# 17.12 Persistent problems and recovery after criti

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ESSENTIALS Post-intensive care syndrome is defined as new or worsening impair- ment in cognition, mental health, or physical function that persists after a critical illness. The complexities of post-intensive care syn- drome come from the interactions of the patient's premorbid mental health and physical function, the acute physiologic derangements and acute organ injury of the critical illness, and the side effects of procedures, treatments, and potential complications incurred during the critical illness. Problems are better described as challenging syndromes rather than specific actionable diagnoses, with the four major functional problems for patients being weakness, cognitive impairment, psychological problems, and new or worsened organ dysfunction. The sequelae of critical illness often extend beyond pa- tients and impact the families of critically ill patients. The clinical approach to post-intensive care syndrome includes preventive strategies during the critical illness and a standardized ap- proach to patients recovering from critical illness. Clinicians should be encouraged to engage the family in care and decision-making to mitigate the risk of psychological distress for the patient and family. The intensive care unit diary is an established means to reduce psy- chological distress in survivors and family members. Repeated and ongoing physical therapy may serve to both prevent deconditioning and to develop compensatory strategies for weakness that may have developed. Post-intensive care syndrome (PICS) Most patients cared for in intensive care units (ICUs) survive that hospitalization.

As a result an increasing number of patients are surviving critical illness but suffering a constellation of problems previously unrecognized or uncommon in general medical care. While many survivors will flourish after a critical illness, many ex- perience neuropsychological and physical function impairments that impact their long-term health, ability to return to work, and quality of life. The residual health effects of critical illness have been termed post-intensive care syndrome (PICS). Definition and conceptual overview Post-intensive care syndrome is defined as new or worsening im- pairment in cognition, mental health, or physical function that persists after a critical illness. Memory and executive function are the cognitive domains most likely to be impaired; anxiety, depres- sion, and post-traumatic stress disorder are common psychiatric symptoms. ICU-acquired weakness, also common after critical illness, can be due to myopathy, neuropathy, or a combination of the two, termed critical-illness neuromyopathy. At the same time, it is also common for patients surviving critical illness to have exacerbations of previously well-controlled chronic illnesses, or new conditions that were either not present or not previously diagnosed. The complexities of post-intensive care syndrome come from the interactions of the following (Fig. 17.12.1): • The patient's premorbid mental health and physical function • The acute physiologic derangements and acute organ injury of the critical illness • The side effects of procedures, treatments, and potential complica- tions incurred during the critical illness These lead to four major functional problems: weakness, cognitive impairment, psychological problems, and new or worsened organ dysfunction. These functional problems can lead to disability, in- ability to return to social roles or prior employment, high recurring healthcare needs, and substantial burdens on caregivers, culmin- ating in an increased risk of death that may persist for years after the apparent resolution of critical illness. Epidemiology and specific manifestations The risk factors associated with these impairments are multiple, complex, and (at present) incompletely understood. Factors thought to contribute include critical illness-associated inflammation and ischaemia, hypotension, hypoxaemia, and hypoglycaemia, and con- sequences of the acute illness and treatments received (e.g. immobil- ization and delirium due, in part, to the use of sedative medications and mechanical ventilation) (Fig. 17.12.1). 17.12 Persistent problems and recovery after critical illness Mark E. Mikkelsen and Theodore J. Iwashyna

 While some acute intensive care unit experiences are associated with an increased prevalence of subsequent problems, causal rela- tionships have not been proven. For example, the presence of de- lirium, a common development in the ICU, does not predict poor long-term outcomes with sufficient accuracy for prognostication in individual patients although there is a strong association at the population level. Equally true, the absence of specific problems in the ICU or immediately afterwards does not exclude the possibility of a patient experiencing post-ICU sequelae. The frequency of reported cognitive, mental health, and func-tional impairments vary by study population and by the timing of assessments in relation to intensive care unit and hospital discharge (Table 17.12.1). At three months, 40% of survivors of shock or re- spiratory failure have cognitive impairment consistent with that present in patients three months after moderate traumatic brain injury, 37% experience symptoms of mild depression or worse, and 32% have disabilities that limit basic activities of daily living. Symptoms of anxiety and post-traumatic stress disorder after critical illness are similarly common. While the definition of post-intensive care syndrome focuses on neuropsychological and physical function, the effects of a crit- ical illness extend beyond these domains. Sexual dysfunction, nu- tritional deficiencies, loss of muscle mass, joint contractures, and scarring all occur after critical illness. Collectively, these changes contribute to the lower quality of life observed in survivors of crit- ical illness. Impairments

