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CRITICAL CARE

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**32ND INTERNATIONAL SYMPOSIUM
ON INTENSIVE CARE AND
EMERGENCY MEDICINE**

Brussels, Belgium
20-23 March 2012

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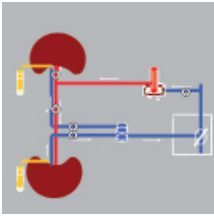
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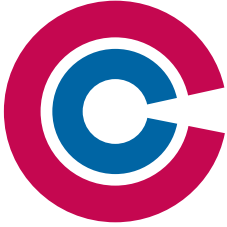
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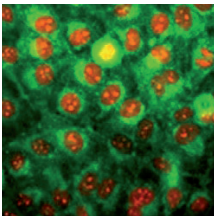
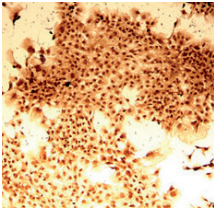


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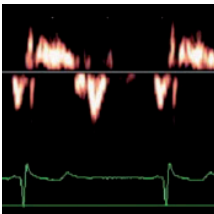
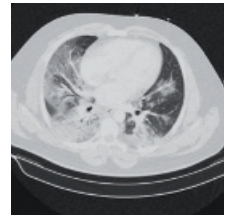
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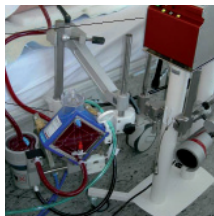
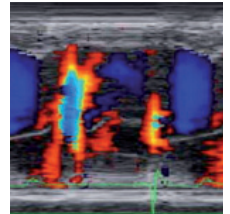
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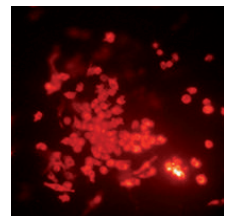
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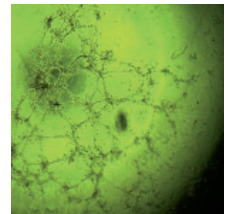
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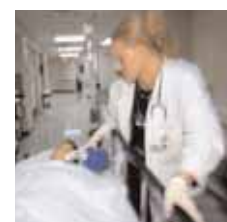
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Impaired innate and adaptive immunity of accelerated-aged Klotho mice in sepsis

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Introduction Sepsis is primarily a disease of the aged and 60% of sepsis occurs in patients older than 65 years, 80% of deaths due to sepsis occur in this age group. Klotho knockout mice (Klotho mice) develop a syndrome resembling human aging, and exhibit shortened life spans (8 weeks); however, details regarding the immunity of and immunological changes in Klotho mice after sepsis are still unclear. The purpose of the study is to elucidate the immunological changes that occur in Klotho mice after sepsis in order to identify therapeutic targets for sepsis that occurs in aged individuals.

Methods (1) Survival study: cecum ligation puncture (CLP) was performed to Klotho and wild-type (WT) mice and 4-day survivals were compared. (2) Cell analysis study: mice were sacrificed at 8 hours post CLP or sham surgery. Spleens, thymus, and serum were harvested for FACS analysis using caspase 3 as a marker for apoptosis, and blood for serum cytokine assay. Bacterial colony count in peritoneal lavage was also analyzed.

Results (1) Klotho septic mice started to die from 8 to 12 hours after CLP, and final survival of Klotho mice with CLP was significantly lower than that of WT with CLP (0% vs. 100%, $P < 0.01$). (2) Increased bacterial count in peritoneal cavity and decreased recruitment of neutrophils and macrophages to the peripheral cavity were observed in Klotho-CLP mice. Serum concentration of IL-6, TNF, and IL-10 were significantly higher in Klotho-CLP mice than those in the WT-CLP mice. A dramatically increased caspase 3 positive proportion in Klotho-CLP mice was observed in both flow cytometric and immunohistological analysis ($P < 0.01$).

Conclusion Poor survival in Klotho-septic mice may be associated with impaired bacterial clearance with decreased recruitment of neutrophils/macrophages in peritoneal cavity, elevated cytokines in serum, and increased apoptosis in thymus and spleen, following to impaired innate and adaptive immunity.

P2

IL-17A rs1974226 GG genotype is associated with increased susceptibility to Gram-positive infection and mortality of severe sepsis

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Introduction IL-17A plays a key role in host defense against microbial infection including Gram-positive bacteria. Genetic factors contribute

to the host defense. Whether genetic variation of IL-17A is associated with altered clinical outcome of severe sepsis is unknown.

