

Aging and Post-Intensive Care Syndrome (PICS): A Critical Need for Geriatric Psychiatry

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Highlights

- The number of older ICU (intensive care unit) survivors is rapidly growing due to aging of the population and improved ICU care.
- The long-term cognitive, psychological, and physical sequelae after ICU hospitalization is known as post-intensive care syndrome (PICS).
- Many older ICU survivors suffer from long-term cognitive impairment from ICU-related delirium and mental health symptoms.
- PICS-family describes the mental health symptoms that family members can experience after their loved ones are hospitalized in the ICU.
- Geriatric psychiatrists may be able to play an important role in collaborative care clinics designed to care for ICU survivors.

ABSTRACT

Due to the aging of the intensive care unit (ICU) population and an improvement in survival rates after ICU hospitalization, an increasing number of older adults are suffering from long-term impairments due to critical illness, known as post-intensive care syndrome (PICS). This paper focuses on PICS-related cognitive, psychological, and physical impairments, and the impact of ICU hospitalization on families and caregivers. The authors also describe innovative models of care for PICS, and what roles geriatric psychiatrists could play in the future of this rapidly growing population.

I. INTRODUCTION

As survival rates from intensive care unit (ICU) hospitalization have increased over the past few decades, the long-term cognitive, psychological, and physical impairments from their critical illness have now become the "defining challenge of critical care medicine."^{1,2} These long-term impairments are known as post-intensive care syndrome (PICS).¹⁻³ In 2012, the Society of Critical Care Medicine (SCCM) organized a task force on PICS to define the syndrome and raise awareness regarding the long-term consequences of critical illness on patients and their families.³

PICS has become an increasingly important phenomenon in older adults for several reasons.^{1,4-7} First, the number of older adults with critical illness is rapidly increasing as the population ages. Patients 65 and over already account for 50% of ICU admissions, and patients 85 and over make up the fastest growing age group for ICU admissions.⁴⁻⁷ Second, over 70% of older adults hospitalized in the ICU develop delirium,⁸ which is a major risk factor for developing ICU acquired cognitive impairment.^{8,9} Third, cognitive and functional impairment before an ICU hospitalization increases the likelihood of cognitive and functional decline afterwards.¹⁰⁻¹² This review discusses aging and PICS, with a special emphasis on aspects of PICS that geriatric psychiatrists can play a critical role in improving clinical care for these older ICU survivors and their families.

II. POST-INTENSIVE CARE SYNDROME (PICS) AND AGING

II.A. Epidemiology

About 50-70% of all ICU survivors suffer from at least one PICS-related impairment, and these effects can persist for as long as 5-15 years after discharge.² Almost one half of all ICU survivors discharged from the ICU have PICS-related physical impairments, and 30-80% will have PICS-related cognitive deficits.^{12,13} The prevalence of physical and cognitive impairments

in older ICU survivors are quite high. Iwashyna *et al.* examined the outcomes of 1,520 ICU hospitalizations in Medicare beneficiaries (mean age 76.9) with severe sepsis.¹⁴ Up to 60% of hospitalizations were associated with worsened cognitive and/or physical functioning at one year after hospitalization.¹⁴ 16.7% of survivors had moderate to severe cognitive impairment one year after hospitalization, compared to 6.1% before ICU hospitalization.¹⁴ In another study examining 291 ICU admissions in older adults (average age 83.7), 51% were severely disabled at discharge from ICU.¹⁵ In a study of 77 patients (median age 61), nearly 80% of ICU survivors had cognitive deficits on 3 month follow up, and 71% at 12 month follow-up.¹⁵ Another study showed that 15% of older ICU survivors had a new diagnosis of dementia 3 years after follow-up, with almost 40% of new dementias being diagnosed within the first year.¹⁶

