lungs to 375 ± 37 mmHg in damaged lungs. Response surface analysis showed highly nonlinear effects of both PEEP and RR upon amplitude, with substantial interactions between PEEP and RR. Partial F testing for the amplitude model showed that PEEP was the strongest predictor of oscillatory amplitude of paO<sub>2</sub>, but RR was nearly as predictive as PEEP. DeltaP had much less effect on paO<sub>2</sub> oscillatory amplitude.

**CONCLUSION.** Large paO<sub>2</sub> oscillations were found in a mechanically ventilated rabbit saline-lavage ARDS model. High PEEP levels and high RR, i. e., features of protective lung ventilation, were most effective in mimicking these oscillations. PaO<sub>2</sub> oscillations in this model of acute lung injury most likely reflect cyclically varying shunt fractions due to ventilation-induced recruitment and collapse of atelectasis, which has been suggested to be a source of stretch injury in VALI. In addition, large swings in PaO<sub>2</sub> may also contribute to VALI directly by intermittent hypoxic stimulation of inflammation.

**REFERENCES.** [1] Neumann et al., J Appl Physiol, 1998 [2] Markstaller et al., Br J Anaesth, 2001 Grant. NIH-GM59274, NIH-HL59052, AHA-0151528U, DFG-Ma2398/2, DFG-Pf

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## PLATELET-ACTIVATING FACTOR ACETYLMYRINOLASE DECREASES MORTALITY IN PATIENTS WITH ORGAN DYSFUNCTION

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**INTRODUCTION.** Platelet-activating factor (PAF) and related oxidized phospholipids (OX-PL) are potent pro-inflammatory mediators that have been implicated in the pathogenesis of severe sepsis and organ dysfunction (OD). Pafase is a recombinant form of the naturally occurring human enzyme that inactivates OX-PL and degrades PAF to lyso-PAF, an inactive metabolite. Pafase decreases acute lung injury and increases survival in animal models after endotoxin challenge.

**METHODS.** Patients were randomized < 12 hours of developing severe sepsis (ACCP/SCCM Consensus Conference definition) to receive Pafase (1 or 5 mg/kg) or placebo (vehicle) administered IV daily for five consecutive days. The number of OD (sustained hypotension, lactic acidosis, oliguria, coagulation abnormality, thrombocytopenia, or alteration in mental status) present at study entry were determined with definitions established a priori. Differences in 28 day all cause mortality were evaluated post-hoc using logistic regression with the number of OD present at study entry included in the model as a covariate.

**RESULTS.** A total of 127 patients with severe sepsis were enrolled (124 evaluable). Groups were similar at study entry for age, APACHE II score, and number of OD. We previously reported (Intensive Care Med 2000;26:S321) that Pafase 1 mg/kg significantly decreased 28 day all cause mortality compared to placebo (21.4% vs 44.2%, p = 0.026) and was well tolerated and did not increase the incidence of serious bleeding. An analysis of 28 day all cause mortality adjusted for the number of OD is summarized below. The number of OD after adjusting for treatment was not predictive of mortality (p = 0.414).

|              | Pafase 1 mg/kg (n/N, %) | Placebo (n/N, %) |
|--------------|-------------------------|------------------|
| 1 OD         | 3/17 (17.6%)            | 9/22 (40.9%)     |
| 2 OD         | 3/14 (21.4%)            | 3/12 (25.0%)     |
| 3 OD         | 1/5 (20.0%)             | 5/6 (83.3%)      |
| 4 or More OD | 2/6 (33.3%)             | 2/3 (66.7%)      |

28 day all cause mortality (n = # of deaths; N = # of patients).

**CONCLUSION.** Pafase 1 mg/kg resulted in a consistent decrease in 28 day all cause mortality independent of the number of sepsis-induced OD present at study entry. A Phase III trial is currently in progress in patients with severe sepsis to confirm these observations.

**REFERENCES.** Phase II Pafase ARDS Prevention Study Group and ICOS Corporation, Bothell, WA, United States

Grant. ICOS Corporation

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## REVERSAL OF IMMUNOPARALYSIS BY GRANULOCYTE-MACROPHAGE COLONY STIMULATING FACTOR-PROOF OF PRINCIPLE

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**INTRODUCTION.** The objective of this study was to evaluate the effect of recombinant human Granulocyte-Macrophage Stimulating Factor (rhGM-CSF) on immunoparalysis as defined by a sustained decrease of HLA-DR expression on monocytes from patients with severe sepsis.

**METHODS.** We included nine consecutive patients from an operative ICU with severe sepsis and a HLA-DR expression on peripheral monocytes of <150 mean fluorescence intensity (MFI) over a period of at least 48 h prior to intervention. For FACS measurement of HLA-DR the blood samples were stained with FITC-labelled anti-CD14 and PE-labelled anti-HLA-DR antibodies and with FITC-labelled anti-CD14 antibodies and PE-labelled anti-IgG1 antibodies as control for non-specific binding (monoclonal antibodies for CD14 and HLA-DR by Becton Dickinson, San Jose, CA; for IgG1 by Coulter, Marseille, France). Monocytes were identified by forward and side scatter and by cell-specific binding of anti-CD14 antibodies. HLA-DR expression was calculated as mean fluorescence intensity (MFI) in the histogram (CellQuest® software). For TNF ex-vivo production, whole heparinized blood (50 ml) was spiked with LPS in culture media at a concentration of 500 pg/ml and incubated at 37±1°C (Milena® Ex Vivo Stimulation Kit, DPC Biermann, Bad Nauheim, Germany). After four hours TNF was measured in the supernatant using an ELISA system (IMMULITE® DPC, Los Angeles, CA).

**RESULTS.** Mean MFI was 69.4±13.2 24h before and 56.7±8.2 on the day of the administration of 300 mg rhGM-CSF. Within 24h a significant increase of HLA-DR expression to a mean of 327.7±78.8 MFI was observed in all patients (p<0.01 post- vs. pre-intervention). It was maintained on days 2, and 5-9. It was accompanied by a significant rise in total WBC. The ex-vivo TNFα production in whole blood after LPS-stimulation increased significantly from a mean of 82±29.2 pg/ml (before rhGM-CSF) to 793±546.8 pg/ml (after GM-CSF) and remained at a higher level when compared to pre-intervention values. No side effects were recorded. Over the course of the observation period, IL-6, CRP, PCT and LBP levels showed a consistent decline. No increase in pro-inflammatory (IL-6, CRP) or infectious markers (LBP, PCT) was seen following rhGM-CSF. There were no adverse reactions when looking at fluid balance, catecholamine doses, PaO<sub>2</sub>/FiO<sub>2</sub> ratio and maximum body temperature. Mortalities were 3 out of 9.

**CONCLUSION.** This preliminary study demonstrates for the first time that the administration of rhGM-CSF reliably and safely upregulates HLA-DR expression on monocytes in severely compromised septic patients with multiorgan dysfunction. Moreover, with the concomitant increase of the ex-vivo whole blood TNFα response, we could show that this upregulation of a monocytic activation marker is also accompanied by a functional recovery. A randomized, controlled trial addressing the clinical impact of such an intervention will therefore be initiated.

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## VALIDATION OF AN ICD-9 BASED STRATEGY TO IDENTIFY SEVERE SEPSIS AND FORECAST DROTRECOCIN ALFA USE

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**INTRODUCTION.** Estimating drotrecogin alfa (activated)[DAA] use is challenging as there is no specific International Classification of Diseases, Ninth Revision (ICD-9) code for severe sepsis (SS) and not all patients with SS will be candidates for DAA therapy. The search strategy reported by Angus et al. using concomitant ICD-9 codes for infection and organ dysfunction estimates the national incidence of SS to be 2.26 cases/100 hospital admissions and has been used by many institutions to predict SS incidence and DAA utilization.<sup>1</sup> This search strategy, however, does not account for the presence of the systemic inflammatory response syndrome (SIRS), consider the temporal relationship between infection, organ dysfunction and SIRS, consider severity of illness nor identify patients for whom DAA may be contraindicated. We attempted to validate the use of the ICD-9 based search strategy proposed by Angus et al. at our 340-bed, urban, level-one, trauma center as a strategy to estimate the incidence of SS and forecast DAA use.

**METHODS.** All patients discharged from our institution over a one year period were electronically identified using this ICD-9 based search strategy. For the first quarter, consecutive patient records were reviewed to determine: 1) incidence of SS based on both ACCP/SCCM guidelines and PROWESS study criteria,<sup>2,3</sup> and 2) potential DAA use based on both institutional DAA prescribing guidelines and PROWESS study criteria.

