ΑΝΑΣΚΟΠΗΣΗ ΤΗΣ ΓΕΝΙΚΗΣ ΟΡΓΑΝΩΣΗΣ, ΤΟΥ ΦΑΣΜΑΤΟΣ ΠΑΘΗΣΕΩΝ ΚΑΙ ΤΩΝ ΔΥΝΑΤΟΤΗΤΩΝ ΠΟΛΥΠΑΡΑΓΟΝΤΙΚΗΣ ΠΑΡΑΚΟΛΟΥΘΗΣΗΣ ΤΗΣ ΝΕΥΡΟΛΟΓΙΚΗΣ ΛΕΙΤΟΥΡΓΙΑΣ ΣΕ ΜΟΝΑΔΕΣ ΝΕΥΡΟΕΝΤΑΤΙΚΗΣ ΘΕΡΑΠΕΙΑΣ

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Περίληψη

Η νοσηλεία ασθενών σε εξειδικευμένες μονάδες νευροεντατικής θεραπείας έχει εξελιχθεί τις τελευταίες δεκαετίες και αποτελεί πλέον ξεχωριστά οργανωμένη ειδικότητα σε πολλά συστήματα υγείας. Η νευροεντατική θεραπεία χρησιμοποιεί ομάδες πολλαπλών ειδικοτήτων, γίνεται χρήση συγκεκριμένων πρωτοκόλλων θεραπείας και παρακολούθησης νευρολογικών λειτουργιών, καθώς επίσης διεξάγει έρευνα και αναπτύσσει περαιτέρω η ίδια το πεδίο αυτό. Το φάσμα της έχει επεκταθεί σημαντικά και οι τεχνολογικές εξελίξεις επιτρέπουν τη δυνατότητα παράλληλης παρακολούθησης των νευρολογικών λειτουργιών με διάφορους τρόπους, αν και το τελικό αποτέλεσμα στη διαχείριση των ασθενών και την λειτουργική τους κατάσταση απαιτεί περαιτέρω έρευνα. Αν και υπάρχουν σαφή στοιχεία ότι η νευροεντατική θεραπεία μπορεί να βελτιώσει την έκβαση και την ποιότητα ζωής των ασθενών που είναι σοβαρά άρρωστοι, η κατανόηση της δομής της, της κλινικής της εφαρμογής και την ταυτόχρονης παρακολούθησης των νευρολογικών λειτουργιών μέσω διαφορετικών μεθόδων είναι ουσιαστική για την περαιτέρω εξέλιξη το τομέα. Για τον λόγο αυτό, παρουσιάζουμε εδώ την ιστορική εξέλιξη των μονάδων νευροεντατικής φροντίδας και της σύγχρονης δομής τους, όπως και το φάσμα των ασθενειών που νοσηλεύονται σε αυτή, καθώς και τις διαθέσιμες δυνατότητες παρακολούθησης της νευρολογικής λειτουργίας.

Λέξεις ευρετηρίου: neurointensive care units, multimodal neuromonitoring, neurointensivist / νευροεντατική θεραπεία, πολυπαραγοντική παρακολούθηση νευρολογικής λειτουργίας, νευροεντατικολόγος

GENERAL ORGANIZATION, DISEASE SPECTRUM AND MULTIMODAL MONITORING IN NEUROCRITICAL CARE UNITS; A REVIEW

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Abstract

Neurocritical care has further evolved in the last decades and is currently part of many health systems as separately organized specialty. Neurocritical care involves interdisciplinary teams, protocol implementation and neuromonitoring as well as research and further development of the filed. Its spectrum has drastically been expanded and technological developments have improved multimodal monitoring capacities, although its impact on patients' management and functional status requires further research. Although there is clear evidence that neurocritical care can improve outcomes and quality of life of patients who are severely ill, understanding its structure, clinical practice and multimodal neuromonitoring is essential for further development of this field. We present herein the historical evolution of neurocritical care units and their current organization, as well as the spectrum of neurocritical diseases and available modalities for neuromonitoring.

Introduction

Critical care medicine and the concept of intensive care unit is fast 70 years old and was evolved after mechanical ventilation with positive pressure was shown to be a solution for polio victims with respiratory insufficiency[1]. The rapid grow up of the specialty in the following years resulted in the establishment of specialized intensive care units (ICU), such as postoperative neurosurgical units and, later, neuroscience ICUs, which was dedicated to the treatment of critically ill neurological patients[2].

As a continuously evolving subspecialty of intensive care medicine, critical care and management of neurosurgical and neurological patients is a developing concept involving many clinical entities and new technological modalities. Recently, with the rapid development of acute stroke care and endovascular therapy, neurological critical care units (NCCUs) covered further clinical problems, expanding their spectrum of critically ill patients[3].

As the clinical spectrum and therapeutic complexity of critically ill neurological patients admitted to NCCU is continuously evolving, dedicated specialized multidisciplinary teams are required to optimal management of acutely ill patients with life threating neurological problems. In this context, a new subspecialization in neurology has emerged, individuals trained to deal with the complexity of these issues, called neurointensivists. These experts are not only involved in the treatment of primary or secondary neurological problems, they are also dedicated to the development of this field as well as they play a key role in the function of the multidisciplinary team of NCCUs[4],[5].