II.B. Physical impairment

Only about half of all older adult ICU survivors have functional recovery after their critical illness, with a median recovery time of 3 months.¹⁰ Older survivors of severe sepsis developed 1.5 new activities of daily living (ADL) limitations compared to 0.5 of their non-ICU counterparts.⁶ Likewise, older survivors who were mechanically ventilated were 30% more likely to have an ADL disability compared to hospitalized older adults who were not mechanically ventilated.¹⁷ These physical impairments translate into increased need for support outside of the hospital. In a study of 291 ICU patients, 72.2% of patients required services on discharge and 58.3% required institutionalization for nursing care or rehabilitation.¹⁵ Vision and hearing impairment prior to ICU hospitalization were associated with poorer post-ICU recovery in older adults, whereas higher body mass index and functional self-efficacy were associated with better post-ICU recovery.¹⁰ The connection between persistent physical impairments and mental health quality of life need further study, but BRAIN-ICU study found physical disability was a significant contributor to depression at three and 12 months following ICU hospitalization.¹⁸

II.C. Long-term cognitive impairment (LTCI)

Risk factors for ICU-acquired long-term cognitive impairment (LTCI) in older adults include neurologic dysfunction, infection or severe sepsis, and acute dialysis.¹⁹ Duration of delirium is a risk factor for LTCI for adults of any age.^{12,20} The interaction between LTCI, age, and delirium, however, is complex. Age is a major risk factor for delirium in both the general hospital and ICU settings.^{21,22} Older adults without premorbid cognitive impairment who develop delirium in both the general hospital and ICU settings have an increased risk of dementia compared to older adults without delirium. This shows delirium itself increases the risk of dementia.^{19,23,24} However, the current evidence does not strongly support that older adults are at substantially higher risk than younger adults for LTCI. In a prospective observational study of 821 ICU subjects, adults 65 and over had similar global cognition and executive functioning scores to those younger than them at 3 and 12 months post discharge.²⁰ In a retrospective study of 10,348 Medicare beneficiaries, the absolute risk of dementia was only increased 3% in older intensive care patients compared to the general population, and this risk was mostly due to their critical illness rather than premorbid conditions.¹⁹

One possible explanation is that the mechanisms causing LTCI from delirium may be distinct from Alzheimer's disease (AD) and other types of dementias. Figure 1 shows the relationship between risk factors for delirium and the underlying pathophysiologic mechanisms that could lead to delirium associated long-term cognitive impairment. While age, premorbid cognitive impairment, and underlying neurodegenerative pathology may increase susceptibility to delirium,²⁵ long-term cognitive impairment from delirium appears to be caused by hypoxia and pro-inflammatory cytokines.²⁶ This theory is consistent with the observation that the onset of LTCI from delirium appears to depend on the duration of exposure to the pathophysiologic processes of delirium.

Medications may also modify the effect between delirium and LTCl either by exaggerating an underlying pathology described above or through mechanisms unique to classes of medications. There is currently a paucity of research explaining the relationship between medications and LTCl among survivors of critical illness. It is unknown whether LTCl is influenced by long-term exposure to certain medications, such as anticholinergics and benzodiazepines, prior to an acute illness;²⁷⁻²⁹ it is also unclear whether exposure to certain medications in the acute, critically ill period, and in the immediate recovery period influence LTCl.³⁰⁻³² Because medications are often used as the primary method to manage many acute and chronic disease, understanding the role of medications in the trajectory of LTCl could significantly shape pharmacologic strategies for acute and chronic treatments in this vulnerable population.

LTCl from delirium appears to differ from AD in several important ways. First, LTCl appears to affect multiple cognitive domains (executive functioning, memory, and attention) rather than primarily memory.²⁰ Second, many patients' LTCl improve within the first year, although they can persist for many years in some individuals. This profound drop in cognition is quite different from the progressive nature of AD. Third, executive functioning in LTCl is associated with worse severity of depression and poorer mental health quality of life.³³ Finally, LTCl may be associated with smaller superior frontal lobes, thalamus, and cerebellar volumes and white matter damage, whereas AD is classically associated with hippocampal atrophy.^{34,35} Interestingly, however, smaller hippocampal volumes are also associated with longer duration of delirium.³⁵

II.D. Mental health impairments

Depression, anxiety and post-traumatic stress disorder are the best-characterized mental health impairments in PICS. Among adult ICU survivors, prevalence is 19-37% for depression,^{18,36,37} 32-40% for anxiety,^{38,39} and 19-22% for PTSD.^{18,40} Two major factors complicate the clinical picture. First, psychiatric comorbidity (the presence of multiple psychiatric disorders) in ICU

survivors is 4-6 times more common compared to the general population (25-33% of ICU survivors versus 6% for the general population).⁴¹⁻⁴⁴ Second, studies suggest that those who have mental health symptoms after critical illness have premorbid psychiatric disorders.^{45,46} Patients who develop critical illness may be more likely to have premorbid psychiatric illness compared to those hospitalized in general wards and the general population.⁴⁶