**RESULTS.** The ICD-9 based search strategy identified 821 patients (6/100 admissions). Review of 188 patient records revealed that only 50 (27%, 1.5/100 admissions) and 47 (25%) had SS based on the ACCP/SCCM and PROWESS criteria, respectively. Common reasons why SS was not identified during the review process include: 1) organ dysfunction criteria not met (82%), 2) temporal relationship not evident (11%), and 3) SIRS not present (6%). Of the patients who had confirmed SS, 17/47 (0.5/100 admissions) were candidates for DAA based on institutional prescribing guidelines and 14/47 based on PROWESS study criteria. Contraindications to DAA therapy included: 1) increased bleeding risk (42%), 2) concomitant anticoagulant therapy (25%), and 3) therapeutic futility (19%). Based on this analysis, it is estimated that 74 courses/year of DAA will be used at our institution (0.5 courses/100 admissions).

**CONCLUSION.** The ICD-9 based search strategy proposed by Angus et al. appears to overestimate the incidence of SS and is an imprecise strategy for forecasting DAA utilization. Retrospective cohort analysis may be a better strategy to identify the incidence of SS and forecast DAA utilization.

**REFERENCES.** 1. Angus DC et al. Crit Care Med 2001;29:1303-10. 2. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference. Crit Care Med 1992;20:864-74. 3. Bernard GR et al. N Engl J Med 2001;344:699-709.

## 9

**EFFECT OF HYDROCORTISONE BOLUS ON THE SYMPATHETIC CARDIOVASCULAR MODULATION DURING SEPTIC SHOCK.**

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**INTRODUCTION.** During septic shock impaired sympathetic modulation of heart and vessels contribute to circulatory failure. Human and animal experimental studies shown that hydrocortisone was able to restore the sensibility to catecholamine during septic shock. Objectives: to study the effect of a single 50 mg intravenous hydrocortisone bolus on the sympathetic modulation of heart rate and blood pressure.

**METHODS.** In septic shock and age and sex matched healthy volunteers, systolic (SBP), diastolic (DBP) and mean blood pressures (MBP), heart rate (HR), low frequency (LF), high frequency (HF) components of HR and BP signals, overall variability (area under curve) for heart rate (AU-HR) and diastolic blood pressure (AU-DBP) were recorded by FINAPRES before and 1 hour after 50 mg i.v. of hydrocortisone hemisuccinate(HSHC). Patients and controls were perfused with 3 mg/kg/min of phenylephrine. Variables were compared by ANCOVA (2 grouping factors) for repeated measures ( $p < 0,05$ ).

**RESULTS.** 5 subjects with septic shock (4 M, 1F, age 56±17 years, IGS 2 : 56±23) et 6 controls (2 M et 4 F, age 37±14 years) were included. Results are summarized in the table:

|          | Before HSHC | Controls After HSHC | Shocks Before HSHC | After HSHC | F and p     |
|----------|-------------|---------------------|--------------------|------------|-------------|
| SBP      | 168±17      | 158±25              | 115±26             | 126±26     | 17.9/<0.001 |
| DBP      | 77±11       | 80±6                | 58±1               | 67±20      | 19.6/<0.001 |
| MBP      | 107±9       | 106±9               | 77±15              | 87±21      | 20.4/<0.001 |
| LF- DBP  | 7.25±3.2    | 6.23±1.8            | 6.4±1.6            | 5.5±3.6    | 10.2/<0.001 |
| LF-HR    | 9.4±6.5     | 6.2±2.7             | 10.4±8.3           | 9±10.7     | 3.3/0.087   |
| HF- DBP  | 7.1±3.2     | 5.1±1.9             | 10±3.9             | 7.1±5.7    | 12.6/0.002  |
| HF-HR    | 13.3±10.5   | 8.4±3.3             | 24±16.2            | 17.5±20.4  | 6.4/0.022   |
| AUC- DBP | 30.9±11.8   | 26.3±48.2           | 40.3±11.6          | 28.8±19    | 11.6/0.003  |
| AUC-HR   | 47.2±34.7   | 30.9±10.8           | 73.5±53.3          | 53.7±61.2  | 5.9/0.027   |
| LF/HF HR | 0.74±0.14   | 0.74±0.12           | 0.47±0.17          | 0.52±0.28  | 61.9/<0.001 |

**CONCLUSION.** One intravenous bolus of 50 mg hydrocortisone hemisuccinate improve the cardiac and vascular variability and particularly the vascular sympathetic modulation during septic shock.

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**IMPACT OF ANTIBIOTHERAPY ON THE OUTCOME OF PATIENTS ADMITTED TO THE ICU FOR SEPSIS**

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**INTRODUCTION.** To evaluate the impact of an adequate empirical antibiotherapy(A-EA) on early (<3 days), 28 days and in-hospital mortalities in patients admitted to ICU for sepsis.

**METHODS.** Prospective cohort study in a 40 beds medical-surgical ICU. Variables: Demographic data, co-morbidities, APACHE II score and predicted mortality, SOFA score, microbiologic documented infection, UCI and hospital mortalities. Univariate and multivariate analysis were performed using SPSS 10.0.

**RESULTS.** Four-hundred and six patients were included. Microbiological documentation of sepsis was obtained in 67.3% of the cases. At admission, clinical picture of sepsis was present in 25.9% of the cases, severe sepsis in 28,6% and septic shock in 45.6%. A-EA was recorded in 224 cases (83%). In multivariate analysis, inappropriate EA in the patients with no-surgical sepsis (OR 7.9 CI 95% 3,9-16,3;  $p < 0,001$ ), respiratory failure at admission (OR 3,4 CI 95% 1,7-7,1;  $p < 0,001$ ), APACHEII score (OR 1.1 CI 95% 1-1,2;  $p = 0,04$ ), SOFA score at the admission (OR 1,2 CI 95% 1,1-1,3;  $p < 0,001$ ), and focus of infection (OR 9,4 CI 95% 3-29,3;  $p < 0,001$ ) were factors independently associated with both 28 days and in-hospital mortality. A-EA in surgical sepsis has been shown to be a protective factor (OR 0,4 CI 95% 0,1-0,7;  $p = 0,001$ ). Immunosuppression, renal and respiratory failure at admission were associated with early mortality.

**CONCLUSION.** An adequate initial empirical antimicrobial treatment is crucial in terms of outcomes in patients admitted to the ICU for sepsis, although early mortality was unaffected.

**Oral Presentations  
Preload/volume therapy – 11-15**

## 11

**INTEREST OF CLINICAL ASSESSMENT IN PREDICTION OF FLUID RESPONSIVENESS IN CRITICALLY ILL PATIENTS**

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**INTRODUCTION.** Volume expansion (VE) can be deleterious in critically ill patients thus reliable predictors of fluid responsiveness are needed at the bedside. We compared clinical signs (passive legs raising (PLR), capillary refill (CR) and shock index (SI = heart rate (HR) / systolic arterial pressure (SAP))) with respiratory cyclic changes in arterial pulse (dPP)[1] before VE in patients in the ICU.

**METHODS.** Clinical (PLR, CR, SI) and hemodynamic (dPP, HR, Mean arterial pressure (MAP), SAP) measurements were performed twice, first before VE and then 5 min after VE using 500 ml gelatin. The effects of VE on hemodynamic parameters were assessed using a non parametric Mann-Whitney U test. Before VE, a dPP value of 13% was used for discrimination between VE responders and VE nonresponders.

**RESULTS.** 36 series of measurements were performed on 26 consecutive patients. The PLR, CR, SI had respective sensitivity values of (69, 61, 77%), specificity of (21, 60, 70%), positive predictive values of (33, 47, 59%), negative predictive values of (56, 74, 84%) compared to threshold responder of dPP. The presence of the 3 clinical criteria (n=7) is associated with a mean dPP = 28%, 2 criteria: dPP = 12%, 1 or 0 criterion: dPP = 9%. VE increased MAP significantly in patients with positive PLR before VE.

**CONCLUSION.** dPP is an accurate indicator to assess changes in cardiac index induced by VE [1] so we chose it as an index of reference. In these preliminary results, SI is the most closely related to dPP. The association of PLR + CR + SI allows a better prediction of fluid responsiveness. PLR is correlated with VE-induced changes in MAP which is the hemodynamic criterion usually used by the clinician. In conclusion, a fast, clinical and strictly noninvasive assessment of the need of fluid expansion is possible but larger studies are necessary to support the results of this study.