In this review article, we present the spectrum of neurological patients treated in NCCUs, the existing modalities of neurointensive monitoring, as well as proposed organization and infrastructure of a NCCU.

Historical Evolution of NCCU

Although care of highly complex critically ill patients was always challenging in medicine, progress in this filed was intensified in the second part of 20th century[2]. Currently COVID-19 pandemic triggered further advancement in vaccine development. Similarly, it was poliomyelitis epidemic, which catalyzed the evolution of critical care of patients. Although units for intensive care of postoperative neurosurgical patients were already existed, it was the pandemic, which led to a further development of the concept of intensive care units[6].

In the early 1950s, Lassen and Ibsen, amid the pandemic of a virulent strain of poliomyelitis, utilized manual mechanical ventilation to improve clinical outcome of patients with respiratory failure or bulbar weakness. Emergency tracheostomy and respiratory support with manual bag ventilation (conducted by medical students) simplified care of critically-ill patients and resulted to a mortality drop from 80% to 50%[1],[7]. That led to a further sophistication and improvement of care, practice and technical equipment; a multidisciplinary special ward called intensive care unit was developed and expanded to the majority of large hospitals[8],[9].

Improving technology with advances in mechanical ventilation, monitoring of invasive hemodynamics and incubators for newborns led to the development of more specialized units, such as surgical ICUs, coronary care units, trauma and neonatal ICUs. Evidence was provided suggesting a significant decline in mortality of patients treated with mechanical ventilation in ICUs compared with those in general wards[10], leading to the acceptance and further expansion of this concept. In this aspect, care of traumatic brain injury in specialized ICUs was the initial step for the evolution of neurocritical care[2]. The close cooperation of neurosurgeons and consulting neurologists led to the first neuroscience ICUs, treating both neurosurgical as well as neurological patients with meningitis and status epilepticus[11].

The specialty of critical care and emergency neurology was further developed in following decades focused on stupor and coma as well joined training of neurologists and intensivists and leading positions of neurologists in NCCUs, while acute brain injury and its complications along with recognition and treatment of acute medical and surgical acute neurology was recognized as important additional skill of neurologists[2],[12]. Societies for intensive or neurocritical care, such as the international Neurocritical Care Society or the national Deutsche Gesellschaft für Neurointensiv- und Notfallmedizin were founded, guidelines and special specialization programs were development to sufficiently train and qualify neurologists for neurocritical care [13]-[15]. Currently, NCCUs are mostly units treating neurologic and neurosurgical patients, so that patients could benefit from both expertise in dealing with their complex problems. Future perspectives may include a board certification through neurologic societies. Neurocritical care is expected to expand to other fields of expertise, such as pediatrics with the recognition of a sub-specialized field of pediatric neurocritical care[16], while development in multimodal monitoring requires further research and standardization[17],[18] for the future.

General Organization and Infrastructure

Most modern NCCUs are mixed units treating neurological and neurosurgical patients, functioning either inside a general ICU as dedicated beds or in separate autonomous units. A survey in Germany showed that only 20% of NCCUs functioned as independent intensive care units of neurology or neurosurgical departments. The majority of neurocritical beds were part of interdisciplinary units, where only 25% of them had a neurologist in their team[19],[20].

The organization of NCCUs is not always clearly defined. An ICU can be open, semi-open and closed. By an open ICU any physician can admit and care for ICU patients, while in a semi-open ICU involves consulting intensivists, while patients are admitted from other physicians. By the closed ICU, which is typical for medical ICUs, intensivists admit and attend all ICU patients[21]. Team composition may vary and can include a large variety of specialists.

Given this lack of organizational criteria for the development of NCCUs, Neurocritical Care Society tried to outline a recommend framework for the structure, personnel and processes for a successful neurocritical care program[22].

Three levels of NCCUs can be defined. Level I units are comprehensive centers of neurocritical care equipped and able to provide expert and interdisciplinary care, featuring a wide spectrum of advanced monitoring and surgical and medical treatment, while offers advanced professional training. Level II units are able to stabilize acutely ill patients and treat stable neurocritical diseases. A Level III unit can evaluate and stabilize neurological emergencies, while facilitates transfer to Level I and II units[22]-[24].

A good coordinated, multidisciplinary team is critical prerequisite for the optimal function of the unit. It has been shown that an interdisciplinary team with expertise in neurocritical care can achieve better outcomes regarding mortality, functional outcomes and resource management [25]-[27]. Standards for continuous training and physician staffing of the interdisciplinary team have been proposed in detail[2][2].

Similarly, adequate nurse training and competency in neurocritical care is required to provide safe and quality care in NCCUs. Skill and competency of the nurses should be assessed periodically using quality indicators describing nursing care[28]. Staffing ratios for an optimal nursing care have been also proposed[22]. Specialty certifications are also an indicator of quality of care and should be encouraged as it may be also associated to improved patients' outcomes[29],[30].

Of interest is the important role of pharmacists as essential members of the interdisciplinary team of the NCCU. Studies suggest that intensive care pharmacists may lead to improvement of care and patients' outcome, due to reduce of adverse drug reactions[31]-[33], decrease ventilator days [34] and improvements in morbidity, mortality and length of stay[35],[36], while there are also evidence suggesting an optimized resource management by reducing medication costs[37].

