Critical care & neurotraumatology

EP3216

Potential risk factors and value of bedside examination in critical illness polyneuropathy and myopathy

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Introduction: Neuromuscular complications are quite common in the intensive care unit. It is a common cause of failure of weaning from ventilation, and substantially contributes to mortality and rehabilitation problems. However pathomechanism and the actual etiological factors are poorly understood. In this retrospective study, we analysed the utility of bedside clinical examination, blood tests and etiology of critical illness myopathy and polyneuropathy.

Methods: Medical records of 142 patients diagnosed with critical illness myopathy and neuropathy between 2000 and 2013 were reviewed. Multiple linear regression tests were generated between blood test parameters, time on respirator, age and gender, etiology, muscle strength, pneumonia, sepsis, antibiotics, muscle relaxants as well as clinical outcome variables. Furthermore we compared laboratory and clinical parameters between the subgroup of patients admitted with respiratory failure and were treated only 7-10 days on respirator versus patients with multiple organ failure long time respirator treatment and sepsis.

Results: Clinical outcome was significantly correlated with age at admittance (p<0.001), positively correlated with muscle strength at time of the neurophysiology examination (p<0.001). From the laboratory parameters creatine phosphokinase was the only significant predictor of outcome (p=0.045) There were no significant differences in laboratory parameters and outcome at follow-up between the subgroup of patients with isolated respiratory failure and multiple organ failure. Duration of mechanical ventilation had no effect on long term outcome of the patients.

Conclusions: Careful clinical and laboratory examinations could help the early diagnosis and may prevent serious neuromuscular complications in the intensive care unit.

Disclosure: Nothing to disclose

EP3217

Does therapeutic hypothermia affect the prognostic accuracy of a clinical neurological examination and SSEP?

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Introduction: Therapeutic hypothermia is recommended in guidelines as neuroprotective treatment after cardiac arrest (CA). However, it has become increasingly clear that the reliability of several prognostic variables has changed since its introduction. The specific aim of this study is to determine whether hypothermia affects the prognostic accuracy of clinical findings and somatosensory evoked potential (SSEP).

Methods: The data were drawn from the Target Temperature Management trial (TTM) which is an international, multicenter, randomized, assessor-blinded clinical trial of temperature management in CA-survivors. A total of 950 patients were randomized to treatment at 33°C or 36°C after return of spontaneous circulation (ROSC) between Nov 2010 and Jan 2013. Neurological prognostication including results of a clinical neurological examination (motor response to pain, pupillary and corneal reflexes) and neurophysiological investigations (electroencephalogram, EEG and SSEP), were protocolized and systematically recorded. In this study we compared the predictive value (sensitivity, false-positive rate) of clinical findings and SSEP between the two intervention groups at the time of prognostication (72 h after the end of the intervention period). Sensitivity, specificity, and false positive rates for each predictor were calculated.

Results: The results of the data analysis are currently being compiled.

Conclusions: The TTM trial is the largest randomized controlled trial on comatose CA-patients and the database contains a collection of systematically assessed prognostic parameters from two temperature intervention groups. Our results are highly relevant and will be presented at the meeting.

Disclosure: Nothing to disclose
EP3218
Outcomes for different levels of hospitals in major trauma patients with head injury: a nationwide population-based study in Taiwan
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Introduction: Since Trunkey described the concept of the “golden hour,” outcomes for trauma patients in different levels of hospitals become of particular interest.

Methods: All the major trauma patients with head injury were identified by ICD-9-CM system from one million beneficiaries data of NHI claim data (2006 to 2008). ICD-MAP was used to calculate the injury severity score (ISS). The major trauma patients were defined as having an ISS more than fifteen. The Charlson Comorbidity Index (CCI) was used for controlling comorbidity. All these factors were adjusted in a logistic regression model for analysis.

