ICU
MANAGEMENT & PRACTICE
@ICU_Management
2024
VOLUME 24
ISSUE 4

Mobilisation

icu-management.org

INTENSIVE CARE | EMERGENCY MEDICINE | ANAESTHESIOLOGY | CARDIOLOGY | MANAGEMENT | LEADERSHIP

Luca Cabrini
Professor of Anesthesia and Intensive Care
Biotechnologies and Life Sciences Department
Insubria University
General and Neurosurgical Intensive Care Units
Ospedale di Circolo e Fondazione Macchi
Varese, Italy
l.cabrini@asst-settelaghi.it

Omar Saleh
General and Neurosurgical Intensive Care Units
Ospedale di Circolo e Fondazione Macchi
Varese, Italy
omar.saleh@asst-settelaghi.it

Giada Spinazza
General and Neurosurgical Intensive Care Units
Ospedale di Circolo e Fondazione Macchi
Varese, Italy
giada.spinazza@asst-settelaghi.it

Mary Ann Belli
Department of Anesthesia and Intensive Care
IRCCS San Raffaele Scientific Institute
Milan, Italy
maryannbelli94@gmail.com

Early Mobilisation, Delirium Prevention and Long-Term Cognitive Function

Early mobilisation showed promising positive effects in preventing and shortening delirium and improving long-term cognitive function. Further research is required to confirm its benefits and to identify the best protocol.

Introduction

In recent years, an increasing demand for critical care services (and Intensive Care Unit (ICU) admissions) has been reported, together with a decrease in short-term mortality (Needham et al. 2012; Dinglaset al. 2018; Hiser et al. 2023). Consequently, the number of ICU survivors is growing. Unfortunately, ICU survivors often present new or worsened long-lasting impairments affecting mental, physical and cognitive health status, ultimately lowering the quality of life. In a seminal paper published in 2012, Needham et al. reported the findings of a conference held two years before by the Society of Critical Care Medicine, which focused on the long-term consequences of critical illness. The international group convened at the conference created Post-Intensive Care Syndrome (PICS) as an umbrella term to raise awareness of those impairments and facilitate screening and research on the issue (Needham et al. 2012).

PICS prevalence in ICU survivors is reported to range between 25% and 40% three months post ICU discharge (Pandharipande et al. 2013), but prevalence higher than 80% has been reported when comprehensive cognitive batteries are used for evaluation instead of subjective assessment or less sensible objective tests like the Mini-Mental State Examination (Honarmand et al. 2020). In PICS, cognitive impairments include deficits in memory, attention, executive function, mental processing speed and visuospatial ability. Of note, almost half of ICU survivors still present cognitive impairment two years after ICU discharge. Cognitive decline has a major negative impact on post-ICU quality of life and carries huge costs on society and a relevant burden on caregivers (Honarmand et al. 2020). Finally, cognitive function is among the most highly rated patient-important outcomes, while survival is among the lowest (Dinglas et al. 2018).

ICU-related cognitive impairment presents non-modifiable risk factors, namely female gender, advanced age, previous mental illness, severity of illness and admission due to acute respiratory distress syndrome (ARDS) (Needham et al. 2012; Honarmand et al. 2020; Hiser et al. 2023). Other risk factors associated with post-ICU long-term cognitive impairment may be modifiable; in particular, negative patient experience in the ICU and delirium are significantly associated with long-term cognitive function and mental outcomes (Hiser et al. 2023).

Delirium in ICU is an acute brain dysfunction manifesting as an impairment or fluctuation in mentation, disorganised thinking, inattention, and altered level of consciousness. It can coexist with other neurological diseases like stroke or traumatic brain injury, but it is not fully explained by these or by other causes (Mart et al. 2020; Palashkappa and Hough 2021). It can present with three main psychomotor manifestations: hyperactive (the easiest to be detected but also the less common), hypoactive, and mixed. Delirium can affect 20-50% of ICU patients, but its prevalence can be as high as 80% in ventilated patients (Palashkappa and Hough 2021). Delirium is independently associated with an increased risk of death, prolonged ventilation, longer ICU and hospital stay, increased costs, and a higher risk of being discharged to a long-term facility. In particular, the hypoactive form showed the worst outcomes (Mart et al. 2020; Palashkappa and Hough 2021).

