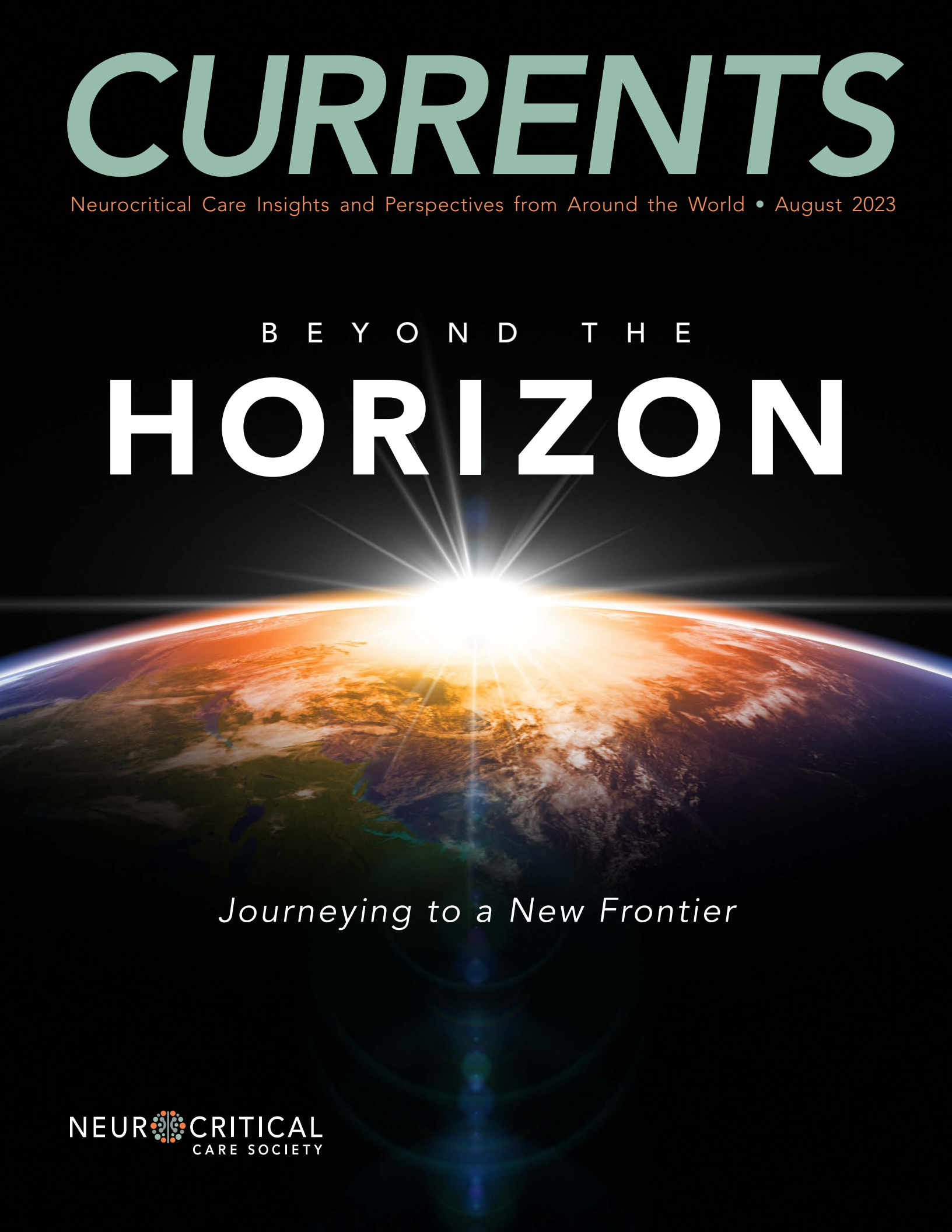
CURRENTS

Neurocritical Care Insights and Perspectives from Around the World • August 2023

BEYOND THE HORIZON



Journeying to a New Frontier

NEUROCRITICAL CARE SOCIETY

CURRENTS

News magazine of the Neurocritical Care Society

August 2023

Neurocritical Care Society

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MESSAGE FROM THE EDITOR

Dear Colleagues,

Welcome to the 2023 annual issue of *Currents*, presented in conjunction with the 21st NCS Annual Meeting! Each year we gather to commemorate the exploration of new frontiers in neurocritical care, and this year's meeting theme reflects our commitment to pushing the boundaries of knowledge and innovation in our field. Whether you are joining us virtually or in person, we look forward to gathering with you all as we embark on a journey "Beyond the Horizon."

We at *Currents* strive to reflect the society's optimism for the future, both for our patients and for our field as a whole. This year, our pursuit of new frontiers aims to broaden our horizons as we reach for the greatest horizon of all—hope. And the spotlight on our profession has never shined more brightly, as neurocritical care was prominently featured in headlines stemming from several newsworthy events this year, including an NFL athlete surviving and recovering from an on-field cardiac arrest and a Hollywood actor suffering from an aneurysmal subarachnoid hemorrhage. As the world becomes increasingly more aware of our strengths and achievements, we are excited to share an even brighter future of cutting-edge care with the world.

Within the pages of this annual issue, you will find articles that embrace innovation and challenge the boundaries of what we once thought possible. We delve into technological and scientific advances of all kinds, including a new artificial intelligence-enhanced management system for patients with severe traumatic brain injury, advances in health equity for acute neurological diseases, and clinical trials of surgical treatment for refractory intracranial hypertension and anti-seizure prophylaxis in intracerebral hemorrhage. In our travels across the globe, our articles span countries far and wide, with contributions from our colleagues in Africa, the Middle East, and South America, among others. These international articles provide valuable context for NCS priorities like the Curing Coma Campaign and standardized ICU EEG nomenclature while raising awareness for important considerations that can help pave the way for more widespread adoption.

Among our most popular articles of the year, we are proud to feature contributions from a diverse group of authors, including physicians, pharmacists, APPs, nurses, and trainees. Our pharmacy section has been especially prolific, and this issue features two great articles about relevant pharmacy concerns that arise at night and facilitating a hospital-wide transition from alteplase to tenecteplase for the management of acute ischemic stroke. Meanwhile, our business section explains new billing updates that every neurointensivist should know about, and our ethics section discusses timely and important topics relevant to both our clinical practice and our lives outside the hospital. We've also got a case from our POCUS section that provides a great lesson on bedside echocardiography, along with helpful pearls for career success from our trainee section. Last but definitely not least, our Stories of Hope series remains foundational to *Currents* and a standard-bearing part of the society's mission. We've featured many outstanding stories this year and have included two especially uplifting highlights in this annual issue. But this is just a taste of what *Currents* has to offer—for more of these and other stories, check out our website to revisit all of our content from the past year.

As Editor-in-Chief, I am immensely proud of the continued growth and evolution of *Currents*. We owe this accomplishment to the dedicated members of our editorial board and the numerous contributors who share their expertise, perspectives, and stories with us. Your commitment to advancing our profession is truly commendable, and we are grateful for your invaluable contributions. To our readers, thank you for your engagement, enthusiasm, and support. You are the driving force behind our endeavors, and we can't wait to hear your thoughts about this issue. As always, if you have an article to submit or would like to brainstorm ideas, please **reach out** to discuss further.

As we embark on a year of exploration and progress, I encourage you to embrace forward-thinking and the momentum that propels us toward the horizon and beyond. We eagerly look forward to your presence at the 22nd Annual Meeting in sunny San Diego, California, where we will undoubtedly be making waves together.

Sincerely,
Michael Reznik, MD
Currents Editor-in-Chief

NEUROCRITICAL CARE SOCIETY

NCS Leadership 2022-2023

Welcome to the NCS 21st Annual Meeting in vibrant Phoenix, AZ! We are thrilled to have you join us for what promises to be a scientific oasis amidst these busy and hot summer months.

Throughout the week, you will have the opportunity to immerse yourself in a diverse array of activities, fostering both professional growth and personal wellness. Our meeting theme, "Beyond the Horizon," will delve into the near-term frontier view of neurocritical care, exploring the latest developments in science, practice, and delivery.

As you prepare for the event, make sure to check out this year's Currents Annual Issue. And don't forget to build your personalized agenda on our mobile app, where you can discover and plan for the sessions that resonate most with you.

We have an outstanding lineup of speakers, including Dr. Azra Bihorac, a renowned authority on AI in critical care, and Dr. Monisha Kumar, who will deliver the Inclusion in Neurocritical Care (INCC) keynote, discussing the impact of changing patient autonomy on health care disparities in our field. Lastly, our closing panel, "Leadership Vision for The Strategic Future of Neurocritical Care," hosted by our current officers and selected past presidents esteemed colleagues, will be your opportunity to ask important questions about the vision of the NCS.

The workshops, in collaboration with the American Society of Neuroimaging, focus on practical and advanced concepts on imaging and ultrasound promise to offer both didactic and hands-on learning experiences. Additionally, prepare to be energized by the late-breaking clinical trial presentations, hot-of-the-press release of new guidelines in neurocritical care, special informal oasis roundtable discussion sessions, and the latest updates from the Curing Coma Campaign's prospective studies.

Beyond the educational components, I am personally looking forward to reconnecting with fellow neurocritical care colleagues, united in our enthusiasm for the inspiring event ahead. Together, we aim to advance patient care and research, and I am confident that our collective time here will foster further progress.

While we anticipate busy days, I would like you to consider carving out some time to engage with the NCS Foundation. Be sure to visit their site to learn more about their valuable work. Also, take part in their special raffle, where you have a chance to win one of four $250 gift cards. To be eligible, simply be a current member of the Neurocritical Care Society and donate $50 or more to the Foundation between August 1 and August 20, 2023. The winners will be randomly selected and notified via email following the Annual Meeting.

Our bustling exhibit hall awaits your exploration, so drop by Booth 410 – the NCS Connect Booth – to engage with our team and discover our range of educational offerings that will keep you learning year-round. Explore Neurocritical Care ON CALL® and ENLS, among other network favorites.

Lastly this event is an extraordinary opportunity to broaden our horizons, gain valuable insights, and contribute to the collective neurocritical care field and we can't continue to strengthen this experience without your feedback. So please be sure take the attendee evaluation when it becomes available on Friday, August 18th.

Once again, welcome to the 21st NCS Annual Meeting! Let's make this week unforgettable as we come together to shape the future of neurocritical care.

Sincerely,
Paul Vespa, MD, FCCM, FAAN, FNCS, FANA
Vice President

Story of Hope: William

By Kimberly Nokes Wilson; Hana Nobleza, MD, MSCI; Lauren Koffman, DO, MS

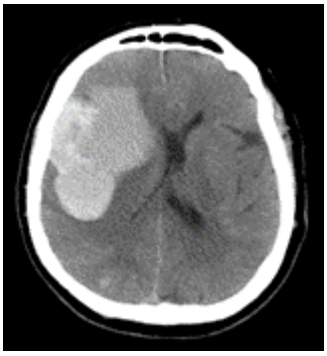


On the morning of April 19, William woke up with some pain in his arm, along with other symptoms he had previously experienced when having a massive heart attack many years ago. After speaking with his cardiologist they decided he would need to come to the office for an evaluation. William was in the bathroom about to brush his hair when he suddenly realized he was not able to pick up the brush with his left hand. He quickly called out to his wife to come help him. She noticed right away that the left side of his face was drooping slightly and his speech seemed different. His wife Pat was on the phone with their daughter and as she was explaining the situation she realized this could be a stroke. William was convinced they could just go to the cardiologist's office but reluctantly agreed to call an ambulance. After William was assessed, he was taken to Baptist Memorial Hospital-DeSoto in Southaven, Mississippi to evaluate him for stroke. Their suspicions were confirmed, and because there was a high concern for stroke, he was given a clot busting medicine called tPA and then transferred to Baptist Memorial Hospital-Memphis for close monitoring.

William in the ICU after undergoing brain surgery

Hanging on by a Thread

While in the ambulance, William's head began to hurt severely, and a follow-up CT scan that was performed upon his arrival in Memphis discovered a brain bleed. He was one of the unfortunate few people to bleed after receiving the clot busting medication. His healthcare providers gave him medications to help stop the bleeding and the rest of the night was a waiting game. William was watched closely in the Neurocritical care unit (NCCU), where staff performed frequent neurologic checks on him.



William's follow-up head CT scan that showed hemorrhagic conversion after receiving tPA

"We were desperately hoping and praying the bleeding would stop throughout the night and that he would not have to have surgery. We were told that if it continued to bleed and he declined, he would need life-saving surgery. We were completely devastated and very scared when it was apparent he had to have surgery. We held on tight to the thread of hope the neurosurgeon gave us due to knowing my dad—the competitor and fighter he has always been. Our entire family was on a roller-coaster of emotions: scared, sad, confused, and mad about the clot buster wondering what his prognosis would be if he had not had it. Despite this we were hopeful and thankful due to the wonderful medical staff working at Baptist Memorial Hospital-Memphis. My mother was burdened with feelings of guilt from consenting to the clot busting medication. Everyone reassured her it was not her fault at all."

By the early morning hours, it was becoming obvious that his condition was worsening and that the bleeding had increased, meaning surgery was becoming more and more likely. William's

Connected to EEG monitoring to look for seizure activity

family was advised by the medical staff that the surgery could save his life, but that he would most likely be permanently weak in his left arm and leg. His close-knit family were all very thankful that the hospital allowed them to gather on April 20, as the odds did not seem to be in their favor. "Hanging on by a thread" were the words that played over and over in their minds after having discussions with the neurosurgical team. Dr. Kenan Arnautovic, of Semmes-Murphey Clinic in Memphis, was the one to offer the surgery, and William's family were appreciative of him for taking on this challenge.

The Pepsi Fight

After the surgery, William had a series of battles ahead of him. He would have to fight to wake from the sedation, fight to breathe on his own, and fight to be able to move his left side. The road to overcoming these challenges was long, and who knew if there would be new obstacles along the way. But as William would say, when a person is surrounded by loved ones, wonderful medical staff, and a great therapist, there is hope that the battle can be won.

As William was breathing on his own and showing signs of improvement, the doctors decided to remove his breathing tube. His family was rejoicing in what seemed to be a step in the right direction, but it turned out to be premature. There was initial excitement when William became awake enough to ask for a Pepsi, but soon afterwards his daughter noticed fluttering eye movements and called his nurse. Ernest Almeria came to assess

> "That glimpse of their William asking for a Pepsi was enough for his family to continue the fight. Nobody was ready to give up, and thankfully William wasn't either."

William and immediately became worried this could be a seizure. The staff responded quickly and connected him to an EEG machine to monitor his brain wave activity; as suspected, he was suffering from seizures.

As part of the treatment for his seizures, William had to be heavily sedated, which meant that a breathing tube had to be replaced so that the ICU could treat the seizures safely. What seemed to be a step forward now led two steps back. But that glimpse of their William asking for a Pepsi was enough for his family to continue the fight. Nobody was ready to give up, and thankfully William wasn't either. The seizures proved difficult to control and many medications and sedatives had to be added. When the ICU team ultimately decided it was safe to reduce the sedation, William did not wake up immediately, and after some time had passed without a return to wakefulness, he underwent a tracheostomy and feeding tube placement. It was very scary for his family not knowing if he would ever open his eyes again and talk, but he eventually started waking up and following some simple commands on his right side.

Time to Transition

One of the hardest decisions William's family had to make would be moving him to another facility. The Baptist Memphis NCCU staff had become their friends and family away from home. They helped and supported the whole family through so many low points, and spent lots of time explaining everything in a way that the family could understand. While William's family had

> "After the surgery, William had a series of battles ahead of him. He would have to fight to wake from the sedation, fight to breathe on his own, and fight to be able to move his left side."

William with his sister on her birthday

grown comfortable in the ICU, it was time for him to transition to a long-term acute care facility that specialized in taking care of patients with brain injuries after they were safe to leave the hospital.

As time went on, William became stronger each day. Eventually he reached a point where the tracheostomy could be removed, though his continued difficulty with swallowing meant he still needed a feeding tube. As his therapy continued, it seemed like things were looking up, and he was starting to regain some function of his left arm and leg as well. Despite his progress, he was not yet ready to go home, so he was relocated to a skilled nursing facility. But his family knew he needed intensive inpatient rehabilitation, even if it was hard to convince others how much of a fighter he was. And there was still so much fight left in him!

William would get another chance to show his determination. On May 26, he developed problems with his breathing and had to be readmitted to Baptist Memphis, where he was diagnosed with a blood clot in his lungs. But while many would see this as a setback, he used it as an opportunity to show how much he had improved. When he was reassessed by physical therapists at the hospital, they decided that he now qualified for admission to Baptist Memorial Rehabilitation Hospital. He then proceeded to gain so much strength and movement from his therapies at Baptist Rehab Hospital that everyone was amazed with his progress. He was even able to start eating again and was finally able to enjoy that Pepsi he had been longing for. William's entire family participated in his rehab and learned ways to help him so that he could regain his independence and be ready to go home.

