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Neurological examination of critically ill patients: a pragmatic approach. Report of an ESICM expert panel

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Abstract *Objective:* Many patients admitted to the intensive care unit (ICU) have pre-existing or acquired neurological disorders which significantly affect their short-term and long-term outcomes. The ESICM NeuroIntensive Care Section convened an expert panel to establish a pragmatic approach to neurological examination (NE) of the critically ill patient. *Methods:* The group conducted a comprehensive review of published studies on the NE of patients with coma, delirium, seizures and neuromuscular weakness in critically ill patients. Quality of data was rated as high, moderate, low, or very low, and final recommendations as strong, weak, or best practice. *Summary and Conclusions:* The group made the following recommendations: (1) NE should be performed in all patients admitted to ICUs; (2) NE should include an assessment of consciousness and cognition, brainstem function, and motor function; (3) sedation should be managed to maximize the clinical detection of neurological dysfunction, except in patients with reduced intracranial compliance in whom withdrawal of sedation may be deleterious; (4) the need for additional tests, including neurophysiological and neuroradiological investigations, should be guided by the NE; (5) selected features of the NE have prognostic value which should be considered in well-defined patient populations.

Keywords Coma · Neurological examination · Critical illness · Sedation · Delirium · Neuroimaging

Introduction

Clinical examination is the cornerstone of the assessment of patients with primary neurological conditions leading to intensive care unit (ICU) admission, and also for the detection of neurological disorders complicating critical illness. It is the basis for neuroanatomical localization of a disease process. It may help to identify a previously undiagnosed neurological disease, such as myasthenia gravis in a patient who is failing liberation from the ventilator, or pre-existing cognitive decline in a patient who develops delirium. The diagnosis of neurological disorders in the ICU may lead to therapeutic interventions, because a specific treatment is needed (e.g., the institution of anticonvulsant therapy) or contraindicated (e.g., therapeutic anticoagulation in a patient with intracerebral hemorrhage), or to determine physiological goals (e.g., management of blood pressure in ischemic stroke). The identification of a neurological disorder will also orient prognosis and the need for and type of rehabilitation. Critical care providers need skills to (1) determine nature and severity of neurological dysfunction, (2) establish a neurological differential diagnosis, and (3) to determine a plan for further neurological testing and treatment. Currently, there are no recommendations for NE of critically ill patients. To address this gap, the ESICM NeuroIntensive Care Section (NIC) convened an expert panel of intensivists, neuro-intensivists, anesthesiologists, and neurologists to establish a pragmatic framework for the NE of critically ill adult patients.

Methods

Expert panel

The members of the expert panel were nominated at a meeting of the NIC in March 2010. Participants are senior academic intensivists with training in anesthesiology, critical care medicine, and neurology. The panel-members were asked to perform an evidence-based review and to write a concise summary with grading of the level of evidence and recommendations. These summaries were merged in a single manuscript which was then reviewed and edited by the entire panel.

Questions addressed by the panel

The group identified nine key domains relating to the clinical NE of critically ill patient and each panel member was tasked with responding in their summaries to one or two of the questions:

1. What are the essential components of the clinical neurological assessment in the ICU?
2. Which critically ill patients should be examined neurologically?
3. How should sedation be managed to facilitate neurological assessment?
4. How should coma be assessed in critically ill patients?
5. How should delirium be assessed in critically ill patients?
6. What are the clinical criteria which should prompt magnetic resonance imaging in patients who are admitted without primary neurological diagnosis?
7. How should patients be evaluated for ICU-acquired muscle weakness?
8. What are the clinical criteria which should prompt nerve conduction studies and electromyography?
9. What is the prognostic value of neurological signs?

The place of EEG in the neurological assessment and monitoring of critically ill patients has been extensively addressed in a recent systematic review by Claassen et al. [1].