**REFERENCES.** [1] F. Michard et al. Am J Respir Crit Care Med 2000, 162 : 134-8

## 12

**MARKERS OF PRELOAD IN PATIENTS WITH SEVERE LIVER DISEASE AND INTRAABDOMINAL HYPERTENSION**

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**INTRODUCTION.** Severe liver disease is often complicated by systemic vasodilatation and low effective intraarterial blood volume leading to arterial hypotension. Furthermore there is a high incidence of raised intra abdominal pressure (IAP) in this patient group which make commonly used markers of preload such as central venous pressure (CVP) unreliable. We tried to investigate whether volumetric parameters such as intrathoracic blood volume (ITBVI), measured via transpulmonary thermodilution or a dynamic parameter such as stroke volume variation (SVV, pulse contour analysis) are superior to filling pressures under above circumstances.

**METHODS.** Simultaneous measurements of CVP, ITBVI, cardiac index (CI), stroke volume index (SVI) and SVV in patients with raised IAP. CI, SVI, ITBVI and SVV were measured using the PiCCO system (Pulsion, Munich). Statistics: Spearman's rho correlation for all measurements.

**RESULTS.** Sixty two recordings were performed in 12 patients with severe liver disease. The median IAP was 18.5 mmHg (16-34). All patients were ventilated and in sinus rhythm. SVV (median 8) correlated best with CI ( $p = 0,001$ ) and SVI ( $p < 0,001$ ). ITBVI was high (median 1152) and only correlated with SVI ( $p = 0,001$ ) but not with CI. There was no correlation of CVP with CI or SVI.

**CONCLUSION.** In patients with decompensated liver disease and intraabdominal hypertension CVP is an unreliable estimate of preload. ITBVI, although high in this patient group, or preferably SVV, if patients are ventilated and in sinus rhythm, are superior markers of preload.

## 13

## EVALUATION OF RESPONSE TO FLUID CHALLENGE WITH PREEJECTION PERIOD VARIATION AFTER CARDIAC SURGERY

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**INTRODUCTION.** Preejection period (PEP), the time interval between the beginning of the Q wave on the ECG and the upstroke of the radial arterial pressure may be used to predict the fluid responsiveness in mechanically ventilated (MV) patients. The hypothesis of the present study was that ventilatory variation of preejection period (DPEP), measured before fluid challenge, correlated with changes in stroke volume index (DSVI) induced by iv volume expansion (VE) in MV critically ill patients.

**METHODS.** Eight post coronary artery bypass surgery patients, hemodynamically stable, deeply sedated and under MV were prospectively included. All patients were equipped with a pulmonary artery catheter (PAC) to measure CI by thermodilution. PEP was measured using a calliper (Agilent® technologies M3150A). DPEP was defined as the difference between expiratory PEP (EPEP) and inspiratory PEP (IPEP) measured over one respiratory cycle. EPEP and IPEP were measured respectively at the minimal and at the maximal systolic pressure value on arterial pressure trace over the same respiratory cycle. DPEP (%) was calculated as  $100 \times (EPEP - IPEP) / (EPEP + IPEP / 2)$ . The SVI and DPEP were obtained both before and after a 30 min infusion of NaCl 0.9% 500 ml. Then, we correlated DPEP and DSVI in percent after VE using linear regression.

**RESULTS.** In all patients systolic arterial pressures was higher during the inspiratory than during the expiratory period. Before VE, DPEP ranged from 8 to 16.7 (mean  $\pm$  SD =  $11.3 \pm 2.7$ ) % and SVI ranged from 24 to 37 ( $29 \pm 4$ ) ml.m<sup>-2</sup>. After VE, DPEP ranged from 0 to 7.4 ( $5.4 \pm 2.5$ ) % and SVI ranged from 28 to 42 ( $34 \pm 4$ ) ml.m<sup>-2</sup>. A positive correlation ( $r^2 = 0.57$ ,  $p = 0.03$ ) was found between DPEP before VE and change in DSVI (in %) after VE.

|   | Before Volume Expansion mean $\pm$ SD | After Volume Expansion mean $\pm$ SD | p (paired t test) |
|---|---------------------------------------|--------------------------------------|-------------------|
| DPEP (%)                                | 11.3 $\pm$ 2.7                        | 5.4 $\pm$ 2.5                        | 0.0021            |
| SVI (ml.m <sup>-2</sup> )               | 29 $\pm$ 4                            | 34 $\pm$ 4                           | 0.0002            |
| DO <sub>2</sub> (ml.min <sup>-1</sup> ) | 596 $\pm$ 159                         | 611 $\pm$ 120                        | 0.6               |
| VO <sub>2</sub> (ml.min <sup>-1</sup> ) | 192 $\pm$ 61                          | 186 $\pm$ 40                         | 0.6               |

**CONCLUSION.** These results suggest that in sedated post cardiac surgery ventilated patients, DPEP is a valid predictor of the hemodynamic effects of VE. Indeed, the higher DPEP is before VE, the greater will be the percent increase in SVI after VE.

**REFERENCES.** <sup>1</sup>: Bendjelid K et al, Crit Care Med 2000, 28 (12-S): A72.

## 14

## ITBV-GUIDED VOLUME THERAPY DIMINISHES DETRIMENTAL EFFECTS OF PEEP ON LIVER PERFUSION AND OXYGENATION

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**INTRODUCTION.** The detrimental effects of the application of PEEP on liver perfusion and oxygenation are well described. Furthermore it has been demonstrated, that volume loading diminishes these effects. But there is no evidence how to guide volume therapy and it remains unclear, whether volume loading alone restitutes liver perfusion and oxygenation at PEEP levels above 10 cm H<sub>2</sub>O. Therefore we investigated the effects of PEEP in an animal model of itbv-guided volume loading.

**METHODS.** 14 anesthetized and ventilated pigs were studied. Ultrasonic flow probes were placed around the hepatic artery and portal vein, catheters were inserted into the femoral artery, portal and hepatic veins. Animals were randomly assigned to two groups: group1, n=7 animals received fluid administration of 10 ml/kg/h cristalloids and group2, n=7 animals received additional colloid to maintain itbv at baseline level. After preparation, animals were allowed to stabilize for 2h before baseline values at ZEEP were taken. Then further measurements were made at PEEP levels of 5, 10, 15 and 20 cm H<sub>2</sub>O. ITBV was measured by the PICCO-System, oxygen metabolism was calculated according to Fick's Law.

**RESULTS.** see Table 1, all data are mean  $\pm$  sd, \*p < 0.05 vs. ZEEP, §p < 0.05 vs. group2

|                              | ZEEP group1 / PEEP 5 group1 group2 | PEEP 10 group1 / group2          | PEEP 15 group1 / group2         | PEEP20 group1 / group2          |
|------------------------------|------------------------------------|----------------------------------|---------------------------------|---------------------------------|
| MAP mmHg                     | 82 $\pm$ 5 / 81 $\pm$ 6            | 80 $\pm$ 11 / 80 $\pm$ 4         | 77 $\pm$ 9 / 82 $\pm$ 5         | 74 $\pm$ 9*§ / 88 $\pm$ 10      |
| Cardiac Output ml/min/kg     | 218 $\pm$ 39 / 213 $\pm$ 23        | 172 $\pm$ 34 / 189 $\pm$ 25      | 156 $\pm$ 34 / 169 $\pm$ 18     | 120 $\pm$ 29*§ / 177 $\pm$ 36   |
| ITBV ml/kg                   | 46 $\pm$ 9 / 38 $\pm$ 5            | 37 $\pm$ 9 / 38 $\pm$ 8          | 33 $\pm$ 7 / 36 $\pm$ 6         | 31 $\pm$ 5*§ / 37 $\pm$ 5       |
| HABF ml/min/kg               | 3.4 $\pm$ 1.1 / 4.5 $\pm$ 0.9      | 2.5 $\pm$ 0.8§ / 4.2 $\pm$ 0.8*§ | 2.1 $\pm$ 0.8*§ / 3.8 $\pm$ 1.0 | 1.7 $\pm$ 0.8*§ / 3.6 $\pm$ 0.9 |
| PVBF ml/min/kg               | 31 $\pm$ 7 / 31 $\pm$ 2            | 28 $\pm$ 7 / 28 $\pm$ 1          | 28 $\pm$ 8 / 28 $\pm$ 2         | 22 $\pm$ 3* / 25 $\pm$ 2*       |
| THBF ml/min/kg               | 34 $\pm$ 6 / 35 $\pm$ 2            | 31 $\pm$ 7 / 32 $\pm$ 1          | 30 $\pm$ 8 / 32 $\pm$ 2         | 24 $\pm$ 3*§ / 29 $\pm$ 2       |
| DO <sub>2</sub> liver ml/min | 82 $\pm$ 31 / 85 $\pm$ 15          | 72 $\pm$ 27 / 87 $\pm$ 16        | 63 $\pm$ 21 / 73 $\pm$ 15       | 53 $\pm$ 12*§ / 66 $\pm$ 15     |
| VO <sub>2</sub> liver ml/min | 20 $\pm$ 7 / 22 $\pm$ 2            | 22 $\pm$ 5 / 28 $\pm$ 6          | 21 $\pm$ 6 / 27 $\pm$ 1         | 27 $\pm$ 8 / 31 $\pm$ 3         |

**CONCLUSION.** ITBV-guided volume loading maintains hepatic arterial blood flow and total hepatic blood flow up to a PEEP level of 15 cm H<sub>2</sub>O. Furthermore the decrease in oxygen delivery to the liver is significantly diminished, while oxygen consumption remained unchanged. Nevertheless volume loading alone does not reconstitute liver perfusion and oxygenation above a PEEP level of 15 cm H<sub>2</sub>O.