Delirium is also associated with significant long-term impairments in physical, psychological and cognitive functions. It was associated with cognitive decline at 1-year follow-up or later in 30%-70% of survivors who had experienced it during their ICU stay. Moreover, delirium was associated with an increased risk of developing dementia or of worsening pre-existing dementia (that is by itself a risk factor for delirium) (Mart et al. 2020; Palashkappa and Hough 2021). Unfortunately, so far, no effective pharmacological treatment or prevention for delirium has been found (on the contrary, some drugs like benzodiazepines are known risk factors). The focus remains almost exclusively on non-pharmacological approaches aimed to prevent delirium: preserving non-fragmented sleep, providing visual and hearing aids if needed, preserving space and time orientation (with clocks and calendars, for instance), minimising noise, avoiding physical restraints, providing cognitive stimulating activities, avoiding as far as possible deep sedation and promoting early mobilisation (Mart et al. 2020; Palashkappa and Hough 2021).

Early mobilisation (EM), from passive motion to ambulation, is safe and was associated with reduced risk of delirium and improved long-term cognitive outcomes. (Mart et al. 2020; Palashkappa and Hough 2021). In 2018, the Society of Critical Care Medicine published the international clinical practice guidelines for the prevention and management of delirium and cognitive impairment, among other purposes, in the critically ill (PADIS Guidelines) (Devlin et al. 2018). The authors stated that delirium incidence and cognitive outcomes could be positively influenced by the application of non-pharmacological interventions, such as early mobilisation, with better results when applied in a comprehensive bundle.

In the present review, after briefly defining EM, we report the main findings of trials evaluating the effects of EM in ICU on delirium and long-term cognitive function. We also expose the supposed brain mechanisms mediating this effect and consider the barriers that hinder the application of EM.

Early Mobilisation Effects on Delirium Prevention

In the first review following the Pain Agitation/Sedation Delirium Immobility Sleep Disruption (PADIS) guidelines (Devlin et al. 2018), Kang et al. (2018) aimed to evaluate non-pharmacological interventions that could reduce delirium incidence and duration. Interruption of sedation, exercise, patient education, automatic warning systems, cerebral haemodynamic improvement, family participation and sedation-reducing protocols appeared effective in preventing and shortening delirium (Kang et al. 2018). Single intervention analysis showed similar results, with early physical exercise showing the best efficacy, leading the authors to recommend consistent application of such strategies but also pointing out the lack of strong evidence.

Liang et al. (2021) published a systematic review of non-pharmacologic treatments for delirium, with EM resulting as the most promising strategy. The five considered studies, including randomised and non-randomised trials, showed medium-quality evidence of reduction of delirium incidence (odds ratio (OR) of 0.33) when EM was compared to usual care (Liang et al. 2021).

A similar study with the addition of a network meta-analysis was performed by Chen et al. (2022). The authors only included randomised controlled trials, ranging over a wide variety of non-pharmacological interventions. Overall, the 29 included studies showed for the first time an advantage in the application of these interventions when applied as a multi-component bundle, but with a strong superiority of EM (reduction of incidence and duration of delirium: respectively OR 0.12 and mean reduction of delirium duration -1.34 days) and family participation when compared to other single strategies. The most recent systematic review and meta-analysis investigating the effects of EM alone on delirium analysed 13 recent studies, randomised trials and quality-improvement projects (Nydahl et al. 2023). Higher heterogeneity impaired the analysis; nonetheless, at least three studies with low risk of bias showed a reduction in delirium duration of up to two days when EM was implemented alone.

Other studies which had not been included in the previously described reviews add further data on the role of EM.

A recent randomised trial by Nydahl et al. (2020) evaluated EM as part of a multidisciplinary intervention. The incidence of delirium was a secondary outcome. Lack of adherence to exercise protocols is often pointed out as the main problem in studies in which EM resulted ineffective. This study had a protocol adherence >90% resulting in improved patient mobilisation; nevertheless, it found no difference in delirium incidence.

Delirium, as well as cognitive decline, are common after coronary artery bypass grafting. Physical rehabilitation is widely applied in cardiac surgery patients, and expertise is crucial to improve adherence to mobilisation protocols. A randomised trial by Shirvani et al. (2020) investigated very early mobilisation protocols (first 48h post-surgery) versus usual nursing. Delirium was less common in the interventional group.

Finally, a randomised trial conducted in four ICUs in Germany and UK showed the feasibility of patient mobilisation during the evening, resulting in a tendency towards less delirium (Nydahl et al. 2021).

Early Mobilisation Effects on Long-Term Cognitive Outcome

Few studies have evaluated early mobilisation as a strategy to reduce post-ICU cognitive decline; comprehensive cognitive assessment is neither easy nor quick.

The Australian and New Zealand Intensive Care Society recently published a randomised trial combining early mobilisation with protocolised interruption of sedation (TEAM Study Investigators and the ANZICS Clinical Trials Group 2022). In this study, interventional EM did not improve the days alive and out of hospital, and no improvement in cognition, ADLs and psychological function were found between the groups.