in these domains frequently coexist, and im- pairment in one domain can exacerbate impairment in another Fig. 17.12.1 Interactions in the critically ill patient leading to adverse long-term outcomes. Pathways to functional impairments and disability are hypothesized but not yet fully described. Inspired by Creditor, M. C. (1993). ‘Hazards of hospitalization of the elderly.’ Ann Intern Med, 118(3): 219–223. Table 17.12.1 The relationship between morbidity after critical illness and timing of assessments ICU discharge Hospital discharge 3 months post-discharge 12 months post-discharge Cognitive Impairment 84% 46–64% 40% 34% Anxiety 24% Depression 37% 28–33% Post-traumatic stress disorder 22% Functional impairment (activities of daily living) 32% 27% Contracture, functionally significant 34% 23% Sexual dysfunction 44%

17.12 Persistent problems and recovery 3927 (e.g. cognitive impairment may undermine coping strategies and exacerbate pre-existing or new psychiatric disorders) or re- sult in new impairment (e.g. post-discharge depression predicts incident physical impairment). PICS-Family Unfortunately, the sequelae of critical illness often extend beyond pa- tients and impact the families of critically ill patients. Termed ‘PICS- Family’ (PICS-F), family members of both surviving and deceased critically ill patients frequently experience psychological distress, including anxiety, depression, complicated grief, and post-traumatic stress disorder, in addition to sleep disorders and panic attacks. As a result, family members may experience a reduced quality of life and reduced ability to care for and support the recovering patients. Risk factors associated with psychological distress include suffering the loss of a loved one, playing an active role as a surrogate decision- maker, ineffective communication from medical and nursing staff during the acute episode, and avoidant coping strategies during the acute events and afterwards. These effects can endure for months or years. Recovery after critical illness Post-intensive care syndrome is a useful construct to conceptualize the impairments that survivors of critical illness may experience, yet it is incomplete as a guide to caring for individual patients. In par- ticular, the concept of PICS may emphasize new problems caused by the critical illness. Yet, whether impairment is attributable to critical illness or not is less important than the degree and duration of impairment experienced by the patient. Further, patients often do not experience post-intensive care syndrome as a fixed burden. Instead, it is a dynamic process of physiologic repair, ongoing med- ical needs, personal rehabilitation efforts, and psychological, social, and pragmatic adaptation to these changes. Current evidence sug- gests that this process is most dynamic during the first 3–6 months after critical illness, although problems may persist for years. This is especially true if intercurrent illnesses stall recovery or precipitate further decline. In the 90  days following critical illness, survivors are com- monly re-admitted to hospital. As many as one in four of these re- admissions require intensive care unit admission. Patients who have survived sepsis appear to be a particularly vulnerable population at high-risk for re-admission to hospital. Two observations have been made about these hospital re-admissions. First, while many hos- pital re-admissions are for new or recrudescent infections, a large number (either a substantial minority or clear majority, depending on the study) are for problems that do not appear immediately re- lated to the cause of the patient’s initial intensive care unit stay. Second, many hospital re-admissions are for problems which, if an- ticipated, may be averted by appropriate primary care in the early post-hospitalization period; examples include congestive heart failure, acute renal failure, and aspiration pneumonitis. Clinical approach The clinical approach to post-intensive care syndrome includes pre- ventive strategies during the critical illness and a standardized ap- proach to patients recovering from critical illness. Whether encountering a patient after critical illness in an acute care hospital, a post-acute care facility, or in the outpatient setting, a standardized approach should be used to examine the patient’s experiences and assess