Search strategy

The PubMed database was searched (from 1996 to September 2012) for observational studies and clinical trials in adults using the following terms: “coma”, “delirium”, “confusion”, “agitation”, “consciousness”; “psychosis”, “encephalopathy”, “brain dysfunction”, “seizure”, “muscle weakness”; “paresis”, “critical illness polyneuropathy”, “critical illness myopathy”, “critical illness neuromyopathy”; with one of the following: “critical illness”, “critically ill patients”, “intensive care”, “sepsis”, “sedation”, “mechanical ventilation”. Only studies containing a description of the NE in critically ill populations were included. Review articles, animal studies, and studies conducted in pediatric populations were excluded.

Rating of evidence and recommendations

Quality of data and strength of final recommendations were rated high, moderate, low, or very low, and recommendations were rated as strong or weak. Some recommendations were based not on published evidence but on clinical standard of care acknowledged by all the experts. These were designated as “best practice recommendation”. All the recommendations were reviewed and approved by all members of the panel. In cases of disagreement, recommendations were modified, in order to be unanimously accepted. Therefore, all the members agreed with the content of the manuscript and the recommendations proposed here.

Question 1: what are the essential components of the clinical neurological assessment in the ICU?

Disturbances in neurological function are prevalent in the ICU, both as expressions of primary neurological injury and of systemic organ failure. Neurological signs indicate severity of illness and independently predict outcome [2–9]. Altered consciousness, delirium, agitation, anxiety, pain, sedation, neuromuscular blockade, hypothermia, intubation/mechanical ventilation, and surgical or traumatic lesions of the extremities may confound neurological assessment in the ICU [10]. Notwithstanding, NE is feasible in the ICU and has major diagnostic and prognostic significance [2, 11, 12].

The structure of the NE is determined by the level of consciousness:

(a) In the conscious patient, the clinician assesses cognition (orientation, language, attention, memory), cranial nerves, motor and sensory function, reflexes, and coordination. The comprehensiveness and structure of this examination must be adapted to the underlying neurological process. Serial examinations are necessary to discern trends and evidence of deterioration. Once sedation is interrupted [13], delirium and coma should be scored using validated instruments [4, 14, 15], as detailed below. Muscular strength should be tested using the validated Medical Research Council (MRC) scale [6, 16] (Table 1).
(b) In the comatose patient, neurological assessment considers level of arousal, brainstem function, motor responses, and respiratory pattern [15]. Numerical scales generally used for this purpose are the Glasgow Coma Scale (GCS) [17] or The Full Outline of Unresponsiveness (FOUR) scale, as detailed in Table 2 and below [18] (see also Figs. 1, 2). In both traumatic and post-anoxic coma, brainstem semiology is critical: absence of pupillary reactivity and abnormal motor responses are prognostically significant [11, 19, 20], while loss of the corneal response signals poor outcome in post-anoxic coma [11].

Recommendations

1. Interpretation of neurological signs must consider confounding by sedation, neuromuscular blockade, pain, delirium, anxiety, metabolic and physiological disturbances, and the physical limitations caused by injuries and intubation—low evidence, best practice recommendation.
2. Frequency of NE should be determined by the nature and severity of the underlying cause of neurological dysfunction. At a minimum, NE should be performed upon admission to the ICU and once daily—moderate evidence, best practice recommendation.
3. Coma, delirium, and motor strength should be evaluated using validated scales (respectively GCS or FOUR; CAM-ICU or ICDSC; and MRC—moderate evidence, strong recommendation.

Question 2: which critically ill patients should be examined neurologically?

Neurological dysfunction including altered consciousness, delirium, seizures, and muscle weakness are exceedingly common in critically ill patients [21]. More than 80 % of mechanically ventilated patients may experience delirium in the ICU [22]. Depressed consciousness is the major contributor to prolonged ventilation in a third of those who need it and a significant factor in an additional 40 % [23, 24]. Neurological complications increase both the length of stay in hospital and the likelihood of death [23]. The mortality rate for patients with neurological complications is 55 % compared to 29 % for those without [25]. Critical illnesses have been associated with substantial long-term declines in neuropsychological function [26, 27, 28].

Recommendations

1. All critically ill patients should undergo routine NE—moderate evidence, best practice recommendation.

Question 3: how should sedation be managed to facilitate neurological assessment?