Results: There were 2,034 major head injury patients during these years. There were 772 patients treated in the trauma centers, 1,262 patients treated in non-trauma centers. The total mortality rate was 14.45%. After controlling all these variables, compared with the risk of mortality in trauma centers, the risk of mortality was 1.31 times higher in the non-trauma centers (p=0.09). However, the odds ratio of mortality was 1.25 in the youngest patients (p=0.50), 1.11 in the older patients (p=0.75), and 1.61 in the oldest patients (p=0.03). There was insignificant difference between two levels of hospitals. But, only in the oldest group (>60 y/o), the survival rate was significantly better in trauma centers.

Conclusion: Based on the insignificant difference in mortality rates between trauma centers and non-trauma centers, major trauma patients with head injury could also be transferred to non-trauma centers. But, the patients older than sixty should still be transferred to the trauma centers.

Disclosure: Nothing to disclose

EP3219
Outcomes analysis for direct versus indirect transport to trauma centers in major trauma patients with head injury. A nation-wide population based research in Taiwan
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Introduction: Since Trunkey described the concept of the “golden hour,” outcomes for trauma patients with direct or indirect transfer to the trauma centers become of particular interest.

Methods: All the major trauma patients with head injury were identified by ICD-9-CM system from one million beneficiaries data of NHI claim data (2006 to 2008). ICD-MAP was used to calculate the injury severity score (ISS). The major trauma patients were defined as having an ISS more than fifteen. The Charlson Comorbidity Index (CCI) was used for controlling comorbidity. All these factors and the condition of transfer were adjusted in a logistic regression model.

Results: We excluded the patients direct and indirect-transferred to the local hospitals, and the patients who died in emergency departments. There were 1,398 major trauma patients with head injury in these years. There were 448 patients direct-transferred to trauma centers, 759 patients direct-transferred to regional hospitals, and 191 patients indirect-transferred to trauma centers from the other hospitals. The total mortality rate was 19.9%. After controlling all the variables, compared with the patients who were indirect-transferred to trauma centers, the risk of mortality was insignificantly higher in the patients direct-transferred to the trauma centers (OR=1.26, p=0.39). But the risk of mortality was significantly higher in the regional hospitals (OR=1.65, p=0.04).

Conclusions: Based on the non-significant difference in the risk of mortality between direct-transferred and indirect-transferred patients, major trauma patients with head injury should be transferred (directly or indirectly) to the trauma centers.

Disclosure: Nothing to disclose
EP3220

Long-term cognitive and functional outcome after cardiac arrest and therapeutic hypothermia: a prospective study

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Introduction: The vast majority of studies investigating cardiac arrest (CA) patients categorize outcome as “good” (Cerebral Performance Categories: CPC 1-2) versus “poor” (death or severe functional impairment: CPC 3-5). We characterized long-term cognitive and functional outcome of CA survivors using a comprehensive neuropsychological assessment. These refined outcome measures may help establishing which early variable could provide functional prognostic information.

Methods: Consecutive survivors after CA treated with therapeutic hypothermia (TH) between September 2012 and May 2013 were followed prospectively. Detailed neuropsychological assessments (testing 10 cognitive domains) at 6 months categorized cognitive impairment as absent (no or minimal impairment in <2 domains) versus moderate/severe (≥3 domains significantly impaired). Early prognostic variables (demographics; clinical, biochemical and neurophysiological evaluations) were correlated with long-term outcome.

Results: 20/33 patients (61%) survived CA, and 15 (75% of survivors; 11 men; age 55.3±14.2 years) were included. At 6 months, all patients lived independently and had CPC 1-2; out of these 15 patients, 7 (47%) had moderate/severe cognitive impairment (mainly reduced processing speed and attention deficits) and 5 had serious cognitive complaints (33%); 33% of those previously working did not return to work; quality of life was subjectively impaired in 2 patient (13%). Early predictors failed to predict outcome in this preliminary cohort.

Conclusions: All CA survivors had CPC 1-2 and were living independently; however, a refined evaluation identified cognitive difficulties in a substantial proportion, so far without correlation with early prognostic variables. This cohort is ongoing; updated results will be presented at the meeting.