functional impairments. At present, there are few proven therapies for specific post-ICU syndromes. Instead, practitioners should focus on recognizing conditions that exist and applying good clinical practice developed outside of the post-ICU setting. There are some strategies that can be recommended as pre- ventive strategies, and others that use a targeted diagnostic approach to patients with potential post-intensive care syndrome complaints. Preventive strategies Strategies to prevent the development of post-intensive care syndrome should begin in the intensive care unit. Evidence-based strategies to decrease the duration of mechanical ventilation and ICU length of stay, duration of delirium, and increase functional independence are incorporated in the 'ABCDE' Bundle. The ABCDE bundle includes strategies to coordinate sedation and ventilator practices to achieve earlier liberation from mechanical ventilation, delirium assessment and management, and early ambulation to promote physical recovery. The ICU Diary, a detailed account of events that occur in the ICU which are documented by both staff and family, is a strategy begun in the ICU and reviewed with the patient and family as an outpatient. It is an established means to reduce psychological distress in sur- vivors and family members who may have limited or confused recall of events during the ICU stay. In conjunction with the review of the ICU Diary as an outpatient, clinicians should take the time to educate patients and caregivers about post-intensive care syndrome as they assess the patient and caregivers for symptoms consistent with this syndrome. To mitigate the risk of psychological distress for the patient and family, clinicians should engage the family in care and decision- making in the ICU and thereafter. Early and effective communica- tion, within the first 48–72 hours of the ICU stay, is recommended, in partnership with open visitation policies and the use of patient- and family-centred ward rounds. Priorities following discharge include assessment for post-intensive care syndrome, coupled with education to provide patients and care- givers with relevant information. There is currently active research on several possible strategies to facilitate recovery and prevent post- intensive care syndrome. Repeated and ongoing physical therapy has strong face validity and plausibility, and may serve to both prevent deconditioning and—as in the pulmonary rehabilitation model used in COPD—to develop compensatory strategies for weakness that may have developed. Several groups are exploring whether psychological or cognitive rehabilitation strategies are beneficial, but the effective- ness of these strategies has not yet been proven. Early and intensive primary care access and close monitoring might be of benefit to accel- erate recovery and prevent recurrent illness. Finally, there is growing interest in (but little evaluation of) the role of peer support groups for patients and families in improving recovery. In some cases, this preventive care will be delivered in post-ICU follow-up clinics. Post-ICU follow-up clinics are an established prac- tice in the United Kingdom and an emerging option within the United States, especially after stroke, trauma, or neonatal care. Yet, there is currently no consensus on their effectiveness or optimal structure.

Section 17 Critical care medicine 3928 Medication reconciliation after the ICU While there is nothing specific to medication reconciliation after in- tensive care unit treatment, it is clear that many medications are in- appropriately stopped and started there. Population-based research in Ontario suggested that HMG-CoA reductase inhibitors (statins), antiplatelet agents, anticoagulants, and thyroxine were frequently discontinued inappropriately after hospital admissions that included an ICU stay. Conversely, medications that may be reasonable for short-term treatment in the intensive care unit may be inappropri- ately continued after discharge; attention to the potential effects of medications on cognitive health is warranted. Offenders in one or both of these categories may include antipsychotics (used to prevent or treat delirium in the ICU), short-acting antihypertensives (used during transient hypertensive urgencies), proton pump inhibitors (used for