In the ICU, routine interruption of continuous sedation (ICS) has been associated with reduced duration of mechanical ventilation and decreased overall ICU length

Table 1 Medical Research Council (MRC) sumscore

Score for each movement
0 = no visible contraction
1 = visible muscle contraction, but no limb movement
2 = active movement, but not against gravity
3 = active movement against gravity
4 = active against gravity and resistance
5 = active movement against full resistance
Movement tested
Upper limbs
Wrist flexion
Forearm flexion
Shoulder abduction
Lower limbs
Ankle dorsiflexion
Knee extension
Hip flexion

From 0 (min) to 36: quadriplegia to severe quadriparesis
From 36 to 48: mild quadriparesis
From 48 to 60 (max): normal strength

Table 2 Glasgow Coma Scale and Full Outline of UnResponsiveness (FOUR) score

	Glasgow coma scale	FOUR score
Eye response	4 = eyes open spontaneously 3 = eyes opening to verbal command 2 = eyes opening to pain 1 = no eyes opening	4 = eyelids open or opened, tracking, or blinking to command 3 = eyelids open but not tracking 2 = eyelids closed but open to loud voice 1 = eyelids closed but open to pain 0 = eyelids remain closed with pain
Motor response	6 = obeys commands 5 = localizing pain 4 = withdrawal from pain 3 = flexion response to pain 2 = extension response to pain 1 = no motor response	4 = thumbs-up, fist, or peace sign 3 = localizing to pain 2 = flexion response to pain 1 = extension response to pain 0 = no response to pain or generalized myoclonus status
Verbal response	5 = oriented 4 = confused 3 = inappropriate words 2 = incomprehensible sounds 1 = no verbal response	
Brainstem reflexes		4 = pupil and corneal reflexes present 3 = one pupil wide and fixed 2 = pupil or corneal reflexes absent 1 = pupil and corneal reflexes absent 0 = absent pupil, corneal and cough reflex
Respiration		4 = not intubated, regular breathing pattern 3 = not intubated, Cheyne-Stokes breathing pattern 2 = not intubated, irregular breathing 1 = breathes above ventilator rate 0 = breathes at ventilator rate or apnea
Max–min	15–3	16–0

of stay [29], and in the prevention and early treatment of evolving neurological deterioration [29, 30]. The strategy of ICS may allow a downward titration of sedative infusion rates over time, minimizing the tendency for accumulation [29, 31–34]. In one trial, paired sedation interruption and spontaneous breathing trials were linked to reduced 1-year mortality [33]. The strategy of daily ICS and neurological evaluation has been demonstrated as