Furthermore, respiratory therapists applying protocols and procedures regarding mechanical ventilation and tracheostomy[38], as well as physical, occupational and speech therapists and qualified dietitians[39] may improve outcomes and cost-effectiveness as well as successfully evaluate and dealing with the complexity of problems regarding neurocritical care.

Of importance regarding processes and safety in NCCU is the building and implementation of protocols and guidelines combined with the evaluation of outcomes[40]. Safety of patients' care is also an essential part of ICU structure and the quality control of the unit's function. Standardized processes, guidelines, protocols and checklists can help reducing errors and building a culture of safety, which affects patient outcomes. Recurrent evaluation and improvements in quality of neurocritical care as part of the structure of a NCCU is essential for the maintenance of a safe environment for patients and staff[41]-[45].

Multimodal monitoring in NCCU

As most of the patients with severe neurological and neurosurgical diseases in NCCU are sedated and intubated, neurologic examination, although essential for clinical evaluation of the patient, may be extremely difficult and insufficient. Thus, neurocritical monitoring parallel to the monitoring of systemic parameters, such as cardiac rhythm, arterial blood pressure, oxygen saturation, temperature etc. is of essential importance for the implementation and response of the patient to therapeutic interventions, as well as detection of early signs of a neurological decompensation. In addition, neurocritical monitoring may help understanding the complexity of the underlying disorders, detecting an early neurological deterioration, guiding individualized care decisions and implementing therapeutic protocols and eventually improving neurological outcome and quality of life of patients with severe neurological illnesses[46].

Global neurologic status remains a tool to evaluate patients' clinical status and is recommended to be routinely performed. However, a change in neurological status may often present too late to inform therapeutic management. Therefore, various neuromonitoring tools have been development for different physiologic parameters, which can adequately reflect patients' pathology[47].

The concept of multimodal monitoring aims to detect a secondary brain injury and guide therapeutic decisions. Monitor of intracranial pressure (ICP) is a wide spread technique used mainly to detect elevated intracranial pressure and imminent brain herniation in high-risk patients with acute brain trauma and imaging or clinical features suggestive of increased intracranial pressure[48].

Monitor of ICP can be done either through a ventriculostomy or using intraparenchymal monitoring, as these are the gold standards for measuring ICP. Other invasive methods of ICP monitor exist, however their measurements are less accurate[49]. Alternatively, a noninvasive method to monitor ICP can be used, although there are not very accurate too. Transcranial Doppler can be used to predict ICP, by evaluating various parameters, however accuracy of this method is low[50]. Tympanic membrane displacement is another method based on the transmission of the CNS pressure to the perilymph of cochlea, however this technique is characterized from several limitations[5][1].

Electroencephalography is frequently implemented in NCCUs not only in the context of status epilepticus and for the detection of epileptiform activity in general, but also after cardiac arrest and prediction of cerebral vasospasm after subarachnoidal hemorrhage. As a monitor of cortical function, EEG reactivity and burst suppression musters are markers predicting recovery after a cardiac arrest, while changes in EEG pattern may predict changes in cerebral blood flow in the context of vasospasm after subarachnoid hemorrhage[52].

Transcranial Doppler sonography in neurointensive care can have many applications as an inexpensive and non-invasive method. Monitoring of vasospasm following a subarachnoid hemorrhage can predict the onset of ischemia, as increased systolic flow velocities are related to delayed cerebral ischemia and poor outcomes. Although TCD has been shown to be highly sensitive and offering a negative predictive value for delayed ischemia[53],[54], lack of studies regarding the impact of TCD on clinically relevant outcomes has limited its use. Furthermore, indications for TCD in NCCUs are the detection of microembolic signals due to carotid stenosis, helping estimating the stroke risk, the evaluation of cerebrovascular reserve and the assessment of cerebral autoregulation[55]. Although not typically part of a multimodal neuromonitoring, these TCD applications may inform clinical decision making in NCCUs and lea to improvements in patients' outcomes.

Cerebral microdialysis is a technique involving a catheter inserted in brain parenchyma and allowing frequent sampling and analysis of various markers of interest, such as glucose, glutamate, lactate and pyruvate. Although relative safe, this method has many limitations such as episodic collection of samples and right placement of the probe in the parenchyma. In addition, lack of evidence and trials regarding cerebral microdialysis limits practical interpretation of findings and development of recommended practices[56].

Sensors for brain tissue oxygenation can be implanted to evaluate brain tissue oxygen tension. There is evidence of a correlation between reduced brain tissue oxygenation tension and worse outcome[57]. Monitoring of ICP in combination with measurements of brain tissue oxygenation compared to ICP monitoring alone resulted in a significant decrease of average duration and depth of tissue brain hypoxia and a trend toward lower mortality and favorable outcomes[58]. Further, near-infrared sprectroscopy measures the attenuation of reflected light, which depends on the level of oxygen saturation in blood. Noninvasive sensors can measure brain parenchyma oxygenation, although their use can be limited from factors such as skin tone or scull thickness. Additionally, although there is still a lack of evidence in literature regarding the impact of this modality in patients' outcome, its combined use with other modalities can be implemented in monitoring cerebral autoregulation[59]. Alternatively, jugular venous bulb oximetry is an invasive method less frequently used and is subject to many limitations, such as low accuracy and secondary complications, such as infection and jugular venous thrombosis and should be used only as part of a multimodal monitoring[52].

