

ICU and Post-ICU Strategies to Improve Cognitive Function after Critical Illness

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Time	Section
01:37	<u>Introduction of John Devlin (first speaker) and Leanne Boehm (second speaker)</u>
03:19	<u>Flow Chart</u> <ul style="list-style-type: none"> • When people become critically ill, there are a lot of symptoms and other interconnected things that happen to these patients (pain, disrupted sleep, delirium, sedation → drug induced coma) • Goal: patients to survive their critical illness • Realized that not everybody, in particular older adults, can get back to their usual activities before their critical illness
04:42	<u>ICU Delirium</u> <ul style="list-style-type: none"> • Prevalence: 20-70% <ul style="list-style-type: none"> ○ Broad range driven by variability in predisposing and precipitating factors between patients (severity of illness is a key driver of daily occurrence) • Associated with: <ul style="list-style-type: none"> ○ Substantial distress to patients, families, and caregivers ○ Increased short- and long-term mortality ○ Prolonged mechanical ventilation and ICU/hospital length of stay (increased healthcare costs) ○ Reduced long-term cognitive decline (dementia)
05:40	<u>Risk Factors for ICU Delirium</u> <ul style="list-style-type: none"> • Patient and host factors → not particularly modifiable • Dementia in any patient is a very important predisposing risk factor for delirium • Acute illness factors → some controllable, some not • Potentially modifiable factors → big focus here to try to prevent delirium: avoid deep sedation, medications associated with delirium, sleep-related circadian-related issues, immobilization
06:50	<u>Select Studies of Delirium and Long-Term Cognitive Outcomes in Patients with Critical Illness</u> <ul style="list-style-type: none"> • Review article in BMJ by Liz Wilcox and Tim Girard • Has consistently shown that the duration of delirium is independently associated with long-term cognitive impairment in patients
07:36	<u>Long-Term Cognitive Impairment after Critical Illness</u> <ul style="list-style-type: none"> • Brain ICU Study (NEJM in 2013) <ul style="list-style-type: none"> ○ N=826 critically ill adults ○ They evaluated cognition at 3 months and 12 months using the RBANS Global Cognition score ○ Both at 3 months and 12 months, patients had a high degree of cognitive dysfunction on average ○ When broken down by age group, even younger patients had substantial reduction in their cognitive function ○ Happens quickly because happening at 3 months, and is also long-term at 12 months ○ Adjusted global cognition score at 12 months with days of delirium (graph on next slide) <ul style="list-style-type: none"> ▪ Found an association between the longer patients had delirium in the ICU, the greater the likelihood of an association with worse global cognition at 3 months and 12 months
10:42	<u>Is there a Causal Link between ICU Delirium and Dementia?</u> <ul style="list-style-type: none"> • Postulated explanations for an association between delirium and dementia • 1. Delirium itself causes dementia • 2. Delirium is a marker of vulnerability to dementia • 3. Delirium in an intermediate factor in the development of dementia