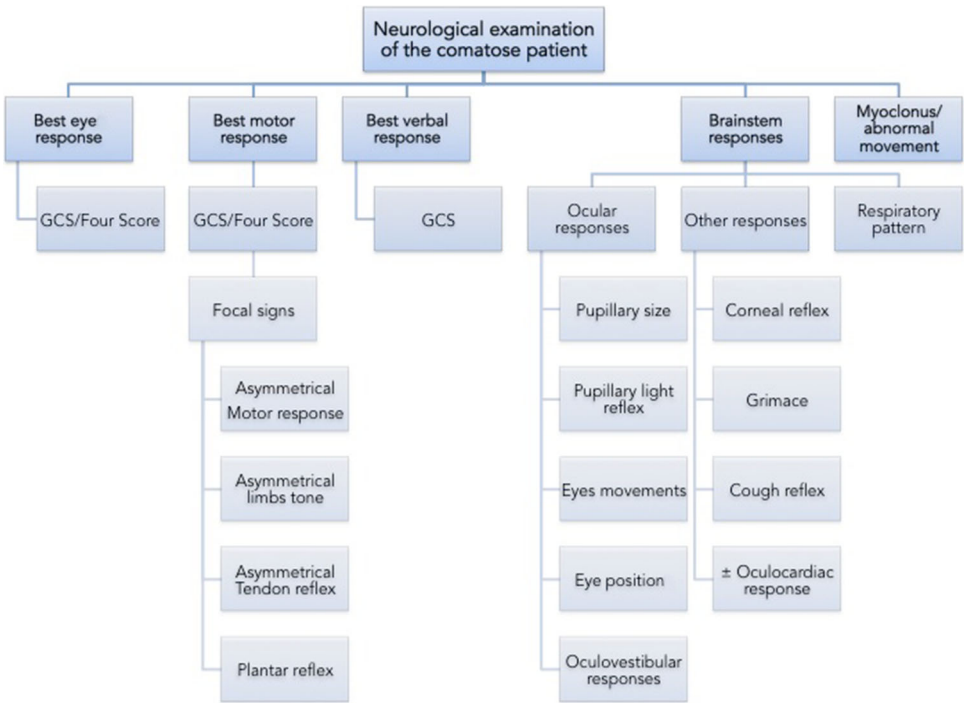

Fig. 1 Neurological examination of a comatose patient. *GCS* Glasgow coma scale, *FOUR score* Full Outline of UnResponsiveness

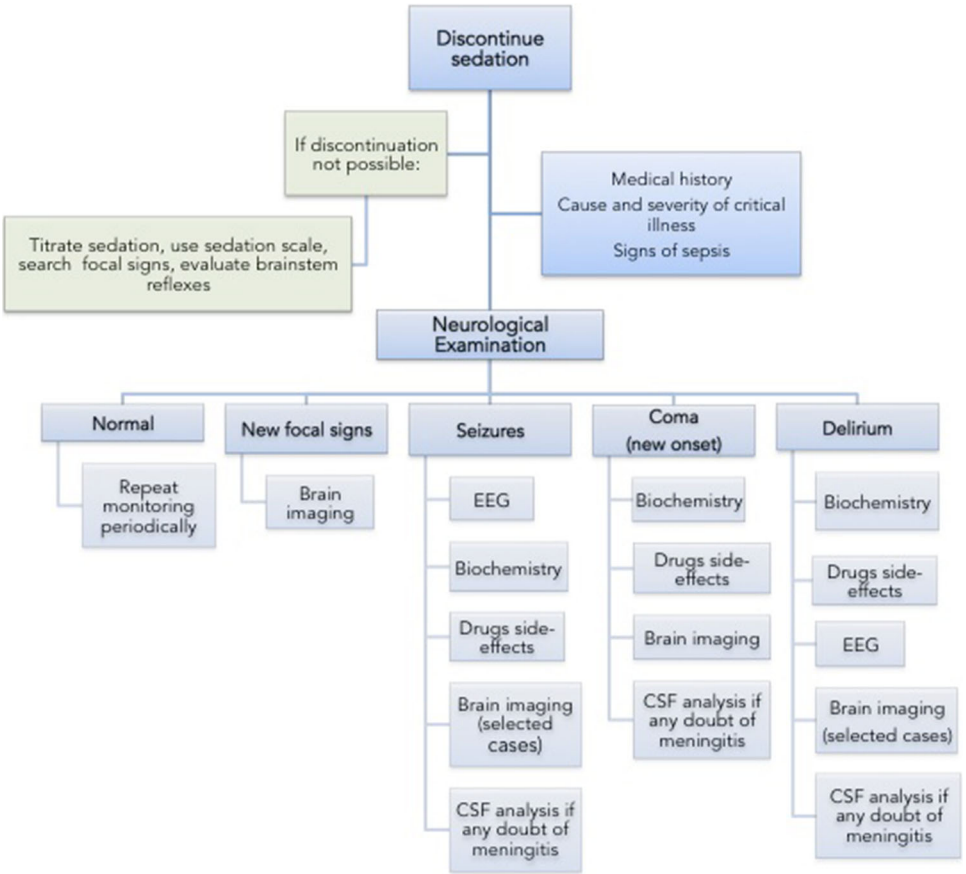

Fig. 2 Diagnostic approach to acute brain dysfunction in ICU. *CSF* cerebrospinal fluid

beneficial, but the role of more frequent evaluation needs further study [35]. Also, the relative benefits of ICS as opposed to protocolized sedation were not clearly demonstrated in one recent multicenter trial [30].