Disclosure: Nothing to disclose

EP3221

Investigating the effects of memantine and melatonin treatment after traumatic brain injury in mice

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Introduction: Brain injury following head trauma occurs after complex pathophysiological processes including activation of N-methyl-D-aspartate receptor, disruption of intracellular calcium (Ca+2) homeostasis and oxidative stress. Extrasynaptic NMDA receptor inhibitor, memantine, and free radical scavenger, melatonin, have fewer side effects and are used in humans in treatment of neurodegenerative disorders.

Methods: In this study, the effects of memantine and melatonin on traumatic brain injury was investigated in male Balb/C mice. Brain trauma was generated by cold injury; liquid nitrogen filled tube was exposed to animals brain to following areas; 2.5mm lateral, 2.5mm posterior from bregma on the skull, under rompun and ketasol anaesthesia. Immediately after trauma memantine, melatonin and memantin/melatonin combination were administrated.

Results: In these studies, both agents reduced traumatic brain injury and DNA-fragmentation but it was not at the significant level. However, melatonin/memantine combination reduced brain injury and DNA-fragmentation significantly further as compared with melatonin and memantine treated animals which was associated with reduced stress kinases JNK-1/2 and p38 activations. Behavioral tests revealed that the animal- activity, anxiety and depression were improved in all treated animals.

Conclusions: Here, we provide evidence that both clinical safe agents reduce traumatic brain injury especially when combined.

Disclosure: Nothing to disclose
**EP3222**

**Prognosis of severe Guillain-Barré syndrome clinical course**

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**Introduction:** Guillain-Barré syndrome (GBS) is one of severe neurological diseases in which the correct therapy allows to get a complete recovery. The early prognosis of clinical course might be helpful for the timely diagnosis of the life threatening disturbances. We investigated the prognostic role of the neurofilament heavy chains (NfH) in the clinical course of GBS.

**Methods:** The NfH level in serum and cerebrospinal fluid (CSF) of 61 patients who fulfilled GBS diagnostic criteria were analysed at the admission. We also measured the NfH concentration in serum of 15 healthy persons to estimate the normal level of NfH. All patients were divided into groups depending on presence of respiratory failure and dysphagia and their serum and CSF concentrations of NfH were compared.

**Results:** We estimated normal concentration of NfH in serum (Me=0.020 [LQ=0.015, UQ=0.025]). We determined the good correlation between NfH level in serum and CSF and severity of GBS by R Hughes-score in admission (R=0.424 (p=0.014) and R=0.467 (p=0.005) respectively). The concentration of NfH was significantly higher in CSF (p=0.028) and in serum (p=0.020) in patients who developed respiratory failure. We also determined the significantly higher NfH level in CSF (p=0.014) and in serum (p=0.007) among patients with dysphagia. The serum level of the NfH>0.144ng/mL could predict the respiratory failure (AUC 0.804, p<0.0001) and the serum level NfH>0.094 ng/mL indicating the development of dysphagia (AUC 0.773, p=0.001).

**Conclusions:** Serum level of NfH can be the prognostic marker in the clinical course of GBS.

**Disclosure:** Nothing to disclose

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**EP3223**

**Early robot-assisted therapy in patients with stroke in an Intensive Care Unit**

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**Introduction:** Pulmonary embolism (PE) increases risk of unfavorable outcome and mortality in stroke.

**Methods:** This case-control study included 66 patients (49 males, 17 females, median age 59.3) within 7 days from onset of ischemic and hemorrhagic stroke, admitted to the Intensive Care Unit from November 2010 to November 2012. We used National Institutes of Health Stroke Scale (NIHSS) and Glasgow Coma Scale (GCS) scores and assessed the rate of deep vein thrombosis (DVT) revealed with ultrasound scanning, the rate of PE and mortality from admission to Day 21.