11:39	<p><u>Conceptual framework for exploring inter-relationship between delirium and long-term cognitive impairment and between delirium and acceleration of dementia</u></p> <ul style="list-style-type: none"> • Important to realize we're really focused here on epidemiology and clinical assessment • To sort all of this out, will take a lot more research than we currently have
12:33	<p><u>Clinical phenotypes of delirium during critical illness and severity of subsequent long-term cognitive impairment: a prospective cohort study</u></p> <ul style="list-style-type: none"> • What patients are at greater risk for long-term cognitive impairment if they develop delirium during the ICU? • Combined cohort from Brain ICU study and MIND ICU haloperidol delirium treatment, randomized control study • Identified 5 different phenotypes of delirium a priori <ul style="list-style-type: none"> ○ <u>Sedative associated delirium</u> (Receipt of benzodiazepine or propofol or opioid or dexmedetomidine) ○ <u>Hypoxic delirium</u> (hypoxemia or shock) ○ <u>Septic delirium</u> (known or suspected infection and ≥ 2 systemic inflammatory response syndrome criteria) ○ <u>Unclassified delirium</u> (none of the other criteria met) ○ <u>Metabolic delirium</u> (blood urea nitrogen >17.85 mmol/L or glucose <2.5 mmol/L or INR >2.5 and AST or ALT >200 U/L, sodium <120 mmol/L or sodium <160 mmol/L) • Found a strong relationship with hypoxic, septic, and sedative delirium, but no relationship with metabolic delirium at 3 and 12 months (graphs showing this on the next slide)
14:51	<p><u>Data-derived subtypes of delirium during critical illness</u></p> <ul style="list-style-type: none"> • Used MIND USA and Brain ICU cohorts • Used machine learning (latent model) to develop the factors that a priori identified to categorize in different delirium subtypes • Heat map of different subtypes • When they looked at delirium/coma free days they found that subtype 2 and 4 had significantly greater number of delirium and coma free days • But when they looked at 3-month cognition and 12-month cognition among the subtypes, there was actually no difference across the 3 subtypes
16:35	<p><u>ABCDEF Bundle Elements</u></p> <ul style="list-style-type: none"> • A → Access, prevent, and manage pain • B → Both SAT and SBT • C → Choice of analgesia and sedation • D → Delirium: assess, prevent, and manage • E → Early mobility and exercise • F → Family engagement and empowerment
17:32	<p><u>Caring for Critically Ill Patients with the ABCDEF Bundle: Results of the ICU Liberation Collaborative in Over 15,000 Adults</u></p> <ul style="list-style-type: none"> • Large 68 hospital cohort that implemented the bundle in over 15,000 adults across the US • Table of outcomes for patients with complete ABCDEF Bundle Performance <ul style="list-style-type: none"> ○ It showed substantial improvement in critical patient outcomes, including delirium • Results: Symptom-Related Outcomes <ul style="list-style-type: none"> ○ Hard to deliver every component of this bundle to every ICU patient on a daily basis ○ The more of the bundle elements that are delivered to each patient every day has a dose-related effect, so even if implementing only 2 or 3 elements, you will be reducing delirium
19:32	<p><u>Does Daily Use of the ABCDEF Bundle Improve Long-Term Cognitive Cognition?</u></p> <ul style="list-style-type: none"> • We are not sure yet... will go through some of the evidence
20:00	<p><u>Both SAT and SBT</u></p>

	<ul style="list-style-type: none"> • Efficacy and safety of a paired-sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (awakening and breathing controlled trial): a randomized controlled trial <ul style="list-style-type: none"> ○ Found that if patients were woken up and put on a spontaneous breathing trial, they'd get off the ventilator faster, out of the ICU faster, and there was a mortality benefit. No difference in days spent with brain dysfunction • Long-term Cognitive and Psychological Outcomes in the Awakening and Breathing Controlled Trial <ul style="list-style-type: none"> ○ Did not find a relationship in long-term cognitive outcome with using the ABC intervention ○ To keep in mind: did not show a difference in delirium, and we know the strong relationship between delirium and long-term cognition • Nonsedation or Light sedation in Critically Ill, Mechanically Ventilated Patients <ul style="list-style-type: none"> ○ Found no difference in days free from coma or delirium within the first 28 days ○ Small subgroup analysis of one of the study centers, they found no difference in severe cognitive impairment
21:32	<p><u>Choice of Analgesia or Sedation</u></p> <ul style="list-style-type: none"> • Benzodiazepines are really an important risk factor for delirium in the ICU, and have dramatically reduced the use of these agents • Recommendation: <ul style="list-style-type: none"> ○ We suggest using either propofol or dexmedetomidine over benzodiazepines for sedation in critically ill mechanically ventilated adults (conditional recommendation, low quality of evidence) • MENS-2 Study: found no difference in days without delirium or coma at 14 days between dex and propofol groups and no difference in 6-month cognition between the two groups
22:51	<p><u>Delirium</u></p> <ul style="list-style-type: none"> • Antipsychotic vs. None (Treatment) <ul style="list-style-type: none"> ○ Rational includes: no benefit for any critical outcomes, Not routinely (vs. never) given that patients with fear, anxiety or agitation not-related to pain may still benefit from a short-course of antipsychotic therapy, unnecessary continuation causes significant morbidity & cost ○ Recommendation: <ul style="list-style-type: none"> ▪ We suggest NOT routinely using haloperidol and atypical antipsychotic to treat delirium (conditional recommendation, low quality of evidence) • Haloperidol and Ziprasidone for Treatment of Delirium in Critical Illness <ul style="list-style-type: none"> ○ Found no difference in days alive without delirium or coma between Ziprasidone, haloperidol, and two different antipsychotics and the control placebo • Long-term evaluation of the MIND USA study looking at cognition at 3 months and 12 months and found no difference in patients that had gotten placebo versus haloperidol • Sleep Promoting Protocol <ul style="list-style-type: none"> ○ Sleep is very hard to measure in the ICU ○ Recommendation: <ul style="list-style-type: none"> ▪ We suggest using a sleep-promoting, multicomponent protocol in critically ill adults (conditional recommendation, low quality evidence)
24:35	<p><u>Early Mobility and Exercise</u></p> <ul style="list-style-type: none"> • Lancet study: <ul style="list-style-type: none"> ○ Showed that early mobile exercise and mobility was associated with a significant reduction in duration of ICU delirium and mechanical ventilation • Recommendation: <ul style="list-style-type: none"> ○ We suggest performing rehabilitation or mobilization in critically ill adults (conditional recommendation, low quality evidence) • Effect of early mobilization on long-term cognitive impairment in critical illness in the USA: a randomized controlled trial