> "William's entire family participated in his rehab and learned ways to help him so that he could regain his independence and be ready to go home."

Going Back Home

June 30 was a great day for William. He was finally going home to sleep in his own bed. His home may have needed some modifications like handrails and other safety devices, and he needed to use a walker to get around, but he had made it home.

William is now in outpatient therapy three times a week and continues to make strides in his recovery. He credits his wife Pat with his tremendous progress. Since returning home, his feeding tube has been removed and he is spending as much time as he can doing what he loves most—spending time with his family, and especially with his grandchildren. He even surprised his sister by attending her 90th birthday party, which made the day even more special for everyone.

William, his family, and the Baptist Memphis team have all learned a great deal from his experience, and they want others to remember to keep fighting, even when faced with tragedy and the odds seem to be against you. If they can find hope, then so too can others. ●

Story of Hope: Kaitlyn McCaffery

By Angie Murkins, MSN, FNP-BC; Honey Beddingfield, MSN, AG-ACNP, CCRN, CNRN; Lauren Koffman, DO, MS



In 2021, Kaitlyn McCaffery was a 27-year-old professional guide who had traveled to more than sixty-two countries. She had graduated from Cal State Fullerton, where she received a degree in Entrepreneurship and Business. After college she began her adventures around the globe, with a particular interest in physical outdoor activities including rock climbing and hiking.

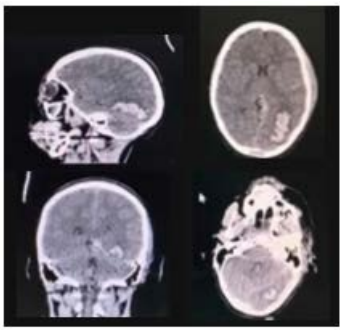
Her latest endeavor led her to Bali, where she planned to open a travel business. After living in Bali for several months, Kaitlyn's world would change on July 31, 2021, when she was found unconscious on the side of the road, presumably having suffered a traumatic injury.

She was taken to Sanglah General Hospital, the largest hospital in Bali, where she was admitted to the intensive care unit and found to have a severe traumatic brain injury (TBI). She was unable to breathe on her own and a drain was placed into her brain to relieve high pressure resulting from the injury and subsequent brain swelling. Head imaging showed multiple severe injuries, including bleeding into and around the brain, as well as a tear in the internal carotid artery, a major blood vessel that supplies blood to the brain. Not only were there neurologic injuries, but she unfortunately also sustained facial fractures, injuries to her cervical spine, and extensive blood clots in her left leg. Without a doubt, there would be a long road to recovery, and she was so far from home.

> "[Her] head imaging showed multiple severe injuries, including bleeding into and around the brain, as well as a tear in the internal carotid artery, a major blood vessel that supplies blood to the brain."

Initially Kaitlyn's local friends were allowed to visit her in the Bali hospital, but she was not awake to realize she had visitors. Unfortunately, Kaitlyn would test positive for COVID soon afterwards, and those visitors were no longer allowed. Kaitlyn's mother, Janine, was unable to get a visa in time to visit her prior to the COVID diagnosis, which meant they were limited





Kaitlyn's initial head CT on arrival

> When she was asked about what good things have come with her recovery, she first mentioned relearning how to swallow and getting her feeding tube taken out.

to interacting over video. In the meantime, Janine started a GoFundMe account to help bring her daughter home to California, which required a transoceanic medical flight costing about $250,000. After successfully raising the necessary funds, Kaitlyn was flown to California, and for the first time since the accident, her family was able to see and touch her after she landed at the airport on August 18, 2021, 18 days after her initial injury. Kaitlyn was then taken directly to Stanford Health Care's Neuro Intensive Care Unit (NICU).

She remained hospitalized at Stanford for over two months while dealing with one crisis after another. The first obstacle to overcome was status epilepticus, with continuous seizures that required heavy sedation to manage and treat. Once the seizures were controlled, her medical team discovered she had developed a tracheoesophageal fistula, which required several surgeries and a long and painful recovery. Despite these challenges, Kaitlin became more and more conscious while in the hospital, and as she became more awake and aware of what was going on, she became overtaken by depression and could not imagine making it through the long road to recovery. In retrospect, she finds this hard to believe, as it is the opposite of her usual bright and positive spirit.

Kaitlyn cannot recall any memory of her hospitalization in Bali or Stanford but is able to remember being moved to a bright and sunny room in a rehabilitation center, which she thinks may have helped jumpstart her memories. After spending almost three months at Stanford, Kaitlyn was finally well enough to transfer to a respiratory rehabilitation center, where she still needed help with breathing and clearing her secretions. She stayed at this rehabilitation center for about six weeks and continued receiving intensive therapy for about three hours a day, five days a week. Once her breathing had improved, she was moved to an acute rehabilitation center, where she spent another month working intensely with therapy services for three hours a day, six days a week.

After rehab, life as Kaitlyn knew it had changed. When she was asked about what good things have come with her recovery, she first mentioned relearning how to swallow and getting her feeding tube taken out. After six months of having the feeding tube, Kaitlyn had set her mind to regaining her ability to swallow with the goal of getting her feeding tube out in one month, and she successfully did so within a day of her ambitious goal. However, she was initially disappointed to find that all food seemed to taste bad, and it took months for her to truly experience flavors again. Kaitlyn had also enjoyed wine prior

to her injury, but she can now no longer drink alcohol due to interactions with her medications. However, once she was swallowing well and her feeding tube was removed, her speech therapist surprised her with a bottle of non-alcoholic wine, which has been a game changer for her recovery. She is now learning to enjoy and discover the large variety of non-alcoholic alternative drinks.

Although she has had to adjust to some new tastes and flavors, she has been able to participate in some other familiar activities since being discharged back home. She has become involved in Rehab Without Walls, an organization that brings rehabilitation out into the real world and which has helped Kaitlyn start rock climbing again.

Kaitlyn is now back at home and has a new priority—helping others. Kaitlyn has come full circle and is now reaching out to help other patients with traumatic brain injuries by sharing her experience. Although she joined a local brain injury support group, she felt that she needed support from survivors her own age. As a result, she started her own local brain injury support group for young adults aged 18-to-35 years old, called Beat the Bias. Not only do they have Facebook and Instagram pages (ig: @Beat.the.Bias) to encourage new membership, but a side group has been formed for caretakers as well. Kaitlyn truly enjoys spending time with her new friends and the positivity from this group has been amazing. Now, a year and a half removed from her injury, Kaitlyn is back at school taking college classes and continuing her pursuit of rock climbing. Despite her past, she is hopeful to return to Bali to make new memories. #fearlesstravelers ●

> "She felt that she needed support from survivors her own age, [so] she started her own local brain injury support group for young adults aged 18-35 years old."

> "Now, a year and a half removed from her injury, Kaitlyn is back at school taking college classes and continuing her pursuit of rock climbing."

The Artificial Intelligence-Enhanced Management of Severe Traumatic Brain Injury (AIMS-TBI) Project: Bringing Data Science to the Bedside for TBI Patients

By Robert McNamara, FCICM; Andrew Udy, FCICM, PhD; Shiv Meka



As part of the Artificial Intelligence-Enhanced Management of Severe Traumatic Brain Injury (AIMS-TBI) project, up to ten trauma ICUs in Australia will begin real-time streaming of traumatic brain injury patient monitoring data to the project's data cloud by the end of this year. Once operational, the scalable AIMS-TBI cloud architecture, developed in collaboration with the Pawsey Supercomputing Center (PSC), Royal Perth Hospital (RPH), The Alfred Hospital, the Royal Melbourne Hospital (RMH), and Curtin and Monash Universities, will enable the timely delivery of monitoring-dependent machine learning and/or deep learning algorithms to the bedside of TBI patients in participating hospitals. The project is currently on hold as the PSC upgrades its facilities to house the first exascale (1018 flops) supercomputer in Australia and the Southern Hemisphere. Full operation of the AIMS-TBI system is contingent upon the PSC. Upon completion of the installation of new infrastructure, the PSC is anticipated to resume full service later this year. In April, RPH began limited operations of the AIMS-TBI system utilising Amazon Web Service (AWS) Cloud infrastructure. Additional AIMS-TBI sites are expected to go live in the coming months.

The three-year development of the AIMS-TBI system required extensive effort and resources. Using high resolution ICM+ data from the three founding hospitals, several hundred thousand hours of high-performance computer processing time were required to develop the algorithms and architectures. The custom system (**Figure 1**) is hosted on a hybrid data cloud that combines the scalability, flexibility, and geographic reach of Amazon Web Service's data cloud with the processing power of the PSC. Using this equitable approach, the system can be delivered scalably to patients in regions lacking the necessary processing resources and expertise.

The AIMS-TBI system is designed to capture and process data streamed from the bedside monitor of TBI patients during operation. On data capture, data is initially pre-processed by a pipeline of algorithms which package, compress/expand, clean, align, interpolate, and/or convolute the data. Upon completion of initial pre-processing, the data is split into two distinct streams. The first is to archive the cleaned data on the project's time series database to allow for further analysis and storage. The second stream involves the operation of clinically relevant algorithms. Currently, a number of traumatic intracranial hypertension (tIH) prediction algorithms operate on this stream, each with its own unique data pre-processing requirements. A handful of AIMS-TBI tIH prediction algorithms are currently undergoing real time observational testing, with testing of other larger tIH prediction as well as other types of algorithms on hold pending restoration of full PSC operations.

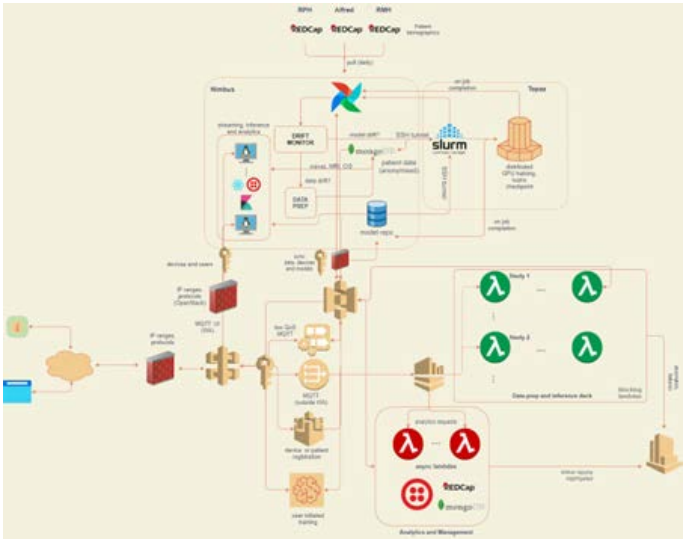
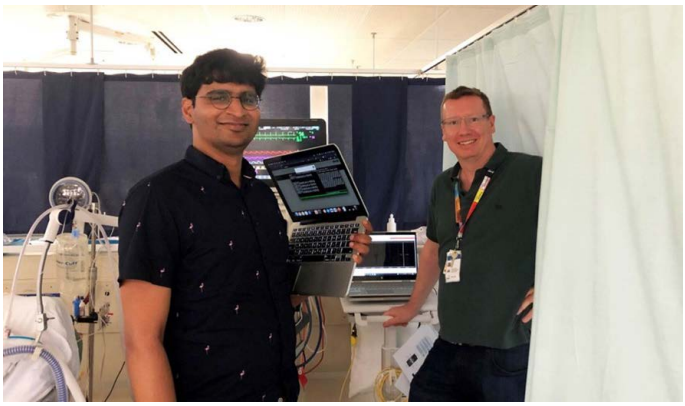


***Figure 1**: Schematic of AIMS-TBI hybrid cloud architecture (Nov 2022). The AIMS-TBI hybrid cloud consists of 32 separate sub applications. Note that this configuration will change with the upgrade in PSC facilities.*

The implementation of the AIMS-TBI system promises to revolutionize the management of severe traumatic brain injury patients by providing healthcare professionals with timely, accurate, and actionable insights derived from advanced machine learning and deep learning algorithms. These insights have the potential to improve patient outcomes by enabling clinicians to make more informed decisions based on individualized patient data.

Benefits of AIMS-TBI System

1. **Personalized Patient Care:** By leveraging the power of machine learning and deep learning algorithms, the AIMS-TBI system can identify patterns and trends in patient data that may not be readily apparent to healthcare providers. This can help tailor treatment plans to the specific needs of individual patients, potentially improving the overall effectiveness of the care they receive.
2. **Early Warning System:** The intracranial hypertension prediction algorithms employed by the AIMS-TBI system can serve as an early warning system for healthcare providers, allowing them to take preventative measures to avoid or mitigate the effects of potentially life-threatening complications.
3. **Improved Clinical Decision-Making:** The AIMS-TBI system can provide clinicians with valuable insights into the underlying causes and progression of traumatic brain injuries, leading to better-informed treatment decisions and hopefully ultimately improved patient outcomes.
4. **Data Sharing and Collaboration:** The AIMS-TBI project's data cloud enables seamless sharing of information between participating hospitals and research institutions, fostering collaboration and the development of new treatment approaches for traumatic brain injuries.
5. **Scalability:** The hybrid data cloud architecture allows the AIMS-TBI system to be delivered to hospitals and healthcare facilities regardless of their location or available resources, ensuring that all patients can benefit from the advancements provided by this cutting-edge technology.



AIMS-TBI project data Scientist Mr. Shiv Meka (left) and Project lead Dr. Robert McNamara (right) during the first live testing of the AIMS-TBI system. (Photo courtesy of the Pawsey Supercomputing Center).

> "The AIMS-TBI system promises to revolutionize the management of severe traumatic brain injury patients ... with timely, accurate, and actionable insights derived from advanced machine learning and deep learning algorithms."

Challenges and Future Directions

While the AIMS-TBI system represents a substantial advance in the treatment and management of severe traumatic brain injuries, there are still challenges to be addressed. These include the validation of the system's predictive algorithms, ensuring data privacy and security, and the integration of the AIMS-TBI system into existing hospital workflows and electronic health record systems.

Validation of Predictive Algorithms: The accuracy and reliability of the AIMS-TBI system's predictive algorithms are crucial for its clinical usefulness. Rigorous validation through large-scale, multi-center clinical trials will be essential to establish the effectiveness of these algorithms in identifying early warning signs and guiding treatment decisions for TBI patients. Additionally, continuous refinement and improvement of the algorithms based on real-world data design feature of the AIMS-TBI system to maintain algorithm accuracy and relevance over time. This later feature of the system requires validation and monitoring to ensure proper operation and utility.

Data Privacy and Security: With the increasing use of cloud-based systems and the collection of vast amounts of patient data, ensuring the privacy and security of this sensitive information is paramount. Robust data encryption and protection measures must be implemented to safeguard patient data from unauthorized access, data breaches, and potential cyberattacks. Furthermore, adherence to regional and international data protection regulations is essential to maintain compliance and trust among patients and healthcare providers.

As the AIMS-TBI project moves into the next phase of implementation, ongoing research and development efforts will focus on refining the system's predictive algorithms, incorporating additional data sources, and exploring the potential applications of the technology in other areas of medicine. With the full operation of the Pawsey Supercomputing Centre and the continued collaboration between participating institutions, the AIMS-TBI project stands poised to make a significant impact on the lives of patients suffering from traumatic brain injuries. ●

Does Surgical Treatment of Refractory Traumatic Intracranial Hypertension Improve Outcomes? 24-month Follow-up of RESCUEicp

By Wazim Mohamed, MD; Sara Stern-Nezer, MD, MPH

Kolias AG, Adams H, Timofeev IS, et al. "Evaluation of Outcomes Among Patients With Traumatic Intracranial Hypertension Treated With Decompressive Craniectomy vs Standard Medical Care at 24 Months: A Secondary Analysis of the RESCUEicp Randomized Clinical Trial." JAMA Neurol. 2022;79(7):664–671. doi:10.1001/jamaneurol.2022.1070

Background

Guidelines for decompressive craniectomy (DC) for intracranial pressure (ICP) control after traumatic brain injury (TBI) center around the DECRA trial, published in 2011. This study looked at bifrontal decompressive hemicraniectomy compared to standard of care in patients who had sustained ICP >20mmHg for >15 minutes despite optimized non-surgical interventions.[1] DECRA found that patients who underwent DC had similar mortality rates compared to standard care and higher rates of poor functional outcomes at 6 months. The trial was criticized for aggressive treatment of patients with elevated ICP not consistent with standard practice as well as a restrictive criteria for inclusion, limiting its applicability to most patients with severe TBI.[2] To that end, Hutchinson et al, and the RESCUEicp investigators published their results of a second randomized controlled trial comparing DC with medical management. The RESCUEicp authors utilized methodologies that were more consistent with current practice, utilizing DC as a last-tier intervention for sustained, refractory elevations in ICP and was designed to be more generalizable. Their results demonstrated a significant mortality benefit at both 6 and 12 months in the surgical group at a cost of more patients left in a vegetative state or with severe disability at similar time points.[3] This study evaluates outcomes for these same participants at 24 months to determine if there is any differential effect of DC on late-outcomes after severe TBI.[4]

"The RESCUEicp authors utilized methodologies that were more consistent with current practice, utilizing DC as a last-tier intervention for sustained, refractory elevations in ICP and was designed to be more generalizable."