## 15

## ROLE OF ATRIAL STRETCH IN THE ACUTE RELEASE OF ATRIAL NATRIURETIC PEPTIDE

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**INTRODUCTION.** Atrial natriuretic peptide (ANP), a hormone secreted by the cardiac atria in response to changes in pressure as measured by stretch receptors in the atria wall, has a spectrum of renal, hemodynamic and endocrine actions, all of which serve to reduce the elevated blood volume. In patients (pts) with cirrhosis of the liver plasma levels of ANP are attributable to several factors: high blood volume, effective hypovolemia, hyperdynamic circulation, posture, intraabdominal and intrathoracic pressure, sodium intake and drug administration. The aim of the study was to assess postparacentesis hemodynamic and neurohumoral changes and the influence of the paracentesis, bed rest 24 hr before and after the paracentesis and volume replacement on the acute release of ANP in pts with tense ascites in Child-Pugh C cirrhosis.

**METHODS.** 40 pts with Child-Pugh C liver cirrhosis and tense ascites, without toxic cardiomyopathy, were randomly allocated into 4 groups. 30 pts (groups 1,2,3) were treated with paracentesis (6 l) associated with plasma volume expansion (200 ml 20% HA, 600 ml FFP, 900 ml solution of synthetic gelatin, which were doses with comparable oncotic power) and bed rest 24 hr before and after the procedure vs. 10 pts (group 4) treated with paracentesis, no volume replacement and bed rest. MAP, pulse rate, plasma renin activity, plasma aldosterone concentration, plasma ANP levels, urine flow rate and creatinine clearance were measured before, 6 hr after start of the trial and on the 2nd 3rd and 6th day.

**RESULTS.** Paracentesis of 6 l of ascites without plasma volume expansion and no bed rest 24 hr before and after the procedure is associated with statistically significant hypotension ( $p = 0.000$ ), tachycardia ( $p = 0.000$ ), increase in plasma renin activity ( $p = 0.024$ ), increase of plasma aldosterone concentration ( $p = 0.000$ ), decrease in plasma ANP levels (NS) and renal impairment measured with creatinine clearance ( $p = 0.046$ ). There was no statistically significant difference in basic plasma ANP levels (pg/ml) between groups 1,2,3 ( $38,87 \pm 67,84$ ) and group 4 ( $18,60 \pm 18,86$ ). 6 hr after the procedure there were marked (NS) increases in plasma ANP levels in group 1 ( $50,40 \pm 27,33$ ), group 2 ( $54,60 \pm 88,40$ ) and group 3 ( $72,90 \pm 118,82$ ) in contrast to group 4 ( $23,90 \pm 20,03$ ). Increase in plasma ANP levels was proportional to amount of volume replacement. On the 2nd day ANP levels were: groups 1,2,3 ( $42,20 \pm 88,03$ ) and group 4 ( $12,80 \pm 8,57$ ). On the 3rd day ANP levels had further decreases for groups 1,2,3 ( $35,67 \pm 66,42$ ), but they were never as low as in group 4 ( $16,00 \pm 16,65$ ). On the 6th day plasma ANP levels were similar to basic levels for all groups: groups 1,2,3 ( $35,30 \pm 61,71$ ) and group 4 ( $15,20 \pm 11,60$ ).

**CONCLUSION.** The results of our investigation indicate that cardiac release of ANP in response to volume expansion is not impaired in patients with Child-Pugh C cirrhosis of the liver and tense ascites. The main mechanism stimulating the acute release of ANP is atrial stretching, induced with volume replacement and is proportional to its amount.

## Oral Presentations

## The critically ill patient after ICU discharge – 16-20

## 16

## IS THE READMISSION RATE A USEFUL INDICATOR OF ICU QUALITY?

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**INTRODUCTION.** There is great need for useful quality indicators allowing better insight into the process of care. Monitoring of readmission (RA) to the ICU has been proposed, assuming that it may directly reflect the quality of care. However, regarding time span and population, RA has never been clearly defined. We wanted to know whether the inclusion of RA monitoring into a formal ICU quality assessment program was worthwhile in terms of identifying risky and potentially preventable situations resulting from premature ICU discharge.

**METHODS.** Descriptive study in a 10 bed multidisciplinary ICU of a 300 bed teaching hospital. RA was defined as any repeated admission of an ICU patient within 365 days. RA was further broken down into four categories (cat): (A: early in-hospital, B: late in-hospital, C: new hospitalization and, coronary heart disease). Included were all patients admitted at least once between Jan 94 and Dec 98. Cat A RA, defined as occurring within 4 days and with problems unresolved or undiagnosed during the ICU stay, were the main focus of interest.

**RESULTS.** During 5 years, among 4028 discharges, 428 individuals were readmitted on 516 occasions (some patients (pts) readmitted more than once). An average of  $83 \pm 11$  pts per year (11.6% of discharges) were readmitted within 365 days (interval: 51.8  $\pm$  6 days after discharge). Their SAPS II at RA within 365 days was significantly higher than on first admission (29.2 vs. 27.6;  $p = 0.048$ ). 204 (40%) of all RA took place during the first 4 days, 96 were classified as cat A. Average initial length of stay (LOS) of RA of cat A was 0.5 days longer than the following one ( $p < 0.05$ ) and the overall SAPS II per admission at the moment of RA was 2.8 points lower than on first admission. Cat A pts to be readmitted later on had a higher initial SAPS II, a longer initial LOS and were older than the non-readmitted. Of the 96 RA in cat A 65 were considered as non-preventable and 31 RA as preventable. Reasons for RA in this group were: respiratory, cardiovascular (coronary syndromes excluded), gastrointestinal, neurologic and postoperative. The largest number of potentially preventable RA was found in the respiratory group (19 out of 22), the identified reason being insufficient respiratory care at the time of ICU discharge. The 2nd largest group was the one with neurological problems where 5 out of 14 (38%) were considered preventable. In the other 3 subgroups less than 4% of the RA were considered preventable. 65% of the 31 RA considered preventable occurred within one day and another 19% on day two.

**CONCLUSION.** Monitoring of RA to the ICU is worthwhile, provided that only early events (within 2 days) and only selected pathologies are followed. Monitoring of respiratory RA within 2 days and of neurological RA within 1 day are useful markers of ICU quality allowing us to identify cases with insufficient care. Monitoring of RA due to other problems is not useful. Unspecific monitoring of RA without a narrow time limit and without targeting specific pathologies seems not worth the effort

## 17

## READMISSION TO THE ICU : A REVIEW OF RISK FACTORS AND OUTCOMES

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**INTRODUCTION.** The aim of the study was to determine the incidence, clinical features, causes and outcomes of patients readmitted during the same hospitalization in a multidisciplinary 10-bed intensive care unit in a 700-bed university teaching hospital during a 7-year period.

**METHODS.** Retrospective chart data review collected on all ICU admissions between January 1, 1995 and March 31, 2002. Data included patient demographics, ICU admission diagnosis patient co-morbid conditions, APACHE II and S.O.F.A admission scores in all patients and ISS scores in trauma patients. Length of mechanical ventilation and sedation, presence of tracheostomy, use of CPAP or T-piece during the weaning process, episodes of hypoxia, use of inotropes, length of ICU stay, time to readmission and outcome for every ICU admission were also recorded. Readmissions were classified as emergency or planned (elective surgery). Risk factors between survivors and nonsurvivors after readmission were analysed. Statistical analysis was performed with Chi-square test, independent T-test and Pearson's correlation. A p value < 0,05 was considered statistically significant.