	<ul style="list-style-type: none"> ○ Randomized patients to an aggressive early mobilization intervention and found a 20% reduction in cognitive impairment at 1 year and a significant reduction in MoCA scores
25:57	<p><u>Conclusions</u></p> <ul style="list-style-type: none"> ● ICU delirium (and its duration) is strongly associated with long-term cognitive impairment/dementia: <ul style="list-style-type: none"> ○ Causal relationship not established ○ Patients with baseline dementia excluded from most studies ○ Mechanisms not well-investigated ● While the ABCDEF bundle reduces ICY delirium, unclear if it improves long-term cognition ● Only one ICU intervention (mobility) shown to reduce ICU delirium has been rigorously shown to improve long-term cognition
27:50	<p><u>Post-ICU Strategies to Improve Cognitive Function after Critical Illness (Leanne Boehm)</u></p>
28:12	<p><u>The Evolving Definition of PICS</u></p> <ul style="list-style-type: none"> ● Post Intensive Care Syndrome (PICS): new or worsening impairments in physical, cognitive, or mental health status arising after critical illness and persisting beyond acute care hospitalization ● Prevalence up to 50% ● Heterogenous manifestation ● Requires specialized assessment and care ● 4 elements: <ul style="list-style-type: none"> ○ Cognitive (memory problems, concentration) ○ Physical (fatigue, chronic pain, muscle weakness, balance problems, mobility issues) ○ Mental health (anxiety, depression, PTSD, mood problems) → social isolation ○ Socio-Economic (employment problems, financial strain) → social isolation
31:09	<p><u>One or more PICS problems are present in most ICU survivors</u></p> <ul style="list-style-type: none"> ● Looked at co-occurrence of these symptoms of PICS problems that were present in ICU survivors ● Venn diagrams of symptoms <ul style="list-style-type: none"> ○ Cognitive impairment was the most commonly occurring of these symptoms ● Also found that more years of education and less clinical frailty were protective factors (more likely to be PICS free)
33:51	<p><u>Establishment of Collaborative & Research Priorities</u></p> <ul style="list-style-type: none"> ● Has helped to figure out what patients need and want to help them with their PICS ● CARIN study interviewed over 60 patients to find out about their recovery experience and over 20 caregivers to find out about the ICU recovery experience ● THRIVE initiative led to the expansion of services to help with PICS, specifically ICY recovery clinics and post ICU peer support groups
34:51	<p><u>Society of Critical Care Medicine consensus conference recommends to risk stratify who should be assessed for long-term impairments after critical illness</u></p> <ul style="list-style-type: none"> ● Consensus statement about cognition: 92% agreement and 80% agreement that we should be evaluating patients that have preexisting cognitive impairment before the ICU (those will be the ones who will have problems afterwards) ● Strong recommendation that the way we should be evaluating them for cognitive impairment is with MoCA
37:06	<p><u>ICU Recovery Clinics</u></p> <ul style="list-style-type: none"> ● An intervention to help patients transition back to their normal lives and address any physical, cognitive, psychological, or social issues that may have arisen during their ICU stay ● Figure of services provided in an ICU recovery clinic <ul style="list-style-type: none"> ○ Pharmacy, durable medical equipment, subspecialty medical care, optimal rehabilitation therapy, improving health habits, diagnosis and management of cognitive impairment, diagnosis and management of mental health problems