Methods

Patients were eligible for inclusion if they were aged 10-65 with abnormal CT and ICP monitoring with ICP>25mmHg refractory to initial medical treatments. Patients were excluded if they had clinical findings consistent with devastating brain injury (i.e., fixed and dilated pupils) or coagulopathy. All patients received initial 'stage 1' treatment for elevated ICP consisting of targeting cerebral perfusion pressures >60mmHg, hypocarbia, normothermia, and normal blood glucose. Persistent ICP>25mmHg led to 'Stage 2' treatments, consisting of inotropes, ventriculostomy, hyperosmolar therapy, hypothermia and loop diuretics. If patients continued to have ICP>25mmHg for 1-12 hours despite both stage 1 and 2 therapies, they were randomized to surgery or medical therapy. Patients randomized to surgery received either a unilateral or bilateral fronto-temporo-parietal craniectomy at the discretion of the surgeon. Those randomized to medical management continued 'stage 2' treatments and were placed in a barbiturate coma for refractory ICP elevation. Barbiturates were not permitted in the stage 2 treatment phase. The primary outcome was the extended Glasgow outcome score (GOS-E) measured at 24 months assessed by mail or telephone interview.

Results

Of 408 patients initially randomized, 356 (87%) were included in the 24-month analysis. The between-group difference, initially seen at 6 and 12 months, was maintained at 24 months (x2=24.20, p=0.001). Additionally, the significant mortality benefit noted at 6 and 12 months in the surgical group was maintained at 24-months with an absolute percentage difference of -20.5% (95% CI -30.8% to -10.2).

Furthermore, in this analysis, the initial 6-month mortality benefit associated with DC was offset by an equivalent number of patients left in either a vegetative or severely disabled state. However, at 24 months the allotment was no longer similar as a disproportionate number of patients in the surgical group improved by at least 1 point on the GOS-E scale (30.4% vs 14.5%) compared to the medical group, respectively. Rates of good recovery at 24 months were similar between the surgical and medical groups, with lower good recovery in 7.7% vs 5.2% and upper 3.3% vs 5.7%, respectively.

Commentary

This study found that surgical treatment of sustained refractory intracranial hypertension demonstrated continued mortality benefits at 24 months without an increase in good recovery but with increased rates of vegetative state, severe disability and moderate disability. Patients in the surgical group were more likely to improve by at least 1 GOS-E grade. Compared to the prior DECRA trial by Cooper et al, RESCUEicp's methodology was more applicable to current practice of severe TBI. However, much of the criticism aimed at the initial RESCUEicp trial, evaluating 6 and 12-month outcomes, is also applicable to this secondary analysis reporting 24-month outcomes.[2-4] Bifrontal craniectomies outnumbered hemicraniectomies by approximately 2-to-1, but these rates appear inconsistent with common practice. The number of patients crossing over between

> "This study found that surgical treatment of sustained refractory intracranial hypertension demonstrated continued mortality benefits at 24 months without an increase in good recovery but with increased rates of vegetative state, severe disability and moderate disability."

groups was high with almost 40% of patients randomized to medical treatment receiving DC and 7% of patients randomized to surgery treated medically. Large-scale crossover such as this can lead to decreased statistical power favoring the null hypothesis. Fortunately, in this trial that does not appear to be the case, but nonetheless the treatment effect of DC may have been blunted due to this imbalance. Differences between those lost to follow-up between 6, 12 and 24 months may also have an unclear effect on the analysis that may bias results. Finally, the issue of timing of cranial reconstruction after DC is poorly referenced in both the trial text and supplementary appendices. Smaller studies and pooled meta-analyses have reported benefits with earlier cranioplasty (<90 days) compared to those beyond (>90 days). As an improvement in GOS-E of at least one point was noted in 30% of those randomized to surgery at 24 months' time, future trials regarding DC should require collection of data pertaining to this variable.[5] ●

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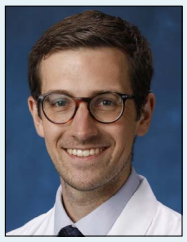
Levetiracetam Prophylaxis is Safe and May Reduce Seizures in Acute Intracerebral Hemorrhage: Results of the PEACH Trial

By Matthew Bower, MD; Sara Stern-Nezer, MD, MPH



Original Article: Ruijter B, Keijzer M, et al. Treating Rhythmic and Periodic EEG Patterns in Comatose Survivors of Cardiac Arrest. NEJM (2022). DOI: 10.1056/NEJMoa2115998

Summary

Spontaneous intracerebral hemorrhage (ICH) accounts for 15% of all strokes and a significant burden of neurological morbidity and mortality affecting 2 million people per year. While organized neurological systems of care have improved outcomes, ICH remains stubbornly resistant to medical interventions. Seizure occurs in 6-15% of ICH patients with recent data reporting up to 30% when continuous EEG (cEEG) is used to identify subclinical seizures. Current literature is mixed on whether seizures affect long-term outcome. Prior studies were limited as they depended on clinical seizures, failing to capture subclinical seizures, and utilized older antiseizure medications (ASM) that have unfavorable side effect profiles which may themselves affect outcome. This study sought to evaluate the safety and efficacy of levetiracetam for primary prevention of seizures in a parallel-group, double-blind, randomized, placebo-controlled trial.

> “Current literature is mixed on whether seizures affect long-term outcome. Prior studies were limited as they depended on clinical seizures, failing to capture subclinical seizures, and utilized older antiseizure medications.”

Methods

The trial included patients >18 years with a spontaneous ICH presenting within 24 hours. Patients with known seizures, seizure after presentation but before intervention, current ASM use, psychiatric history, or terminal illness were excluded. Levetiracetam 500mg twice daily or placebo was given within 24 hours of randomization and patients were monitored on cEEG for 48 hours. Treatment was continued for 30 days followed by a 2-week taper. Primary efficacy outcome was the occurrence of one clinical seizure within 72 hours or one electrographic seizure on cEEG. Secondary efficacy outcomes included the number and duration of seizures on cEEG, paroxysmal interictal patterns, change in ICH volume or midline shift at 72 hours, seizures during the follow up period, and function and quality of life measures. Secondary safety outcomes were medication side effects, psychiatric symptoms measured by the Hospital Anxiety and Depression Scale (HADS), and all-cause mortality. Analysis was performed using modified intention-to-treat analysis utilizing logistic regression, adjusted for randomization factors.

Results

50 patients were enrolled in the study, 24 assigned to levetiracetam and 26 to placebo. For the endpoint analysis, 19 were included in the treatment group and 23 in the placebo group. Patients were excluded because of issues with cEEG access or other technical issues. Any patient who initiated treatment was included in the safety analysis. The treatment group had more women (38% vs 27%), was older (77.5, IQR 72.5-81, vs 66.5, IQR 53-86), had more baseline disability (mRS 0 in 71% of treatment and 92% of placebo), and had a lower NIHSS (7.5, IQR

> This study has significant limitations due to the small sample size and unbalanced groups, given the number of differences in the age, pre-stroke mRS, gender, ICH volume and NIHSS between the two groups.

5-13.5, vs. 12.5, IQR 8-15). Median GCS was 15 (IQR 14-15) in both groups. The treatment group also had a higher percentage of lobar hemorrhage compared to the placebo group (42% vs 19%). Median hematoma volume was 9.2 ml (IQR 3.1-24.4) in the treatment group and 18 ml (IQR 7.2-27) in the placebo group. Seizures occurred in 3 patients in the treatment arm and 10 patients in the placebo arm (16% vs 43%; OR 0.16, 95% CI, 0.03-0.94; P=.043). The median duration of seizures was lower in the treatment group compared to the placebo group (67 sec, IQR 46-300, vs 780 sec, IQR 380-1980, p=0.028). These differences did not translate into any difference in the number of seizures within 30 days, 12 months, the mRS change between inclusion and 3 or 6 months follow-up, or 12 month mortality. No statistical difference was found in changes in ICH volume nor in midline shift at 72 hours between the two groups. There was no difference in adverse events between the two groups nor in depression or anxiety at followup.

Commentary

This parallel-group, double-blind, randomized, placebo-controlled trial suggests that levetiracetam is safe and may reduce seizures after ICH. Interestingly, this effect on seizure frequency in the acute phase did not translate to lower risk of late onset seizures nor to improved functional outcome, quality of life, or mortality. However, this study has significant limitations due to the small sample size and unbalanced groups, given the number of differences in the age, pre-stroke mRS, gender, ICH volume and NIHSS between the two groups. Additionally, the treatment group had higher rates of diabetes (33% vs 8%) and hypertension (73% vs 50%). Most importantly, ICH location was more often lobar and ICH volume was smaller in the levetiracetam group, both of which may influence seizure risk as well as outcome, which may have had differential effects that washed out any true difference between the levetiracetam and placebo groups.

This study reinforces the emerging data showing seizure occurrence has been underestimated and further supports current AHA/ASA and the American Clinical Neurophysiology Society recommendations for EEG monitoring in supratentorial ICH with altered mental status, although this can be challenging in limited resource settings. Some studies have shown that seizures may worsen outcomes due to hematoma expansion and impaired brain-oxygenation with one prospective study showing a worse functional outcome with early seizures, however this study did not find a difference in hematoma expansion nor midline shift from baseline between the two groups. As such, this data is compelling despite the limitations and warrants a larger study powered to evaluate outcomes. ●

Advancing Health Equity in Acute Neurological Diseases and Neurocritical Care: The Path Forward

By Hera Kamdar, MD; Minjee Kim, MD; Jennifer Kim, MD, PhD; Shraddha Mainali, MD




The pursuit and understanding of health equity is an integral guiding principle for quality and comprehensive healthcare. Health equity refers to the equal access and universal allowance of the highest level of healthcare to all individuals, regardless of their socioeconomic status, race, ethnicity, gender, or geographical location. Achieving health equity is essential. However, as many know, numerous disparities persist within and beyond the healthcare system perpetuating inequalities in healthcare and health outcomes.

Within the rapidly growing field of Neurocritical Care, there is a lack of longstanding, high-quality research guiding the care of individuals with acute neurological diseases. These diseases, which encompass a wide range of conditions including stroke, traumatic brain injury, epilepsy, brain tumors, and infections, require not only advanced medical treatments and interventions that are still under study, but also a vital understanding of a patient's social determinants of health (SDOH) to provide comprehensive care and improve health care outcomes. Patients who experience an acute neurological disease may also lose decision-making capacity for their health, which makes this population particularly vulnerable to additional stressors.

Understanding this need, the National Institute of Neurological Disorders and Stroke (NINDS), aligned with the U.S. Department of Health and Human Services, established the Healthy People 2030 initiative. This initiative aims to promote research efforts to improve healthcare by facilitating a variety of health opportunities, and further fortifies the enduring importance of health equity in healthcare research. The additional traction from this initiative has resulted in a shift in focus regarding how to best conduct this type of research and translate it into actionable change to optimize equity for all.

Dr. Nirupama Yechoor, a Neurocritical Care physician at Massachusetts General Hospital with a research focus on health equity and SDOH in stroke patients, commented on refocusing how to best approach the problem: "The traditional approach [to studying health equity] is looking to see what makes our patients different that they have worse outcomes. For example, we study race and income as determinants of clinical outcomes. However, I think a new way forward could be [asking] how do we, as the health system, make decisions differently based on factors that lead to worse health outcomes. This shifts the paradigm to modifying our care, which is possible, and not simply focusing on factors we can't modify, such as someone's race."

Given her passion for health equity research, Dr. Yechoor recently spoke at both the Neurocritical Care Society's World Coma Day and the American Heart Association's International Stroke Conference. In her presentations, she shared that "social and structural determinants of health can seem overwhelming and intimidating. But there are several feasible and actionable steps towards starting this work, especially in our neurological patients. [And] understanding [SDOH] is just one way to build a bridge between clinical medicine and public health."

Additional studies have shown that the knowledge gaps arising from a lack of exposure to racial and ethnic diversity and sexual and gender minorities may lead to barriers in access to clinical care for disadvantaged populations. Simpkins et. al. also highlighted the need for transdisciplinary team science and diversity enhancement to address unconscious decisions that limit accessibility for diverse populations, whether influenced by implicit biases of individual providers or larger-scale systemic biases. Diversity in the neuroscience workforce and a push towards team-based science can help improve research innovation and creativity while offering a broad scientific perspective. The field of neurocritical care, as a fast growing and multidisciplinary community, is at the forefront of leading such initiatives. We stand at the brink of new and exciting research that will lead the path forward to improve healthcare and outcomes through optimizing health equity, particularly in our vulnerable population of patients with acute brain injury. ●

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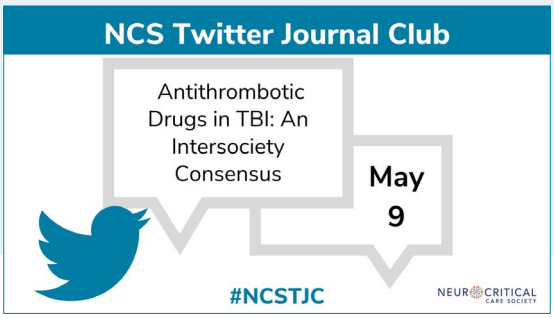
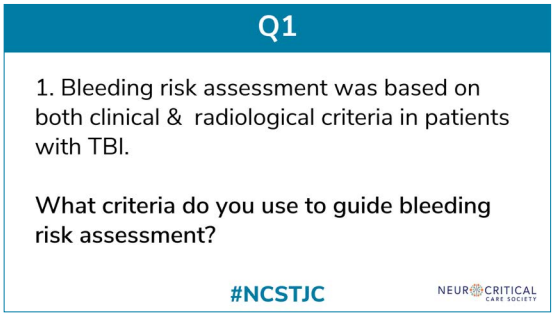
NCS Twitter Journal Club Round-Up #NCSTJC: May 2023

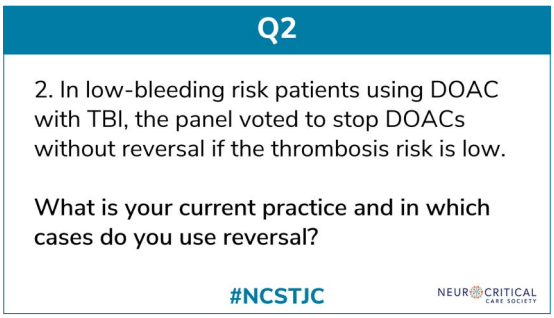
By Eric Lawson, MD



Link to Twitter Thread: **https://twitter.com/neurocritical/status/1651625300155826177**

Moderator: @tchaaban





Featuring a large virtual attendance, the May Neurocritical Care Society Twitter Journal Club featured a lively discussion on the article, "Management of Antithrombotic Drugs in Patients with Isolated Traumatic Brain Injury: An Intersociety Consensus Document" by Corraddo Iaccarino et al. The article was the culmination of a collaborative effort of a working group endorsed by the Neurotraumatology Section of the Italian Society of Neurosurgery, the Italian Society for the Study about Haemostasis and Thrombosis, the Italian Society of Anaesthesia, Analgesia, Resuscitation, and Intensive Care, and the European Association of Neurosurgical Societies. The working group developed 28 statements on the management of antiplatelets, vitamin K antagonists, and direct oral anticoagulants in traumatic brain injury. The authors noted the low strength of evidence in previously published consensus documents due to their reliance on lower quality studies.