**RESULTS.** A total of 3063 patients were admitted and overall mortality was 16,63 %. Readmission rate was 1,9% (n=60) with overall mortality of 16,7% (n=10). Neurological diagnoses (35%) and trauma (28,3%) were the most frequent reasons of admission. Patients with gastrointestinal diagnoses (GI) had the higher mortality rate (85,7%). Cardiorespiratory failure was the most prominent cause of emergency readmission (51,7%). Patients discharged from ICU with tracheostomy had better survival rate (96,15%) compared to those discharged with an oxygen mask (73,6%). Concerning all other studied parameters there were no significant differences between survivors and nonsurvivors.

|                       | Nonsurvivors<br>(n=10) | Survivors (n=50) | p value |
|-----------------------|------------------------|------------------|---------|
| APACHE II 1           | 11.6±5.46*             | 12.20±5.49*      | ns      |
| APACHE II 2           | 15.4±4.01*             | 10.98±6.48*      | 0.01    |
| SOFA 1                | 2.9±1.79*              | 3.72±2.32*       | ns      |
| SOFA 2                | 5.8±1.62*              | 3.70±2.81*       | 0.004   |
| Length of 1. ICU stay | 3.6±4.35*              | 11.78±12.19*     | 0.01    |
| Length of 2. ICU stay | 18.7±20.54*            | 10.76±15.91*     | 0.05    |
| Readmission           | 10/0                   | 32/18            | 0.02    |
| emerg./planned        |                        |                  |         |
| Tracheostomy          | 1                      | 25               | 0.02    |

\*values are mean±SD

**CONCLUSION.** Patients with trauma, GI and neurological diseases are at highest risk of requiring ICU readmission with cardiorespiratory failure being the main cause. Severity of illness, organ dysfunction, the presence of tracheostomy and emergency readmission seem to influence ICU outcome in an important manner. Intermediate care areas may help to avoid ICU readmission, prevent death and conserve hospital resources.

## 18

## ICU READMISSION AFTER "FAST-TRACK" CARDIAC SURGERY

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**INTRODUCTION.** The introduction of "fast-track" management to cardiac surgery has significantly shortened ICU length of stay (LOS). However, the effect of decreasing the ICU LOS on the readmission rate, has not been well studied and this was the aim of the present study.

**METHODS.** We prospective studied the incidence, causes, risk factors, secondary ICU LOS and mortality for ICU readmission. All patients were assessed by the modified Parsonnet score. Patients were divided into 2 groups: group 1, requiring readmission to ICU, and group 2, not readmitted to ICU.

**RESULTS.** Over the study period, 1572 patients (63.3% of total surgeries) were managed by the "fast-track". The readmission rate was 3.1% (49/1572 patients). Initial cardiac procedure was CABG in 41 cases, AVR in 6 and other procedures in 2 cases. Primary ICU LOS was 14.2(±2.9) hours for group 1 and 13.5(±3.1) hours for group 2 (p=NS). Secondary ICU LOS was 3.8(±2.1) days. Mortality rate was 5.7% (group 1) vs.0% (group 2). The modified Parsonnet score was significantly higher in group 1 (12.9 vs. 20.2, p<0.05). The reasons for readmission were respiratory distress (36.7%), renal insufficiency (14.3%), bleeding (12.2%), arrhythmia (10.2%), severe agitation (8.1%), CVA (4%) and other causes (7%). Predictors of ICU readmission were a "Modified" Parsonnet score > 15, poor LV function and a history of previous CHF.

**CONCLUSION.** The most common causes for readmission after "fast-track" cardiac surgery were related to respiratory and renal complications and these patients had a high mortality rate. Patients with poor preoperative cardiac function were at highest risk and the use of "fast-track" management in this group should be reassessed.

## 19

## A MODEL FOR PREDICTING HOSPITAL OUTCOME IN SURVIVORS AFTER INTENSIVE CARE DISCHARGE\*

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**INTRODUCTION.** The aim of this study was the development and validation of a predictive model to estimate the probability of hospital mortality in survivors at ICU discharge.

**METHODS.** A total of 962 consecutive critically ill patients who were ICU survivors were studied during a 4 year period. Coronary care or cardiac surgery patients, and those under 18 year-old were excluded. Clinical variables, demographic data, and length of ICU stay were recorded. Severity scores at ICU admission APACHE II, APACHE III (APS III), and SAPS II, and individual probabilities of hospital mortality from APACHE II, SAPS II, and MPM II (0 and 24 hours) were calculated in the first ICU day. APACHE II, APS III, and SAPS II scores were also calculated at ICU discharge. Decreases or increases in APACHE II, APS III, and SAPS II points at ICU discharge with respect to ICU admission (D) were calculated in each patient. After follow-up, the hospital outcome was recorded.

**RESULTS.** Variables found as predictive of hospital mortality after ICU discharge by discriminant analysis were: age, MPM II-24, length of ICU stay, and difference between APS III values at ICU discharge and ICU admission (D<sub>APS III</sub>). The logistic model was developed on the first 481 consecutive patients, and it showed the following regression coefficients: b<sub>0</sub> = -5.1835; b<sub>1</sub> = 0.0352; b<sub>2</sub> = 3.0190; b<sub>3</sub> = 0.0182; and b<sub>4</sub> = 0.0295, and logit = b<sub>0</sub> + b<sub>1</sub> (age) + b<sub>2</sub> (MPM II-24) + b<sub>3</sub> (days of ICU stay) + b<sub>4</sub> (D<sub>APS III</sub>), where the probability of hospital mortality after ICU discharge is given by Pr = e<sup>logit</sup> / (1 + e<sup>logit</sup>). Model validation on the next 481 cases showed values of Hosmer-Lemeshow C statistic = 14.82 (10 degrees of freedom; p = 0.15); and area under the ROC curve = 0.703.

**CONCLUSION.** Risk estimation of hospital mortality after ICU discharge may be a useful parameter for the evaluation of the efficiency of intensive care units in the future.

**REFERENCES.** \*The EPICURE Study ([www.epiCure.org](http://www.epiCure.org)) = Epidemiological Projects for ICU Research and Evaluation

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## 20

## ELDERLY PATIENT IN CRITICAL CARE UNIT: FOLLOW UP 8 MONTHS AFTER HOSPITAL DISCHARGE.

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**INTRODUCTION.** The current opinion that elderly have poor benefits of critical care unit (CCU) stay, increase sometimes suffering or serious social cases. That's why we're frequently collated with ethical and economic problems, which difficut the decision respects to the elderly interment in CCU.

**METHODS.** It was included in the study, all the elderly with >65 years old, interned in the CCU, during a 4 years period between 1/1/1997 and 31/12/2000. The clinic evolution was evaluated by daily doctor's registers observed elderly hospital evolution until discharge. The severity of illness index was evaluated by the Acute Physiology and Chronic Health Evaluation APACHE II scoring system. QOL of survivors was evaluated in follow up interview 8 months after discharge by Barthel index that includes 30 questions that approach the activities daily living (ADL), classifying the patients on: self-sufficient (SS), partially dependents (PD) and disability (D). The data were analysed using the Student t test and expressed as mean ±SD was considered significant a p<0.05. Commercial software package (SPSS version 7.5).

**RESULTS.** In that period 176 elderly patients with >65 years old were admitted in CCU who represented 35.3% (502) of general population in the same period. 51.7% male and 48.3% female. The average age was of 72.2±5.4 years. The input average APACHE II was 20.7±6.5. The admission diagnostic was: respiratory failure 92 (Pneumonia, chronic bronchia disease, cardiac failure, trauma patient and sepsis), 63 programmed surgeries, 15 emergent surgeries and other situations 7. The totality of elderly needed artificial ventilation for average time 6, 3 days, and the length stay in CCU was 8, 7 days. Mortality in CCU elderly 27 (17, 2%); in hospital 37, after transference from CCU (in-hospital mortality 36.4%). Got discharge 112 (63, 6%) with check consultation for 8 months later. In this period they death at home 14, lacked to consultation 22, in 14 cases QOL test was made by telephone and 62 was present at interview. We included in the survival and QOL study 76. Cumulative survival was 87,5% at 8 months, TI=56(73.7%), D=14(18,4%) and PD=6 (7,9%), 41(53,9%) kept their previously interment activity. It did not have statistically significant differences (p<0.05) between deceased and survivors respect to age, sex, length stay in ICU and artificial ventilation time. The statistic difference was significantly higher for APACHE II and risk of mortality calculated to admission, to deceases respect survivors.

**CONCLUSION.** APACHE II was an efficient predictor of prognostic and the mortality of elderly in ICU. Eight months after hospital discharge a great number of survivors kept the daily living activities (QOL)(73, 7%) and 53.9% kept their previously interment way of life.