Methods We tested for genetic association of IL-17A SNPs with susceptibility to infection and clinical outcome of severe sepsis using two cohorts of European ancestry (St Paul's Hospital (SPH) derivation cohort, $n = 679$; Vasopressin and Septic Shock Trial (VASST) validation cohort $n = 517$). The primary outcome variable was susceptibility to Gram-positive bacterial infection. The secondary outcome variable was 28-day mortality.

Results Of four tested tag SNPs (rs4711998, rs8193036, rs2275913, rs1974226) in the IL-17A gene, rs1974226 SNP was associated with altered susceptibility to Gram-positive bacterial infection in the derivation cohort (corrected $P = 0.014$). Patients who have the GG genotype of the rs1974226 SNP were more susceptible to Gram-positive bacterial infection, compared to the AG/AA genotype in the two cohorts of severe sepsis (SPH, $P = 0.0036$; VASST, $P = 0.011$) and in the subgroup having lung infection ($P = 0.017$). Furthermore, the G allele of the IL-17A rs1974226 SNP was associated with increased 28-day mortality in two cohorts (SPH, adjusted OR 1.44, 95% CI 1.04 to 2.02, $P = 0.029$; VASST, adjusted OR 1.67, 95% CI 1.17 to 2.40, $P = 0.0052$).

Conclusion IL-17A genetic variation is associated with altered susceptibility to Gram-positive infection and 28-day mortality of severe sepsis.

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P3

Prevalence of TLR4 single nucleotide polymorphisms (ASP299GLY, THR399ILE) in healthy subjects and septic patients, and association with outcome

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Introduction Our study aimed to determine the prevalence of functional SNPs (Asp299Gly, Thr399Ile) of TLR4 receptors, in healthy volunteers and septic patients in a Brazilian population and to correlate the presence of these polymorphisms in septic patients with clinical outcome.

Methods We verified the presence of polymorphisms ASP299GLY, THR399 ILE by PCR-restriction fragment length polymorphism followed by digestion with enzymes *NcoI* for SNP 299 and *HinfI* for SNP399 followed by electrophoresis for identification of alleles.

Results We observed a statistically significant difference between the genotypes of the Thr399Ile polymorphism and respiratory dysfunction, indicating a higher frequency than wild-type genotype in subjects with respiratory dysfunction than those without this condition ($P = 0.001$). We also observed a statistically significant difference between genotype groups formed by the Asp299Gly and Thr399Ile polymorphisms and respiratory dysfunction more often featuring group 299Selv/399Selv grupo299Het/399Het and less frequently in individuals with respiratory dysfunction than those without this condition ($P = 0.003$).

P83

Digitalized acoustic monitoring of lung congestion

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Introduction Changes in lung water are known to change breath sound acoustics [1]. Using two pig models, we observed that continuous elevation of lung sound amplitude may indicate an increase in total lung water content [2]. Here we report three cases of ventilated patients in whom continuous acoustic monitoring was done during extravascular lung water (EVLW) measurements.

Methods We retrospectively analyzed cases in which EVLWi (PiCCO) and other clinical parameters were measured, during continuous acoustic monitoring (VRI), using eight small sensors adhered to the anterior chest. A transmission factor (TF) was calculated, using the sound transfer function between different sensors. The TF changes in correspondence to changes in tissue density [1]. The difference in TF was calculated between recordings when pulmonary edema was observed (>7 ml/kg threshold accompanied with an increase of 2 ml/kg in the EVLWi) and when absent. Statistical analysis was made using a *t* test.

Results A total of 336 continuous acoustic recordings in three patients (acoustic monitoring was applied together with EVLWi measurements) were analyzed (146 recordings when lung edema was present; 190 with no edema). In all patients, the acoustic profile corresponded to changes in the clinical picture. In two of the cases, changes in acoustic profile were similar to the ones in the EVLWi and other clinical parameters (Figure 1). In one case, where there was stability in lung sound acoustics, EVLWi and other clinical parameters were also stable. Significant differences existed between recordings with edema (-3.61 ± 0.39) and without edema (-5.71 ± 0.15) ($P < 0.001$).

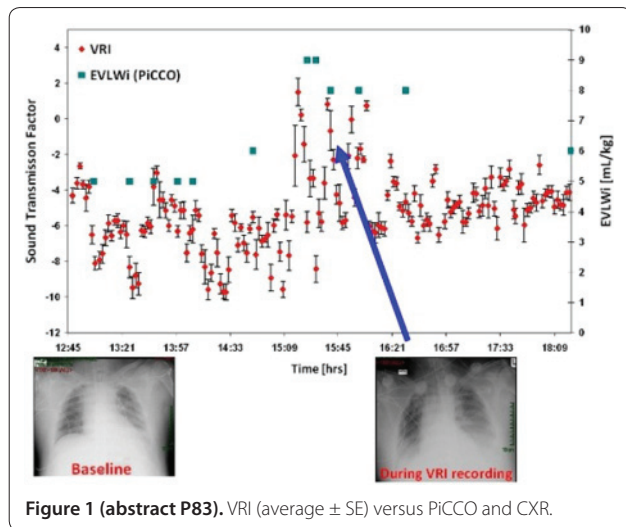


Figure 1 (abstract P83). VRI (average \pm SE) versus PiCCO and CXR.