Finally, regional cerebral flowmetry is a method used to monitor cerebral blood flow. Using a thermal diffusor flowmeter, blood flow can be estimated from thermal loss along two elements. This method has its limitations, as it is highly sensitive to positioning and its accuracy depends on patient temperatures. There is also a lack of evidence regarding its predictive role. Alternatively, a laser doppler flowmeter measures erythrocyte flux directly, however its use is still experimentally[56].

Neurological Diseases and Outcomes

Although initially neurocritical care involved brain injury and neurosurgical patients, it currently involves a broad spectrum of neurological diseases and conditions related to disorders of consciousness, circulatory or respiratory functions as a result of a neurological disease or complications of a neurological disease such as infections, sepsis, aspiration etc. Next to traumatic brain or spine injury, neurologic diseases associated with neurocritical care are acute cerebrovascular disorders, infectious disorders, such as encephalitis or abscesses, or inflammatory disorders, such as NMDAR-encephalitis or severe Guillain-Barre syndrome, refractory status epilepticus or brain tumors. More rarely, disorders associated with neurodegenerative diseases, such as a Parkinson crisis or respiratory insufficiency by ALS, as well as hypoxic or metabolic encephalopathies, tetanus, intoxications or a malignant neuroleptic syndrome may necessitate treatment in NCCUs[60].

There is robust evidence that neurocritical care improves outcomes, especially when specialized neurointensivists are involved[61],[62]. A reduction of length of stay, without increase in complications and increased chances of discharge to home have been related to more clinician experience due to patient volume, adherence to protocols, earlier catheter removal and mobilization and use of improved technology and neuromonitoring data[61],[63]-[66].

Outcomes of patients with acute cerebrovascular disorders have been improved due to the development of stroke units[67]. Neurocritical care has also been associated to better outcomes of stroke patients. A benefit for patients with ischemic stroke, as well as intracerebral hemorrhage, has been found regarding length of stay, decreased mortality and increased rate of return to pre-stroke function when neurointensivists were involved in patients' treatment. Similarly, improved outcomes have been shown for patients with intracerebral hemorrhage treated in NCCUs [68]-[71]. Regarding subarachnoidal hemorrhage, there is evidence of decreased length of stay in hospital, decreased rate of ventriculoperitoneal shunting, decreased mortality and increased rate of favorable disposition with increased rate of good functional outcome for patients treated in specialized neurocritical units with presence of neurointensivists[72]-[74].

Apart from acute cerebrovascular disorders and traumatic brain injury, data regarding other diseases are scarce in literature and not always consistent due to heterogeneity. In one study patients with status epilepticus admitted to NCCU were more likely to become continuous electroencephalograms and less likely to be intubated compared to patients treated in a medical ICA, however the overall mortality, length of stay and outcome was not different between these two groups[75]. Outcome of cerebral venous sinus thrombosis was improved after institution of NCCU, however data for other diseases are in general rare[21].

In addition, there are evidence of a financial benefit of a NCCU. Although neurocritical illnesses are costly and resource demanding [76], NCCUs staffed with neurointensivists can lead to lower costs due to decrease in length of stay and lower total costs of care[77],[78]. While in another study a dedicated NCCU was related to higher costs, lower mortality and better quality of life outweighed the extra NCCU costs resulting eventually to improved cost-effectiveness[79].

Conclusions

Neurocritical care has been evolved in the last decades and is now an essential part of critical care in many health systems worldwide. The spectrum of neurological illnesses treated in an NCCU has similarly been evolved. There is convincing evidence of improved outcomes of neurocritically ill patients, however functional outcomes remain oft poor. Beside improvements in protocols and training of neurointensivists, technological advances have improved neurocritical monitoring. However, multimodal monitoring needs further research to elucidate its role in informing therapeutic decisions. Patients' outcomes depend on the interpretation of data from multimodal monitoring, implementation of informed protocols regarding patients' management and developing and implementation of therapy according to changes detecting in multimodal monitoring. Neurointensivists and NCCUs with their interdisciplinary teams are expecting to have a leading role not only in treating neurocritically ill patients, but also in research and further scientific advancement of this field.

References

[1] Lassen HC. A preliminary report on the 1952 epidemic of poliomyelitis in Copenhagen with special reference to the treatment of acute respiratory insufficiency. ***Lancet***. Jan 3 1953;1(6749):37-41. doi:10.1016/s0140-6736(53)92530-6

[2] Wijdicks EF. The history of neurocritical care. ***Handb Clin Neurol***. 2017;140:3-14. doi:10.1016/B978-0-444-63600-3.00001-5

[3] Michalski D, Jungk C, Beynon C, et al. [Focus on neurological intensive care medicine 2022/2023 : Summary of selected intensive medical care studies]. ***Anaesthesiologie***. Dec 2023;72(12):894-906. Fokus Neurologische Intensivmedizin 2022/2023 : Zusammenfassung ausgewahlter intensivmedizinischer Studien. doi:10.1007/s00101-023-01352-7

[4] Ropper AH. Neurological intensive care. ***Ann Neurol***. Oct 1992;32(4):564-9. doi:10.1002/ana.410320413

[5] Smith M. I. Neurocritical care: has it come of age? ***Br J Anaesth***. Dec 2004;93(6):753-5. doi:10.1093/bja/aeh275

[6] Hilberman M. The evolution of intensive care units. ***Crit Care Med***. Jul-Aug 1975;3(4):159-65. doi:10.1097/00003246-197507000-00006

[7] Ibsen B. The anaesthetist's viewpoint on the treatment of respiratory complications in poliomyelitis during the epidemic in Copenhagen, 1952. ***Proc R Soc Med***. Jan 1954;47(1):72-4.