**REFERENCES.** 1. Capuzzo M, Bianconi m, Contu P, Pavoni G, Gritti G; Survival and quality of life after intensive care. Intensive Care Medicine(1996) 22(9):947-953

## Oral Presentations Auditing ICU practice – 21-25

21

### ERRORS IN ICU: ROLE OF AUDIT LOOP

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**INTRODUCTION.** The increasing technology and workload of an intensive care unit lead to a number of adverse incidents, whose 63% are due to human errors. Some of these could be easily avoided by analysing their incidence, cause and nature, and by consequently modifying ICU habits. An observational study had been conducting in our ICU (13 beds in 7 rooms) when a failure of the gases delivery system happened, forcing us to temporarily reduce the ICU in 4 rooms with 8 beds, without central monitoring. The aim of our study was to compare between the 12 beds and 8 beds ICUs, to obtain data that could be used for the project of the new ICU.

**METHODS.** Two periods of 6 weeks were considered, before and after ICU move (7 Oct – 17 Nov 2001; 16 Jan – 26 Feb 2002). Anonymous forms 2 were administered to the involved staff: anaesthetists (experts and residents), nurses and auxiliaries. Critical incident reporting were collected, including date, hour, kind of error, eventual injury and solution of the incident. Errors were classified into: patient area, equipment, nursing, transfusions and drugs. Infections were not included in our study.

**RESULTS.** 48 and 27 patients were respectively admitted in the ICU (median SAPS2 42 vs 45). 45 vs 33 errors were recorded in 33 (68.75%) vs 20 (74.1%) patients, at a rate of 1.36 vs 1.65 errors for involved patient. Types of errors, observed before and after ICU move, are shown in table 1. 21 of 33 errors (64%) were recorded in the first 10 days after ICU move (last column table 1). 8.24% vs 9.82% (26.25% in the first 10 days) errors per total stay in hospital days were reported. None of the errors resulted in patient death.

|              | 42 days BEFORE | 42 days AFTER | First 10 days AFTER |
|--------------|----------------|---------------|---------------------|
| Patient area | 2 (4.4%)       | 3 (9.1%)      | 2 (66.7%)           |
| Equipment    | 6 (13.3%)      | 8 (24.2%)     | 6 (75%)             |
| Nursing      | 20 (44.4%)     | 10 (30.3%)    | 5 (50%)             |
| Transfusions | 0              | 1 (3%)        | 1 (100%)            |
| Drugs        | 17 (37.7%)     | 11 (33.3%)    | 8 (72.7%)           |

**CONCLUSION.** Increased incidence of errors after ICU move, especially in the first 10 days, could be explained with the reduced area available for every patient, the absence of central monitoring and the changed identification number of beds. Despite this general raise, paradoxical reduction in the most frequent types of errors (nursing and drugs) was observed, due to increased nurse/patient ratio (1:1.8 vs 1:1.1). The study demonstrates that most of the errors in ICU must be considered a preventable phenomenon, even in temporary conditions. Errors reporting and following staff discussion, on obtained data, close the audit loop and can be used to focus where to address resources and how to improve patients' safety.

**REFERENCES.** 1 K.E.J. Gunning Intensive Care Med (2000) 26:8-10  
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### COMPREHENSIVE CRITICAL CARE, A MODERNISATION PROGRAMME FOR THE DEVELOPMENT OF CRITICAL CARE SERVICES

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**INTRODUCTION.** In May 2000, the Department of Health published a review of adult critical care services, Comprehensive Critical Care. It outlined a radical modernisation programme to develop consistent and inclusive critical care services in England. It described a speciality that is based on the severity of illness of each patient. The service is to be delivered to specified uniformed standards regardless of location and parent speciality, with staff numbers, skills and expertise reflecting the complexity generated by the condition of individual patients. The characteristics of the service were considered to be: An integrated, hospital wide approach to critical care services; a networked service across hospitals in a defined geographical area; standardisation of work force planning; a data collecting culture promoting evidence based practice.

**METHODS.** GBP 142.5 million was allocated to the development of innovative critical care services in 2000 including GBP 2.5 million for a National Comprehensive Critical Care. As part of the Modernisation Agency, the Programme is using established collaborative methodology aimed at improving access, experience and outcomes for patients with potential or actual need for critical care. Each hospital with critical care services has been supported in developing a multiprofessional, inclusive Critical Care Delivery Group which takes responsibility for the delivery of a whole hospital integrated critical care service. Each hospital has to be affiliated to a network that takes responsibility for service provision to all critically ill patients in the network. These are managed by multiprofessional Steering Groups. A project team in each network is planning, implementing and analysing local improvement projects using Rapid Cycle, Small Scale Change and Redesign methodology. The national team has organised a series of learning events, workshops and seminars so that training, experiences and good practice are shared. All professional bodies with an interest in the care of the critically ill have been involved in the programme.

**RESULTS.** The majority of the 228 hospitals in England with critical care services have Critical Care Delivery Groups and all are members of one of the 29 Critical Care Networks. Each network is developing common standards, policies and audit tools based on nationally agreed guidelines. The number of critical care beds in England has increased by 28% since January 2000 from 2362 to 3030, with more equipped to the highest level. The number of reported transfers of critically ill patients for non-medical reasons has dropped by 32% over 12 months. 185 improvement projects are in place across England with a system being developed for identifying patient and carer experiences.

**CONCLUSION.** The implementation of the recommendations contained in Comprehensive Critical Care is leading to changes both in the organisational structure and in the way that critical care services are delivered. The hope is that these improvements will lead to a patient focused, sustainable, cost effective, quality service

**REFERENCES.** Comprehensive Critical Care, Department of Health, London, England

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### PATTERNS OF UTILIZATION OF INTENSIVE CARE BEDS FOR INTERMEDIATE CARE IN A FLEXIBLE ICU

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**INTRODUCTION.** Intermediate care units mitigate personnel and financial requirements of health care systems and offer advantages for the moderately ill patient. Many hospitals still lack intermediate care (IC) units and utilize the post-anesthesia care unit (PACU) as an overflow location. Objective: To prospectively document total and IC patient bed occupancy in a flexible general intensive care unit (GICU) over a period of 41 months. Hypothesis: A flexible ICU accommodates IC patients irrespective of total ICU bed occupancy.

**METHODS.** A prospective observational study, performed in an 11 bed GICU of a tertiary medical care facility where overflow of GICU patients is admitted to the PACU. Data for the study was obtained from an 08:00 AM registry performed daily by the senior staff physicians of the GICU. The registry included the total number of GICU patients and "intent to treat" plans regarding same-day discharge or discharge-delay of patients designated as IC. Patients were designated as IC according to 4 clinical requirements: 1. Physiological monitoring; 2. Intensive nursing care; 3. Respiratory care; 4. Continuous intravenous drug therapy.

**RESULTS.** Bed occupancy in the unit fluctuated between 4 to 16 beds, exceeding the allotted number of beds (11) in 377 days out of 1285. Relative flexibility allowed the daily bed occupancy to distribute in a Gaussian-like manner around the formally allotted number of beds in the unit (Table, last row). No change in the average number of IC patients scheduled to remain in the GICU was observed as bed occupancy rose. The number of IC patients scheduled to be discharged increased slightly with increasing bed occupancy (Table, center rows). Average daily bed occupancy rose from 9.7±1.7 (SD) in 1997 to 11.07±1.9 in 2000. A rise was also observed in the average daily number of IC patients scheduled to be discharged from the unit: from 0.4± 0.6 in 1997 to 0.6±0.8 in 2000, while in patients scheduled to remain no difference was found: 1.3±1.0 in 1997 and 1.4±1.2 in 2000.

| Bed occupancy               | 4 | 5 | 6  | 7  | 8   | 9   | 10  | 11  | 12  | 13  | 14 | 15 |
|-----------------------------|---|---|----|----|-----|-----|-----|-----|-----|-----|----|----|
| Avg. # IC pts to remain     | 1 | 0 | 1  | 2  | 1.4 | 1.5 | 1.6 | 1.6 | 1.5 | 1.6 | 2  | 1  |
| Avg. # IC pts for discharge | 0 | 0 | 0  | 0  | 0.3 | 0.3 | 0.5 | 0.7 | 0.7 | 0.8 | 1  | 1  |
| Incidence of bed occupancy  | 1 | 5 | 17 | 40 | 103 | 174 | 284 | 284 | 210 | 107 | 49 | 9  |

Table : Flow of IC Patients as a Function of Bed Occupancy (27/7/97 – 31/12/00)

**CONCLUSION.** The model of a flexible ICU allows apparent freedom in triage decisions, with the PACU acting as a buffer to absorb part of the GICU workload. There was a rise in the scheduled discharge of IC patients with rising bed occupancy, while the proportion of IC patients scheduled to remain did not show a similar trend. This may have contributed to the relatively low percentage of IC patients. Utilization of the PACU as a buffer for ICU expansion may be a practical and cost effective option, allowing concurrent care for intensive and IC patients.