ICS may have adverse effects in patients with reduced intracranial compliance resulting in deleterious ICP and CPP changes [36, 37]. These patients, and also patients without ICP monitoring in whom low intracranial compliance is suspected, should be excluded from ICS and information should instead be gathered from other neuromonitoring methods in combination with neuroradiological evaluation. Recent evidence suggests that assessment of brainstem responses is feasible even when sedation is maintained, and that loss of selected responses is predictive of mortality and altered mental status [12].

Recommendations

1. Daily interruption or reduction of sedation is recommended in mechanically ventilated patients to enhance NE and improve short- and long-term outcomes—moderate evidence, strong recommendation.
2. Sedation interruption is not recommended in patients with intracranial hypertension—moderate evidence, strong recommendation.

Question 4: how should coma be assessed in critically ill patients?

Examination of the comatose patient should include assessment of the best responses to graded stimulus starting with verbal order and progressing to noxious stimulus, brainstem reflexes, motor responses, and respiratory pattern [15]. The noxious stimulus can evoke localizing movements, withdrawal, posturing reflexes, or no response. Brainstem examination includes an assessment of pupils and pupillary reactivity, spontaneous eye position and movements, vestibulo-oculocephalic reflex, corneal reflex, cough, and gag reflexes [12, 38].

There are various scales that assign a numerical value to the level of consciousness. The GCS remains the most widely used [17]. Its main limitations are that verbal responses are not assessable in mechanically ventilated patients and that brainstem examination is not directly considered. More recently, the FOUR score has been designed and validated for use in mechanically ventilated patients [18]. It assesses eye response, motor response, brainstem reflexes, and respiratory pattern and has been tested in a range of clinical settings and in different countries [39–42]. Patients with the lowest GCS score can be further differentiated using the FOUR score (Table 2);

however, evidence that the FOUR has greater inter-rater reliability or prognostic value than the GCS is limited [18, 39].

Recommendations

1. Examination of the comatose patient should include graded stimulus, brainstem evaluation, motor responses, and respiratory pattern—moderate evidence, best practice recommendation.
2. Coma examination should include a validated objective scale such as the GCS or the FOUR score—moderate evidence, strong recommendation.

Question 5: how should delirium be assessed in critically ill patients?

Delirium is a pathological alteration in cerebral function associated with inattention, a fluctuating course, and an underlying illness or physiologic/metabolic imbalance [43]. Delirium is independently linked to hospital mortality and length of stay [7, 44, 45], posing a major public health burden [46, 47]. Delirium also increases the likelihood of post-discharge death [48], functional disability [49], cognitive impairment [26, 28], and dementia [50]. The risk of delirium is particularly high in the elderly, following major surgery [51] and in the ICU [14]. Up to 80 % of mechanically ventilated patients experience delirium, which is independently associated with a higher risk of death during and after hospitalization [14, 44, 48, 52].

Delirium is under-recognized and inadequately treated in ICU patients [53]. There is broad acceptance of the Diagnostic and Statistical Manual of mental disorders (DSM) criteria for delirium [43]; however, implementation of DSM in the ICU is hindered by sedation and endotracheal intubation. The Confusion Assessment Method for the Intensive care Unit (CAM-ICU) assesses four items (acute change of or fluctuating mental status, inattention, altered level of consciousness, and disorganized thinking), two of which require active patient participation [14]. The Intensive Care Delirium Screening Checklist (ICDSC) has eight items (level of consciousness, inattention, disorientation, hallucination/delusion/psychosis, psychomotor agitation or retardation, inappropriate speech or mood, sleep/wake disturbance, and fluctuation of symptoms), none of which require direct patient cooperation [4]. The feasibility of CAM-ICU and ICDSC screening has been demonstrated in different ICU settings and in many countries [52, 54–57]. The validity and reliability of the two instruments when compared to a diagnostic gold standard (DSM) is mixed [4, 14, 56], as is their comparative accuracy [13, 58, 59]. Delirium screening is not practicable in the unconscious patient, and the value of delirium screening in sedated patients needs further study.

Recommendations

1. All critically ill patients who are not comatose should be screened routinely for the presence of delirium—high evidence, strong recommendation.
2. Delirium should be assessed using a score validated in the ICU, such as the CAM-ICU or the ICDSC—moderate evidence, strong recommendation.
3. Delirium screening should be repeated at scheduled intervals to increase diagnostic sensitivity and monitor response to interventions—low evidence, strong recommendation.