[8] Bryan-Brown CW. My first 50 years of critical care (1956-2006). ***Am J Crit Care***. Jan 2007;16(1):12-6.

[9] Rosengart MR. Critical care medicine: landmarks and legends. ***Surg Clin North Am***. Dec 2006;86(6):1305-21. doi:10.1016/j.suc.2006.09.004

[10] Rogers RM, Weiler C, Ruppenthal B. Impact of the respiratory intensive care unit on survival of patients with acute respiratory failure. ***Chest***. Jul 1972;62(1):94-7. doi:10.1378/chest.62.1.94

[11] Wijdicks EF, Worden WR, Miers A, Piepgras DG. The early days of the neurosciences intensive care unit. ***Mayo Clin Proc***. Sep 2011;86(9):903-

6. doi:10.4065/mcp.2010.0815
[12] Borel C, Hanley D. Neurologic intensive care unit monitoring. ***Crit Care Clin***. Jul 1985;1(2):223-39.
[13] Smith WS, Weingart S. Emergency Neurological Life Support (ENLS): what to do in the first hour of a neurological emergency. ***Neurocrit Care***. Sep 2012;17 Suppl 1:S1-3. doi:10.1007/s12028-012-9741-x
[14] Diringer MN, Bleck TP, Claude Hemphill J, 3rd, et al. Critical care management of patients following aneurysmal subarachnoid hemorrhage: recommendations from the Neurocritical Care Society's Multidisciplinary Consensus Conference. ***Neurocrit Care***. Sep 2011;15(2):211-40. doi:10.1007/s12028-011-9605-9
[15] Wijdicks EF. The journal and its first decade. ***Neurocrit Care***. Feb 2014;20(1):1-2. doi:10.1007/s12028-013-9943-x
[16] Murphy SA, Bell MJ, Clark ME, Whalen MJ, Noviski N. Pediatric Neurocritical Care: A Short Survey of Current Perceptions and Practices. ***Neurocrit Care***. Oct 2015;23(2):149-58. doi:10.1007/s12028-015-0120-2
[17] Le Roux P, Menon DK, Citerio G, et al. Consensus summary statement of the International Multidisciplinary Consensus Conference on Multimodality Monitoring in Neurocritical Care : a statement for healthcare professionals from the Neurocritical Care Society and the European Society of Intensive Care Medicine. ***Intensive Care Med***. Sep 2014;40(9):1189-209. doi:10.1007/s00134-014-3369-6
[18] Bouzat P, Marques-Vidal P, Zerlauth JB, et al. Accuracy of brain multimodal monitoring to detect cerebral hypoperfusion after traumatic brain injury*. ***Crit Care Med***. Feb 2015;43(2):445-52. doi:10.1097/CCM.0000000000000720
[19] Bosel J, Kowoll C, Kahmann J, Dziewas R, Schirotzek I, Dohmen C. [Survey study: update on neurological intensive care in Germany 2012: structure, standards and scores in neurological intensive care units]. ***Nervenarzt***. Dec 2012;83(12):1609-18. Umfragestudie „Update Neurointensiv Deutschland 2012": Struktur, Standards und Scores auf deutschen Neurointensivstationen. doi:10.1007/s00115-012-3541-6
[20] Busse O, Hillmann S, Grond M. [Neurointensive care in Germany : Results of an inspection of intensive care units]. ***Nervenarzt***. Feb 2018;89(2):147-155. Neurointensivmedizin in Deutschland : Ergebnisse einer Begehung von Intensivstationen. doi:10.1007/s00115-017-0446-4
[21] Busl KM, Bleck TP, Varelas PN. Neurocritical Care Outcomes, Research, and Technology: A Review. ***JAMA Neurol***. May 1 2019;76(5):612-618. doi:10.1001/jamaneurol.2018.4407
[22] Moheet AM, Livesay SL, Abdelhak T, et al. Standards for Neurologic Critical Care Units: A Statement for Healthcare Professionals from The Neurocritical Care Society. ***Neurocrit Care***. Oct 2018;29(2):145-160. doi:10.1007/s12028-018-0601-1
[23] Rosenberg DI, Moss MM, American Academy of Pediatrics Section on Critical C, American Academy of Pediatrics Committee on Hospital C. Guidelines and levels of care for pediatric intensive care units. ***Pediatrics***. Oct 2004;114(4):1114-25. doi:10.1542/peds.2004-1599
[24] Marshall JC, Bosco L, Adhikari NK, et al. What is an intensive care unit? A report of the task force of the World Federation of Societies of Intensive and Critical Care Medicine. ***J Crit Care***. Feb 2017;37:270-276. doi:10.1016/j.jcrc.2016.07.015
[25] Suarez JI, Zaidat OO, Suri MF, et al. Length of stay and mortality in neurocritically ill patients: impact of a specialized neurocritical care team. ***Crit Care Med***. Nov 2004;32(11):2311-7. doi:10.1097/01.ccm.0000146132.29042.4c
[26] Kramer AH, Zygun DA. Do neurocritical care units save lives? Measuring the impact of specialized ICUs. ***Neurocrit Care***. Jun 2011;14(3):329-33. doi:10.1007/s12028-011-9530-y
[27] Lott JP, Iwashyna TJ, Christie JD, Asch DA, Kramer AA, Kahn JM. Critical illness outcomes in specialty versus general intensive care units. ***Am J Respir Crit Care Med***. Apr 15 2009;179(8):676-83. doi:10.1164/rccm.200808-1281OC
[28] Brown DS, Donaldson N, Burnes Bolton L, Aydin CE. Nursing-sensitive benchmarks for hospitals to gauge high-reliability performance. ***J Healthc Qual***. Nov-Dec 2010;32(6):9-17. doi:10.1111/j.1945-1474.2010.00083.x
[29] Fleischman RK, Meyer L, Watson C. Best practices in creating a culture of certification. ***AACN Adv Crit Care***. Jan-Mar 2011;22(1):33-49. doi:10.1097/NCI.0b013e3182062c4e
[30] Leyden C. Certification as a Quality Initiative. ***J Nurs Adm***. Oct 2015;45(10):467-8. doi:10.1097/NNA.0000000000000234
[31] Leape LL, Cullen DJ, Clapp MD, et al. Pharmacist participation on physician rounds and adverse drug events in the intensive care unit. ***JAMA***. Jul 21 1999;282(3):267-70. doi:10.1001/jama.282.3.267
[32] Ng TM, Bell AM, Hong C, et al. Pharmacist monitoring of QTc interval-prolonging medications in critically ill medical patients: a pilot study. ***Ann Pharmacother***. Apr 2008;42(4):475-

