

MEETING ABSTRACTS

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000085

Cross-sectional validity of the Chelsea Critical Care Physical Assessment tool (CPAx) in critically ill adults

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Introduction: The Chelsea Critical Care Physical Assessment tool (CPAx) is a performance-based measurement instrument to evaluate respiratory function, functional mobility and grip strength in critically ill adults [1]. The CPax has established construct validity and high interrater reliability in a general ICU population [2], but little is known about its validity to measure change over time (cross-sectional-validity).

Objectives: The current study investigated cross-sectional validity at three relevant, pre-specified timepoints across the ICU and hospital stay in critically ill adults on prolonged mechanical ventilation.

Methods: This prospective, longitudinal, clinimetric study was conducted in a mixed ICU of a Swiss academic hospital. Participants were assessed by certified physiotherapists at three predefined timepoints: ICU baseline (between 72-144 h after the onset of mechanical ventilation), ICU discharge and hospital discharge. We hypothesized that the relationship of the CPax with other measurement tools would differ between these timepoints due to temporal changes in the measured characteristics. Based on this theoretical model we determined 22 a-priori defined hypotheses about the relationship of the CPax-GE with other instruments such as the Medical Research Council sum score (MRC-SS), ICU Mobility Scale (IMS) or Sequential Organ Failure Assessment (SOFA)

Results: CPax data of 58 participants (70.7% male) with a median age of 68 years (IQR 56-73), APACHE II score of 32 (28-36) and ICU stay of 7.97 days (6.69-12.85) were analysed. Cross-sectional validity was excellent with 86% (6 out of 7), 89% (8 out of 9) and 83% (5 out of 6) of the a-priori hypotheses accepted at ICU baseline, ICU discharge and hospital discharge, respectively. Floor (10%) and ceiling effects (6%) were likewise highly acceptable.

Table 1 Selection of a-priori hypothesis and test-results

Hypothesis	n	Spearman's rank correlation coefficient (r)	confirmed
ICU Baseline			
CPAx with MRC-SS (r=0.5 to 0.8)	58	0.639	yes
CPAx with IMS (r=0.6 to 0.9)	58	0.711	yes
CPAx with SOFA (r= -0.4 to -0.7)	58	-0.341	no
ICU Discharge			
CPAx with MRC-SS (r=0.6 to 0.9)	50	0.809	yes
CPAx with IMS (r>0.7)	50	0.883	yes
CPAx with SOFA (r= -0.4 to -0.7)	50	-0.482	yes
Hospital Discharge			
CPAx with MRC-SS (r=0.5 to 0.8)	31	0.674	yes
CPAx with IMS (r>0.7)	32	0.856	yes

Conclusion: The CPax demonstrated cross-sectional validity as an indicator of change over time. Floor and ceiling effects were low enabling therapists to detect change across the ICU and hospital stay. The CPax can therefore be recommended to assess physical function and activity in critically ill adults from ICU baseline to ICU and hospital discharge.

Reference(s) and grant acknowledgment(s)

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3. Research grant from physiswiss
4. PhD Grant from the Swiss Foundation for Physiotherapy Science

000074

Efficacy and Safety of Imipenem/Cilastatin/Relebactam Versus Piperacillin/Tazobactam in Patients With Hospital-Acquired Bacterial Pneumonia/Ventilator-Associated Bacterial Pneumonia by Geographic Region

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Conclusion: Both piperacillin and tazobactam are measurable in stool during therapy; after discontinuation of therapy, piperacillin can be detected in feces for up to 6 days. This may have important consequences for disturbances of the microbiome and the impact of antibiotic therapy.

000402

Impact of high doses of antibiotics and sequence on bacterial clearance in a rat model of E coli peritonitis-induced septic shock

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Introduction: Septic shock is one of the deadliest diseases worldwide, with a mortality rate of 30-50%. Antibiotic delay and higher microbial loads are known to increase morbi-mortality in sepsis.

Loading doses achieve faster appropriate concentrations in plasma, allowing for a better bacterial kill. Bacterial kill and patient outcomes may be further improved by synergistic combination therapy, which is best established for betalactams and aminoglycosides. However, how the sequence of antibiotic administration impacts this synergy is unknown. While *in vitro* work suggests that giving the betalactam first improves bacterial clearance, the effect of antibiotic sequence has not been studied *in vivo*.

Objectives: Determine whether the sequence of antibiotic administration impacts bacterial kill and cytokine production in a monomicrobial rat model of septic shock.