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### FUNDAMENTAL CRITICAL CARE SUPPORT (FCCS) IN BRAZIL: THE IMPACT ON CRITICAL CARE STAFF EDUCATIONAL PR

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**INTRODUCTION.** Several studies support the argument that trained critical care staffing is related to better patients outcome. The Brazilian Critical Care Society (AMIB) has identified the FCCS multidisciplinary staff training course to be applied through the continuing education in Brazil.

**METHODS.** The Brazilian FCCS committee was approved by AMIB and FCCS/SCCM to implement FCCS in Brazil. An editorial staff started translating the textbook to Portuguese. An advanced instructor FCCS course was conducted to recognized Brazilian physicians leaders in critical care education from different states of the country. Therefore, regional instructors and training units could start at almost all places from Brazil to become easily available for continuing education and reducing costs. The FCCS board is composed by consultants responsible for maintaining the quality, previously approved by FCCS/SCCM, a director team who organize the courses and a secretary coordination that provides the background. The course follows the same model of organization as FCCS/SCCM. The staff is composed by 1 consultant, 1 director, 3 instructors. The provider course is offered to physicians, nurses and therapists. The requirements for successful completion of the provider course is the same of FCCS/SCCM. To become an FCCS Brazilian instructor, the physician might have the specialist title recognized by AMIB, have passing grades >8 (post- test), and indicated by the consultant after satisfactory performance in 3 skill stations. The course, the instructors and the director are submitted to student's evaluation and further to the consultant committee who reviews policies and procedures.

**RESULTS.** From January 2000 to August 2001, there were 67 FCCS provider courses through Brazil, applied to 1716 health professional; 72.03% reached the requirements for successful. The number of courses were proportional to the ICU's numbers on each state, mostly concentrated in the southeast (58%) and south Brazil (18%). Satisfaction index was high among the participants.

**CONCLUSION.** Conclusions: The FCCS course had a good impact in a continental country. It is a way to provide the same information among intensivists and non specialists improving quality of critical care education.

**REFERENCES.** Data base Brazilian Society of Critical Care Medicine

## 25

## EVALUATION OF PERFORMANCE IN NINE INTENSIVE CARE UNITS

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**INTRODUCTION.** Scoring systems to predict hospital mortality may be used to measure the effectiveness in intensive care by Quality of Care Index (QCI). The length of stay (LOS) adjusted for severity of illness (Resource Use Index-RUI) has been used as an indirect indicator of efficiency. Recently, the APACHE III has been customized to Spanish intensive care units. The objective was to evaluate performance using customized APACHE III and adjusted LOS in 9 ICUs in Spain.

**METHODS.** Prospective multicenter study in nine mixed medical-surgical ICUs. 1784 patients were admitted consecutively from November 1999 to March 2000. Patients under 16 years old, length of stay in ICU less than 24 hours, admitted to implant pacemaker or readmitted in ICU in the same stay hospital were excluded. Predicted hospital mortality rates were calculated using the logistic regression model detailed in the original article. LOS was computed as exact-LOS. Effectiveness (QCI) was computed as the mean observed mortality to mean expected mortality ratio with confidence interval 95%. Efficiency (RUI) was obtained by dividing the mean of observed weighted hospital days (WHD) by mean of expected WHD in each ICU. WHD is a measure of resource use which weights ICU days more heavily than non-ICU days. Expected WHD was adjusted by diverse variables with a model of multiple linear regression.

**RESULTS.** 1210 patients were included. Median ICU length was 3.06 days

|       | Number patients | Age (mean) | Observed Mortality | QCI (CI 95%)     | RUI  |
|-------|-----------------|------------|--------------------|------------------|------|
| 1     | 188             | 65.7       | 30                 | 0.83 (0.58-1.08) | 0.94 |
| 2     | 110             | 67.1       | 23                 | 0.80 (0.54-1.07) | 0.79 |
| 3     | 93              | 51.6       | 31                 | 1.16 (0.87-1.44) | 1.70 |
| 4     | 84              | 63.0       | 14                 | 0.86 (0.48-1.23) | 0.90 |
| 5     | 113             | 60.5       | 38                 | 0.87 (0.67-1.07) | 1.07 |
| 6     | 111             | 58.9       | 30                 | 0.98 (0.71-1.24) | 1.24 |
| 7     | 136             | 63.3       | 39                 | 0.95 (0.74-1.17) | 0.83 |
| 8     | 253             | 61.7       | 32                 | 0.82 (0.58-1.07) | 0.98 |
| 9     | 122             | 60.5       | 25                 | 0.90 (0.62-1.17) | 0.99 |
| Total | 1210            |            | 262                | 0.90 (0.82-0.99) | 1.00 |

**CONCLUSION.** In our study, the confidence interval 95% QCI included 1 in eight hospitals. Three hospitals obtained RUI over 1

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## Oral Presentations

### To die (from nosocomial infection) ... or not to die – 26-30

## 26

## OUTCOME EVALUATION IN ICU PATIENTS WITH CATHETER-RELATED BLOODSTREAM INFECTIONS.

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**INTRODUCTION.** Catheter-related bloodstream infection (CR-BSI) is a frequent complication in ICUs, associated with considerable mortality.

**METHODS.** To investigate the clinical impact of CR-BSI, a retrospective matched cohort study (Jan 1992-Dec 2000) was performed in which all ICU patients with CR-BSI were defined as cases (n=156). Cases were matched with control subjects (1:2-ratio), (n=312) on basis of the APACHE II system: an equal APACHE II score ( $\pm 2$  points) and diagnostic category. As expected mortality can be derived from this severity of disease scoring system, this matching procedure results in an equal expected mortality for cases and controls.

**RESULTS.** 46% of CR-BSI were due to coagulase-negative Staphylococci, 20% due to other gram-positive bacteria (9% Staphylococcus aureus), 24% due to gram-negative bacteria and 12% due to Candida species. Eighty-five% of the catheters were removed within a one day delay. There was no difference between cases and controls in age (resp. 52 $\pm$ 17.8 vs. 54 $\pm$ 17.8 year; P=0.228) and APACHE II scores (resp. 21 $\pm$ 8.2 vs. 21 $\pm$ 8.0; P=0.982). Cases had more respiratory failure (90.4% vs. 75.3%; P<0.001), acute renal failure (25.0% vs. 13.1%; P=0.001) and hemodynamic instability (72.4% vs. 50.3%; P<0.001). Cases had a longer ICU stay (39 $\pm$ 31.4 vs. 12 $\pm$ 13.2 days; P<0.001) and length of mechanical ventilation (31 $\pm$ 23.4 vs. 11 $\pm$ 12.6 days; P<0.001). Hospital mortality rates for cases and controls were not different (resp. 28.8% vs. 32.7%; P=0.398). In a multivariate survival analysis the APACHE II related expected mortality was the only variable independently associated with mortality (HR: 1.55, 95% CI: 1.04-2.31; P=0.029).

**CONCLUSION.** Our data revealed that, after careful adjustment for severity of underlying disease and acute illness, CR-BSI are not associated with higher mortality in ICU patients. They are, however, associated with a significant morbidity and excess length of ICU stay.

**REFERENCES.** None

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## EVALUATION OF THE OUTCOME OF CATHETER-RELATED BLOODSTREAM INFECTION: IMPORTANCE OF THE PATHOGEN

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**INTRODUCTION:** To define the attributable mortality and the increase in length of stay due to catheter-related bloodstream infection (CRBI), differentiating episodes caused by coagulase negative staphylococcus (CNS) from high pathogenic microorganisms.

**METHODS.** Paired case-control study (1:1). As cases were included all ICU-acquired CRBI (>48 hours), requiring for the diagnosis a positive blood culture and concomitant isolation of the same microorganism in a semiquantitative culture of the catheter tip. Duration of venous catheterization for control subjects was always at least as long as the cases. The other conditions necessary to constitute a matched pair were: (1) the level of severity measured by APACHE II score at admission to the ICU ( $\pm 4$  points), (2) same diagnostic category according to Knaus classification, (3) age ( $\pm 5$  years). Statistical analysis was done using McNemar's and Wilcoxon's test for paired data.