82. doi:10.1345/aph.1K458
[33] Rivkin A, Yin H. Evaluation of the role of the critical care pharmacist in identifying and avoiding or minimizing significant drug-drug interactions in medical intensive care patients. ***J Crit Care***. Feb 2011;26(1):104 e1-6. doi:10.1016/j.jcrc.2010.04.014
[34] Marshall J, Finn CA, Theodore AC. Impact of a clinical pharmacist-enforced intensive care unit sedation protocol on duration of mechanical ventilation and hospital stay. ***Crit Care Med***. Feb 2008;36(2):427-33. doi:10.1097/01.CCM.0000300275.63811.B3
[35] MacLaren R, Bond CA, Martin SJ, Fike D. Clinical and economic outcomes of involving pharmacists in the direct care of critically ill patients with infections. ***Crit Care Med***. Dec 2008;36(12):3184-9. doi:10.1097/CCM.0b013e31818f2269
[36] Netzer G, Liu X, Shanholtz C, Harris A, Verceles A, Iwashyna TJ. Decreased mortality resulting from a multicomponent intervention in a tertiary care medical intensive care unit. ***Crit Care Med***. Feb 2011;39(2):284-93. doi:10.1097/CCM.0b013e3181ffdd2f
[37] Weant KA, Armitstead JA, Ladha AM, Sasaki-Adams D, Hadar EJ, Ewend MG. Cost effectiveness of a clinical pharmacist on a neurosurgical team. ***Neurosurgery***. Nov 2009;65(5):946-50; discussion 950-1. doi:10.1227/01.NEU.0000347090.22818.35
[38] Kollef MH, Shapiro SD, Silver P, et al. A randomized, controlled trial of protocol-directed versus physician-directed weaning from mechanical ventilation. ***Crit Care Med***. Apr 1997;25(4):567-74. doi:10.1097/00003246-199704000-00004
[39] Task Force of ASPEN, American Dietetic Association Dietitians in Nutrition Support Dietetic Practice G, Russell M, et al. American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) and American Dietetic Association (ADA): standards of practice and standards of professional performance for registered dietitians (generalist, specialty, and advanced) in nutrition support. ***Nutr Clin Pract***. Oct 2007;22(5):558-86. doi:10.1177/0115426507022005558
[40] Stockwell DC, Slonim AD. Quality and safety in the intensive care unit. ***J Intensive Care Med***. Jul-Aug 2006;21(4):199-210. doi:10.1177/0885066606287079
[41] Huang DT, Clermont G, Kong L, et al. Intensive care unit safety culture and outcomes: a US multicenter study. ***Int J Qual Health Care***. Jun 2010;22(3):151-61. doi:10.1093/intqhc/mzq017
[42] Dykes PC, Rozenblum R, Dalal A, et al. Prospective Evaluation of a Multifaceted Intervention to Improve Outcomes in Intensive Care: The Promoting Respect and Ongoing Safety Through Patient Engagement Communication and Technology Study. ***Crit Care Med***. Aug 2017;45(8):e806-e813. doi:10.1097/CCM.0000000000002449
[43] Wick EC, Galante DJ, Hobson DB, et al. Organizational Culture Changes Result in Improvement in Patient-Centered Outcomes: Implementation of an Integrated Recovery Pathway for Surgical Patients. ***J Am Coll Surg***. Sep 2015;221(3):669-77; quiz 785-6. doi:10.1016/j.jamcollsurg.2015.05.008
[44] Pronovost PJ, Weast B, Holzmueller CG, et al. Evaluation of the culture of safety: survey of clinicians and managers in an academic medical center. ***Qual Saf Health Care***. Dec 2003;12(6):405-10. doi:10.1136/qhc.12.6.405
[45] Curtis JR, Cook DJ, Wall RJ, et al. Intensive care unit quality improvement: a "how-to" guide for the interdisciplinary team. ***Crit Care Med***. Jan 2006;34(1):211-8. doi:10.1097/01.ccm.0000190617.76104.ac
[46] Yang MT. Multimodal neurocritical monitoring. ***Biomed J***. Jun 2020;43(3):226-230. doi:10.1016/j.bj.2020.05.005
[47] Peacock SH, Tomlinson AD. Multimodal Neuromonitoring in Neurocritical Care. ***AACN Adv Crit Care***. Summer 2018;29(2):183-194. doi:10.4037/aacnacc2018632
[48] Le Roux P, Menon DK, Citerio G, et al. The International Multidisciplinary Consensus Conference on Multimodality Monitoring in Neurocritical Care: a list of recommendations and additional conclusions: a statement for healthcare professionals from the Neurocritical Care Society and the European Society of Intensive Care Medicine. ***Neurocrit Care***. Dec 2014;21 Suppl 2(Suppl 2):S282-96. doi:10.1007/s12028-014-0077-6
[49] Eide PK, Sorteberg W. Simultaneous measurements of intracranial pressure parameters in the epidural space and in brain parenchyma in patients with hydrocephalus. ***J Neurosurg***. Dec 2010;113(6):1317-25. doi:10.3171/2010.7.JNS10483
[50] Brain Trauma F, American Association of Neurological S, Congress of Neurological S, et al. Guidelines for the management of severe traumatic brain injury. VI. Indications for intracranial pressure monitoring. ***J Neurotrauma***. 2007;24 Suppl 1:S37-44. doi:10.1089/neu.2007.9990
[51] Shimbles S, Dodd C, Banister K, Mendelow AD, Chambers IR. Clinical comparison of tympanic membrane displacement with invasive intracranial pressure measurements. ***Physiol Meas***. Dec 2005;26(6):1085-92. doi:10.1088/0967-