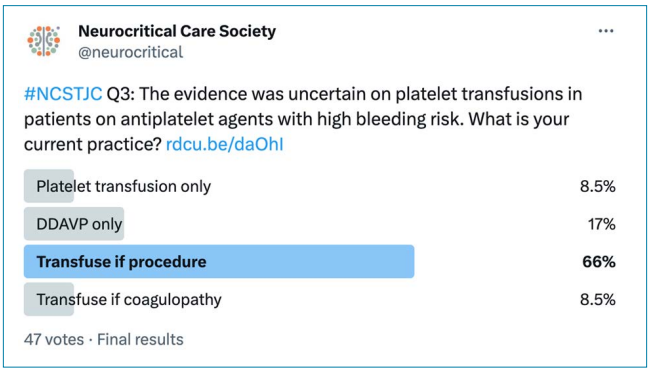
A vibrant discussion was held on Twitter through #NCSTJC, and we will review the discussion topics and opinions expressed.

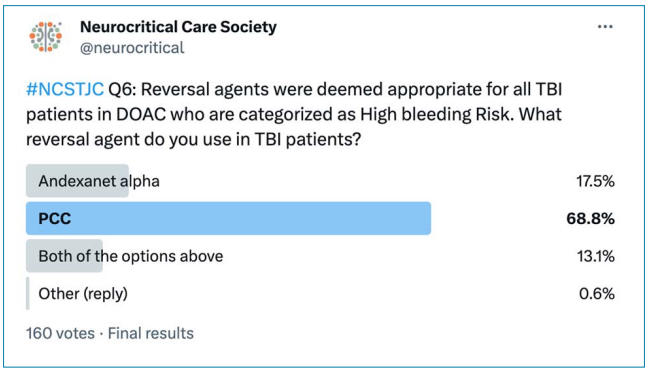
The discussion on bleeding risk assessment was kicked off by @tchaaban who noted: "Bleeding volume/thickness, coexisting coagulopathy, need for intervention, bleed stability are important factors." He also linked to the criteria utilized by the working group authors. Other respondents generally agreed that bleed volume, hematoma expansion, and other underlying coagulopathy are important factors in guiding their risk assessment.

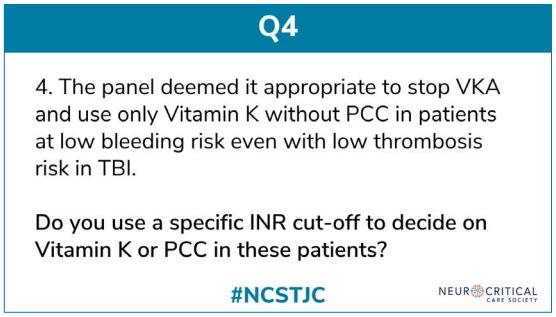
The second question asked participants to indicate their current DOAC reversal practice in otherwise low risk patients. @dcm7200 and @TJUHNeuroCrit both discussed utilizing TEG and ROTEM to assess bleeding risk to help guide both transfusion thresholds and DOAC reversal. @EderCaceres5 indicated: "Low bleeding risk: stop DOACs and clinical and imaging follow up. Bearing in mind when was the last dose of DOAC taken." @Tchaaban1 had a pragmatic view of the authors approach stating that it "…totally makes sense in the absence of high-quality evidence. Cost and thrombosis risks are not to be underestimated."

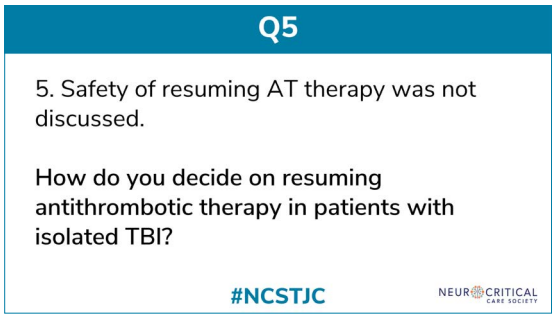
Question 3 featured a poll regarding the uncertainty of utilizing platelet transfusions in patients at high risk for bleeding who were on antiplatelet agents. The poll asked participants about their current practice, with the majority choosing to transfuse only in situations where a procedure was required. Some utilized DDAVP to potentially reverse the antiplatelet effects, with fewer respondents choosing to transfuse if a coagulopathy exists.

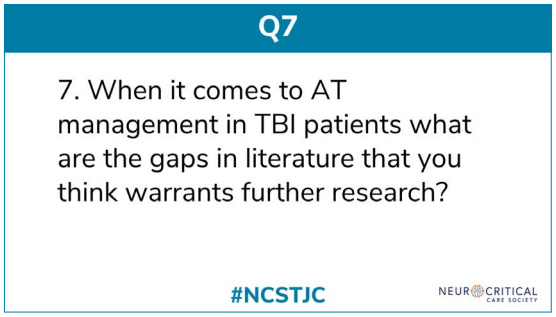
The discussion on question 4 was initiated by @tchaaban1 stating: "Our cut off is 1.5 in patients who have traumatic intracranial hemorrhage. We delay/avoid reversal if minimal bleed with very high thrombosis risk ie mechanical MVR and recent (<1month) VTE". @Apaulsonrngmai1 indicated: "We tend to treat around 1.5 to 1.7 but do a lot of wait and see –











follow up CT and good neuro exams make a difference". Most agreed that mechanical valves complicate the decision and many defer vitamin K in this specific population. @TheABofPharmaC indicated: "…We do the combination of both PCC and Vitamin K in most cases of acute TBI on VKA therapy". @NezerSara raised the important point that more patients are on DOAC these days, so the INR target is often no longer relevant.

The working group did not specifically address the safety or timing of resuming antithrombotic therapy on isolated traumatic brain injury patients. @KeatonSmetana noted: "Indication and severity of injury are critical determinants for resuming antithrombotic therapy in TBI patients." Many, including @paulsonrngmai1, @TJUHNeuroCrit, and @EderCaceres5 noted patient specific factors and provider opinions are important indicators in the ultimate decision. Multiple participants also noted the importance in understanding the underlying reason for antithrombotic therapy, both in determining the need for early reinitiation and in considering whether the medication is still indicated.

Question 6 featured another poll with potentially interesting results especially given ongoing clinical trials featuring the use of andexanet alfa. When considering reversal agents for DOACs in patients with high bleeding risk, a vast majority of respondents voted for PCC as their agent of choice. Some indicated a preference for using both, while others solely utilized andexanet alfa. @gdomeni raised an important point regarding the availability of andexanet alfa: "In low and middle income countries is very difficult the access to andexanet". Many hospitals in the United States also do not have the medication on their formulary, which may have influenced the overall preference toward PCC as well.

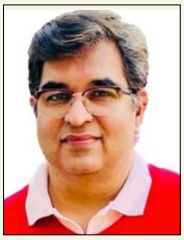
As a final summary discussion, the last question asked participants to consider the literature gaps which warrant further research to help bring clarity to the topic. @NezerSara indicated "…using TEG and other assays of functional clotting are the next step to balance understanding of clotting vs bleeding risk". Her response referenced an additional discussion between @GilbertPharmD, @KeatonSmetana, and @tchaaban1 on the utilization of lab measures such as PT/INR, anti-Xa, and functional assays like TEG/ROTEM to assess the need for reversal. Variability across labs, institutions, and time to results were all indicated as factors in the decision to utilize lab or functional assays to guide reversal.

The May edition of the #NCSTJC featured a vibrant discussion regarding the management of antithrombotic agents in traumatic brain injury. The online discussion indicated both consensus on components, such as the reversal of DOAC with PCC, and only utilizing platelets in the setting of procedures. An area identified for potential exciting advancements was the utilization of functional clotting assays such as TEG and ROTEM to guide reversal and risk of antithrombotic agents. ●

Read the full article here: **https://link.springer.com/article/10.1007/s12028-023-01715-3**

Curing Coma® Campaign Through the Lens of Low- And Middle-Income Countries (LMICs)

By Gentle Sunder Shrestha, Tribhuvan University Teaching Hospital, Maharajgunj, Kathmandu, Nepal; Hemanshu Prabhakar, All India Institute of Medical Science (AIIMS), New Delhi, India



Neurological disorders remain the leading cause of global disability-adjusted life years (DALYs).[1] The burden of acute neurological diseases is even higher in low- and middle-income countries (LMICs) and is expected to continue rising in the future.[2] Coma and disorders of consciousness are common manifestations or sequelae of a variety of neurological disorders. Thus, coma is a commonly encountered entity among a highly heterogenous group of patients. The outcomes of these patients vary significantly, ranging from complete recovery or partial recovery to long-term states of unconsciousness.[3]

NCS has launched the Curing Coma Campaign (CCC) with the aim of improving the outcome of patients with coma and disorders of consciousness. This overarching "Blue Ocean" strategy is a much needed and highly ambitious project, which has a global vision and aims to embrace health care workers from different backgrounds who are involved in the management of patients with coma and disorders of consciousness. Three major pillars were identified to attain the goals of the project, including endotyping of patients with coma and disorders of consciousness, biomarkers, and proof of concept studies. Subsequent proceedings have identified specific research priorities and existing gaps. However, LMICs have several unique limitations that can potentially complicate the implementation and expansion of CCC, such that LMIC perspectives are imperative to consider to ensure CCC's global success.[4]

There is wide variability on the definition and understanding of coma, with differences in treatment strategies and prognostication of comatose patients. This was evidenced by NCS's recently conducted multinational COME TOGETHER survey involving 41 nations and 258 health care professionals.[5] There is also significant variability in the delivery of neurocritical care globally, and the international PRINCE study was conducted to explore this variability.[6] Such international epidemiological studies are important early steps on the CCC roadmap. Unfortunately, LMICs remain largely under-represented in these studies. To ensure that such studies are truly globally representative, more LMICs need to be proactive and get involved in future surveys. In conjunction, NCS should strive to recruit more LMICs through regional chapter leads and by identifying regional champions.

Because patients with coma are highly heterogenous, endotyping and identifying sub-groups of patients is highly desirable. The majority of recent clinical trials have yielded neutral results, much of which is likely explained by their use of a one-size-fits all approach while enrolling a highly heterogenous patient population.[7] In patients with coma, incorporating biomarkers and other precision-based medicine approaches could potentially help identify subgroups of patients with a higher likelihood of recovery.[8] Though the application of advanced endotyping tools like functional MRI and task-based EEG seems promising, such technologies are largely unavailable in LMICs, thereby limiting their applicability.[4] Instead, most clinicians typically base their prognostication on the etiology of a patient's coma along with their neurological examination findings and neuroimaging. Only a small minority of clinicians have also incorporated tools like functional MRI, EEG, and laboratory biomarkers.[5] Future research should explore how currently available and utilized modalities can be better implemented for endotyping. For example, preliminary studies have revealed that simple bedside evaluations like the FOUR score, ocular tracking, and spontaneous eye blinking can have prognostic significance in patients with coma.

> "Considering the complexity of managing patients with coma in LMICs, focusing on acute treatments is not enough—effective preventive measures to minimize the burden of diseases that lead to coma should also be prioritized."

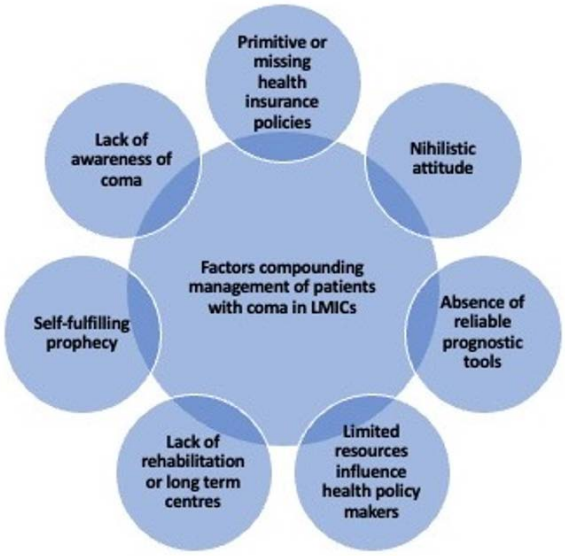


Figure 1. *Barriers for management of patients with coma in LMICs.*

Figure 2. *Proposed measures to enhance success of CCC in LMICs.*

The management of patients with coma in LMICs is complicated by multiple factors (**Figure 1**). Health insurance policies are either primitive or non-existent in many regions, and as a result, the cost of health care is often borne by patients and their families. There is also a lack of public awareness about coma, while health care workers are predisposed to prevailing attitudes of nihilism and self-fulfilling prophecy that are further confounded by an often protracted clinical course and an absence of reliable prognostic tools. Post-acute care is an additional issue, as rehabilitation centers and long-term care centers are not well developed in many places. Finally, because of the limited resources available in most LMICs, most government authorities and public health policy makers tend to consolidate their resources into preventive measures like vaccination against common infectious diseases.

Considering the complexity of managing patients with coma in LMICs, focusing on acute treatments is not enough—effective preventive measures to minimize the burden of diseases that lead to coma should also be prioritized (**Figure 2**). For CCC to be successfully implemented in LMICs, we need detailed epidemiological data and further research on optimal utilization strategies for the resources and expertise that are available. There is a critical need for reliable prognostic tools that are locally implementable in order to divert limited resources to comatose patients with a higher likelihood of recovery. Cost-effectiveness analyses should also be performed to help convince policy makers to allocate more resources for these patients. More well-designed clinical and translational research is ultimately needed to minimize these gaps in evidence and practice. ●

> “There is a critical need for reliable prognostic tools that are locally implementable in order to divert limited resources to comatose patients with a higher likelihood of recovery.”

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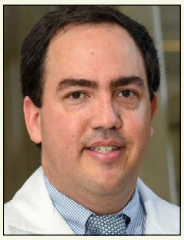
The Tower of Babel: Translating the ICU-EEG Nomenclature to Spanish

By Clio Rubinos, MD, MS; Andres Fernandez, MD, MSEd; Maria Jose Bruzzone, MD


Read the article in Spanish >>

In the last few decades, continuous electroencephalography (cEEG) has become increasingly adopted as part of the standard management of critically ill patients in many centers.[1,2] The use of cEEG has grown in large part due to the increasing recognition that most acute symptomatic seizures (ASyS) are solely electrographic and do not have detectable clinical signs at the bedside.[3] Similarly, there has been a greater awareness of previously described EEG patterns such as lateralized periodic discharges (LPDs), lateralized rhythmic delta activity (LRDA), and generalized periodic discharges (GPDs), which are critically important patterns due to their association with seizure risk or outcome.[4,5]

In response to these findings, the American Clinical Neurophysiology Society (ACNS) proposed new terminology in 2005 to improve scientific communication and establish a consistent approach to studying ictal-interictal continuum (IIC) patterns.[6] The initial establishment of ACNS critical care EEG terminology made some key changes, which included removing the word epileptiform from the names of these discharges to highlight the uncertainty regarding their underlying association with seizures. The ICU-EEG literature has continued to grow, and the most recent revision of the terminology last year introduced definitions for other observed patterns, such as cyclic alternating pattern of encephalopathy (CAPE), brief potentially ictal rhythmic discharges (BIRDs), and multifocal lateralized periodic discharges.[7]

> "The goal of this group is to translate the English version of the cEEG nomenclature into Spanish to promote research and collaboration with and among Spanish-speaking countries, and to further promote academic diversity in our field."

The increase in cEEG utilization that has paralleled efforts to create a standardized nomenclature has led to more interest in the topic across the globe, including in non-English speaking countries. However, while the ICU EEG nomenclature has an acceptable interrater reliability for the main terms,[8] they have so far only been used in English, limiting the extrapolation of scientific knowledge to Spanish-speaking countries and other non-English speaking settings.

The lack of a common Spanish language terminology to communicate cEEG findings amongst Spanish-speaking colleagues is a challenge akin to the one that prompted the development of the original English language cEEG nomenclature. This need catalyzed the formation of the "Consorcio Hispano de Monitoreo Encefalografico," a group formed by Hispanic physicians coming from Spain, North, Central, and South America. The goal of this group is to translate the English version of the cEEG nomenclature into Spanish to promote research and collaboration with and among Spanish-speaking countries, and to further promote academic diversity in our field.

Due to the nature of the Spanish language and its regional variations, a consensus between different geographical regions was thought necessary to reflect the most accurate terms that would be more broadly accepted in the diverse Spanish communities where it is intended to be applied. To reflect this diversity, we are working with physicians who are members of the neurology, epilepsy, and neurophysiology societies in several countries to help us achieve a more generalizable Spanish translation of the ICU-EEG nomenclature.

We have also decided to follow a rigorous methodology for the translation process that follows qualitative methodologic principles, rather than simply submitting the original English language document to a translation service. The first step was creating three working subgroups to iteratively translate each nomenclature section. The sections were 1) EEG background, 2) periodic and rhythmic patterns, and 3) electrographic and

> During those meetings, specific terms were recognized as especially challenging to translate given the vast amount of Spanish terms that are used for a given word.

electroclinical seizures. Each subgroup met regularly to discuss progress with the translation. During those meetings, specific terms were recognized as especially challenging to translate given the vast amount of Spanish terms that are used for a given word. When a subgroup-level consensus for a Spanish term was not reached, a general group-level meeting was organized, where we discussed the Spanish translation options and kept the words that were more frequently used. The discussions of all subgroup and general group-level meetings were recorded in a tracking document.