stress ulcer prophylaxis), opioids and benzodiazepines (used for procedural pain, sedation, or unclear indications in the ICU). Clinicians should be aware that, due to insomnia and psychi- atric symptoms, psychiatric medications are prescribed in up to 20% of patients in the year after a critical illness; the appropriateness of this is unclear. Colourful stories are often told of patients who resume taking one full set of medications they were prescribed before the in- tensive care unit, and an entire second set of medications with which they were discharged: many duplicative, some unnecessary, others contraindicated. Diagnostic approach A comprehensive clinical evaluation after ICU treatment should re- view the details of the recent critical illness and intervening events, including locations of care post-discharge, in addition to conducting a physical examination. Based on the unique challenges faced by survivors of critical illness and the prevalence of neuropsychological and physical impairments, additional elements of the history and physical examination should be included as an initial screening strategy (see Table 17.12.2). A structured approach that ties together a health narrative precritical illness to the present state post-critical illness can be used to identify new and unmasked health needs Clinical investigations Neuropsychological assessment Because informal assessments of neuropsychological problems are known to have low sensitivity, survivors of critical illness should be screened for cognitive impairment and mental health disorders, including depression, anxiety, and post-traumatic stress disorder. Several simple, validated screening tests are avail- able for use (Table 17.12.3). Formal neuropsychological assess- ment by a trained neuropsychologist may be useful to further characterize the type and severity of impairment in those who screen positive or are experiencing symptoms. The effectiveness of neurocognitive rehabilitation has not been fully studied after critical illness. However, given its utility in other disease states (e.g. traumatic brain injury), early referral to an interested prac- titioner is reasonable. Those identified to have significant psy- chiatric symptoms should be considered for referral to a mental health expert, in addition to consideration of prescribing psychi- atric medications. Functional assessment Assessment of activities of daily living should be performed to assess for functional disability, which may guide referral to phys- ical or occupational therapists to develop compensatory strat- egies or assistive devices. In addition, the ‘Timed Get Up and Go’ test in which the patient is asked to stand up from a seated position, walk 3 metres, and return back to the seated position is a simple test to assess for functional status problems patients may not self-report. Lung function In survivors who experienced acute respiratory failure, and acute respiratory distress syndrome (ARDS) in particular, lung function Table 17.12.2 A targeted approach to the history and physical examination after critical illness, accounting for health pre- and post-critical illness Critical illness history Physical examination Acute event Complications, including detailed review of acute infections during the hospitalization Focused assessment for: Mobility Joint contractures Body composition Post-procedural scars Medication reconciliation, including antibiotics, psychiatric prescriptions, and sleeping aid prescriptions Post-illness review of symptoms, including constitutional (fatigue, weight change, pain), cognition (memory, ability to think clearly), anxiety, depression, post-traumatic stress disorder, insomnia, sensory changes (hearing, taste, vision), cardiopulmonary (dyspnoea, cough), musculoskeletal changes (loss of strength, mobility) Dependent on screening, post-illness functional assessment, including neuropsychological assessment, physical function, lung function, sexual function, nutritional, and sleep hygiene assessment Recovery history post-discharge, including locations of care and present support structure Table 17.12.3 Suggested strategies for assessments post-critical illness Domain assessment Instrument Cognitive function Modified Mini-Mental State Montreal Cognitive Assessment Mental health Hospital Anxiety and Depression Scale Post-traumatic stress syndrome 10-questions inventory (PTSS-10) Functional

assessment Activities of daily living Instrumental activities of daily living Timed Get Up and Go Testa Lung function Pulmonary function tests, in those with symptoms or clinical history suggestive of lung dysfunction Ancillary tests (imaging, laboratory testing) Neither routine imaging or laboratory testing are recommended in general; assessments for those recovering from an infection are recommended to ensure resolution and for secondary prevention a In this test, patients are asked to stand up from a seated position, walk 3 metres, and return back to the seated position. A normal time to accomplish the task is 10 seconds or less in healthy elders and longer times are associated with increased fall risk.