Question 6: what are the clinical criteria which should prompt neuroimaging in patients who are admitted without a primary neurological diagnosis?

Neuroimaging with computed tomography (CT) may reveal brain infarction, intracranial hemorrhage, or cerebral edema, and is generally the first neuroimaging study in patients where clinical instability or local resource limitation makes magnetic resonance imaging (MRI) inaccessible. In the same sitting, CT may be coupled with (1) CT angiography which may be useful in the diagnosis of intracranial aneurysms, vasospasm, arterial occlusion, stenosis or dissection, and cerebral venous thrombosis, and (2) CT perfusion to evaluate regional cerebral blood flow abnormalities.

Brain MRI has greater sensitivity to early infarction and is substantially superior to CT in identifying lesions in the posterior fossa. Brain MRI may have prognostic value in patients with hypoxic-ischemic [60] or septic [61] encephalopathy. Imaging findings are not diagnostic in isolation; consequently, the prescription of neuroimaging studies is recommended only once clinical history and NE define a reasonably high a priori probability of brain injury.

Recommendations

1. Computed tomography (CT) is a reasonable initial imaging modality for the evaluation of patients with focal neurological deficits or unexplained depression of consciousness, particularly when the need for continuing organ support and/or local resource limitation makes MR logistically difficult—high evidence, best practice recommendation.
2. Brain MRI is recommended in the following conditions:

Table 3 Semiology of main peripheral nervous system syndromes

	Motor neuron disease	Neuropathy	Myasthenic syndrome	Myopathy
Symmetry	Bilateral ± symmetrical	Variable MM: asymmetrical PN: symmetrical PRN: symmetrical	Bilateral and symmetrical	Bilateral and symmetrical
Proximal vs. distal	Proximal or distal	MM: distal PN: distal PRN: proximal	Proximal++	Proximal++
Topography	Limbs, bulbar, respiratory	MM: ≥1 nerve PN: limbs ± respiratory PRN: limbs, trunk, bulbar, facial, respiratory	Variable Limbs, facial, bulbar, trunk or respiratory Ptosis (often unilateral) and diplopia PLR preserved (except botulism)	Variable Limbs, facial, bulbar, trunk, respiratory
Tone	Flaccidity	Flaccidity	Flaccidity	Flaccidity
Tendon reflexes	Lost or pyramidal signs (ALS)	Lost or decreased	Preserved	Preserved
Idio-muscular response	Preserved	Preserved	Preserved	Absent
Atrophy	Pronounced	Pronounced	No	Variable
Other motor signs	Fasciculation	–	Fatigability Fluctuation	Myalgia Myotonia
Other neurological signs	Cramps	±Sensory loss ±Dysautonomia	No sensory loss (except L. Eaton)	No sensory loss

Neuronopathy designates primary loss or destruction of lower motor neuron (i.e. poliomyelitis) or sensory neurons in dorsal root ganglion cells with resultant degeneration of their entire peripheral and central axons
MM mononeuropathy multiplex, *PN* polyneuropathy, *PRN* polyradiculoneuropathy, *ALS* amyotrophic lateral sclerosis, *PLR* pupillar light reflex

(a) In patients developing acute neurological deficits or an acute change in mental status not explained by CT-scan—high evidence, strong recommendation;
(b) In patients with refractory status epilepticus, who cannot be evaluated clinically due to the concurrent use of major neurodepressants—high evidence, best practice recommendation;
(c) In case of suspicion of cerebral fat embolism, osmotic myelinolysis, or posterior reversible encephalopathy syndrome—high evidence, best practice recommendation;
(d) In patients not recovering after hypoxic-ischemic injury or prolonged hypoglycaemia—high evidence, best practice recommendation;
(e) In patients with sepsis associated with altered mental status, focal neurological signs, and/or abnormal brainstem reflexes—low evidence, best practice recommendation.

Question 7: how should patients be evaluated for ICU-acquired muscle weakness?