The next step in this process will be the creation of focus groups with professionals residing in Spanish-speaking countries to obtain a consensus of individuals who will use the nomenclature in their local settings. This is a work in progress, and we are still recruiting volunteers for the focus groups. If you are a potential target audience for the Spanish version of the nomenclature and are interested in contributing to the focus groups, we encourage you to fill out this form. **https://forms.gle/NvQUcL3S4By6NvbU8** ●

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Why Hold an In-Person Neurocritical Care Regional Meeting in the Era of Virtual Meetings?

By Yasser Abulhasan, MBChB, FRCPC, FNCS

Shortly after the introduction of the 1st Neurocritical Care Regional Meeting in the Middle East and Africa in 2019, the SARS-CoV-2 pandemic disrupted in-person medical conferences globally and caused virtual/hybrid meetings to flourish instead. A year later, we all realized that there is considerable fatigue associated with attending conferences virtually. More importantly, real human interactions and discussions of new 'blue ocean' projects and collaborations—especially those coupled with conferences in developing regions—cannot truly get off the ground during virtual meetings.

Third Regional Meeting

The 3rd Neurocritical Care Regional Meeting, in conjunction with the 18th edition of the Emirates Critical Care Conference (ECCC), took place in 2022. Although it was planned as a hybrid conference (both in-person and virtual) from May 13-15, 2022, in-person attendance by speakers and other attendees was impressive and actually exceeded the virtual turnout.

As part of the neurosciences sessions, the scientific program included ENLS (May 13) and the full-day neurocritical care track (May 14), the latter of which focused on: (1) Disorders of Consciousness, (2) the NCS Curing Coma Campaign, (3) the new NCS SAH Guidelines, (4) Prognostication after Cerebrovascular Diseases, (5) Cerebrovascular Disease in Children, (6) Pro and Con Debates on Mechanical Thrombectomy in the Elderly and Daily Wake Up Trials, and (7) Infectious Diseases in Neurocritical Care. This was followed by a half-day Neurocritical Care Nursing workshop which discussed practical nursing issues surrounding neurological and neurosurgical patients in the ICU. All accepted abstracts submitted to the Regional Meeting were ultimately published in *Neurocritical Care*.

> "More importantly, real human interactions and discussions of new 'blue ocean' projects and collaborations … cannot truly get off the ground during virtual meetings."

Overall, the conference was attended by over 1500 delegates (both in-person and virtually). Of the 246 speakers, 38% were international, 36% local, and 26% regional, representing a total of 37 countries. There were 8 workshops including ENLS and Neurocritical Care Nursing. Kudos to all speakers and attendees who joined worldwide.

Brain Death Determination Workshops

Meanwhile, one day before the conference, representatives from NCS leadership were invited to Abu Dhabi for a high-level dialogue with healthcare representatives from the UAE to discuss the possibility of training and certifying physicians in the UAE in

Brain Death Determination. This ambitious request was followed by virtual meetings which resulted in a collaborative partnership between the UAE Ministry of Health and Prevention, the ECCC, and NCS to train over 200 healthcare professionals during and after the 2023 ECCC meeting. There are now three workshops scheduled from May 14-16, 2023, with over 20 speakers/faculty involved in training over 200 participants. Details of outcomes and possible research opportunities are expected to follow this event.

Global Partnership Milestones

Since 2011, the NCC-MENA chapter of IPACCMS has been one of the foremost global partners of NCS, and NCS leadership has participated in the open annual NCC-MENA chapter meeting. Over the years, the neurocritical care track of the ECCC has also continued to grow. ENLS was first offered in 2016, then in 2018, 2019 (in person), 2021 (hybrid), and 2022 (in person). In October 2018, NCS confirmed the first Middle East/Africa member to represent the region on its Board of Directors. In April 2019, the 1st NCC Middle East/Africa Regional Meeting was conducted in person in Dubai, and in June 2021, the hybrid

format 2nd Regional Meeting, and 3rd Regional Meetings were conducted in conjunction with the 15th, 17th, and 18th editions of the ECCC, respectively. In 2022, a formal dialogue was initiated between the UAE team and NCS to hold Brain Death Certification workshops in the UAE.

Our Mission

Overall, Critical Care representation of neurosciences in our region remains strong and vital, and has contributed significantly to spreading the mission and vision of NCS globally. And to answer the title question justifying in-person Regional Meetings: the effort, diligent planning, and follow-up of discussions during an in-person Regional Meeting all result in a level of scientific and societal advancement that a virtual meeting simply cannot replicate.

Acknowledgements

I would like to acknowledge the strong partnership between the International Pan Arab Critical Care Medicine Society (IPACCMS) and NCS, with especially strong leadership from both societies ensuring a high yield meeting despite all the challenges encountered. Additionally, I would like to acknowledge the efforts of our esteemed group of speakers and moderators who volunteered to participate, and sincerely thank them for their role during the meeting.

Regional Meeting track/ENLS/Nursing workshop speakers and moderators (in-person and virtual): Tamer Abdelhak, Yasser Abulhasan, Maha Aljuaid, Sana Alkhawaja, Omar Ayoub, Mary Kay Bader, Ahmad Bayrlee, Jamil Dibu, Michael Diringer, Hussam Elkambergy, Saef Izzy, Kalpana Krishnareddy, Sarah Livesay, Majid Mokhtari, Laura Nedolast, Marco Pallavidino, Lucie Pelunkova, Harsh Sapra, Wade Smith, Othman Solaiman, Jose Suarez, Gene Sung, Panayotis Varelas, Katja Wartenberg, and Khalil Yousef. Additionally, I would like to acknowledge Katja Wartenberg for directing the ENLS course, and Sarah Livesay and Khalil Yousef for co-leading the Neurocritical Care Nursing workshop. Sincere thanks go to Hussain Al Rahma (conference chairman) and team, and Katja Wartenberg for co-organizing the 3rd Regional Meeting with me. ●

Transitioning Alteplase to Tenecteplase for Acute Ischemic Stroke

By Brian W. Gilbert, PharmD, MBA, BCPS, BCCCP; Danielle S. Murray, PharmD; Peter Tran, PharmD; Kathryn E. Qualls, PharmD, BCPS, BCCCP




The transition from alteplase (ALT) to tenecteplase (TNK) in the management of acute ischemic stroke (AIS) has been an exciting and thoroughly discussed topic within the neurocritical care community. Although debates on the clinical efficacy and safety of TNK for AIS have subsided somewhat in light of recently published data, what remains lacking is a clear "road map" for institutions on how to properly implement the transition in thrombolytics. This article will attempt to serve as a guide for those evaluating the transition from ALT to TNK for AIS and shares the experience from our institution's rollout.

Safety

With respect to the most feared adverse event with TNK use, symptomatic hemorrhagic conversion, data suggest that incidence rates are relatively similar to ALT. However, other safety concerns exist that have been omitted in the literature.

First, angioedema is a known non-hemorrhagic adverse sequela associated with thrombolytic use and has a paucity of evidence on management. Since there are relatively few articles addressing this event with ALT, future data will be needed to study the phenomenon with TNK given the pharmacodynamic and pharmacokinetic differences between the agents.

Another large concern for stroke programs is ensuring that appropriate dosing is utilized for AIS. This may seem like a relatively simple concept, but TNK is currently supplied in a box that emphasizes dosing for myocardial infarction. This could lead to the possibility that in a critical moment, the wrong dosing could be utilized for AIS. To mitigate this, many programs have removed TNK from the manufacturer-supplied box entirely and utilized custom "stroke kits" (**Figures 1 & 2**).

Lastly, TNK has multiple indications for use—some FDA approved and some not—and it is imperative to have a discussion on the extent of TNK use for non-AIS indications. There are minimal data for TNK use in the pulmonary embolism literature but extensive data on its use in myocardial infarction. Additionally, stroke programs must consider which thrombolytic will be used and how it should be supplied for cases of AIS that require intra-arterial administration.

For all the reasons presented above, each institution should discuss current indications where thrombolytics have a place in therapy and decide which agent will be utilized for that situation. In evaluating these situations, institutions should also determine where thrombolytics will be stocked/located (i.e., central pharmacy, satellite pharmacy, or automated dispensing cabinet [ADC]), and whether medication errors can be mitigated by removing one or the other, while also considering the time sensitive nature associated with thrombolytic use. If multiple thrombolytics will be stocked in the ADC, safeguards should be present in terms of override capability and user access. The final safeguards that can be utilized to prevent errors are personnel double checks and warnings within the electronic health record (EHR).

Education

Proper education of staff involved in handling TNK and responding to stroke alerts is a vital step in the transition from ALT to TNK. Education will help to ensure that institutional guidelines are being followed and staff are maintaining patient safety. This education should be widespread and include pharmacy staff, providers, and nursing colleagues. Pharmacy

> "Proper education of staff involved in handling TNK and responding to stroke alerts is a vital step in the transition from ALT to TNK."

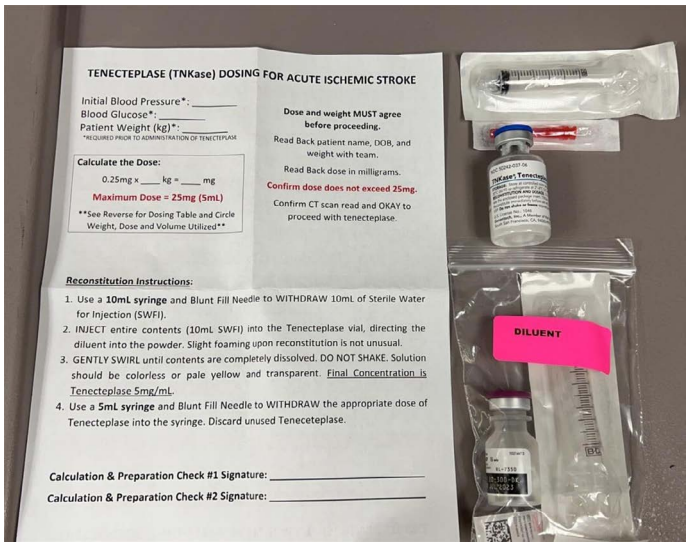
> Pharmacists will need to play a key role at the bedside to ensure safe, accurate, and timely administration of the medication.

staff will need education on the process of how TNK will be supplied, whether in dedicated TNK "stroke kits" or in the current manufacturer-supplied box. If a "stroke kit" is being used, there should be specific education on the contents of the kit to ensure accuracy. Further, the location of TNK should be identified for pharmacists and nursing staff to ensure timeliness of administration.

Providers should also be educated on how to order TNK and how the order may differ from ALT. Implementation of TNK order sets for AIS can help streamline the order entry process and mitigate dosing errors. It will also be important to note the differences in order sets depending on the indication. For institutions that will have both TNK and ALT on their formulary, education on when to use each agent and the correct order set for that agent and indication will be necessary.

Nursing staff should be educated on the proper dilution, dosing, and administration of TNK. It is important to differentiate the dosing for AIS and other indications and ensure nursing staff is aware of the maximum dose for AIS. Nursing should also be educated that TNK is given as a one-time bolus instead of a bolus with an infusion like ALT. However, it should be emphasized that patients who receive TNK should be monitored just as closely as those who had received ALT in the past, even though the administration time is shorter. Continuous education should also be given based on an institution's progress with the transition and to address any issues that may arise. Lastly, all personnel should be educated on how to report adverse events and voice concerns to ensure problems are addressed in a timely manner.

Figure 1. *Example of a custom "stroke kit."*



Operational Concerns & Preparation

There are many moving parts when discussing the operational aspects of changing from ALT to TNK for AIS. The first step after the decision to switch is made is to discuss implementation policies and guideline changes with your institution's pharmacy and therapeutics committee. You should also coordinate with your telestroke services, neurology providers, and other collaborators to inform them of the switch to maintain clear, streamlined communication. Orders sets will also need to be updated and tested in the EHR. As discussed above, education should be completed in a systematic way to ensure all team members involved in the AIS pathway are educated prior to the go-live date.

If an institution decides that moving toward a custom "stroke kit" for AIS is appropriate, the contents of the kit should be thoroughly discussed. In order to prepare the "stroke kit" for use in AIS, the TNK should be removed from the manufacturer's box and package insert, as the kit should include all necessary items for mixing and dosing. TNK dosing cards with weight, dose, and volume should be included to assist with dosing and avoid medication errors in case a pharmacist is not available at the bedside. In order to create an effective kit, we recommend the following in a sealable plastic bag:

- TNK vial
- 2 alcohol pads
- 5 mL dose syringe
- dosing card
- blank label
- needleless cannula
- separate sealable plastic bag for the diluent materials (which includes the diluent, 10 mL diluent syringe, and needleless cannula)

Pharmacists will need to play a key role at the bedside to ensure safe, accurate, and timely administration of the medication. Communications departments should therefore be made aware to ensure stroke pages include clinical pharmacists. Pharmacists can also assist in assessing the blood pressure and recommending pharmacologic agents to reduce the blood pressure levels to goal prior to administration of TNK. Additionally, they can make sure a blood glucose level has been drawn, as TNK is incompatible with dextrose-containing fluids. It is also recommended to have a second check dose calculation to ensure the appropriate dose is administered.

Table 1. *Tenecteplase for Institutional Transition Checklist*

Safety	• Dosing and indication differences » Implementation of TNK kits with clear instructions • Automatic dispensing cabinet » Assess need to stock both TNK and ALT » Override capabilities, user access, and second check for thrombolytics
Education	• Implementation of new order sets • Indications • Dilution and dosing » Max dose is no more than half the volume of the diluted product • Administration » Push dose vs. bolus with infusion • Monitoring » Blood pressure, neuro exams, etc.
Operational/ Preparation	• TNK Kits » Removal of TNK from manufacturers box to mitigate dosing errors in AIS • Prepared zip lock med kit and separate diluent kit inside » Med kit: TNK vial, 2 alcohol pads, 5 mL syringe, label, needleless cannula » Diluent kit: diluent, 10 mL syringe, needleless cannula » Dosing card: weight, dose, volume
Cost/Billing/ Other	• Review TNK cost and billing practices with the finance department or pharmacy representative • Ensure the TNK is built within the electronic medical record system appropriately charge in multiple instances

Cost & Billing

One of the big discussion points on the change from ALT to TNK revolves around the cost of the medications. Average wholesale prices of TNK are lower than ALT both within the United States and in most other countries. From a drug billing standpoint, AIS is typically placed in a diagnosis-related group (DRG) that confers a standardized hospital reimbursement. In turn, all the care provided for a patient with AIS is billed as a package option and covered under this reimbursement. DRG-based billing is commonly used by Medicare, Medicaid, and some commercial insurances which is important given that the amount of drug used versus wasted should be accounted for in these billing practices.

These factors are important when creating orderable items for TNK and on the backend for billing purposes. The change from a clinical standpoint is a rather easy process, but the process of changing billing mechanisms is more complicated and one that should be thoroughly discussed prior to the go-live of the new AIS protocol.

Figure 2.

