

## EDITORIAL, DISCUSSION Deployment of Artificial Intelligence in Neurocritical Care

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Readers of Telehealth and Medicine Today might ask, "What is the relevance of artificial intelligence (AI) to telehealth and telemedicine?" Not surprisingly, the answer lies, at least in part, in the application of AI through telehealth to mediate the issues of misdistribution of the demand versus supply of healthcare services. That and more are probably possible. Understanding the current status of AI in healthcare is the first step and the goal of this editorial.

In the last few years, we have witnessed unprecedented growth and development in the deployment of AI in healthcare. Simultaneously, super-specialization and sub-specialization niches in clinical areas have also increased. Neurocritical care (NCC) is one such area. This communication discusses the present status of some of the clinical challenges within NCC that AI could address. This includes unlocking clinically relevant information hidden in massive amounts of data. In an NCC setup, there are limitations and even inefficiencies in traditional approaches. It is possible that, eventually, AI could help mitigate some of these issues. However, at present, we are in a stage of transition. We still do not have enough data to unequivocally identify all the use cases for AI in an NCC unit. The purist may require double-blind, randomized controlled, multi-institutional cross-over studies before advocating the use of AI in an NCC. However, this is a time-consuming, labor-intensive procedure with several challenges.

The "A" in artificial intelligence should ideally stand for Augmenting, Amplifying, Accelerating, and

Assisting in an Ambient milieu.<sup>1</sup> Today, AI is being adopted for the management of critically ill patients in an NCC unit. Immersed in voluminous dynamic data, secondary to multimodality monitoring (MMM), an intensivist could benefit from predictive analytics. Components of AI used in clinical practice include machine learning (ML), deep learning (DL), natural language processing (NLP), fuzzy logic (FL), convolutional neural networks (CNN), and data mining (DM). Big data (BD) are large, complex data sets that cannot be analyzed using traditional statistical modeling. These components of AI are increasingly being used in NCC.<sup>2</sup> Converting computing power to meaningful clinical information is a challenge. The use of AI needs a thorough, systematic evaluation before incorporation into management.

NCC is primarily real-time, dynamic management of critically ill patients with neurological disorders with multi-factorial compromised brain functions. Management includes real-time analysis of large volumes of scores from different types of data. MMM includes close monitoring of ventilation parameters, intracranial pressure (ICP), hemodynamics, body temperature, fluid intake-output, and serial neurological examinations. In addition to electrophysiological monitoring of brain and cardiac functions, AI predicts earlier neurological deterioration, enabling better management and outcomes. Predicting a rise in ICP, sub-clinical seizures, and maintaining pulmonary functions are AI-enabled illustrations.<sup>3</sup>

<sup>\*</sup>The Appendix after the References defines the acronyms used in the article.

#### **Challenges for NCC Teams**

The complexity of data from each patient often overburdens the NCC teams. In a state-of-the-art neuro ICU, there might be 200 variables to analyze. The Miller principle states that humans can only consider two variables efficiently and concurrently in a decision-making process. This capacity is lost when dealing with more than seven variables.<sup>4</sup> The "black box" factor makes it impossible to understand how an ML model came to a particular conclusion. In addition, intensivists cannot precisely compute how they arrive at a final decision. The AI decision is based on the analysis of voluminous, reliable, relevant data. Regulations suggest that the beneficiary (the patient) has a right to an explanation as to how recommendations were made by models and algorithms.<sup>5</sup> The author has, in a previous publication, pointed out that "ever-changing, futuristic, user-friendly, uncomplicated regulatory requirements promoting compliance and adherence are needed" for the deployment of AI in clinical practice. This is particularly so for NCC.6

## **Predicting Future Events**

The ability to predict future events and trends is crucial. To this end, digital twins and predictive analytics play a role.