ICU-acquired muscle weakness (ICUAW) is a generalized symmetrical reduction of limb and respiratory muscle strength developing as a complication of critical illness [62]. Manual testing of muscle strength is done using the Medical Research Council [16] (Table 1), or handgrip dynamometry [2] in awake collaborative patients. Critical illness polyneuropathy (CIP) and myopathy (CIM) are the most frequent cause of ICUAW. ICUAW should be differentiated on the basis of clinical history and NE. Differential diagnosis includes concurrent complications, such as electrolyte abnormalities, rhabdomyolysis, nerve compression or entrapment, status epilepticus, surgery, or use of drugs, and pre-existing neuromuscular diseases, particularly in cases of acute onset diseases (Guillain–Barré syndrome, myasthenia gravis, botulin intoxication, hypokalemic periodic paralysis, and various intoxications) [62] (Tables 3, 4).

ICUAW is usually excluded in the presence of the following: clinical signs suggest a central nervous system disease (i.e. Babinski signs, increased deep tendon reflexes, spasticity, widespread muscle fasciculation, and focal neurological signs); facial muscles are involved (i.e. drooping of the eyelids, weakness of extraocular muscles with diplopia, facial nerve palsy with altered patient's expression, and difficulty in speech, chewing or swallowing); distribution of muscle weakness is asymmetrical (i.e. monoparesis or hemiparesis); progression of muscle weakness suggests a specific diagnosis, for example, the pattern is ascending (Guillain–Barré syndrome) or descending (botulin intoxication); muscle weakness is fluctuating and worsens after brief exercise indicating muscle fatigability and neuromuscular transmission defect (myasthenia gravis) or improves

Table 4 Causes of muscle weakness in the critically ill patient (taken from Stevens et al. [78])

Bilateral or paramedian brain or brainstem lesions[a]
Trauma
Infarction
Hemorrhage
Infectious and noninfectious encephalitis
Abscess
Central pontine myelinolysis
Spinal cord disorders[a]
Trauma
Nontraumatic compressive myelopathies
Spinal cord infarction
Immune-mediated myelopathies (transverse myelitis, neuromyelitis optica)
Infective myelopathies (e.g., HIV, West Nile virus)
Anterior horn cell disorders
Motor neuron disease
Poliomyelitis
West Nile virus infection
Hopkins syndrome (acute post-asthmatic amyotrophy)
Polyradiculopathies
Carcinomatous
HIV-associated
Peripheral nervous disorders
Guillain–Barre syndromes[b]
Diphteric neuropathy
Lymphoma-associated neuropathy
Vasculitic neuropathy
Porphyric neuropathy
Paraneoplastic neuropathy
Critical illness polyneuropathy
Neuromuscular junction disorders
Myasthenia gravis
Lambert–Eaton myasthenic syndrome
Neuromuscular blocking drugs
Botulism
Muscle disorders
Rhabdomyolysis
Disuse myopathy
Cachexia
Infectious and inflammatory myopathies[c]
Mitochondrial myopathies
Drug induced and toxic myopathies
Critical illness myopathy
Decompensation of congenital myopathies (e.g., myotonic dystrophy, Duchenne muscular dystrophy, adult onset acid maltase deficiency)

[a] Upper motor neuron signs (increased tone, hyperreflexia) may be absent in the acute setting

[b] Includes acute inflammatory demyelinating polyneuropathy (AIDP); acute motor axonal neuropathy (AMAN), acute motor and sensory axonal neuropathy (AMSAN)

[c] Includes polymyositis, dermatomyositis, pyomyositis

after exercise indicating pre-synaptic neuromuscular defect (Lambert–Eaton syndrome); there are associated abnormalities such as skin rash or abdominal pain pointing to dermatomyositis, vasculitis, porphyria, or diabetes; there are dysautonomic signs (i.e. dilated pupils poorly reactive to light suggesting botulin intoxication, and cardiac arrhythmias or fluctuations in blood pressure as seen in GBS); pharmacological side effects are suspected (i.e. after prolonged administration of neuromuscular blocking agents, steroids, or cancer chemotherapy).

Recommendations

1. We recommend that assessment of ICUAW be made using either the MRC or handgrip dynamometry—low evidence, moderate recommendation
2. Critically ill patients with muscle weakness should be evaluated for plausible etiologies with a careful clinical history and NE—moderate evidence, best practice recommendation.