The role of aging and mental health impairments need to be better understood. Mental health problems after critical illness occur across all age groups. Studies have found that older age is independently associated with increased depression and worse mental health quality of life.^{18,47} Some studies have found that younger age is a risk factor for PTSD,^{48,49} but other studies have found that age is not associated with the risk of PTSD.^{40,51,52}

III. PICS-FAMILY (PICS-F) AND CAREGIVER STRESS

Post-intensive care syndrome-family (PICS-F) describes the psychological impact of ICU hospitalization and post-ICU recovery on family members and other caregivers. PICS-F symptoms can start in the ICU and often persist in the post-ICU phase. Prevalence rates at six months of 15-24% for anxiety, 4.7-36% for depression, and 35-57% for PTSD have been observed.⁵² Complicated grief after the death of the patient is seen in greater than 50% of relatives.⁵³ Demographic risk factors for PICS-F include female gender, younger age of patient, lower education level, spouse of patient, previous history of mental health disorder, and family history of mental health disorder.⁵² The RECOVER study found that caregivers of ICU caregivers who were younger and had less social support were more likely to be persistently depressed at a year. Interestingly, no patient characteristics were associated with poorer mental health outcomes in caregivers.⁵⁴ ICU-related risk factors for PICS-F include perception of patient being very near death, unexpected or sudden patient illness, family members with greater levels of anxiety and depression about the ICU hospitalization, and poor communication between family members and ICU physicians.⁵⁵

Interventions for PICS-F include diaries and educational materials.⁵⁶ Diaries are written by the ICU staff and family, and include photos of patients and family members during the ICU stay. Patients take the diaries with them when they are transferred to a hospital floor or discharged from the hospital. Educational materials include pamphlets or brochures about PICS and informational videos available on the hospital TV and social media. Condolence letters written to family members may actually worsen their depression and PTSD-related symptoms.⁵⁷ Potential areas of study for PICS-F include differences in PICS-F in older versus younger ICU survivors, algorithms to identify caregivers at high risk for PICS-F to deliver depression-focused psychotherapies, and family based interventions to provide emotional support while in the hospital and after discharge.

IV. PREVENTION AND TREATMENT OF DELIRIUM

IV.A. ICU-based interventions

In 2013, the Society of Critical Care Medicine (SCCM) developed the Pain, Agitation, and Delirium (PAD) guidelines.⁵⁸ There are a few practices worth highlighting since they are unique to the ICU and relevant to geriatric psychiatry. However, their impact on LTCl is unknown. First, the guidelines emphasize the use of music therapy and relaxation techniques as nonpharmacologic interventions for pain management. Second, delirium prevention is quite important. Early mobilization, an important delirium prevention strategy, is associated with improved walking distance, functional improvement, shorter duration of mechanical ventilation, shorter length of stay, and decreased cost of stay.⁵⁹ Psychotropics, including antipsychotics, and acetylcholinesterase inhibitors such as rivastigmine have not been shown to prevent or treat delirium.^{58,60} Third, the Confusion Assessment Method for the ICU (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC) are the most valid and reliable delirium monitoring tools in adult ICU patients. Fourth, ICUs need to control light and noise, cluster

patient care activities, and decrease stimuli at night. Finally, psychiatric medications should be restarted if clinically indicated.⁵⁸

The PAD guidelines also highlight the importance of limiting benzodiazepine use to alcohol or benzodiazepine withdrawal and administering non-benzodiazepines whenever possible.

Systematic literature review shows that the use of benzodiazepines and duration of sedation are significant clinical risk factors for the development of post-ICU PTSD.^{40,51} Long-term high doses of benzodiazepine used for sedation increases the risk of longer duration of delirium, the PAD guidelines indicate benzodiazepines may be associated with LTCl, but this question needs further investigation as noted above. Likewise, antipsychotic use should be limited for agitation. Antipsychotic use has not yet been consistently shown to improve duration or severity of delirium, hospital length of stay, or mortality.⁶⁰ Nevertheless, clinicians should minimize use of antipsychotics when treating behavioral disturbances.