## The Digital Twin

Digital twins are digital replicas of the physical environment with voluminous, continually changing data. The methodology for building an NCC digital twin is based on a thorough understanding of underlying pathophysiology. These models enable the testing of clinical decisions in an actionable way, in an "in silico" environment, before executing treatment strategies on living patients. A validated model for training and clinical practice in an NCC unit has been proposed.<sup>7</sup>

### **Predictive Analytics**

Predictive analytics uses data from MMM of complex and dynamic interacting electrophysiologic indices obtained from critical neurologically ill patients to foresee events before their occurrence. Data are visualized on multiple monitors in multiple formats or presented as text displays. This increases the probability of error, as providers must collect, maintain, and integrate data mentally. Taking into account this information overload, data visualization should be intuitive and user-friendly with graphical displays.<sup>8</sup>

## Clinical Use Cases of AI in an NCC Unit

Critical care specialists must quickly process huge volumes of data and act on them urgently. The NCC environment involves EEGs, multimodal intracranial monitoring, and complex imaging. BD focuses on description, prediction, and prescription, which are difficult for a human to do in real-time.<sup>9</sup> As critically ill children with acute neurological injury have higher mortality and morbidity, predictive models would be beneficial. An ML approach independently identified previously known causes of secondary brain injury.<sup>10</sup> In an NCC setting, integrating large volumes of complex critical information into effective clinical decisions to improve patient outcomes is mandatory, and AI could be a valuable aid.<sup>11</sup>

There are many specific clinical use cases where AI interventions have been attempted in an NCC. Every NCC patient has a constellation of multiple, complex, co-existing clinical conditions. Hence, there are major limitations even in describing the current standard of care, challenges, and gaps in clinical management for individual clinical conditions.

At present, AI is primarily contemplated as a use case for a specific clinical condition, not for a combination of multiple clinical conditions, as encountered in the real world. "Standard" protocols are, at best, guidelines and are necessarily individualized in different NCC units. The published literature is insufficient to unequivocally demonstrate how the proposed AI or algorithm would address these challenges. Providing concrete examples and data to support ideas, while necessary to enhance credibility and applicability, may not be possible without more studies.

#### **Acute Kidney Injury**

Acute kidney injury (AKI), which leads to poor prognosis and high mortality, is common in the neuro ICU. Ensemble ML models have been developed for predicting AKI following brain surgery. Four ML algorithms have been used. These include C5.0, support vector machine (SVM), Bayes Optimization, and Extreme Gradient Boost (XGBoost). The incidence of AKI in critically ill patients following brain surgery was reportedly 20.8%. Intra-operative blood pressure, postoperative oxygenation index, oxygen saturation, creatinine, albumin, and urea and calcium levels were associated with postoperative AKI occurrence. The ensemble ML algorithm could be useful in forecasting AKI.<sup>12</sup>

## **Antibiotic Choice**

Long-term effects after the implementation of computer-assisted decision support systems have been studied. Adherence to locally adapted guidelines improved from 60% to 90% (post-implementation), decreasing ICU mortality significantly when implementing rational antibiotic treatment.<sup>13</sup>

#### **Brain Death**

Confirmation of brain death is particularly relevant in an NCC unit.<sup>14,15</sup> Prediction based on ensembled artificial neural networks (ANNs) in a neurosurgical ICU has been reported.<sup>16</sup>

#### **Deep Venous Thrombosis**

An ML-based clinical pre-test probability strategy has been reported for deep venous thrombosis (DVT). Pretest prediction models simplified and improved intervention and diagnostic processes among patients in the neuro ICU with suspected DVT. The study was carried out on 518 patients, where 189 eventually developed DVT.<sup>17</sup>

## Delirium

Earlier identification of delirium in a NICU is possible with AI. Real-time heart rate variability, assisted by ML techniques has been used.<sup>18</sup> Static and dynamic ML algorithms have been trained, tested, and externally validated to predict the earlier onset of delirium. The static model, using data from the first 24h, predicted delirium. The dynamic model predicted delirium up to 12h in advance, enabling proactive intervention.<sup>19</sup> Wang et al.<sup>20</sup> validated and deployed models for predicting delirium in critically ill adult patients on ICU admission. Delirium occurred within 48 h. 24-h models enabled delirium prediction for patients discharged one day after ICU admission.