Olotu et al. (2022) applied a delirium prevention bundle, mainly consisting of early mobilisation, in a group of patients who underwent cardiovascular surgery. The cognitive investigation battery was very extensive and performed both preoperatively and after surgery. No effect of the delirium prevention strategies on cognitive function was observed.

Patel et al. (2023) published a subsequent trial investigating EM alone and assessed cognitive impairment. The results at 12-month follow-up were very promising, as there was an overall risk reduction of cognitive deterioration of almost 20%. However, the authors advocated careful care for the increased rate of adverse events with intense and early mobilisation.

Finally, a recent randomised trial performed in the cardiovascular postoperative setting found a reduction in cognitive dysfunction when patients were treated with a three-phase EM protocol compared with a delayed, four-staged protocol and usual care (Allahbakhshian et al. 2023).

Efficacy of Early Mobilisation When Included in a Bundle

The idea of implementing EM as one of the other interventions in a bundle was already present in the earliest Pain Agitation/Sedation Delirium(PAD) guidelines in 2013 (Barr et al. 2013). More recently, Marra et al. (2017) summarised the evidence on which the 2018 PADIS guidelines were built. The different proposed non-pharmacologic strategies forming the bundle were given a name - the ABCDEF bundle (assessing pain, spontaneous awakening and breathing trials, choice of analgesia and sedation, delirium monitoring/management, early exercise/mobility, and family and patient empowerment) (Balas et al. 2013). An early implementation of the 2013 PAD guidelines was performed in a large cohort of more than 6000 patients (Barnes-Daly et al. 2017). Higher bundle compliance was independently associated with better survival and more delirium-free days.

Following the 2018 guidelines, two main reviews summarised the available evidence. A systematic review with meta-analysis by Zhang et al. (2020) evaluated the impact of bundle interventions on ICU delirium prevalence and duration. Including RCTs and cohort studies, the analysis failed to show that bundle interventions were effective in reducing delirium incidence and stay in the ICU. Nevertheless, the authors reported some efficacy in reducing the proportion of hospital length of stay with coma, which might have a beneficial impact on cognitive function. In the most recent systematic review by Sosnowski et al. (2023), the authors searched for barriers and facilitating conditions that influenced complete bundle application. The authors proposed the assessment of a wide range of patient-important and clinically relevant outcomes for future trials, as, unfortunately, no recent studies evaluating PAD/PADIS/ABCDEF bundles reported the impact on cognition.

Biological Mechanisms Mediating Mobilisation Effects on Cognitive Function

Physical activity appears to influence neurologic function with several mediators. Animal studies suggest that angiogenesis and neurogenesis in the hippocampus (the brain area linked to memory and recall) are promoted by physical exercise (Hopkins et al. 2012). These effects are thought to be muscle-induced through a cytokine-based crosstalk between muscle and specific brain areas (Pedersen 2019). These myokines are of growing interest as they appear to influence several other functions, particularly in patients with sarcopenia (Kim et al. 2019).

In humans, exercise is beneficial to patients suffering from neuro-degeneration due to diseases (Mahalakshmi et al. 2020) or from age-related cognitive impairment (Sujkowski et al. 2022). Promoting mobility is helpful also in other pathological conditions such as COPD (Hopkins et al. 2012) and stroke (Middleton et al. 2013).

Since cognitive impairment and delirium are common in the ICU, there is a strong rationale that mobilisation might benefit critically ill patients as well, also considering the high incidence of sarcopenia and muscle wasting.

Conclusion

In addition to its effects on physical outcomes (such as muscular strength and mobility), EM is one of the few and one of the most promising strategies that could prevent and shorten delirium duration and improve long-term cognitive function. Further research is required to confirm these findings and to identify the best EM protocol (as a stand-alone intervention or included in a bundle) aimed at preventing ICU cognitive decline.

Conflict of Interest

None.

References

Allahbakhshian A et al. (2023) Comparison of early mobilization protocols on postoperative cognitive dysfunction, pain, and length of hospital stay in patients undergoing coronary artery bypass graft surgery: A randomized controlled trial. Appl Nurs Res. 73:151731.

Balas MC et al. (2013) Implementing the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle into everyday care: opportunities, challenges, and lessons learned for implementing the ICU Pain, Agitation, and Delirium Guidelines. Crit Care Med. 41(9 Suppl 1):S116-27.