IV.B. Post-ICU Interventions

There is a need to develop interdisciplinary consensus guidelines for psychotropic stewardship in older ICU survivors. ICU patients are often discharged on inappropriate medications, which they continue to use for a significant duration post discharge, including anticholinergics, opioids, nonbenzodiazepine hypnotics and benzodiazepines, and atypical antipsychotics.⁶¹ Despite the recommendation to minimize use of antipsychotics, almost a quarter of patients were given a new antipsychotic during their hospitalization are discharged on an antipsychotic. Although there are no specific guidelines for discontinuation of antipsychotics in the post-ICU phase, the American Geriatrics Society recommends the use of the lowest dose for antipsychotics for post-operative delirium when given for behavioral disturbances, and soonest possible discontinuation. If clinicians decide to continue psychotropics upon discharge from ICU admission, they should weigh the benefits versus risks, such as the FDA black box warning for antipsychotics.

Another important intervention has been the growth of dedicated post-ICU survivor clinics. Over 80 ICU survivor clinics in the U.K. have been created since 1993. The first ICU survivor clinic in the US, the Critical Care Recovery Center (CCRC) affiliated with Indiana University, was created in 2011. The CCRC utilizes a collaborative care model for ICU survivors, a model that has been shown to be successful in older patients with dementia and late-life depression (Figure 2).^{62,63} At CCRC, patients undergo an initial assessment, which includes a complete diagnostic workup, structured physical and neurological examinations, comprehensive neuropsychological examination, physical function battery, medication reconciliation, and additional blood work and imaging as clinically indicated. Two weeks after the comprehensive assessment, a family conference with the physician, patient, caregiver, registered nurse (RN), the social worker, and a critical care pharmacist is held to discuss an individualized care plan for the patient and caregiver. The care coordinators [registered nurse (RN), social worker] are the key to executing the individualized care plan. The care coordinator functions as the recovery coach who assist patients and family members navigate multiple parts of healthcare system, which happens frequently due to the complexity of PICS. (Figure 2). Cognitive, behavioral, and physical functioning are assessed as part of the physical and neuropsychological examinations, as well as monitors completed by the caregiver or the patient (cite HABC-M). The ICU Recovery Center affiliated with Vanderbilt University Medical Center utilizes a similar interprofessional approach to evaluate and manage PICS and PICS-F.⁶⁴ In 2016, the SCCM sponsored the creation of a national collaborative network of ICU survivor clinics, known as the Thrive Post ICU Clinic Peer Collaborative. Future studies will need to further examine the effectiveness of ICU survivor clinic, but a small longitudinal study of CCRC found beneficial effects on patients' cognitive and functional symptoms.⁶² One major concern is that although psychiatric morbidity in ICU survivors is associated with adverse effects on patients' quality of life and increased acute

care service utilization after discharge from the ICU,^{43,65} the role of mental health professionals in these ICU survivorship models has not been well-defined.

V. FUTURE DIRECTIONS

The rapidly growing population of older ICU survivors presents critical care medicine with an unprecedented clinical challenge. How do we widely disseminate geriatric mental health services for patients with complex psychiatric comorbidities and comorbid cognitive and functional impairments due to critical illness? The current model of primary care or critical care medicine starting a first line antidepressant will not address this population's needs. Nearly one third of adult survivors seen in the Critical Care Recovery Center were on an antidepressant at their initial visit, but half of these treated survivors still had significant depressive symptoms.⁴⁵ To worsen matters, access to geriatric psychiatrists is dropping due to a lack of workforce and the increasing mental health needs of older adults.

Geriatric psychiatrists can play a key role in building and leading new health delivery models for PICS. First, clinical practice guidelines for the neuropsychiatric sequelae in ICU survivors are essentially non-existent. Geriatric psychiatrists need to collaborate with critical care medicine organizations to provide vital guidance on the diagnosis and management of post-ICU cognitive and mental health impairments. Next, geriatric psychiatrists need to work with the hospital leadership and various clinical disciplines to build system wide interventions for older ICU survivors. Figure 3 depicts the vision of a system-based, individualized care plan to address both patients' cognitive and mental health needs and caregivers' mental health needs. There are several notable aspects, which differ from current models of care. First, there should be proactive assessment of psychiatric comorbidity for both patients and caregivers upon admission. This proactive assessment allows for the identification of premorbid psychiatric disorders, which may not be previously diagnosed or adequately treated, and a plan for ongoing