#### **Electrophysiology and Neuroimaging**

DL has been used to classify ICP waveforms and potential clinical applications. Patients with poor outcomes showed a lower incidence of normal waveforms. Analysis of the shape of the ICP pulse waveform and its temporal change was critical. Data were taken from continuous ICP recordings with parenchymal probes. An inverse relationship was found for ICP less than 20 mm Hg, with markedly increased occurrence of pathological waveforms in the unfavorable outcome group.<sup>21</sup>

#### Infections

There is a time delay between the onset of sepsis and changes in laboratory values, which delays the diagnosis of new episodes of sepsis. Incorporating vital signs with electronic health records (EHR) enables accurate ML prediction of sepsis onset 4 to 12 h before clinical identification.<sup>22</sup> Multivariate Logistic Regression (LR), along with the least absolute shrinkage and selection operator regression, has been used to predict the possibility of intracranial infection in patients with external ventricular drainage.<sup>23</sup>

#### **Intracranial Pressure**

DL, a hierarchical form of ML, has been deployed to model the relationship between ICP and waveform morphology, enabling accurate detection of ICP. The algorithm was 92.05%  $\pm$  2.25% accurate. The CNN was effective in learning the properties of ICP beat waveforms.<sup>24</sup>

## **Major Morbidity and Mortality**

Bihorac et al.25 described the development and validation of an ML risk algorithm for major complications and death after surgery. In a single-center cohort of more than 51,000 surgical patients undergoing major inpatient surgery, the authors developed a framework for a preoperative risk algorithm (MySurgeryRisk). Existing clinical data in the EHR were used to predict the occurrence of eight major postoperative complications (AKI, cardiovascular complications, ICU admission >48 h, mechanical ventilation >48 h, neurologic complications, sepsis, venous thromboembolism, wound infections) and death at 1, 3, 6, 12 and 24 months after surgery. These patients were operated on by 590 different surgeons. An algorithm was developed, universally applicable for any type of surgery while using all available data in an EHR platform, with the capacity for automation and implementation in real-time clinical workflow. For each patient, 285 preoperative factors were studied. This is an example of the enormous amount of data that can be analyzed using AI. leading to improved care and outcomes compared with current practices.25

Yu et al.<sup>26</sup> used ML approaches for prediction of mortality in patients undergoing craniotomy for various indications; 67 variables were studied. Optimal parameters for ML algorithm models included LR, random forest (RF), SVM, ANN, and extreme gradient boosting (XGBoost). Python and R were used for statistical analyses. XGBoost was found to be superior to black-box models like SVM and ANN. Multiple variables were found to have statistically significant prognostic value on the outcome of craniotomy using traditional statistical techniques. Using comparative models and application of ML, minimum heart rate, maximum temperature, maximum magnesium, minimum white blood cell (WBC) count, minimum albumin, uric acid, diastolic pressure, minimum and maximum creatine kinase isoenzymes and age at mortality were found to have the greatest impact on the outcome.

#### **Parkinsonism**

Clinical improvements in patients with Parkinson's disease who underwent bilateral deep brain stimulation of the subthalamic nucleus could be predicted based on a multitask DL-based microelectrode recording analysis. This could help determine the appropriate electrode location in new patients.<sup>27</sup>

#### **Postoperative Complications**

Postoperative complications have been predicted using automated real-time EHR data and mobile device outputs.<sup>28</sup> An ML gradient boosting algorithm generates models that predict early postoperative complications (EPC). Pathology and surgery-related variables (anatomical localization, histology, surgical access) were better predictors of EPC. The model predicted complications with 70% accuracy, outperforming conventional statistical methods.<sup>29</sup>

## Seizures

Studies with ML models predicting the onset of early seizures following intracerebral hemorrhage have been reported. Variables considered included cortical hematoma location, volume >10ml, age <65 years, anticoagulant and antiplatelet use, Glasgow Coma Scale (GCS), international normalized ratio, and systolic blood pressure. Reliable prediction could improve patient selection for EEG monitoring and commencement of prophylactic seizure medications.<sup>30</sup>