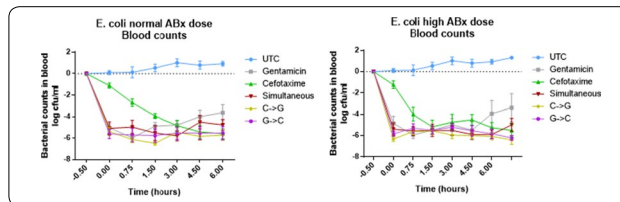
Methods: Our monomicrobial peritonitis rat model of septic shock requires the surgical implant of a gelatin capsule with a fibrinogen clot, alpha cellulose and a known bacterial inoculum (2×10^6 cfu E. coli Bort) in the peritoneum of the rat. This capsule slowly dissolves and generates a progressive peritoneal infection that evolves into septic shock in 12 hours.

After septic shock is established, we fluid resuscitate the rats, connect them to mechanical ventilation, and start vasopressors if needed to achieve a MAP goal of 70 mmHg. We experiment with the order of antibiotics (cefotaxime [cef] and gentamicin [gent]) and compare them to monotherapy, untreated controls and sham controls, for a total of 7 treatment arms and 6 rats per arm. We used two doses of antibiotics: normal (cef 60 mg/kg, gent 10 mg/kg) and high (cef 120 mg/kg, gent 20 mg/kg).

We measure bacterial blood counts, cytokine profile, lactate and renal function at different time points. Following the ethics guidelines of University of Manitoba, we euthanize the rat and measure organ bacterial counts after homogenization.

Results: Rats treated with cefotaxime monotherapy had slow initial bacterial clearance compared to those treated with gentamicin alone. This improved with the higher dose of cefotaxime. Over time the rats treated with gentamicin showed bacterial regrowth (postantibiotic effect); this was delayed in the group treated with a higher gentamicin dose. All combination arms showed a rapid initial bacterial kill and maintained bacterial clearance over time, exhibiting the strengths of gentamicin and cefotaxime, respectively. No significant differences were observed between combination arms.

All treatment arms showed similar bacterial clearance from peritoneal fluid and organs.



Conclusion: Combination therapy showed synergistic effects with a rapid and maintained bacterial clearance from the blood. Altering the antimicrobial sequence had no significant impact in our *in vivo* model of septic shock. Higher doses of antibiotics showed faster initial bacterial kill with cefotaxime monotherapy, and delayed the postantibiotic effect of gentamicin monotherapy.

000423

Too old for the ICU? Long term prognosis of critically ill patients

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Introduction: In the recent years a rapid increase in the age of patients admitted to the Intensive Care Units (ICU) was noted. Fewer limitations are now imposed on performing invasive treatments or surgery in old or even frail patients, especially when complemented by optimal supportive intensive care. However, little is known about the long term follow up of these patients.

Objectives: To evaluate the age stratified long-term all-cause mortality, after admission to the ICU. Secondly, to compare a one-year mortality rate of this cohort of critically ill patients after hospital discharge, with that of a standard population with the same age distribution.

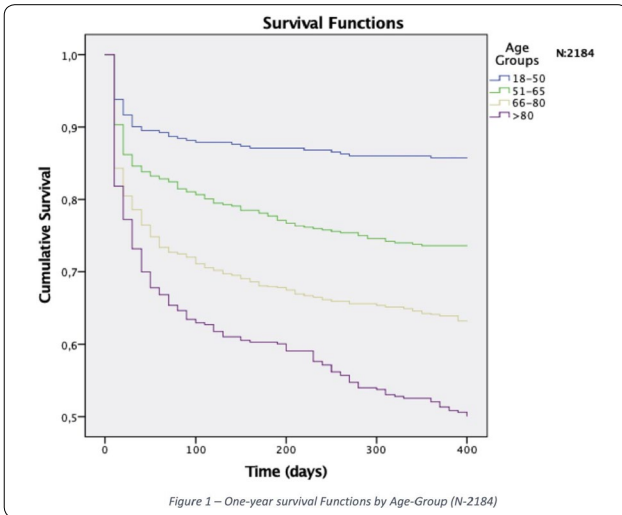
Methods: Retrospective cohort study of all patients admitted to a multipurpose ICU between 2015-2019. Patients < 18 years or admitted for < 24 h were excluded. Only the first ICU admission was considered. Patients were followed until hospital discharge or death, whatever occurred first. One-year all-cause mortality was assessed for all patients. Standard Mortality Ratio (SMR) were determined at hospital discharge and at a 1-year follow-up.

We split the sample in 4 groups according to patients age at admission to the ICU: 18-50 (Adult); 51-65 (Senior); 66-80 (Old); > 80 (Very-old). Survival curves were plotted for all 4 groups according to the time of ICU admission. The ratio between observed and expected mortality was calculated, for patients discharged alive from the hospital and according to age-adjusted tables for the general Portuguese population.

