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The musculoskeletal ultrasound in critical care: Longitudinal evaluation (UK-MUSCLE) study: Severity of acute critical illness determines the degree of muscle wasting

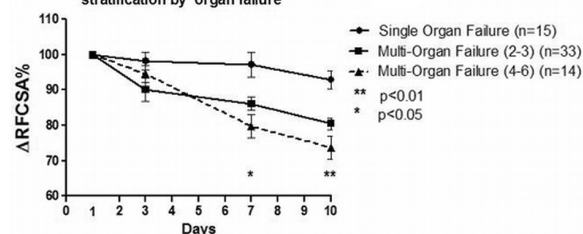
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Acute muscle wasting in critical illness is a major cause of disability amongst intensive care survivors. Limited data exists detailing sequential loss of muscle mass and histological changes. We hypothesised that loss of Rectus Femoris Cross-Sectional Area (RF_{CSA}) would be determined by illness severity and paralleled by reduction in myofibre cross-sectional area.

Methods: Critically ill patients were recruited within 24 hours of admission. Serial RF_{CSA} measurements were taken using B-mode ultrasound and stratified by numbers of failed organ systems. Serial vastus lateralis muscle biopsies were performed.

Results: 63 patients were analysed. The greatest RF_{CSA} reduction was observed in patients with multi-organ failure (MOF); 21.53±10.5% in MOF vs. 7.2±9.7% in 1 organ failure (SOF); $p < 0.0001$.

Time course of acute muscle loss during ICU stay: stratification by organ failure



Greater loss of RF_{CSA} was observed at day 3 in patients with (MOF) compared with (SOF) patients (8.7±16.3% in MOF vs. 1.8±9.6% in SOF; $p < 0.01$). Histological analysis confirmed reduction in type 1 fibre cross sectional area.

Conclusions: Measurement of RF_{CSA} by ultrasound can objectively track muscle loss early in critical illness. Patients with single organ failure tend to have preserved RF_{CSA}, whereas patients with multi-organ failure have significant muscle wasting. This observation is supported by the overall loss of cross-sectional area of type 1 fibres.

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Can lung ultrasound predict prone positioning response in ARDS?

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Introduction: Prone positioning (PP) is an alternative in the management of patients with severe ARDS. Among patients treated with that technique: only 70% are responders as they improve their P/F but at present we are not able to predict the patient's responsiveness. The aim of our study was to determine whether the lung aspect observed with US before PP can predict or not the prone positioning response.

Patients and settings: Prospective monocentric study (medical ICU university hospital Brest France) including patients with severe ARDS (P/F < 200 with FiO₂ ≥ 0.7). A standard lung US exam with 12 lung areas to explore (superior/inferior, anterior/lateral/posterior, right/left) was practiced before prone positioning (12 hours according unit's procedure). Before PP, after 2 hours of PP and 2 hours after turning back the patient supine, haematocrit parameters were collected.

Lung aspect was evaluated *a posteriori* by 3 physicians and graded in 4 stages (normal aspect, and 3 stages of lung compression). Observation of the P/F ratios course permitted to classify patients as responders or non-responders.

Statistics: Fisher's exact test

Results: 17 patients were enrolled in the study.

– For the early response: the absence of lung compression in anterior and superior areas is associated with an improvement of P/F ratio > 20 mmHg, whereas posterior areas aspect is not predictive of the response to PP.

– For the late response, we have not found any relationship between the lung aspect and the pp response.

Discussion: The first analysis showed that lung's US aspect could predict the patient's response to PP and could help physician in routine practice to place or not severe ARDS patient in PP.

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Treatment of hypercapnic respiratory failure with a novel extracorporeal CO₂ removal system

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Background: Extracorporeal CO₂ removal (ECCO₂R), a potentially valuable technique, has not been systematically evaluated in patients with hypercapnic respiratory failure. We describe the application of a novel single venous catheter, low blood flow, ECCO₂R device (Hemolung® Respiratory Assist System, ALung Technologies, Inc.).