3334/26/6/017

[52] Claassen J, Vespa P, Participants in the International Multi-disciplinary Consensus Conference on Multimodality M. Electrophysiologic monitoring in acute brain injury. ***Neurocrit Care***. Dec 2014;21 Suppl 2:S129-47. doi:10.1007/s12028-014-0022-8

[53] Kumar G, Shahripour RB, Harrigan MR. Vasospasm on transcranial Doppler is predictive of delayed cerebral ischemia in aneurysmal subarachnoid hemorrhage: a systematic review and meta-analysis. ***J Neurosurg***. May 2016;124(5):1257-64. doi:10.3171/2015.4.JNS15428

[54] Esmael A, Flifel ME, Elmarakby F, Belal T. Predictive value of the transcranial Doppler and mean arterial flow velocity for early detection of cerebral vasospasm in aneurysmal subarachnoid hemorrhage. ***Ultrasound***. Nov 2021;29(4):218-228. doi:10.1177/1742271X20976965

[55] Bonow RH, Young CC, Bass DI, Moore A, Levitt MR. Transcranial Doppler ultrasonography in neurological surgery and neurocritical care. ***Neurosurg Focus***. Dec 1 2019;47(6):E2. doi:10.3171/2019.9.FOCUS19611

[56] Rivera Lara L, Puttgen HA. Multimodality Monitoring in the Neurocritical Care Unit. ***Continuum (Minneap Minn)***. Dec 2018;24(6):1776-1788. doi:10.1212/CON.0000000000000671

[57] Oddo M, Bosel J, Participants in the International Multidisciplinary Consensus Conference on Multimodality M. Monitoring of brain and systemic oxygenation in neurocritical care patients. ***Neurocrit Care***. Dec 2014;21 Suppl 2:S103-20. doi:10.1007/s12028-014-0024-6

[58] Okonkwo DO, Shutter LA, Moore C, et al. Brain Oxygen Optimization in Severe Traumatic Brain Injury Phase-II: A Phase II Randomized Trial. ***Crit Care Med***. Nov 2017;45(11):1907-1914. doi:10.1097/CCM.0000000000002619

[59] Rivera-Lara L, Geocadin R, Zorrilla-Vaca A, et al. Validation of Near-Infrared Spectroscopy for Monitoring Cerebral Autoregulation in Comatose Patients. ***Neurocrit Care***. Dec 2017;27(3):362-369. doi:10.1007/s12028-017-0421

[60] Bosel J. [Modern principles of neurocritical care]. ***Nervenarzt***. Dec 2018;89(12):1411-1427. Moderne Prinzipien der neurologischen Intensivmedizin. doi:10.1007/s00115-018-0634-x

[61] Kramer AH, Zygun DA. Neurocritical care: why does it make a difference? ***Curr Opin Crit Care***. Apr 2014;20(2):174-81. doi:10.1097/MCC.0000000000000076