TENECTEPLASE (TNKase) DOSING FOR ACUTE ISCHEMIC STROKE

Weight (kg)	Dose (mg)	Volume (mL)
< 40 kg	Manual Calculation	Manual Calculation
≥ 40 kg to < 41 kg	10 mg	2 mL
≥ 41 kg to < 43 kg	10.5 mg	2.1 mL
≥ 43 kg to < 45 kg	11 mg	2.2 mL
≥ 45 kg to < 47 kg	11.5 mg	2.3 mL
≥ 47 kg to < 49 kg	12 mg	2.4 mL
≥ 49 kg to < 51 kg	12.5 mg	2.5 mL
≥ 51 kg to < 53 kg	13 mg	2.6 mL
≥ 53 kg to < 55 kg	13.5 mg	2.7 mL
≥ 55 kg to < 57 kg	14 mg	2.8 mL
≥ 57 kg to < 59 kg	14.5 mg	2.9 mL
≥ 59 kg to < 61 kg	15 mg	3 mL
≥ 61 kg to < 63 kg	15.5 mg	3.1 mL
≥ 63 kg to < 65 kg	16 mg	3.2 mL
≥ 65 kg to < 67 kg	16.5 mg	3.3 mL
≥ 67 kg to < 69 kg	17 mg	3.4 mL
≥ 69 kg to < 71 kg	17.5 mg	3.5 mL
≥ 71 kg to < 73 kg	18 mg	3.6 mL
≥ 73 kg to < 75 kg	18.5 mg	3.7 mL
≥ 75 kg to < 77 kg	19 mg	3.8 mL
≥ 77 kg to < 79 kg	19.5 mg	3.9 mL
≥ 79 kg to < 81 kg	20 mg	4 mL
≥ 81 kg to < 83 kg	20.5 mg	4.1 mL
≥ 83 kg to < 85 kg	21 mg	4.2 mL
≥ 85 kg to < 87 kg	21.5 mg	4.3 mL
≥ 87 kg to < 89 kg	22 mg	4.4 mL
≥ 89 kg to < 91 kg	22.5 mg	4.5 mL
≥ 91 kg to < 93 kg	23 mg	4.6 mL
≥ 93 kg to < 95 kg	23.5 mg	4.7 mL
≥ 95 kg to < 97 kg	24 mg	4.8 mL
≥ 97 kg to < 99 kg	24.5 mg	4.9 mL
≥ 99 kg	25 mg (MAX DOSE)	5 mL

Conclusion

Transitioning from ALT to TNK for AIS remains a widely discussed topic for many stroke programs. There are many factors involved with the transition, including implementation of safeguards to prevent dosing and administration errors, education across all disciplines comprising the stroke response team, and operational considerations that vary between ALT and TNK. A structured checklist-based approach should be considered for programs preparing to make the switch, and hopefully this article can serve as a template. ●

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Don't Be Afraid of the Dark: Neurocritical Care Pharmacy at Night

By Brittny Medenwald, PharmD, BCCCP; Jessie Lipstreuer, PharmD

Healthcare workers face unique challenges during evening and overnight hours: an abundance of unplanned intensive care unit (ICU) admissions, unforeseen patient decompensation, and critical treatment decisions.[1] The majority of overnight neurocritical care (NCC) teams consist of one or two providers, often a resident or advanced practice provider. These providers have fewer resources, less accessibility to consult services, and indirect supervision from senior providers. Other services are also scaled back and frequently consist of less experienced team members on-site, including limited or no access to a clinical pharmacist. Add to that chronic sleep deprivation, which can impair cognitive function,[2] and it is clear to see how most medication errors occur during these hours.

A study conducted in critical care units found the rate of medication errors to be 16.7% during day shift (8 am – 2 pm) vs. 42.7% during evening shift (2 – 8 pm) and 28.7% during night shift (8 pm – 8 am).[3] One way to combat the increase in medication errors seen on evening and overnight hours is to increase access to a clinical pharmacist. The addition of a neurocritical care-trained clinical pharmacist on all shifts would allow real time identification and correction of medication errors before they occur. In fact, the Neurocritical Care Society recommends that in addition to a dedicated clinical pharmacist, neurocritical care units should have 24-hour on call clinical pharmacy support. Furthermore, they recommend that this clinical pharmacist should have additional training in both critical care and neuropharmacology beyond what a typical clinical pharmacist may possess.[4] Specialty training allows the pharmacist to be well versed in the unique challenges and complex medications of this specialized population, resulting in interventions above and beyond the low hanging fruit.

> "The Neurocritical Care Society recommends that in addition to a dedicated clinical pharmacist, neurocritical care units should have 24-hour on call clinical pharmacy support."

Beyond an increase in medication errors, evening and overnight shifts pose other unique challenges that a neurology-trained clinical pharmacist can help mitigate. Obtaining medication records can be quite difficult on these shifts due to limited hours of outpatient facilities and minimal access to family members. A clinical pharmacist is skilled at finding alternative avenues to obtain outpatient medication records. Additionally, they can provide 24-hour monitoring of medications with narrow therapeutic indices such as antiepileptics, antibiotics, and barbiturates. Real-time dose alterations and recommendations as a result of this monitoring can impact the duration of stay for neurologically ill patients. The additional pharmacologic support also allows providers to focus on the bigger picture within patient care and can alleviate some of the increased workload NCC providers face at night.

Our hospital provides 24-hour clinical pharmacy support on evenings and overnights to address some of the many challenges that providers face "after-hours." Our ICU and emergency department (ED) pharmacists on evening shift are heavily integrated into the NCC team. We would like to share our practice model with examples of pharmacy-related challenges and successes.

Emergency Department (ED) After Dark: Jessie Lipstreuer

My name is Jessie, and I am one of two evening shift ED pharmacists for a Level I Trauma Center, Comprehensive Stroke Center and referral center for 21 surrounding counties. I work seven-on/seven-off from 3 pm to 1 am as the sole ED pharmacist. This schedule provides continuity of critical care coverage for our providers and patients, but it is not without challenges from a pharmacist's perspective. There is no ED pharmacist overlap,

so I start my day by receiving hand off from dayshift regarding critically ill patients within the department, as well as any incoming alerts.

Operating during atypical business hours means that primary care offices and urgent cares are closed, which leads to increased ED volume and heavy utilization of ED pharmacy services. With the lack of available information, I utilize my critical thinking to provide more creative medication solutions. In addition, I am routinely in contact with our critical care pharmacist regarding patients being admitted to the ICU, providing updates, differential diagnoses, and recommendations that have not yet been addressed.

As medication experts, ED pharmacists can assist with medication selection for status epilepticus, identification of contraindications to thrombolytic therapy in acute ischemic stroke, anticoagulation reversal in intracranial hemorrhages (ICH), and intubation or resuscitation if necessary. In one recent example in my role as the ED evening pharmacist, I responded to a code stroke with the evening shift nurse practitioner for a transfer patient that had received alteplase at an outside hospital. The patient experienced an acute decline in mentation during transport and required immediate intubation upon arrival. Due to concern for potential

> "ED pharmacists can assist with medication selection for status epilepticus, identification of contraindications to thrombolytic therapy in acute ischemic stroke, anticoagulation reversal in intracranial hemorrhages (ICH), and intubation or resuscitation."

hemorrhagic conversion, I facilitated the rapid ordering and bedside delivery of fibrinolytic reversal with aminocaproic acid and then initiated our code stroke red process once imaging confirmed an acute ICH. My involvement shortened the time it would have normally taken on evening shift for a patient to receive reversal medication and likely improved patient care.

Neurocritical Care After Dark: Brittny Medenwald

My name is Brittny, I am a PGY-2 neurocritical care-trained, critical care pharmacist. I cover the NCC unit and trauma surgical

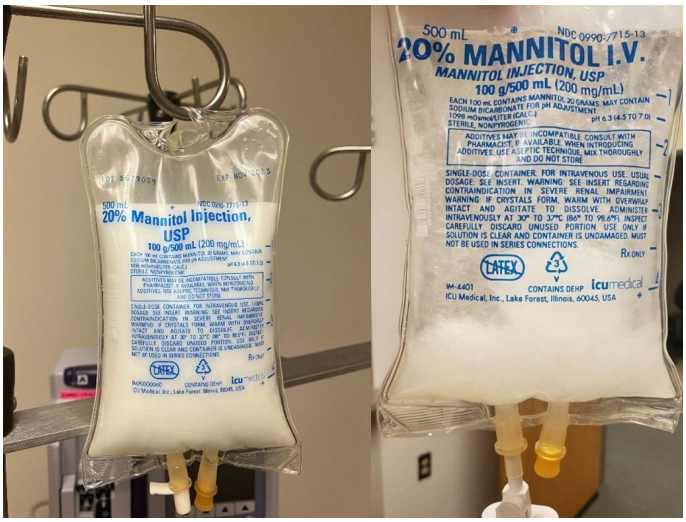

Figure 1. *Crystallized Mannitol*

ICU on evening shift. I also work seven-on/seven-off, however, my hours are from noon until 10 pm. We follow an integrated pharmacy practice model, so I start my shift by providing order entry cross coverage for the dayshift pharmacists. Around 15:00, I receive sign out (a verbal pass-off from the day shift pharmacist) on any medication levels, acute medication issues, or critical patients that need follow up. As I cover multiple ICUs, there are no formal multidisciplinary patient rounds or sign out rounds. Instead, I try to be present when the providers pass off to their overnight counterparts to gain more insight into any patient care changes that occurred on day shift and address any medication-related issues I have come across. Since I respond to inpatient codes and provide back up for the ED pharmacist, I am not always able to attend provider hand offs, making it extremely difficult to know all the patients in as much detail as I would like. My role as the evening critical care pharmacist is to provide support and try to bridge the gap between dayshift and evening shift with respect to the medication therapy that is ordered for patients.

I make myself available to the nursing staff as much as possible and often rely on them for pertinent patient updates. In return, I am often able to provide additional insight on the course of a patient's care in the ED prior to their arrival in the NCC unit as I am in frequent communication with the ED pharmacist. Once the patient arrives, most of my focus and communication is geared toward emergent problems or new issues identified during order verification. The rest of my shift is spent assisting the team in stabilizing new ICU admissions, responding to patients who are decompensating, and following up on the status of critical patients signed out by day shift ICU pharmacists. For example, one evening I noticed a milky bag of fluid hanging on the bedside of an NCC patient who was waiting for a computed tomography (CT) scan. Upon closer inspection, I realized it was a bag of completely crystalized mannitol that was primed and attached to the patient. Mannitol has a propensity for crystallizing at cooler temperatures and sometimes at room temperature (**Figure 1**). After ensuring the medication was

> A neurology-trained pharmacist can serve as a resource to the other evening shift pharmacists who may not be as familiar with these medications.

not yet infusing, I provided nursing education, and expedited a replacement bag of uncrystallized mannitol. This error, and others like it, may not have been caught without the physical presence of a clinical pharmacist on the evening shift. At the end of my shift, I sign out to the overnight pharmacist.

In addition to supporting overnight providers, a NCC pharmacist can also serve as a resource for other evening/night shift pharmacists who may encounter neurology-related issues on non-critically ill patients. With the rapid increase in the approval of monocolonal antibodies for multiple sclerosis, migraine headache, Parkinson's and Alzheimer's disease, patients with these medications are frequently admitted outside of the ICU. Many of these medications are parenteral with unique dosing criteria, adverse effects, and access barriers. In addition, customization of dual antiplatelet therapy is becoming increasingly common. A neurology-trained pharmacist can serve as a resource to the other evening shift pharmacists who may not be as familiar with these medications.

With the exponentially growing pool of neurology literature, a neurology-trained pharmacist has a more thorough understanding of complex neurology topics than a pharmacist with training in a different specialty. This is important because, as anyone who practices in neurology and neurocritical care can tell you, neurology is not black and white. A pharmacist needs to develop the necessary skills and expertise to provide optimal patient care in the "gray areas."

Are You Still Afraid of the Dark?

The Standards for Neurologic Critical Care Units from the Neurocritical Care Society state that pharmacists are an essential member of the interdisciplinary care team, citing their ability to reduce medication-related costs, decrease ICU length of stay, reduce readmission rates, decrease adverse medication reactions/interactions and more. They recommend that in addition to a highly trained and dedicated pharmacist, the NCC unit should have access to 24-hour, on-call clinical pharmacy services.[4] Our hospital amplifies the recommendation by providing a pharmacist in the ED with advanced training and a neurology-trained critical care pharmacist in the ICU to support our providers and decrease medication errors.

Literature shows that medication errors more than double during the evening and overnight hours.[3] The examples we describe are evidence that access to a neurology-trained pharmacist on these shifts can reduce medication errors and prevent serious errors that might not have been caught otherwise due to reduced staffing and increased workload. In addition to preventing medication errors, our skill set was utilized to provide therapeutic alternatives during drug shortages, most recently for the recent national shortage of 3% saline, 23.4% saline, and mannitol. Overall this service takes some of the workload off other overnight providers while enhancing patient safety.

Twenty-four-hour clinical pharmacy support for neurocritical care patients, while not without its own challenges, is a luxury that benefits a hospital system in multiple ways. From increasing neuropharmacologic resources for providers to preventing medication errors, ED and ICU clinical pharmacists with expertise in the care of NCC patients can be beacons of light in the dark. ●

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Business of Neurocritical Care: Billing Updates for 2023

By Ryan Hakimi, DO, MS, NVS, RPNI, CPB, FNCS, FCCM

Just as 2022 restructured the rules associated with outpatient billing and documentation, January 1, 2023 began with substantial changes that surround inpatient billing and documentation. In general, the identity and history associated with patients who present to the emergency department is often unknown. As such, items that have historically been required for documentation within the H&P such as the review of systems, social history, and family history often cannot be obtained at the time of documentation leading to queries from the billing and coding specialists within the hospital and often lead to downgrading of the charge and provider frustration.

With the new changes, only relevant history needed for the care of the patient needs to be documented when billing an Evaluation and Management (E&M) code. For example, the family history of an 80-year-old ICH patient is irrelevant to the patient's care and no longer needs to be documented in the H&P. However, when known, documenting this patient's use of antithrombotics and antihypertensives is relevant and should be documented. Many centers will thus need to restructure their H&P fields to consolidate the fields down to relevant medical history. Here we summarize the variety of inpatient encounter types considering the most up to date requirements.

E&M Encounters with APPs

It is important to note that when an attending physician attests an APP's note during an E&M encounter that he/she document that they performed the substantive portion of the assessment. This simple attestation would then require that the APP's note document what the physician did. As an alternative, and to ensure compliance with this requirement, it is ideal for the attending physician to document at least one of the 3 key elements (the history, physical exam, or the assessment and plan). Therefore, an ideal E&M attestation with an APP would state, "I saw and examined this patient on month/day/year. I have reviewed the note from APP X. I agree with his/her assessment and plan except as noted here. On my examination… OR summarize the history of present illness OR summarize the assessment and plan."

E&M Encounters with Residents/Fellows

For an E&M encounter with a resident or fellow, the attending needs to be physically present for the critical or key portions of the services provided by the resident or fellow and document the attending's involvement in the management of the patient. As in the case with attestation of an APP's E&M service, the attending may document, "I saw and evaluated this patient on XX/XX/XXXX. Discussed with the resident/fellow and agree with the findings and plan as documented in the resident/fellow's note." However, again this would require that the resident/fellow clearly document what the attending did. Therefore, as in the case of the APP, it is best for the attending to document one of the 3 key elements in their attestation.

For critical care patients, those additional history items have never been required for billing critical care, but some health systems have had internal requirements that have mandated that all of the fields be completed leading to provider frustration. Additionally, 2022 marked the allowance of split-share billing with APPs (counting critical care time provided by the APP alone + critical care time provided simultaneously by the attending and APP + critical care time provided by the attending alone). This change led to substantial frustration and many questions. Therefore, in 2023 CMS and CPT offered some clarifications.

> "It is important to note that when an attending physician attests an APP's note during an E&M encounter that he/she document that they performed the substantive portion of the assessment."

New since January 1, 2023, are two key points of clarification regarding time thresholds for billing the add-on code 99292 for CMS patients in comparison to non-CMS patients. First, CMS has a differing opinion than the CPT Committee in that they feel that 99292 can only be billed when a complete additional 30 minutes time increment is met as shown in Table 2. Second, CMS indicated that 99292 can be billed when the appropriate time threshold is met regardless of whether the time is provided by one individual or as a split-share visit and does not require the first provider to provide at least 30 minutes.

Non CMS Patient: Critical Care Provided by APP and Attending in the Same Group

First practitioner (APP or attending) provides first 30 minutes of CC time

Bill 99291 (30-74 minutes) by the practitioner who provided the most critical care time

Ex: APP sees patient first and provides 35 minutes of critical care time; then attending provides critical care with the APP/ completes documentation for 38 minutes of critical care time. Total CC time is 73 minutes which gets billed to the attending.

Bill 99291 and 99292 (total time 75-104 minutes)

Example 1: APP sees the patient first and provides 35 minutes of CC time; then attending provides critical care with the APP/ completes documentation for 45 minutes of critical care time. Total CC time is 80 minutes which gets billed to the attending.

Example 2: Physician A provides 45 minutes CC; Physician B provides 40 minutes of critical care on the same calendar day: total time spent 85 minutes. Physician A would bill code 99291 and Physician B would bill code 99292 x 1 unit.

Example 3: Physician A provides 100 minutes CC; Physician B provides 30 minutes of CC on the same day: total time spent 130 minutes. Physician A would bill code 99291 and 99292 x 1 and Physician B would bill code 99292 x 1 unit.