Barnes-Daly MA et al. (2017) Improving hospital survival and reducing brain dysfunction at seven California community hospitals: Implementing PAD guidelines via the ABCDEF bundle in 6,064 patients. Crit Care Med. 45(2): 171–178.

Barr J et al. (2013) Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. Crit Care Med. 41(1): 263–306.

Chen TJ et al. (2022) Comparative effectiveness of non-pharmacological interventions for preventing delirium in critically ill adults: A systematic review and network meta-analysis. Int J Nurs Stud. 131:104239.

Devlin JW et al. (2018) Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. Crit Care Med. 46(9):e825–e873.

Dinglas VD et al. (2018) Understanding patient-important outcomes after critical illness: a synthesis of recent qualitative, empirical and consensus-related studies. Curr Opin Crit Care. 24:401-09.

Hiser SL et al. (2023) Postintensive care syndrome (PICS): recent updates. J Intensive Care. 11(1):23.

Honarmand K et al. (2020) Natural history of cognitive impairment in critical illness survivors. A systematic review. Am J Respir Crit Care Med. 202(2):193-201.

Hopkins RO et al. (2012) Improving post-intensive care unit neuropsychiatric outcomes. Am J Resp Crit Care Med. 186(12):1220–1228.

Kang J et al. (2018) Effect of nonpharmacological interventions for the prevention of delirium in the intensive care unit: A systematic review and meta-analysis. J Crit Care. 48(1):372–384.

Kim S et al. (2019) Roles of myokines in exercise-induced improvement of neuropsychiatric function. Pflügers Arch. 471(3):491–505.

Liang S et al. (2021) Effects of nonpharmacological delirium-prevention interventions on critically ill patients' clinical, psychological, and family outcomes: A systematic review and meta-analysis. Aust Crit Care. 34(4):378–387.

Mahalakshmi B et al. (2020) Possible neuroprotective mechanisms of physical exercise in neurodegeneration. Int J Mol Sci. 21(16):5895.

Marra A et al. (2017) The ABCDEF bundle in critical care. Crit Care Clin. 33(2):225–243.

Mart MF et al. (2021) Prevention and management of delirium in the intensive care unit. Semin Respir Crit Care Med. 42(1):112-126.

Middleton LE et al. (2013) Physical activity in the prevention of ischemic stroke and improvement of outcomes: A narrative review. Neurosci Biobehav Rev. 37(2):133–137.

Needham DM et al. (2012) Improving long-term outcomes after discharge from intensive care unit: Report from a stakeholders' conference. Crit Care Med. 40:502-09.

Nydahl P et al. (2020) PROtocol-based MObilizaTION on intensive care units: Stepped-wedge, cluster-randomized pilot study (Pro-Motion). Nurs Crit Care. 25(6):368–375.

Nydahl P et al. (2021) Mobilization in the evening to prevent delirium: A pilot randomized trial. Nurs Crit Care. 27(4):519–527.

Nydahl P et al. (2023) Early mobilisation for prevention and treatment of delirium in critically ill patients: Systematic review and meta-analysis. Intensive Crit Care Nurs. 74:103334.

Olotu C et al. (2022) The effect of delirium preventive measures on the occurrence of postoperative cognitive dysfunction in older adults undergoing cardiovascular surgery. The DelPOCD randomised controlled trial. J Clin Anesth. 78:110686.

Palashkappa JA, Hough CL (2021) How we prevent and treat delirium in the ICU. Chest. 160(4):13265-34.

Pandharipande PP et al. (2013) Long-term cognitive impairment after critical illness. N Engl J Med. 369:1306-16.

Patel BK et al. (2023) Effect of early mobilisation on long-term cognitive impairment in critical illness in the USA: a randomised controlled trial. Lancet Respir Med. 11(6):563–572.

Pedersen BK (2019) Physical activity and muscle–brain crosstalk. Nat Rev Endocrinol. 15(7): 383–392.

Shirvani F et al. (2020) Early mobilization reduces delirium after coronary artery bypass graft surgery. Asian Cardiovasc Thorac Ann. 28(9):566–571.

Sosnowski K et al. (2023) The effect of the ABCDE/ABCDEF bundle on delirium, functional outcomes, and quality of life in critically ill patients: A systematic review and meta-analysis. Int J Nurs Stud. 138:104410.

TEAM Study Investigators and the ANZICS Clinical Trials Group (2022). Early active mobilization during mechanical ventilation in the ICU. N Engl J Med. 387(19):1747–1758.

Zhang S et al. (2020) Effectiveness of bundle interventions on ICU delirium: A meta-analysis. Crit Care Med. 49(2):335–346.


ICU
MANAGEMENT & PRACTICE
icu-management.org
@ICU_Management