[62] Finley Caulfield A, Mlynash M, Eyngorn I, et al. Prognostication of ICU Patients by Providers with and without Neurocritical Care Training. ***Neurocrit Care***. Aug 2022;37(1):190-199. doi:10.1007/s12028-022-01467-6

[63] Varelas PN, Conti MM, Spanaki MV, et al. The impact of a neurointensivist-led team on a semiclosed neurosciences intensive care unit. ***Crit Care Med***. Nov 2004;32(11):2191-8. doi:10.1097/01.ccm.0000146131.03578.21

[64] Varelas PN, Hacein-Bey L, Schultz L, Conti M, Spanaki MV, Gennarelli TA. Withdrawal of life support in critically ill neurosurgical patients and in-hospital death after discharge from the neurosurgical intensive care unit. Clinical article. ***J Neurosurg***. Aug 2009;111(2):396-404. doi:10.3171/2009.3.JNS08493

[65] Kramer AH, Zygun DA. Declining mortality in neurocritical care patients: a cohort study in Southern Alberta over eleven years. ***Can J Anaesth***. Oct 2013;60(10):966-75. doi:10.1007/s12630-013-0001-0

[66] Russell D, VorderBruegge M, Burns SM. Effect of an outcomes-managed approach to care of neuroscience patients by acute care nurse practitioners. ***Am J Crit Care***. Jul 2002;11(4):353-62.

[67] Jorgensen HS, Nakayama H, Raaschou HO, Larsen K, Hubbe P, Olsen TS. The effect of a stroke unit: reductions in mortality, discharge rate to nursing home, length of hospital stay, and cost. A community-based study. ***Stroke***. Jul 1995;26(7):1178-82. doi:10.1161/01.str.26.7.1178

[68] Bershad EM, Feen ES, Hernandez OH, Suri MF, Suarez JI. Impact of a specialized neurointensive care team on outcomes of critically ill acute ischemic stroke patients. ***Neurocrit Care***. 2008;9(3):287-92. doi:10.1007/s12028-008-9051-5

[69] Varelas PN, Schultz L, Conti M, Spanaki M, Genarrelli T, Hacein-Bey L. The impact of a neuro-intensivist on patients with stroke admitted to a neurosciences intensive care unit. ***Neurocrit Care***. 2008;9(3):293-9. doi:10.1007/s12028-008-9050-6

[70] Knopf L, Staff I, Gomes J, McCullough L. Impact of a neurointensivist on outcomes in critically ill stroke patients. ***Neurocrit Care***. Feb 2012;16(1):63-71. doi:10.1007/s12028-011-9620-x

[71] Diringer MN, Edwards DF. Admission to a neurologic/neurosurgical intensive care unit is associated with reduced mortality rate after intracerebral hemorrhage. ***Crit Care Med***. Mar 2001;29(3):635-40. doi:10.1097/00003246-200103000-00031

[72] Lerch C, Yonekawa Y, Muroi C, Bjeljac M, Keller E. Specialized neurocritical care, severity grade, and outcome of patients with aneurysmal subarachnoid hemorrhage. ***Neurocrit Care***.

2006;5(2):85-92. doi:10.1385/ncc:5:2:85

[73] Josephson SA, Douglas VC, Lawton MT, English JD, Smith WS, Ko NU. Improvement in intensive care unit outcomes in patients with subarachnoid hemorrhage after initiation of neurointensivist co-management. ***J Neurosurg***. Mar 2010;112(3):626-30. doi:10.3171/2009.8.JNS09441

[74] Egawa S, Hifumi T, Kawakita K, et al. Impact of neurointensivist-managed intensive care unit implementation on patient outcomes after aneurysmal subarachnoid hemorrhage. ***J Crit Care***. Apr 2016;32:52-5. doi:10.1016/j.jcrc.2015.11.008

[75] Varelas PN, Corry J, Rehman M, et al. Management of status epilepticus in neurological versus medical intensive care unit: does it matter? ***Neurocrit Care***. Aug 2013;19(1):4-9. doi:10.1007/s12028-013-9840-3

[76] Raj R, Bendel S, Reinikainen M, et al. Costs, outcome and cost-effectiveness of neurocritical care: a multi-center observational study. ***Crit Care***. Sep 20 2018;22(1):225. doi:10.1186/s13054-018-2151-5

[77] Mirski MA, Chang CW, Cowan R. Impact of a neuroscience intensive care unit on neurosurgical patient outcomes and cost of care: evidence-based support for an intensivist-directed specialty ICU model of care. ***J Neurosurg Anesthesiol***. Apr 2001;13(2):83-92. doi:10.1097/00008506-200104000-00004

[78] Varelas PN, Abdelhak T, Wellwood J, Benczarski D, Elias SB, Rosenblum M. The appointment of neurointensivists is financially beneficial to the employer. ***Neurocrit Care***. Oct 2010;13(2):228-32. doi:10.1007/s12028-010-9371-0

[79] Grieve R, Sadique Z, Gomes M, et al. An evaluation of the clinical and cost-effectiveness of alternative care locations for critically ill adult patients with acute traumatic brain injury. ***Br J Neurosurg***. Aug 2016;30(4):388-96. doi:10.3109/02688697.2016.1161166