Table 1: Non-CMS billing table (not Medicare or Medicaid)

Total Duration of Critical Care	Appropriate CPT Codes
30- 74 minutes	99291 x 1
75- 104 minutes	99291 x 1 and 99292 x 1
105- 134 minutes	99291 x 1 and 99292 x 2
135- 164 minutes	99291 x 1 and 99292 x 3

Table 2: CMS billing table (Medicare or Medicaid)

Total Duration of Critical Care	Appropriate CPT Codes
30- 103 minutes	99291 x 1
104- 133 minutes	99291 x 1 and 99292 x 1
134- 163 minutes	99291 x 1 and 99292 x 2
164- 193 minutes	99291 x 1 and 99292 x 3

New since January 1, 2023, is the allowance of summing of critical care time under split-share when the first practitioner (APP or attending) does not provide at least 30 minutes of CC time. In this case one must follow the rules below:

First practitioner (APP or attending) provides less than 30 minutes of CC time

Bill 99291 (30-74 minutes) by the practitioner who provided the most critical care time

Ex: APP sees patient first and provides 15 minutes of critical care time; then attending provides critical care with the APP/ completes documentation for 35 minutes of critical care time. Total CC time is 50 minutes which gets billed to the attending.

Bill 99291 and 99292 (104-134 minutes)

Ex: APP sees the patient first and provides 25 minutes of CC time; then attending provides critical care with the APP/completes documentation for 80 minutes of critical care time. Total CC time is 105 minutes which gets billed to the attending.

Bill 99291 only (74-103 minutes)

Ex: APP sees the patient first and provides 25 minutes of CC time; then attending provides critical care with the APP/completes documentation for 60 minutes of critical care time. Total CC time is 85 minutes which gets billed to the attending. Note that since the first provider did not provide at least 30 minutes of CC time and the sum of the two providers CC time is less than 104 minutes, only 99291 can be billed.

It is important to note that each institution can choose if they wish to follow CMS rules for all payers or to bill each individual payer by that payer's rules. In other words, your institution may indicate that you must bill for 104 minutes of critical care in order to bill a 99292 even if the patient is covered under a commercial insurance carrier such as Blue Cross. Please consult your hospital's billing and coding department to ensure compliance. ●

What Should Our Daughters Expect? A Neurointensivist's and Mother's Perspective

By Sarah Nelson, MD, MPH

I am a neurointensivist who has cared for several gunshot wound victims, and am also a new mother of a daughter. I feel these roles provide me with perspectives on reproductive rights and gun control that are likely to be shared with others. In this article, I briefly summarize the policies in our country regarding both of these issues, the dangers in not fully addressing them, and the steps we (as neurointensivists and others reading this article) can take to help ensure that evidence-based reproductive rights remain available to all and that our society (and in particular our children) can live without fear of gun violence. While some recent progress has been made regarding both of these issues, much work unfortunately remains.

• • •

I have recently given birth to my first-born – a daughter. I am also a neurocritical care physician who has taken care of gunshot wound victims. Over the last few months, we've lost the abortion rights provided by Roe v Wade[1] and continued to witness repeated episodes of gun violence.[2] I would argue that both issues are relevant to neurointensivists (and other physicians) and parents alike, and further that we can each do our part to ensure a better tomorrow for future generations.

Growing up in the '80s and '90s and completing medical school by 2010, I never considered the magnitude of potential infringements on our rights (including women's rights) that could be possible in the future. We saw important gains in LBGTQ+ rights early in the 21st century. Various contraceptive methods have been in practice for decades. In 2020, we celebrated 100 years of women being afforded the right to vote. We were headed in what I thought was the right direction, especially for future generations—including my daughter.

Though others may have different views, 71% of the US population feel that abortion is a medical issue that exclusively concerns a pregnant person and their doctor.[3] Though of course there is a new life at stake, there is also the mother's life as well, and without a mother there can be no new life. Further, eliminating abortion rights only removes safe abortions in many places but not abortions overall, and there are also now legal risks with self-managed abortions as well as real medical risks to some mothers if required to carry a pregnancy to term.[4]

From a neurocritical care perspective, there may be times when known teratogenic agents are necessary for various conditions (e.g., valproic acid for status epilepticus, cyclophosphamide for autoimmune encephalitis), which could obviously have major implications for unborn children.[5] In addition, there may be other situations in which critical care physicians feel constrained in the patient-care decisions they are able to make if there are concerns about possible undesirable consequences to fetuses and the potential for liability. In other words, they may feel they have little choice but to abide by the law even if it comes into direct conflict with a patient's wishes.

However, given the medical complexity surrounding abortions as well as the attitudes of the US population,[3] one might argue that abortion should not even be a target of legislation to begin with. Though I'm fortunate to live in a state that permits abortions regardless of the recent Supreme Court decision, I worry about my daughter's future and what rights may (or may not) await her when she is of child-bearing age. And it should be acknowledged that the Supreme Court decision will most certainly disproportionally affect those of lower income, those with fewer resources, and those living in states that have historically disenfranchised minorities.[4,5]

There are some potential bright spots with regard to this issue. In the wake of the Supreme Court decision, several leading medical societies released statements supporting the right to abortion. The American Medical Association (AMA) pledged "to protect the patient-physician relationship" and to "oppose any law or regulation that compromises or criminalizes patient access to safe, evidence-based medical care, including abortion."[6] The Neurocritical Care Society (NCS) stated that "Laws that restrict the provision of medical and nursing care based on best scientific evidence is in direct conflict with NCS's Mission and Vision, especially when these rulings impact those in minority or otherwise underserved populations. NCS will continue to advocate for the right of healthcare providers globally to deliver care based on their training, to act based on the best available evidence without threat of criminalization and to support patients to make healthcare decisions based on this advice."[7] On the governmental level, the Biden administration has issued executive orders and guidelines to help protect access to

reproductive services,[3,8] though the right to abortion has yet to be codified into law.

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Gun violence also clearly remains problematic in this country and is also of major concern to physicians and parents. It seems not a week goes by that we don't hear about young lives being taken as a result of firearms, and physicians (including neurointensivists) continue to see gunshot wound victims in our practice settings. I had worked alongside others to help address this at the AMA level a few years ago, including advocating for gun buyback programs and for increasing the age to purchase ammunition and firearms from age 18 to 21. Within the past year, the AMA has continued to release statements in support of curbing gun violence.[9] Fortunately our country recently seems to have made additional strides in this direction.[10,11] In particular, the Bipartisan Safer Communities Act increases funding for mental health services, expands background checks for individuals less than 21-years-old seeking to purchase a firearm, and prevents those convicted of domestic violence offenses from purchasing firearms for 5 years, among other provisions.[11]

But even now, without the support of additional legislation, parents are discussing equipping their children with bulletproof outfits, and active shooter drills are being exercised in schools – previously unimaginable scenarios but seemingly necessary given the ongoing gun violence crisis in our country. And despite what some critics may say, gun violence does affect medical professionals, and they can and should work to address it.[12] Having cared for many of these patients myself, many of whom are unfortunately younger victims, I can personally attest to this issue being in physicians' "lane," and I'm sure many other neurointensivists would agree.

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Despite these recent advances, reproductive rights and gun control are still not completely secured and assured in this country. I am uneasy about what the future holds for the generation that will include my daughter – to have fewer rights than my mother and I had, and to be potentially exposed to gun violence at school. What a scary predicament for physicians and parents alike.

I've always believed in standing up for things when they don't seem right, and I hope to engender this in my daughter as well. I believe I'm speaking for lots of parents and their children that our nation finds itself in a crisis, and I know I speak for many other physicians regarding the tremendous impact of these issues on both doctors and patients.[4,5,9] The US has seemingly taken steps backwards in its protection of rights and safety. As a mother, I want the best for my daughter, including the assurance that healthcare decisions for women will continue to be made based on the best available scientific evidence, and that gun violence will hopefully be a non-issue throughout her life. As a critical care physician, I worry that we will continue to see and manage young victims of gun violence, and that we may be doing pregnant women (and their unborn children) a disservice with limitations on the medical care we are permitted to provide.

It will require concerted and deliberate action by as many stakeholders as possible to ensure that reproductive decisions remain a decision solely between persons born as female and their doctor, and that guns find a decreased presence in society or, at the very least, are placed only in responsible hands. Physicians need to continue to support medical associations such as the AMA and NCS in their advocacy efforts through participation in meetings, phone calls, and emails. All of us must lobby our governmental leaders (including local members of congress) to support these issues via similar mechanisms as well as by votes and/or potentially financial assistance. We must continue to amplify our voices by utilizing social media such as Facebook and Twitter and any other outlets at our disposal. Guaranteeing that reproductive rights remain available and that our society can live and grow without fear of gun violence is critical: the lives of future generations are at stake. ●

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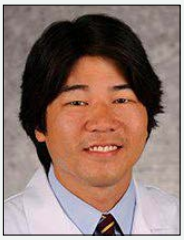
The Ethical Conundrums of Normothermic Regional Perfusion

By Richard Choi, DO; Misti Tuppeny, MSN, APRN-CNS, CCRN, CNRN, CCNS; Alexandra Reynolds, MD



Heart transplantation has proven to be lifesaving for thousands of patients with advanced heart failure since its inception in 1967. Despite our advances, this procedure is performed less than 6000 times a year worldwide[1] and many hundreds of listed patients and thousands of unlisted ones die every year awaiting a transplant. The biggest obstacle limiting expansion of heart transplants is the same one limiting transplantation of other organs: demand far exceeds supply. Hearts are significantly more challenging to attain than other organs because hearts have historically been derived almost exclusively from brain-dead donors (also referred to as Donation after Neurological Death, or DND).

Donation After Circulatory Death

The decision to withdraw life-sustaining therapies (WLST) ensues after determining that further treatment will not enable survival, nor will it produce a functional outcome with acceptable quality of life to that patient.[2] If the patient's medical decision maker agrees to organ donation, donation may occur after compassionate extubation if death by circulatory criteria (ie., cardio-pulmonary arrest) occurs within a previously established timeframe. Controlled donation after circulatory death (cDCD) involves declaration of death after a "hands-off" 5-minute waiting period during which it is ensured that cardiac activity does not spontaneously recur, followed by organ procurement. Of note, a recent international prospective study of 480 patients demonstrated that no patients had circulation beyond 5 minutes, and all patients progressed to death.[3] Currently, cDCD is practiced in 17 countries: Australia, Austria, Belgium, Canada, China, Czech Republic, France, Ireland, Italy, the Netherlands, New Zealand, Norway, Spain, Sweden, Switzerland, the United Kingdom, and the United States.[2]

> "Hearts are significantly more challenging to attain than other organs because hearts have historically been derived almost exclusively from brain-dead donors (also referred to as Donation after Neurological Death, or DND)."

Heart Transplantation after cDCD

Two newer techniques that allow for heart transplantation following cDCD currently in use are: Direct Procurement and Perfusion (DPP) or Thoraco-Abdominal Normothermic Regional Perfusion (TA-NRP).

Direct Procurement and Perfusion (DPP)

In DPP, following declaration of death after the "hands-off" period, the heart is removed, instrumented, and placed into a perfusion device.[4] While this device can measure arterial and venous lactate levels, it is incapable of assessing the mechanical function of the heart. It is unknown if the donor heart, which has now undergone a period of warm ischemia, instrumentation, and machine perfusion, can maintain circulation in the recipient until after the transplant.[1] Hearts procured in this manner are frequently rejected based on their lactate profile, even if usable, and carry a high cost, with the machine costing $270,000 and each perfusion costing an additional $68,800.[5] Outcomes from heart transplants using this procurement method have been shown to be similar to those of DBD.[6]

Normothermic Regional Perfusion

In Normothermic Regional Perfusion (NRP), upon declaration of death by circulatory criteria following the "hands-off" period, the patient is instrumented, and Extra-Corporeal Machine

Oxygenation (ECMO) is started. There are two forms of NRP: Abdominal NRP (A-NRP), where the thoracic aorta is cross-clamped and ECMO started via femoral access to allow for abdominal organ perfusion, and Thoraco-Abdominal NRP (TA-NRP), where the cerebral vessels are either ligated or drained following sternotomy, and the great vessels are cannulated for ECMO to allow for cardiac perfusion. The heart typically restarts following ECMO, allowing for the mechanical evaluation of the heart via direct visualization, transesophageal echocardiography (TEE), and pulmonary artery catheterization prior to transplantation. This technology has already demonstrated an increase in the number of heart transplants compared to baseline, with outcomes comparable to DBD heart transplants.[7,8]

Despite the ligature of the cerebral vessels, the presence of anastomoses via one of several pathways may continue to perfuse areas of the brain and brainstem after both A- and TA-NRP. These include a) thoracic aorta to posterior intercostal to anterior spinal artery; b) inferior epigastric to internal thoracic to subclavian to vertebral arteries; c) thoracic aorta to supreme intercostal to costo-cervical trunk to subclavian to vertebral arteries; and d) thyrocervical trunk to ascending cervical to vertebrobasilar arteries.[9] In a porcine model of NRP, one out of five animals demonstrated collateralization of flow to the brain, though without return of brainstem reflexes nor increase in activity on BiSpectral Index (BIS), electroencephalogram (EEG), or Near-Infrared Spectroscopy (NIRS) monitoring.[10] Testing to assess for the possibility of preserved cerebral perfusion, as is recommended by the European Society for Organ Transplantation, is currently performed in some countries, though not in the US. It is unclear if this technology is sensitive enough to detect small amounts of persistent brainstem flow[11] or what the significance of this flow is.

> "TA-NRP proponents argue that the absence of brain flow by ligation of cerebral arteries maintains a persistent state of death under neurologic criteria, even if the patient's circulation has been restored."

While already performed in many countries, including Belgium, Spain, Italy, the Netherlands, France, and some centers in the United States, TA-NRP is not currently performed in Australia or Canada.[11] The UK, where this technique was developed, has currently paused NRP pending additional research, and a recent exploration of NRP in Canada concluded that while DPP aligns with its current guidelines, NRP requires further work to ensure the absence of brain perfusion.[12,13]

Ethical Principles Guiding Organ Donation

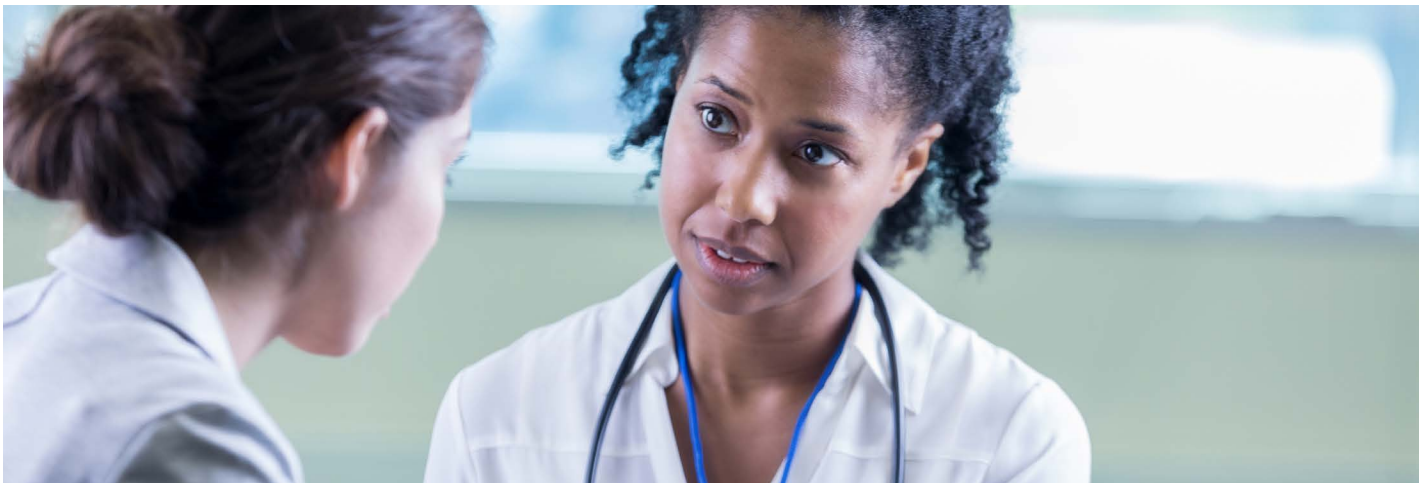
The Dead Donor Rule (DDR) is the main ethical principle guiding organ donation in the United States. The DDR states that "a vital organ cannot be removed until the donor is determined to be dead according to medical standards and legal criteria" and "removing a vital organ cannot cause the death of the donor".[14] The DDR cannot be overridden by an autonomous decision. Thus, even a person's voluntary sacrifice to save another is not considered ethically or morally justifiable.

Ethical Concerns Over TA-NRP

The main ethical concern over TA-NRP is in regard to the Uniform Determination of Death Act (UDDA). The UDDA is the legal basis for death pronouncement in the United States, stating that "[a]n individual who has sustained either (1) irreversible cessation of circulatory and respiratory functions, or (2) irreversible cessation of all functions of the entire brain, including the brain stem, is dead. A determination of death must be made in accordance with accepted medical standards." If the basis for the determination of death during DCD is "irreversible cessation of circulatory and respiratory functions", then restoration of circulation upon initiation of ECMO in TA-NRP may invalidate the death declaration. If the patient's death declaration were annulled, organ procurement would then constitute a violation of the DDR.