Conclusion Changes in lung water tend to result in changes in the sound TF, due to changes in the tissue's density. These preliminary results indicate that monitoring lung sounds has the potential to monitor changes in lung water.

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P84

Usefulness of electrical activity of the diaphragm to detect intrinsic positive end-expiratory pressure during pressure support ventilation

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Introduction Intrinsic positive end-expiratory pressure (PEEPi) may add a substantial workload on respiratory muscles of patients undergoing

pressure support ventilation (PSV). This can be reduced with the application of an external positive end-expiratory pressure (PEEPe) [1]. However, an accurate measurement of PEEPi during PSV is challenging [2]. The aim of the present study is to investigate if the use of the electrical activity of diaphragm (EAdi) may yield the detection of PEEPi in patients undergoing PSV. We reasoned that if PEEPi was present the inspiratory airflow would start after EAdi had reached a given value (EAdi-threshold) necessary to generate the muscle pressure overcoming PEEPi.

Methods Ten patients with a clinical suspicion of PEEPi undergoing PSV were enrolled. Exclusion criteria were: age <18 years, hemodynamic instability, fever and $\text{PaO}_2/\text{FiO}_2 < 100$ mmHg. All patients were tested during PSV for seven steps of 3 minutes each with increasing PEEPe (2, 4, 6, 8, 10, 12, 14 cmH_2O). At the end of each step, PEEPi was estimated with an end-expiratory occlusion maneuver. During the study, we continuously recorded airway pressure, flow, volume and EAdi waveforms for off-line analysis. Data were analysed by linear regression and *t* test. $P < 0.05$ was considered statistically significant.

Results If PEEPi is present, EAdi-threshold is supposed to gradually decrease together with the raise of PEEPe; thus we divided patients into five responders for whom EAdi-threshold was significantly correlated with PEEPe, as opposed to five nonresponders. In the group of responders we observed significant correlations between the reduction of PEEPi and the increase of PEEPe ($r^2 = 0.86$, $P < 0.01$), and between EAdi-threshold and PEEPi at different PEEPe levels ($r^2 = 0.96$, $P < 0.001$). In the same group, respiratory rate (RR) decreased ($r^2 = 0.76$, $P = 0.01$), tidal volume increased ($r^2 = 0.71$, $P = 0.02$) and the peak of EAdi decreased ($r^2 = 0.94$, $P < 0.001$) at increasing levels of PEEPe. On the contrary, in the nonresponder group the increase of PEEPe was associated only with an increase of RR ($r^2 = 0.75$, $P = 0.01$).

Conclusion In five of 10 patients with clinical suspicion of PEEPi, when the PEEPe was increased we observed a decrease of EAdi-threshold, associated with improved respiratory mechanics, suggesting that EAdi-threshold could be a useful indicator for the presence of PEEPi.

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P85

Adequate lung sliding identification is not influenced by the level of academic or ultrasound training

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Introduction Rapid confirmation of the adequacy of endotracheal intubation is critical in the field of emergency medicine (EM). Methods confirming endotracheal tube (ET) position should have accuracy near 100%. Studies confirming ET position using lung sliding (LS) identification were done by physicians with extensive ultrasound (US) training using sometimes lengthy examination. These conditions are not easily reproduced in the emergency department. Our primary objective was to compare the accuracy of EM physicians with different levels of academic and US training to correctly identify presence or absence of LS on random short sequences of lung US. Our secondary objective was to determine if results were better when participants had the choice to abstain themselves in uncertain cases.

Methods We recorded in the operating room 280 short lung US sequences (one respiratory cycle), of present and absent LS of intubated patients and randomly presented them to two groups of EM physicians. Accuracy was calculated for different academic and US training: none, basic Focused Assessment with Sonography in Trauma (FAST), FAST and advanced cardiac US, fellowship in EM US. We compared them using an ANOVA test. Only participants in the second group where instructed to abstain from answering in uncertain cases and accuracy was compared to the first group using a Student's *t* test. The project was approved by the research and ethics committees.

Results Two medical students, 42 EM residents and 31 EM attendings participated. No difference in accuracy was shown between the subgroups of academic training with mean accuracies of 66.3% (medical