Question 8: what are the clinical criteria, which should prompt nerve conduction studies and electromyography?

Nerve conduction studies (NCS) include the measurement of conduction velocity and action potential amplitude in sensory (SNAP) and motor (CMAP) nerves [63]. SNAP and CMAP amplitudes are reduced while nerve conduction velocity is normal in sensory-motor axonal neuropathy such as CIP [64]. Conversely, velocity is reduced while amplitude is normal in demyelinating polyneuropathy. In repetitive muscle stimulation, a brief series of stimulations is applied to a motor nerve, and serial response amplitudes are recorded [63]; a decremented response is shown in disorders of the neuromuscular transmission such as myasthenia gravis or the use of neuromuscular blocking agents.

ICU-AW is established clinically. However, clinical evaluation has limitations particularly in cases of rapid progression of disease causing acute respiratory failure. Some diseases are amenable to specific treatments, for example, immunoglobulins or plasmapheresis in Guillain–Barré syndrome [65], steroids in post-surgical inflammatory neuropathy [66], antitoxin administration in botulism [67], or simply the prompt removal of ticks in tick paralysis [68]. Nerve conduction study, repetitive nerve stimulation, and electromyography can be of value in distinguishing acute axonal neuropathy from demyelinating neuropathy, altered neuromuscular transmission, or acute myopathy.

Recommendations

1. We recommend that NCS and EMG are used whenever a differential diagnosis between ICUAW and other causes of neuromuscular weakness cannot be achieved based on history and clinical features—moderate evidence, best practice recommendation.

Question 9: what is the prognostic value of neurological signs?

Clinical examination is the cornerstone for prognostic assessment following neurological insults [69]. In traumatic

brain injury (TBI), the GCS and pupillary light responses have prognostic significance [70, 71]. Following cardiac arrest (CA), absent pupillary light response, corneal reflexes, abnormal motor response, and the presence of myoclonus status epilepticus have been robustly associated with neurologic prognosis in patients who have not received therapeutic hypothermia [72, 73]. In CA patients who have received therapeutic hypothermia, clinically significant false positive rates have been noted in particular with absent or abnormal with motor responses [19, 74, 75]. The clinical NE also has prognostic significance in non-neurological critical illness, increased weighting of the GCS increases prognostic performance of APACHE II [76], and APACHE III [3]. The FOUR score has prognostic value in a range of illnesses [19, 40, 41, 74]. Impaired brainstem responses, absent verbal responses, or absent withdrawal to pain substantially increase the risk of non-survival or severe disability in comatose critically ill patients [12, 77]. Absent cough or oculocephalic reflexes, even when documented in sedated patients, remain predictive of mortality and post-sedation delirium [12]. Finally, delirium independently predicts mortality and long-term risk of neuropsychological impairment in critically ill patients [7, 26].

Recommendations

1. NE is recommended to assess prognosis following TBI and CA—high evidence, strong recommendation.
2. NE of comatose patients after CA should include: pupillary reflex, corneal reflex, and motor responses—high evidence, strong recommendation.

Concluding remarks

These deliberations of this panel provide pragmatic recommendations on the indications, content, and interpretation of NE, and on the indication for additional testing in order to improve the management of critically ill patients who have, or are at high risk for developing, neurological disorders. A major contribution of the present work is to underscore the need to conduct studies which will define and validate the neurological approach to critically ill patients. Despite technological advances, it is likely that the clinical NE will remain a foundation in the assessment of patients in the ICU.

Limitations of this work must be acknowledged. First, the evidence supporting some of these recommendations is weak or biased. Second, and largely because of the lack of robust studies, this group elected to not undertake a formal evidence-based consensus process. Finally, we have focused our investigation on two major neurological syndromes—alteration of consciousness (i.e. delirium and coma) and muscle weakness—as they are the most frequent neurological manifestations of critical illness. It will be interesting in the future to address other more subtle neurological symptoms such as impairments in attention, memory, and executive function.

Conflicts of interest The authors have no conflict of interest to declare.

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