17.12 Persistent problems and recovery 3929 may be impaired after critical illness, although it is normalized sur- prisingly often. Symptom-directed testing is appropriate. Imaging Routine imaging after critical illness is not recommended. Rather, ancillary testing, including more advanced imaging such as com- puted tomography or magnetic resonance imaging, should be re- served for those with clinical symptoms and signs and based on established, routine health screening recommendations. Ancillary tests There is no formal recommendation to obtain specific labora- tory testing after critical illness. Rather, laboratory testing should be obtained based on routine health maintenance and screening recommendations. In general, clinicians should be aware that an- aemia is common after critical illness and testing should be reserved to examine resolution of acute organ dysfunction or as needed for safety monitoring. Early treatment to avoid re-admission to hospital As noted above, re-admission to hospital for infection as well as other ambulatory-care sensitive conditions is common in the 90- days after discharge, and it may be beneficial to ensure rapid access and lower treatment thresholds for such conditions. Compensation and rehabilitation strategies for identified problems Clinicians should prioritize timely referral to ancillary services based on the patient’s symptoms and testing. While the benefits of strategies to improve outcome of post-intensive care syndrome have not been proven, experts in cognitive and functional impairments can provide strategies to compensate for these impairments. While no post-intensive care syndrome-specific therapies yet exist, pru- dent generalization from experience with other conditions may pro- vide symptomatic relief and improved function. Further, in terms of health trajectory, vigilance is required to ensure that acute condi- tions resolve and new symptoms and conditions are identified and managed in a timely and effective manner. Given the complexity of care after critical illness, communica- tion among care providers is of the utmost importance to help the patient navigate their post-critical illness course. While the most effective strategy remains unclear, identifying an accessible point- person to oversee the coordination of care required after critical illness should be a priority. The number of services and related clin- icians that may needed in the care of patients after critical illness can be substantial (see Table 17.12.4). As a result, communication and coordination from hospital discharge to the outpatient setting is essential. As many survivors of critical illness will be disabled, there are plausible benefits to engaging the patient’s support net- work (family and friends) in the process. At the centre of these communications lies the patient, and while the focus shifts towards rehabilitation and recovery in many, palliative and hospice care may be reasonable considerations for others based on their symp- toms and care preferences. Conclusion The success of critical care medicine in preventing death has led to substantial new challenges for clinicians throughout the healthcare system. Patient who might once have died in the intensive care unit or subsequently in hospital are surviving, often (but not always) with enduring problems—and problems better described as chal- lenging syndromes rather than specific actionable diagnoses. New approaches to diagnosis, classification, treatment, and symptom management are emerging, offering more hope for affected

patients. FURTHER READING Davidson JE, Jones C, Bienvenu J (2012). Family response to critical illness: postintensive care syndrome-family. Crit Care Med, 40, 618–24. Garrouste-Orgeas M, et al. (2012). Impact of an intensive care unit diary on psychological distress in patients and relatives. Crit Care Med, 40, 2033–40. Hua M, et al. (2015). Early and late unplanned hospital readmissions for survivors of critical illness. Crit Care Med, 43, 430–8. Iwashyna TJ, et al. (2010). Long-term cognitive impairment and func- tional disability among survivors of severe sepsis. JAMA, 304, 1787–94. Mehlhorn J, et al. (2014). Rehabilitation interventions for postintensive care syndrome: a systematic review. Crit Care Med, 42, 1263–71. Needham DM, et al. (2012). Improving long-term outcomes after dis- charge from intensive care unit: report from a stakeholders' confer- ence. Crit Care Med, 40, 502–9. Pandharipande P, et al. (2010). Liberation and animation for ventilated ICU patients: the ABCDE bundle for the back-end of critical care. Crit Care, 14, 157. Pandharipande PP, et al. (2013). Long-term cognitive impairment after critical illness. N Engl J Med, 369, 1306–16. Prescott HC, Angus DC (2018). Enhancing recovery from sepsis: a re- view. JAMA, 319, 62–75. Prescott HC, Langa KM, Iwashyna TJ (2015). Readmission diagnoses after hospitalization for severe sepsis and other acute medical condi- tions. JAMA, 313, 1055–7. Table 17.12.4 Potential services and expertise required in the care of the recovering critically ill patient Acute care Post-acute care Outpatient Physical and occupational therapy Acute rehabilitation Physical and occupational therapy Nutrition consultation Home with home
health services Nutrition consultation Respiratory therapy Skilled care facility Mental health services, including grief counselling for family members Case manager to facilitate post-acute care needs Long-term acute care hospital Neuropsychology consultation Palliative care for symptom management Hospice care Palliative care for symptom management and/or hospice care Surgery consultations Support groups

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