## Stroke

AI has been used in early detection, diagnosis, treatment, outcome prediction, and prognosis evaluation in stroke management. Prediction models for 28-day in-hospital mortality in elderly patients with ischemic stroke are available. The XGBoost model based on ML exhibited the best short-term death prediction accuracy compared with traditional LR methods and other ML algorithms. Useful predictors include elevated oxygen saturation, aspartate aminotransferase, neutrophils, heart rate, WBC count, creatinine, BUN level, and lymphocytes.<sup>31</sup>

## Traumatic Brain Injury

A simple ML-based algorithm predicted mortality among ICU patients following traumatic brain injury (TBI). Data were derived from patients with TBI in three ICUs. Algorithms based on ICP, mean arterial pressure, cerebral perfusion pressure, and GCS to predict 30-day mortality had greater than 80% accuracy.<sup>32</sup> ML-based algorithms for prognosticating TBI in the elderly are available. Variables included blood test reports, clinical status, co-morbidities, epidemiological factors, mechanical ventilation, and surgery. Thirty-day mortality was studied. Age, body temperature, pupillary nonreactivity, GCS, Abbreviated Injury Scale score, WBC count, calcium, and mechanical ventilation were independently associated with mortality using LR. ML algorithms showed slightly higher accuracy than LR. AdaBoost and RF performed slightly better than LR in predicting the mortality of geriatric patients with TBI.33

## **Risks and Challenges in Deploying AI in NCC**

Clinical use of AI in an NCC is not without risks. There could be an inadvertent bias even in the development of the initial algorithm. Data used to train an AI system might not be truly representative of NCC patients. Data might be incomplete, or numbers might be inadequate. This could result in a skewed outcome, low accuracy levels, and analytical errors. Challenges include developing an algorithm that is easier to use and better than existing clinical decision support systems. The gold standard is to prove that AI betters healthcare outcome in a patient in the NCC, compared to real-time, evidence-based decisions taken by an experienced neurointensivist. Deploying AI in the NCC should be compared with anticipated benefits such as improved diagnostic accuracy, efficiency gains, or enhanced patient outcomes. Publications dealing with adequate numbers specifically addressing these specific areas are awaited.

## Conclusion

After reviewing the main findings and insights gained, and assessing the pros and cons of implementing AI in NCC, the author concludes that there is a long way to go before any evidence-based conclusion can be drawn regarding the efficacy or otherwise of using AI in an NCC unit. Preliminary reports, however, justify the necessity for detailed studies with much larger populations. The co-existence of multiple clinical conditions in the same individual further compounds the problem of proving a direct cause and effect, even when the assistance of AI is sought for an individual clinical condition.

Time alone will tell if AI in NCC will be a bane or a boon. Remote use of AI designed for NCC in smaller critical care units is possible with a good telemedicine system. After all, distance today is meaningless. AI will be adopted in a neurointensivist's armamentarium when there is evidence that AI betters outcomes cost-effectively. Artificial intelligence should never replace a compassionate intensivist. Hopefully, the AI-enabled intensivist will spend more time empathizing with the family and the patient instead of being drowned in voluminous data. The application of AI in the NICU should, at best, be an enabler, a sophisticated tool to help achieve an end and not an end by itself.

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# Application of Al-Generated Text or Related Technology

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## Appendix: Acronyms used in the article

Al: artificial intelligence AKI: acute kidney injury ANNs: artificial neural networks BD: big data CNN: Convolutional Neural Network DL: deep learning EPC: early postoperative complications FL: fuzzy logic GCS: Glasgow Coma Scale EHR: electronic health records ICP: intracranial pressure LR: logistic regression ML: machine learning MMM: multimodality monitoring NCC: neurocritical care NLP: natural language processing RF: random forest TBI: traumatic brain injury