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Post-intensive care cognitive impairment: questions in mind?

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cognitive function (prospective or retrospective), (2) validated follow-up cognitive tests, (3) clear inclusion and exclusion criteria, and (4) adjustment for confounders such as age and gender. Studies had to evaluate patients more than 2 months after ICU discharge; cardiac surgery patients, case reports, reviews and data from animal studies were excluded. Cognitive impairment tests varied greatly, as did the rate of cognitive impairment, its definition, and time to follow-up (2 months to 13 years). The rate of cognitive impairment was <10 % in three of the five studies that used questionnaires or screening test-based cognition assessments; studies that used gold-standard neuropsychological tests found 45 to 80 % of patients had moderate to severe cognitive impairment at follow-up. Loss to follow-up and study duration varied. In ten of the studies the mean age was 54 years or less at study enrollment. While this review highlights important findings regarding post-ICU cognitive impairment, questions remain regarding mechanisms, risk factors, patients' baseline cognitive function, recovery and effect of rehabilitation, and the relationship of cognitive impairments with quality of life and functional abilities.

Introduction

Each year millions of individuals are admitted and treated in intensive care units (ICUs) [1]. Better care has resulted in reduced mortality with a concomitant increase in ICU survivors, many of whom are left with significant morbidities. Large numbers of ICU survivors have cognitive impairments [2]; these impairments are new [3, 4], affect multiple cognitive domains, and are likely permanent. In this issue of Intensive Care Medicine, Wolters et al. [5] systematically review studies that assess cognitive impairment following critical illness. Quality was ascertained based on: (1) systematic baseline assessment of

What we need to know to improve patient outcomes

Mechanisms of cognitive impairment

The basic pathophysiology of cognitive impairment in survivors of critical illness is poorly understood. The heterogeneity of ICU populations and the lack of identified mechanisms of injury are challenging. In other populations, and probably in the critically ill, the mechanisms of cognitive impairment are complex, multifactorial, and likely interact with risk factors such as the number and type of comorbid disorders or genetic factors. ICU-related cognitive impairment is linked to hypoxemia [6], its duration [7], hypotension [8], glucose dysregulation

[9, 10], and inflammation and cytokine activation [11]. The relative importance of these factors and their interplay are not identified. Whether cognitive sequelae can be modulated in ICU populations, particularly with regard to potentially reversible ICU complications, such as glucose control, has not been tested to date.

Confounding variables

Confounding variables associated with the development of cognitive impairments occur frequently in the critically ill. Age is among them. Many ICU patients are elderly; in Canada patients over 80 years constitute 16 % of ICU admissions. The mean age was 54 years or less in ten of the studies reviewed by Wolters et al. [5]. Although the elderly were under-represented in this review (all studies enrolled older individuals), one study describes cognitive sequelae in ‘older’ (mean age 61) ICU survivors of 80 and 70 % at 3 and 12 months, respectively [12]. Normal aging may be accompanied by cognitive decline or dementia [13]. Cognitive decline may occur as early as 45–49 years, with greater cognitive decline occurring in older individuals (ages 65–70 years) [14]. Wolters and colleagues [5] note that one important but unanswered question is whether the cognitive impairments are due to critical illness and their treatment or to the patients’ poor premorbid health. Most cognitive outcome studies in critically ill populations have excluded patients with prior cognitive impairments or disorders associated with known cognitive impairments including cerebrovascular disease and dementia. Two large longitudinal population-based studies indicate that post-ICU cognitive impairment develops during or after the onset of critical illness [15, 16]. However, patients with hypertension, vascular disease, coronary disease, atrial fibrillation [17], and diabetes have high rates of cognitive impairment [18]; these patients may be over-represented among the critically ill, and as such the type and number of comorbid disorders may be risk factors for cognitive sequelae. For example, critically ill patients commonly develop multi-organ failure including renal failure; dialyzed patients over 55 purportedly have a 70 % incidence of cognitive dysfunction [19, 20]. In cardiovascular disease early investigations attributed cognitive decline to cardiac bypass surgery. However, cardiac populations with similar comorbidities and similarly rigorous cognitive testing without surgery have similar rates of cognitive decline as patients who have undergone surgery [21, 22], suggesting that the use of rigorously selected control groups is important. The relationship between comorbid disorders and development of cognitive impairment in the critically ill has not been studied to date. In addition, surgery and anesthesia are associated with the development of cognitive impairments [23]. Postoperative cognitive dysfunction may affect a significant proportion of patients exposed to

anesthesia, which may confound the cognitive outcome in surgical ICU patients. Whether anesthesia is associated with cognitive abnormalities in ICU survivors is unknown and remains to be investigated.

Baseline cognitive function, natural history of post-ICU cognitive impairment, and its risk factors

Few studies have addressed baseline cognitive function in ICU survivors and compared it to post-critical illness functioning in order to identify which patients recover to their pre-ICU level of function because of the unexpected nature of most critical illnesses. A small proportion (~5–10 %) of ICU survivors are believed to have cognitive impairment prior to ICU admission, based on two large, population-based studies where cognitive function was tested at regular intervals [15, 16]. Features by which risk can be stratified have not been identified. Intensive care unit delirium, a clinical feature associated with post-ICU cognitive impairment [12], may be preventable with measures such as early mobility or pharmacological prophylaxis. Whether depression or post-traumatic stress disorder, commonly described psychiatric morbidities in the critically ill, predict cognitive outcome as well as whether psychiatric symptoms [24] are risk factors for development of cognitive impairments [25] is also not clear.

Recovery and rehabilitation

Survivors of critical illness can have significant cognitive abnormalities at hospital discharge that improve over time. A recent study found variable cognitive outcome trajectories (impaired and stable, normal and stable, improvement, or decline), and further cognitive testing at hospital discharge did not predict 6-month cognitive outcomes in survivors of critical illness [26]. Given the inability to predict who will develop long-term cognitive impairment, treatments to prevent, ameliorate, or remedy cognitive impairments are needed. Limited data suggest that rehabilitation improves physical and cognitive function, but the rate of these changes is unclear, as is whether lifestyle patterns predict or influence its occurrence and speed [27]. Identifying which survivors of critical illness are likely to benefit from rehabilitation specifically targeted at post-ICU cognitive impairments [28] will require information as to mechanisms and risk factors as well as information regarding effectiveness of rehabilitation strategies. Cautious optimism is warranted as cognitive rehabilitation appears promising; a recent study describes a 6-week physical and cognitive rehabilitation protocol that led to better executive functioning than controls

without rehabilitation [29]. We suspect that knowing which patients will benefit from these interventions, when to initiate them, which therapies are effective in ICU populations, and how rehabilitation will be funded will all

remain issues for clinical scientists for many years to come [28].

Conflicts of interest None.

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