**RESULTS.** A CRBI was diagnosed in 57 patients: 27 due to CNS, and 30 to other microorganisms (Staphylococcus aureus 8, Acinetobacter baumannii 6, Candida spp 5, Klebsiella pneumoniae 3, others 9). No controls were found for 6 cases. ICU mortality of cases due to CNS was 17.4 % and 21.7 % for their controls (p value not significant). ICU mortality in non-CNS episodes was 46.4 % in cases and 28.6% in the controls (p=0.06). Among the survivors, the ICU stay was increased only in the episodes caused by non-CNS microorganisms (seven days).

**CONCLUSION.** We fail to demonstrate an attributable mortality due to CRBI. A clear trend to a higher mortality and increase in stay is shown only in non-CNS episodes.

## 28

## IS INFECTION WITH MULTIRESTANT MICROORGANISMS WORSENING THE OUTCOME OF ICU PATIENTS?

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**INTRODUCTION.** Our hypothesis was that the outcome of ICU patients in whom an infection with multiresistant microorganisms was proved could be worse than the outcome of patients infected with sensible strains.

**METHODS.** Data were retrospectively collected for patients admitted between January 1997 and december 2001 in an 8 bed mixed ICU. The following parameters were compared: SAPS II score, length of stay (LOS) in the ICU, LOS in ICU before the infection was proved, mechanical ventilation (MV) free-days, hemodialysis (HD) free-days, the use of antibiotics (AB) before infection was proved (we excluded prophylactic antibiotherapy), ICU and in-hospital mortality. CDC criteria were used to define infection. Data were compared using analyze of variance (ANOVA) method.

**RESULTS.** We included 515 infected patients of whom 136 patients had an infection with multiresistant microorganisms. We found multiresistant species of Pseudomonas aeruginosa in 45 cases, Enterobacter in 38 cases, Acinetobacter baumannii in 28 cases, Enterococcus in 15 cases and MRSA in 10 cases. The results are presented in the following table:

|                                   | Resistant microorganisms | Sensible microorganisms | P value |
|-----------------------------------|--------------------------|-------------------------|---------|
| SAPS II score                     | 30 $\pm$ 2               | 29 $\pm$ 2              | NS      |
| LOS (days)                        | 18 $\pm$ 6               | 12 $\pm$ 3              | 0.03    |
| LOS before infection was proved   | 8 $\pm$ 3                | 5 $\pm$ 3               | 0.03    |
| Mechanical ventilation free days  | 8 $\pm$ 2                | 7 $\pm$ 3               | NS      |
| HD free days                      | 9 $\pm$ 1                | 8 $\pm$ 2               | NS      |
| ICU mortality                     | 40/136 (29%)             | 108/379(26%)            | NS      |
| In hospital mortality             | 8/136(6%)                | 16/379(4%)              | NS      |
| Previous antibiotic therapy(days) | 80/136 (59%)             | 118/379(31%)            | 0.02    |

**CONCLUSION.** Our results show that there is no difference between the outcome of ICU patients infected with multiresistant microorganisms and patients infected with sensible strains.

## 29

## IMPACT OF FUNGAL CANDIDA COLONIZATION AND INFECTION IN CRITICALLY ILL PATIENTS.

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**INTRODUCTION.** Critically ill patients with prolonged stay in the ICU, develop frequent fungal colonization (FC) and infection (FI). Objective To assess the impact on ICU (ICU-M) and hospital mortality (H-M) of FC and FI.

**METHODS.** Multicenter prospective cohort study of Candida spp colonization and infection in critically ill patients admitted to UCI >7 days. Surveillance samples were taken weekly. Definitions: FC: isolation of Candida in surveillance samples and FI in significant samples. Intrinsic and extrinsic risk factors including FC and FI were related to mortality. Statistical analysis: Multiple logistic regression (MLR).

**RESULTS.** A total of 1765 patients were studied; 880 developed FC and 105 FI. In 437 patients, 521 antifungal treatments were done. Five hundred thirty five patients (30%) died in the ICU (UM) and 159 (9%) in wards after ICU discharge, therefore, hospital mortality (HM) was 39%. Patients with FI had an UM and HM of 53,2 and 60,9%; in FC were 25,6 and 33,9 %, and in patients with no colonization no infection. (NCI) of 31,4 and 41,2%, (p<0.001). HM was similar in FC/FI due to C albicans, 41,6 and C no albicans 41,7%. Several RF were related to mortality in UCI, but the study of MLR selected the following (Odds Ratio): mechanical ventilation 2,9, radiotherapy 4,2; extrarenal deuration 3,66; hematological malignancy 3,26, fungal infection 2,21; cardiac failure 1,70; medical pathology 1,62; diabetes 1,50; NPT 1,46; APACHE II >15 1,37; age 1,03 and enteral nutrition 0,43. For hospital mortality, RF were: mechanical ventilation 4,76 medical pathology 2,14; NPT 1,58; surgical patología 1,55; APACHE II>15 1,50; anaerobic antibiotics 1,47; diabetes 1,45 and age 1,03. Finally, the group of patients with fungal infection, independent factors were: medical pathology 7,97; APACHE II>15 2,96; age 1,02 and peritoneal focus 0,32.

**CONCLUSION.** In critically ill patients, fungal infection (but no colonization) was an independent factor for mortality in ICU, but no for hospital mortality. Underlying disease, age and severity were the mayor determinants for the outcome

Grant. Gilead

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## EFFECTS OF SELECTIVE DECONTAMINATION OF THE DIGESTIVE TRACT ON MORTALITY AND ANTIBIOTIC RESISTANCE

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**INTRODUCTION.** Meta-analyses have suggested that Selective Decontamination of the Digestive Tract (SDD) may decrease mortality in critically ill patients, but this has never been shown in individual prospective, controlled, randomized trials. Moreover, fear exists that SDD may increase the emergence of (multi)resistant bacteria in these patients. We set up a study sufficiently powered to determine the effects of SDD on mortality of critically ill patients and on the emergence of antibiotic resistance in colonizing bacteria.

**METHODS.** From September 1999 until December 2001, 934 consecutive patients (both surgical and medical) with an expected duration of mechanical ventilation > 48 h were randomized and treated with either SDD (4 times daily oropharyngeal and intestinal application of tobramycin, polymyxine E and amphotericin B (TPA), and a 4-day intravenous course of cefotaxim) or standard treatment. Rectal, pharyngeal, axillary and wound colonization with methicillin resistant *S. aureus* (MRSA), vancomycin resistant enterococci (VRE), and tobramycin, polymyxin, ciprofloxacin and ceftazidim resistant *P. aeruginosa* and other gram-negative bacteria was assessed weekly. P-values are by Fisher's exact or Mann-Whitney U test.

**RESULTS.** No differences were found in baseline characteristics of both study groups.

|                                    | SDD (n=468) | Control (n=466) | ODDS-ratio (95% CI) | P-value |
|------------------------------------|-------------|-----------------|---------------------|---------|
| ICU-mortality (%)                  | 14.8        | 22.9            | 0.6 (0.4-0.8)       | 0.002   |
| Hospital-mortality (%)             | 24.2        | 31.2            | 0.7 (0.5-0.9)       | 0.02    |
| ICU length-of-stay (days)          | 11.6        | 13.4            |                     | <0.001  |
|                                    | SDD         | Control         | ODDS-ratio (95% CI) | P-value |
| Tobramycin/ <i>P.aeruginosa</i>    | 13          | 13              | 1.0 (.5-2.3)        | NS      |
| Tobramycin/other gram-negative     | 20          | 47              | 0.4 (.2-.7)         | 0.001   |
| Imipenem/ <i>P.aeruginosa</i>      | 1           | 16              | 0.1 (.01-.5)        | <0.001  |
| Imipenem/other gram-negative       | 1           | 10              | 0.1 (.01-.8)        | 0.01    |
| Ciprofloxacin/ <i>P.aeruginosa</i> | 1           | 13              | 0.1 (.01-.6)        | 0.002   |
| Ciprofloxacin/other gram-negative  | 9           | 31              | 0.3 (.1-.6)         | 0.001   |
| Vancomycin/ <i>enterococcus</i>    | 4           | 5               | 0.8 (.2-3.1)        | NS      |
| Methicillin/ <i>S.aureus</i>       | 0           | 0               |                     | NS      |

Colonization with (multi)resistant bacteria (acquired during stay on ICU, number of patients)

**CONCLUSION.** In a setting with low prevalence of MRSA and VRE, SDD significantly decreases ICU- and hospital mortality of critically ill patients and decreases the length of stay on the intensive care unit. Moreover, SDD decreases colonization with (multi)resistant *P.aeruginosa* and other gram-negative bacteria.