Age Groups (years)	N	Predicted Mort. (SAPSII)	I.H Mortality	SMR	Follow-up	
					1 st year	
					Real	SMR
Adult [18-50]	372	60 (16.1%)	40 (9.2%)	0.67	56 (15%)	0.93
Senior [51-65]	507	125 (24.6%)	84 (16.5%)	0.67	136 (26.8%)	1.09
Old [66-80]	892	321 (36%)	199 (22.3%)	0.62	322 (36.1%)	1.00
Very-old >80	413	181 (43.8%)	110 (26.6%)	0.61	200 (48.4%)	1.10
Total	2184	687 (31.5%)	433 (19.8%)	0.63	714 (32.7%)	1.04

Table 1 -Mortality by Age Group. Predicted and observed in-hospital mortality (with SAPSII), and one-year follow-up SMR-Standard Mortality Ratio

Results: A total of 2184 patients were included. Male gender was predominant (57%); mean age and SAPS II Score were 66 ± 15.8 and 40 ± 18.9 . Mean ICU length of stay was 4.23 ± 4.2 days. ICU and Hospital mortality were 12.1% and 19.8% (SMR 0.63). SAPSII performance was accurate to predict one-year mortality, rather than in-hospital mortality, for all age groups (Table 1).



A Kaplan-Meier survival curve (KM) was computed to assess the differences between long term prognosis for the different age groups (Fig 1) and unveiled a statistically significant difference in the survival probability (log rank test, $p < 0.01$). A sharp drop in survival in the first days was noted, corresponding to the in-hospital mortality. A continuous decay in survival was observed in the Old and Very-old groups that was less evident in the younger population.

Age Groups (years)	N	1 st year		Ratio
		After discharge	Population Estimate	
Adult [18-50]	332	14 (4.2%)	1 (0.3%)	14
Senior [51-65]	423	51 (12.2%)	3 (0.71%)	16.9
Old [66-80]	693	125 (18.4%)	16 (2.3%)	8
Very-old >80	302	89 (29.5%)	32 (10.6%)	2.8
Total	1750	535 (30.6%)	69 (3.9%)	7.8

Table 2 - One-year mortality after discharge and age adjusted control population estimate.

One-year mortality rate after hospital discharge was higher in the older patients. The ratio between the observed and expected mortality (for an age adjusted control population) was significantly high for all age groups (Table 2).

Conclusion: The one-year mortality risk of critically ill patients of all age groups is very high, even after hospital discharge, largely above of the general population. SAPSII showed good accuracy to predict one-year mortality in this cohort. Although a continuous decline in survival is noted in the older patients, more than 50% of the Very-old patients are alive 1 year after ICU admission.

Reference(s) and grant acknowledgment(s)

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000426

Prediction of Hypotension Events with Physiologic Vital Sign Signatures in the Intensive Care Unit

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Introduction: Hypotension is known to be the most consistent manifestation of decompensated shock leading to major organ failure, and even brief hypotension is associated with increased morbidity and mortality. Several early warning scores have been introduced to identify patients at risk for decompensation and trigger escalation of care, but most of current scoring systems are unable to provide reliable, continuous feedback to clinicians who need to make time-sensitive decisions for rapidly fluctuating conditions in critically-ill patients.

Objectives: Using common vital sign data, we aim to develop a machine learning model to predict the initial hypotension event among intensive care unit (ICU) patients, and design an alert system for bedside implementation.

Methods: From the Medical Information Mart for Intensive Care III (MIMIC-3) dataset, minute-by-minute vital signs were extracted. An initial hypotension event was defined as at least 5 measurements within a 10-minute period of systolic blood pressure ≤ 90 mmHg and mean arterial pressure ≤ 60 mmHg. The performance of various supervised machine learning models was measured with area under the receiver operating characteristic curve (AUROC) and area under the precision recall curve (AUPRC). A random forest (RF) classifier was selected, trained with 10-fold cross validation method, then applied to an *a priori* separated out-of-sample validation cohort. Risk score trajectory was built from vital signs features on overlapping windows. For an alert system, hypotension alerts were generated using a two-step (stacked) approach. First, positive alerts were identified with risk score thresholds, then a second RF model was used to reduce false alerts, followed by imposing a lock-out time for alerts to decrease alarm fatigue.

Results: We identified 1532 subjects (1946 ICU stays) as the case group (experienced a hypotension event), and 1707 subjects (2585 ICU stays) as the control group. The RF model showed AUROC of 0.93, 0.91, and 0.88 at 15, 30, and 60 minutes before hypotension, AUPRC of 0.77, and a low calibration score (Brier score 0.09). Mean risk score trajectories revealed a clear separation with 80% of cases predicted at 15 minutes before hypotension, and more than 60% at one hour before the hypotension. For the alert system, the stacked machine learning model with lock-out of 15 minutes produced on average 0.79 alerts/subject/hour for future hypotension, with a positive predictive value (probability of developing hypotension) of 65% and sensitivity of 92.4%.

Conclusion: Most clinically significant hypotension events in the ICU can be predicted from bedside physiologic monitoring at least 1 hour before the initial hypotension episode. Designing a practical alert system with high sensitivity and acceptable positive predictive value for hypotension prediction is feasible, with low rate of alerts.

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