**Results:** Patients were equally divided into two homogenous groups—Intervention and Control to receive standard stroke therapy plus daily robot-assisted arm and leg therapy (MOTOmed letto 2) in Intervention group. Groups had similar stroke severity on admission (GCS: Μe=13 [LQ-10, UQ-15] vs. Me=14 [LQ-10, UQ-15], p=0.11; NIHSS: Me=20 [LQ-16, UQ-29] vs. Me=18 [LQ-15, UQ-27]), p=0.5 in Intervention and Control group, respectively). There was no significant difference in neurological outcome on Day 21 (GCS: Me=15[LQ-14, UQ-15] vs. Me=15[LQ-15, UQ-15], p=0.12; NIHSS: Me=11[LQ-8, UQ-25] vs. Me=15 [LQ-10, UQ-19], p=0.4 in Intervention and Control group, respectively), in the rate of DVT on Day 21 (58% vs. 45%, p=0.147; respectively). Rate of PE and mortality on Day 21 were higher in the Control vs. Intervention group (39% vs. 12%, p=0.014 and 39% vs. 12%, p=0.014; respectively).

**Conclusions:** Early robot-assisted therapy in severe stroke patients was associated with significant reduction of PE rate and mortality on Day 21, but did not influence neurological outcome and DVT rate.

**Disclosure:** Nothing to disclose
Light-controlled niche-astrocytes promote neuronal differentiation of human mesenchymal stem cells and improve the neurological deficit in rats with stroke

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Introduction: Astrocytes have been identified as key components of the stem cell niche. However, it is not clear whether astrocyte-derived ATP plays a vital role in modulating the function of mesenchymal stem cells (MSCs).

Methods: We co-cultured MSCs with light-stimulated-channelrhodopsin-2 (ChR2)-astrocytes, and the real-time PCR was used to examine the expression of neuronal markers by MSCs. The light-controlled astrocytes were also co-transplanted with MSCs to the ischemic area of stroke rats for examining the influence of depolarized astrocytes on the MSCs-based therapeutic effects in the stroke rats.

Results: We observed those MSCs expressed more neuronal markers, Tuj1 and NeuN. Furthermore, the ChR2-astrocyte-conditioned medium markedly up-regulated mRNA expression of Tuj1 and Pax6 indicating some component(s) from the photostimulated ChR2-astrocytes contributed to the differentiation-enhancing effects. Optical stimulation of ChR2-astrocytes significantly increased ATP accumulation in their bathing medium without impairing the cell membrane. We further demonstrated either FZD8 or b-catenin mRNA level was significantly increased by ATP, and this effect could be reversed by application of the selective P2X receptor antagonist, TNP-ATP. Finally but importantly, our study also demonstrated that light-controlled astrocytes stimulated endogenous ATP release into the ischemic area to influence the transplanted MSC-niche, resulting in steering the MSCs towards neuronal differentiation and improvements of neurological deficit in the stroke rats.

Conclusions: Together these data provide convergent evidence that ATP from photostimulated-astrocytes, through binding to the P2X receptors expressed by MSCs, activates the wnt/b-catenin signalling, and as a consequence, upregulates neuronal differentiation of MSC within a special niche.

Disclosure: Nothing to disclose

Initial management of mild traumatic brain injury: variability of clinical presentation and accuracy of diagnosis

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Introduction: Reliability of mild traumatic brain injury (MTBI) diagnosis seems to be quite a common problem, because the majority of MTBI symptoms are mainly of a subjective and rapidly reversible character. That is why time of assessment and some other interfering factors significantly influence the patients’ triage and the accuracy of MTBI diagnosis. To improve the standard diagnostic protocols and clarify the significance of some diagnostic criteria we analyzed the structure of the main clinical signs, natural course of recovery and some other features in initial management of MTBI patients.

Methods: This study embraces 184 MTBI patients (aged 16-39) consecutively admitted to the regional hospital. In 61 patients the accident took place on the background of mild and moderate alcohol intoxication. The quantitative analysis (duration/intensity) of MTBI symptoms was carried out.