Methods: Twenty three hypercapnic patients received ECCO₂R. Group 1 (n=7) consisted of patients with chronic obstructive lung disease on noninvasive ventilation with a high likelihood of requiring invasive ventilation, Group 2 (n=2) were patients who could not be weaned from noninvasive ventilation, Group 3 (n=11) were patients who could not be weaned from invasive ventilation, and Group 4 (n=3) were patients on invasive ventilation requiring lung protective ventilation techniques.

Results: The device was well tolerated, with complications and rates similar to those seen with central venous catheterization. Blood flow through the system was 430.5±73.7 ml/min, and ECCO₂R was 82.5±15.6 ml/min. Invasive ventilation was avoided in all patients in Group 1 and both patients in Group 2 were weaned; PaCO₂ decreased significantly ($p < 0.003$) with application of the device. In Group 3, three patients were weaned, in 3 patients ventilatory support was reduced, and one patient died due to a retroperitoneal bleed following catheterization. In Group 4, lung protective ventilation was enhanced by the ECCO₂R device.

Conclusions: This single catheter, low blood flow ECCO₂R system provided clinically useful levels of CO₂ removal in these hypercapnic patients. The system appears to be a potentially valuable additional modality for the treatment of hypercapnic respiratory failure.

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Effect of a closed loop ventilation strategy on the duration of ICU stay: A randomized controlled trial (interim analysis results)

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Background and aim: There are some studies suggesting that adaptive support ventilation (ASV), a closed loop ventilation mode, shortens the weaning duration in some patient groups. We aimed to investigate the effect of ASV on total duration of mechanical ventilation (MV), weaning and intensive care unit (ICU) stay when compared to pressure controlled ventilation (PCV), a conventional mode.

Materials and methods: Patients who were mechanically ventilated longer than 24 hours were randomized into ASV and PCV. Demographic data and total duration of MV, weaning and ICU stay, total number of manipulations, need for sedation and complications (self-extubation, ventilator associated pneumonia) were compared.

Results: Data are expressed as median (IQR). 96 patients (73 COPD) were enrolled between December 2011 and February 2012. Duration of weaning was 2 hours (2–7) in ASV and 4 hours (2–26) in PCV ($p = 0.013$). Number of manipulations were 2 (1–3) in ASV and 3 (1–6) in PCV ($p < 0.001$). When a subgroup analysis was done only on patients who could be weaned, in addition to the results above, duration of ICU stay was 4 days (3–7) in ASV while it was 7 days (5–10) in PCV ($p = 0.039$).

Conclusion: ASV seems to decrease the staff's workload, duration of weaning and ICU stay when performed from intubation until extubation. The present study is continuing until the targeted sample size is reached in order to detect the effects of

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this mode on secondary outcomes such as total duration of mechanical ventilation and need of sedation.

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Diaphragm electromyographic activity as a predictor of weaning failure

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Purpose: To compare breathing pattern descriptors and diaphragm electromyographic activity (EAdi)-derived indices obtained from a Neurally Adjusted Ventilatory Assist (NAVA) catheter during a spontaneous breathing trial (SBT) in patients successfully (SP) and unsuccessfully (UP) separated from the ventilator and to assess their performance to discriminate these two categories of patients.

Methods: 57 ready-to-wean patients were included in a prospective observational study (35 SP and 22 UP separated from the ventilator). During a 30 minutes SBT (pressure support 7 cmH₂O, zero end expiratory pressure), tidal volume (VT) and respiratory rate (RR) were obtained from the flow signal at 3, 10, 20 and 30 minutes. EAdi-derived indices were simultaneously computed: maximum of the EAdi (EAdimax), area under the inspiratory curve of EAdi (EAdiAUC), the difference between EAdimax and EAdimin (Δ EAdi), EAdimax/VT, EAdiAUC/VT and Δ EAdi/VT.