TA-NRP proponents argue that the absence of brain flow by ligation of cerebral arteries maintains a persistent state of death under neurologic criteria, even if the patient's circulation has been restored.[14] When exploring the justifications used to define brain death as human death in 2008, the US President's Council on Bioethics agreed upon the unifying medical concept of death by majority decision.[15] This concept states that death, rather than being an irreversible process, is the permanent termination of brain functions. Proponents therefore argue that the UDDA should not be interpreted literally[2] and the patient remains dead because total or near total permanent brain destruction is the unavoidable result of cDCD, whether with or without TA-NRP.

A counterargument invokes the principle of double effect which states that an action that causes an adverse effect is ethically and morally justifiable if it is meant to provide benefit. WLST is acceptable when the goal is to provide benefit by respecting the patient's autonomy and alleviate suffering – even if the withdrawal is likely to cause the patient to die – as long as death is not the intended result. Instead, if an activity is intended to cause death, it is equivalent to euthanasia and is unethical. If the patient's declaration of death is invalidated by the restoration of circulation, then the cerebral vessel ligature in TA-NRP represents an intentional attempt to cause brain death.[14]



Another major ethical concern lies in the possibility of ongoing cerebral perfusion through collaterals. Even though the European Society for Organ Transplantation guidelines recommend monitoring cerebral perfusion via NIRS, BIS, or EEG[11], these technologies may not be sensitive enough to monitor for the presence of brainstem perfusion. In a study of 3 patients undergoing TA-NRP, 1 patient had approximately 50 mL/min of blood draining from the open distal ends of the cerebral vessels. Though this is far less than the 10-12 mL/100 g brain tissue/min that would be necessary to maintain neuronal membrane integrity and function, the authors conclude that "…TA-NRP … cannot be considered to provide absolute reassurance of the complete absence of brain blood flow or perfusion".[9] Because the brainstem may have retained perfusion, albeit minimal, it remains uncertain if the donor can experience suffering or awareness. Newer techniques aimed at reducing this anastomotic cerebral blood flow that involve leaving the aortic arch vessels open to drainage or to negative pressure have been devised, but are challenging, time-consuming, and complex.[9]

While TA-NRP is already practiced in the United States, several medical societies have voiced concerns over its practice.[16,17]

Ethical Principles vis-a-vis TA-NRP

The main ethical principles that guide medical care remain Autonomy, Beneficence, Non-Maleficence, and Justice.

Autonomy represents respect for a person and the right to self-determination. While the patient in these instances has no say in their own self-determination – the decision to proceed with TA-NRP lies in their medical decision maker – the goal to respect that person's wishes persists. While TA-NRP would allow for the maximization of organs donated and thus respect the donor's desire to help others and their right to self-determination, the principle of double effect would arguably place TA-NRP in direct odds with their right to self-determination. Critical for respect of autonomy is also a clear informed consent process, full transparency in regard to pre- and post-mortem interventions, and the possibility of restoration of cerebral blood flow.

Beneficence denotes the obligation to act in the best interest of the patient. In the case of TA-NRP, the patient's medical decision maker has determined that WLST is in the patient's best interest. The team's responsibility lies in continuing to provide care prior to organ procurement. TA-NRP allows for the maximization of benefit to others by donating organs that would otherwise not be able to be transplanted. NRP would allow for increased availability of hearts that may otherwise not have been able to be transplanted. The lower cost associated with TA-NRP compared to DPP will increase access to hearts for transplantation and make it available in resource-restrained areas.

Non-maleficence, or "do no harm," is discussed as ante- and post-mortem interventions. In Spain, femoral ECMO cannulation is allowed ante-mortem. This practice is not permitted in the UK or the US. Initiation of a heparin infusion ante-mortem can help with organ preservation and is considered ethically acceptable as the potential ill effects of the intervention causing death are not intended (principle of double effect). The main post-mortem concern is that of direct injury and harm to the patient. If the persistent cerebral perfusion via collaterals were sufficient to allow the donor to be aware or experience suffering during organ procurement, it would be ethically unjustifiable to continue the organ procurement process with TA-NRP. For this reason, the European Society for Transplantation has recommended that brain flow monitoring be utilized with a pre-established plan to abort the TA-NRP process if any such flow is detected.[11]

Justice represents the concept of fair and equitable distribution of resources as well as respect for the law. TA-NRP requires equitable distribution of benefits and burdens. The ACP has raised concerns that TA-NRP will disproportionately affect stigmatized populations, though this is not unique to TA-NRP but rather applies to all DCD and DBD donors. The respect of autonomy via the informed consent process is critical to maintain justice, as is the ongoing fair allocation of organs. The ongoing ethical dilemma of death declaration surrounding TA-NRP, where TA-NRP may "bring about" death by restoring the circulation and then ligature of the cerebral vessels, are of potential concern for future litigation. Institutions should abide by their local and state regulations.

> Neurocritical Care Society members are likely to encounter TA-NRP in their local institutions and are particularly adept at understanding the ethical and moral implications of this practice.

Conclusion

TA-NRP presents a true ethical conundrum, driven by the variable interpretation of the UDDA and the prospect of persistent cerebral blood flow. DPP is less ethically controversial but leads to fewer transplants due to its associated higher cost. This piece has highlighted these major ethical controversies and applied an ethical framework for its consideration. Neurocritical Care Society members are likely to encounter TA-NRP in their local institutions and are particularly adept at understanding the ethical and moral implications of this practice. Neurocritical Care Society members should be informed about TA-NRP and local practices in order to help guide further conversations within their institutions. ●

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Signs of Right Ventricular Strain on Point-Of-Care-Ultrasound (POCUS) in the setting of Pulmonary Embolism

By Eric Dornoff, MD; Kelly Rath, DNP; Vasisht Srinivasan, MD



A 38-year-old woman, previously healthy, was admitted to the neuroscience intensive care unit following a thoracic fusion. On post-op day four, the patient suffered a syncopal event and was hypotensive, tachycardic, and hypoxemic. A rapid response was called, she was started on oxygen by nasal cannula, given intravenous fluid boluses, and admitted to the neurocritical unit for further monitoring and work-up. An EKG was obtained, which demonstrated right axis deviation and a right bundle branch block (**Figure 1**). Point-of-care ultrasonography (POCUS) was performed, which revealed right ventricular enlargement and dysfunction, with a D-sign and McConnell's sign (**Figure 2**). A computed tomography scan of her chest was obtained next (**Figure 3**), which demonstrated a large pulmonary embolism (PE) with bilateral clot burden, with suspicion for a saddle clot. She was taken for catheter-directed thrombolysis, followed by a heparin infusion. Over the following three days, she was monitored in the neurocritical care unit. Transthoracic echocardiography repeated on day two post-thrombolysis demonstrated normal right ventricular function, no regional wall abnormalities with the left ventricle, and normal systolic pressures measured in the pulmonary artery. She remained hemodynamically stable and was weaned to room air. She was transitioned to warfarin and the remainder of her hospital course was uneventful. She was ultimately discharged home.

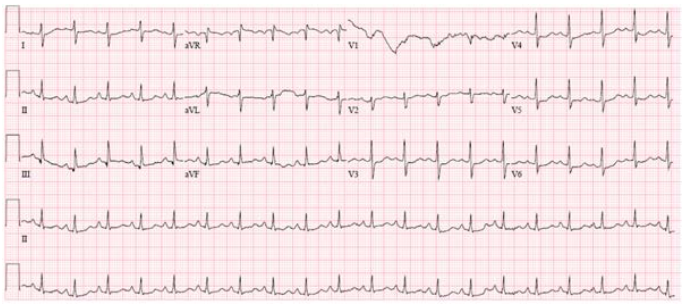
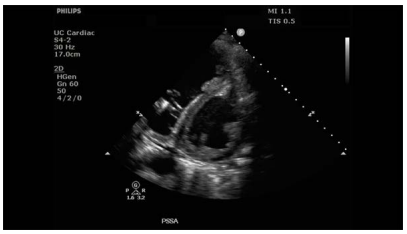
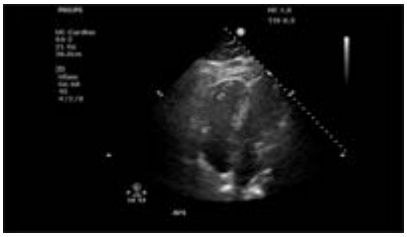


***Figure 1**. Initial electrocardiogram demonstrating the right axis deviation and right bundle branch block.*



A



B

***Figure 2**. Ultrasound images. A – Short axis view. B – Apical four chamber view.*

Evidence, Pathophysiology, Views, and Differential Diagnoses

Pulmonary Embolism (PE) is a life-threatening condition associated with significant morbidity and mortality, and requires prompt diagnosis and management. One of the quickest ways to assess for the presence of PE is through POCUS. Studies have demonstrated that POCUS has a sensitivity ranging from 60 - 83% and specificity ranging from 50 - 90%.[1]

Large PEs will cause elevated pressures in the pulmonary vasculature resulting in right ventricular strain and dilation, manifesting as the so-called 'D-sign' on POCUS. This is seen due to ventricular septal deviation and flattening. Ventricular interdependence causes a reduced left ventricular (LV) diastolic size with impaired LV filling and preload, with subsequent

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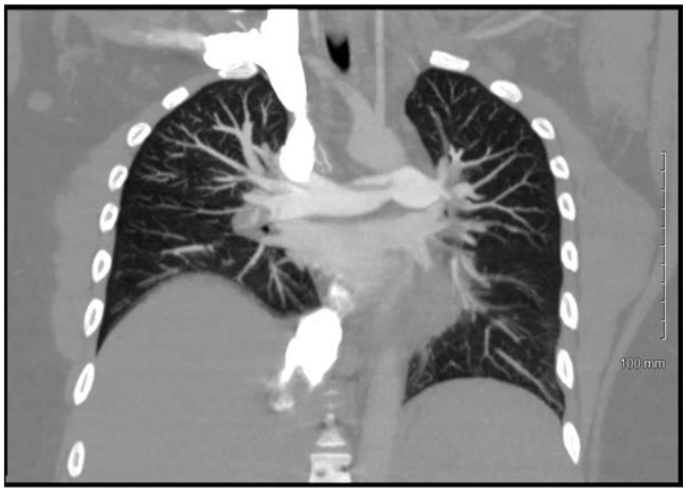

Figure 3. *Initial CTPA (coronal view) demonstrating the pulmonary embolism.*

reduced cardiac output and hypotension.[3] However, both acute and chronic pulmonary hypertension can cause a D-sign, so while sensitive, it is not always specific for pulmonary embolism, and merely indicates the presence of right ventricular strain with pulmonary hypertension. In cases of volume overload, the D-sign will be present only in diastole, whereas in acute pressure overload, it will be seen during the entire cardiac cycle.

In addition, elevated pulmonary vascular pressures may also lead to 'McConnell's Sign' in the right ventricle. McConnell's Sign is defined as hypokinesis or akinesis of the free wall of the right ventricle, with normal function at the apex. The presence of a McConnell's sign has mixed sensitivity and specificity, initially being described with sensitivity and specificity of 77% and 94%, respectively[4] with a more recent study showing its presence in PE in 68% of patients and without PE in 32% of patients.[2] Presence of McConnell's sign mandates further workup for right heart pathology. Absence of McConnel's sign also does not definitively rule out the presence of PE. Overall, however, McConnell's sign is useful to have in mind when PE is on the differential.

Conclusion

POCUS is a useful tool in the early diagnosis and management of pulmonary embolism in unstable patients. While CT scan is the gold standard, the immediacy of POCUS can give early clues into diagnostic probabilities and expedite time to definitive treatment. ●

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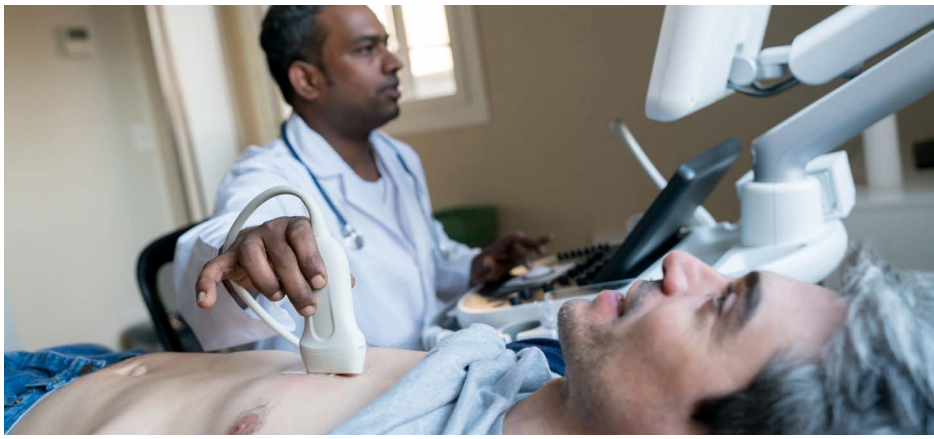

Pearls For Career Success: If I Only Knew What I Know Now

By Paola Martinez, MD; Diana Alsbrook, MD; Naomi Niznick, MD; Stefanie Cappucci, MD; Shweta Goswami, MD; Eunice Lee, MD






The NCS Trainee Section has launched the second year of the Professional and Career Development Workshops Series. This interactive webinar series provides trainees and early career faculty with tools for career planning and is a unique opportunity for networking, collaboration, and resource sharing.

During the first session in September – "If I only knew what I know now" – we had the opportunity to learn from three leaders in the field about their professional development journeys: Dr. Aarti Sarwal, Dr. Shraddha Mainali, and Dr. David Hwang. They each shared their challenges, successes, and pearls they wish they had known when starting their careers. Whether you are job hunting or starting your career, this session provided valuable tools to help navigate challenges and foster success.

Here are ten pearls of wisdom shared:

1. Find your community. Seek allies even in an environment where you don't feel supported. Find collaborators you can trust and rely on. One advantage of professional societies is to find people who want to encourage and mentor you. On the other hand, it is as important to pay it forward to your community when you have the chance. – Dr. Mainali
2. You are your best advocate and you are not on your own. There are many resources out there to help, such as leadership courses, books, video series and podcasts. Life is not always fair, but you have the choice to accept that and make the best of what you have. It is your choice. – Dr. Sarwal
3. When finding a research mentor, one valuable resource is the NIH Reporter website where you can see all researchers' NIH grants. It might help you figure out who you would like to approach. It is also a good place to visit beforehand to have a more efficient meeting. – Dr. Hwang
4. Know that Imposter Syndrome – the feeling where we are constantly doubting ourselves in our talents and accomplishments – is just a feeling. It can affect our work and may breed anxiety and depression. It is common. It is just a mindset that can be changed, and knowing this will be a good place to start seeing yourself in a positive way. – Dr. Mainali
5. Own your journey. We are in an environment where we will always be dependent on others. Medicine is a team sport and there is enough to go around. Promote your colleagues and give them space to grow. Don't compare yourself to others, be proud of who you are. – Dr. Sarwal
6. "Percent effort" is not well defined in critical care and it may take many forms. When navigating details of your first job, understand the concept of percent effort specific to the employer. Specifically, what are the baseline work expectations and how will your time be managed? Ask questions such as: how does the department adjust when you go above your FTE, how does the department value various efforts (research, committee, administrative, etc.)? – Dr. Hwang
7. Instead of trying to find work life balance, focus on organizing your life. Prioritize what is important in your life. Try to outsource things that do not advance you as a person so that you can focus on your life mission and career goals. – Dr. Mainali
8. For building a research career, think long term on how to best position yourself and how you're going to be a team leader. The most successful researchers build a team and master the transition from first author to senior author. – Dr. Hwang
9. It is okay to grow horizontally. You do not have to be checking boxes at every stage of your life, you can just let it run its course. Sometimes you won't know until you try, and life will give you the answer that you did not know you were looking for. At some point you must be honest with yourself and focus on growing vertically. – Dr. Sarwal
10. If you find yourself at a convention and you feel like you don't know anyone, know that it will change. With time, you start to know people, and meetings become fun and a great way to network. Just get out there. – Dr. Hwang

These valuable pearls of wisdom are generalizable and applicable to a variety of practitioners from physicians, advanced practice providers, pharmacists, and nurses. We hope you take advantage of these phenomenal opportunities to continue learning from our speakers and building your community in Neurocritical Care. You can find the recordings for this session and all previous sessions on the NCS Trainee Webinar Series section of the NCS website. ●