	<ul style="list-style-type: none"> • Because of the multi-component kind of intervention that ICU recovery clinics need, that means there's a lot of people that potentially would be involved in this kind of clinic service (pyramid diagram of people) <ul style="list-style-type: none"> ○ Probably no clinic that offers all of these things
41:09	<p><u>Benefits of ICU-Recovery Clinic Participation</u></p> <ul style="list-style-type: none"> • Emerging evidence of: identify PICS, cognition, physical function, self-efficacy, short-term survival, quality of life, return to employment
41:58	<p><u>ICU Recovery Clinic: Models</u></p> <ul style="list-style-type: none"> • Inpatient consultation, face-to-face consultations at home or in a clinic, telephone consultations (could be a combination of these)
43:27	<p><u>Why don't patients attend ICU Recovery clinics?</u></p> <ul style="list-style-type: none"> • Didn't know they had an appointment, financial concerns, transportation challenges, distance to clinic, rurality, tracheostomy, >ICU days, >MV days, shock diagnosis, older age
43:59	<p><u>TelePORT: An ICU Recovery Study (pilot feasibility trial)</u></p> <ul style="list-style-type: none"> • Methods: <ul style="list-style-type: none"> ○ Design: prospective RCT ○ Setting: Vanderbilt University Medical Center ICU Recovery Center ○ Sample: 45 patients with ARDS or sepsis with complete follow up ○ Analysis: fixed effect ANOVA models on post-treatment scores with study and age group as factors and baseline cognitive function as a covariate • Model flow chart of study design (enrolled 91 patients) • Results: <ul style="list-style-type: none"> ○ Mean age= 49; caregivers=51 ○ Mean days: ICU=3; hospital=16 ○ 3-week visit length: 52 minutes ○ 12-week visit length: 36 minutes ○ Found that older patients who received the intervention demonstrated better cognitive outcomes than their younger peers, as compared to the control group ○ Telemedicine ICU Recovery Clinic Implementation → learned that people liked it and it's acceptable, appropriate, and feasible to do ○ Skipping through next few slides due to time • TelePORT Multi-site RCT <ul style="list-style-type: none"> ○ Continuing to look at this as a multi-factorial, multidisciplinary transitional care intervention
47:03	<p><u>Cognitive Rehabilitation/Goal Management Training</u></p> <ul style="list-style-type: none"> • A focused stepwise approach to rehabilitation of executive function by increasing goal-directed behavior and helping patients to learn to be reflective before making decisions and executing tasks and to achieve success in engaging complex tasks by breaking into manageable units
47:30	<p><u>A remotely delivered multicomponent rehab program for ICU survivors was feasible and possibly effective in improving cognitive performance and functional outcomes in 3 months</u></p> <ul style="list-style-type: none"> • After hospital discharge, patients were randomized to receive in-home cognitive rehabilitation and then tele-physical rehabilitation over the course of 3 months, and then evaluated for whether that might have helped with their physical and cognitive function • They found that the multi-component rehab program did help with executive function at 3 months
48:57	<p><u>ICU survivors with cognitive impairment had significant improvement in neuropsychological domains with computerized cognitive rehabilitation (CCR)</u></p> <ul style="list-style-type: none"> • There was improvement over time from their precognitive scores and post computerized cognitive rehabilitation scores
50:18	<p><u>Early cognitive rehabilitation training can improve cognitive impairment in critically ill patients</u></p> <ul style="list-style-type: none"> • Found improvements in cognition for the intervention groups, but lots of items in the intervention, so unsure what specifically helped to improve cognition

51:16	<u>Opportunities for technology to facilitate cognitive recovery after ICU...</u> <ul style="list-style-type: none">• Therapeutic robots to engage in cognitive exercises• Smart wearables/nearables• Remote or web-based cognitive rehabilitation• AI health coach/cognitive rehabilitation• E-health platforms• Recovery coordinators
52:00	<u>Future Directions</u> <ul style="list-style-type: none">• Efficacy and effectiveness of cognitive and multidisciplinary interventions and mechanistic analysis on PICS outcomes (e.g. cognition)• Alternative delivery strategies to improve reach and access• Incorporation of implementation measures to understand fidelity, acceptability, adoption, sustainability• Cost-benefit analysis of interventions and test healthcare system models and technologies that accommodate intervention and early follow-up
52:32	<u>Questions and Answers</u>