Results: At baseline, breathing pattern was similar in the two groups whereas EAdimax and EAdiAUC were significantly lower in the success group ($p < 0.05$). In the failure group, RR and RR/VT increased significantly during the trial, VT decreased, whereas EAdimax and EAdiAUC did not change. At 3 minutes, the areas under the receiver operating characteristic-curve of RR/VT and EAdi-derived indices to predict weaning outcome were: RSBI (0.83), EAdimax/VT (0.84), EAdiAUC/VT (0.80) and Δ EAdi/VT (0.82). During the SBT, the coefficient of variation of VT decreased in the failure group while the one of EAdimax remained unchanged.

Conclusion: EAdi-derived indices provide reliable and early predictors of weaning outcome. However, the performance of these indices is not better than the RR/VT.

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Usefulness of selective neutrophil elastase inhibitor, sivelestat, in ALI patients with SIRS

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Background: Neutrophil elastase is known to be an important mediator of acute lung injury (ALI) in systemic inflammatory response syndrome (SIRS). Sivelestat is a neutrophil elastase inhibitor, but the clinical efficacy of sivelestat in patients with ALI associated with SIRS is now controversial.

Methods: A retrospective data analysis of 110 ALI patients with SIRS was conducted to investigate the effects of sivelestat. The clinical efficacy of sivelestat was evaluated based on the survival rate and ventilator free days (VFD) and changes between before and 7 days after administration of sivelestat in PaO₂/F_iO₂ (P/F) ratio, white blood cell count, levels of C-reactive protein and procalcitonin (PCT).

Results: Sivelestat group included 70 patients, and control group included 40 patients without administration of sivelestat. VFD was significantly higher, and P/F ratio significantly improved in the sivelestat group compared to the control group. Univariate analysis showed that administration of sivelestat is not an independent predictor of survival of ALI patients with SIRS. In non-septic patients, there was no significant efficacy of administration of sivelestat on the survival rate, VFD and changes in P/F ratio. In septic patients, the survival rate was significantly higher in the sivelestat group than in the control group ($p = 0.008$). Administration of sivelestat significantly increased VFD and P/F ratio, and reduced the levels of PCT in septic patients.

Conclusion: Our results suggest that sivelestat might have beneficial effect on the respiratory condition of the ALI patients with SIRS. Furthermore, sivelestat administration tends to associate with survival in patients with ALI with sepsis.

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Biological effects of nanostructured lipid carriers

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Nanostructured lipid carriers (NLC) are a type of drug delivery system offering improved performance in terms of drug loading and long-term stability. Our aims were to test mechanisms of NLC uptake into endothelial cells (EC) and evaluate possible biologic effects of these compounds.

NLC were prepared with triglycerides Miglyol and Softisan and egg-phosphatidylcholine (1:1 by weight) by the double emulsion technique. Cultured mouse lung microvascular endothelial cells (LMVEC) were incubated with curcumin-loaded NLC and uptake was quantified as fluorescence detected in the cell homogenate or by FACS. To test biologic effects, we challenged human LMVEC with thrombin with or without NLC and measured endothelial permeability as flux rate of fluorescent albumin across endothelial monolayers grown on transwell inserts. Alterations were tested in thrombin-induced Extracellular-Regulated Kinase (ERK) activation by immunoblotting and endothelial actin remodelling by fluorescence microscopy. Finally, NLC were delivered intravenously as pre-treatment in a mouse model of hydrochloric acid (HCl) aspiration lung injury.

Using cultured mouse LMVEC we observed that NLC are incorporated into cells more efficiently when caveolin-1, the structural protein of caveolar vesicles, is expressed. Upon challenge of cultured EC with thrombin, NLC attenuated the permeability increase, activation of ERK, cytokine production and actin stress fiber formation. In the HCl-aspiration model, NLC attenuated the increase in bronchoalveolar lavage protein content, inflammatory cells and histological alterations.

Conclusion: Systemically delivered NLC are taken up by EC via caveolae and have endothelial-protective effects of potential relevance to acute lung injury.