Results: Several factors and critical points in regard to clinical presentation and initial MTBI diagnosis were identified: age of patients, mechanism of trauma, history of the accident, traumatic signs of head soft tissues, disorders of consciousness and amnesia at the moment of accident, patterns of posttraumatic headache and some other symptoms, concomitant alcohol intoxication, and time of admission to hospital. Special MTBI diagnostic algorithm based on time scale and constellation of different symptoms allows us to classify the diagnosis of MTBI in three categories of reliability: significant (62%), probable (25%) and possible or doubtful (13%).

Conclusions: Optimal time for the assessment and confidential diagnosis of MTBI seems to be the first three days after the trauma.

Disclosure: Nothing to disclose
EP3226

Significance of unusual movements in the diagnosis of brain death
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Introduction: Reflex movements can observe in brain death and these unusual movements might cause arguments in diagnosis. This prospective study investigates the significance of spinal reflexes in patients who fulfilled the criteria for brain death.

Methods: We evaluated 176 patients with brain death (32% female, 58% male, the mean age 57.2 years. Brain death was caused most commonly by intracranial hemorrhage (39%) and this was followed by subarachnoid hemorrhage (24%), ischemic stroke (16%), tumor (10%), anoxic encephalopathy (6%), traumatic brain injury (3%) and meningoencephalitis (2%).

Results: Thirty-seven (21%) of 176 patients presented unexpected movements spontaneously or during examinations. These movements included undulating toe (10, 31%), increased deep tendon reflexes (6, 19%), plantar flexor or extensor responses (5, 15%), Lazarus sign (4, 12%), flexion-withdrawal reflex (3, 9%), facial myokymia (1, 3%), neck-arm flexion (1, 3%), finger jerks (1, %3) long-lasting fasciculations in the muscles of the extremities, chest, and abdomen (1, 3%).

Conclusions: In comparison, there were no significant differences in age, sex, etiology of brain death and hemodynamic laboratory findings in patients with and without reflex motor movement. Regardless of artificial respiratory and cardiac support, brain death is medically and legally a “whole and certain death. Although brain death implied total unresponsiveness, reflex and spontaneous movements have been previously described in patients with brain death, and these unusual movements might raise a suspicion in diagnosis. Spinal reflexes should be well recognized by the physicians and it should be born in mind that the brain death can be determined in the presence of spinal reflexes.

Disclosure: Nothing to disclose

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EP3227

Brain mapping utilizing quantitative EEG (Q-EEG) with Loretta 3-dimensional source analysis in traumatic brain injury (TBI)
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Objective: Quantitative electroencephalograms (Q-EEGs) were performed on selected patients (n=3) with traumatic brain injury (TBI) to correlate functional brain activity with the results of MRI and neuropsychological tests.

Methods: Three patients with TBI are described: one with seizure; one with diffuse brain injury; and one with focal brain damage. Q-EEG provides a mathematical transformation of raw EEG data which associates specific EEG frequency bands with specific brain states. This, combined with the built-in Loretta MRI template, allows the patient and experimenter to see detailed feedback of brain activity in real time. All analyses were completed using Deymed Hardware and Neuroguide Database. Nineteen cortical sites were monitored in linked ear montage with two ground reference points. Impedance measures were all at acceptable levels and below 25Ω suggesting valid results. Average split half and test-retest correlation coefficients were at 0.96 or higher.

Results: Brain MRI scans revealed focal right frontal atrophy; right hemispheric gliosis (seizure patient) and one was normal. Neurological exams were minimally abnormal. However, neuropsychological testing revealed significant cognitive abnormalities that were confirmed by Q-EEG including focal seizure activity and disrupted cortical activity (e.g., excessive Delta waves). Q-EEG brain mapping correlated with abnormal neuropsychological testing more than minimally abnormal brain MRI and neurological exams.

Conclusions: Q-EEG demonstrated superiority over brain MRI and neurological exams in diagnosing brain injury in TBI. The findings provided by Q-EEG provided crucial information for cognitive therapy.

Disclosure: Nothing to disclose