management throughout their entire hospitalization and in the outpatient setting. Second, a recovery care coordinator must be identified during the ICU hospitalization, so care coordination can start with patient and caregiver during the ICU hospitalization. The recovery care coordinator collaborates with the geriatric psychiatrist to implement the individual care plans, helps to create the post-ICU individualized plan, and ensures that there is a smooth transition of care and follow through on the post-ICU individualized plan in the various outpatient settings. Most importantly, the recovery care coordinator continues to work with the patient and family in the outpatient setting until the care plan goals are achieved. Third, the monitoring and interventions should be protocol driven, and ideally, technology driven to minimize staff burden. The protocol driven component is a key addition to ensure consistency in mental health involvement, rather than completely relying on clinical staff, who change with every shift. Table 1 describes in more detail some possible elements of these individualized care plans.

Geriatric psychiatrists can also be part of interdisciplinary teams by providing clinical services and leading clinical practice and research innovations. Clinical services include diagnostic assessment of cognitive and mental health symptoms, mental health treatment planning, and psychotropic management. Electronic/telephonic consultation or videoconference are novel approaches which can increase access to subspecialty care. Possible clinical practice and research innovations include multisite piloting of in-home cognitive and physical/functional rehabilitation programs,⁶⁶ computer based neuropsychological testing for rapid neurocognitive assessments, development and testing of deprescribing protocols, testing the efficacy of depression-focus psychotherapies delivered via web-based or mobile technology, better characterization and management of post-ICU PTSD in the context of comorbid cognitive and functional impairments, and factors which may increase resilience in both patients and caregivers. Finally, geriatric psychiatrists can increase their impact by educating trainees in the fields of mental health and medical and surgical subspecialties (particularly residents who are

seeking dual training in medicine and psychiatry), other mental health professionals, and medical-surgical subspecialties through clinical case conferences and via teleconferencing. In summary, critical care medicine is facing an unprecedented situation of providing services for chronically ill older patients who have survived their ICU hospitalization. The public, including healthcare professionals in other fields, need to be aware of the impact of aging on the ICU survivor population, and the potential for geriatric psychiatrists to contribute to this increasingly important field.

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Figure 1. Relationship between age and long-term cognitive impairment secondary to delirium.

Figure 2. Collaborative Care Model of Critical Care Recovery Center.

Figure 3. Vision of System-Based Care for Neuropsychiatric Sequelae of Older ICU survivors

MOCA = Montreal Cognitive Assessment. RBANS = Repeatable Battery for the Assessment of Neuropsychological Status. PHQ-9 = Patient Health Questionnaire-9.

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**Table 1. Vision of Individualized Care Plans for Older ICU Survivors and Their Caregivers
In Hospital Individualized Care Plans**

In Hospital Individualized Care Plans	
Patient	Caregiver
Assignment of recovery care coordinator	Assignment of recovery care coordinator
Protocol driven monitoring of cognition and mental health by staff or technology	Protocol driven monitoring of mental health by staff or technology
Protocol-driven assessment and initiation of psychotropic use	Education pamphlets
Ongoing review of psychotropic use	ICU diaries (collaboration with staff)
ICU diaries (collaboration with patient and staff)	In-hospital support groups
Psychiatry inpatient consultation (protocol driven by initial screen, monitors, and clinical staff)	Referral to family counseling and mental health services (protocol driven by initial screen, monitors and clinical staff)
In hospital treatment goals	In hospital treatment goals
Post-ICU Individual Care Plans	
Patient	Caregiver
Ongoing collaboration with recovery care coordinator	Ongoing collaboration with recovery care coordinator
Protocol driven monitoring of cognition and mental health by staff or technology	Protocol driven monitoring of mental health by staff or technology
Protocol-driven assessment and initiation of psychotropic use	Education pamphlets
Deprescribing protocols including identification of target medications and timeline for stopping medications	Ongoing collaboration with primary care services as needed
Outpatient support groups (face to face, mobile technology)	Outpatient support groups (face to face, mobile technology)
Psychiatry outpatient consultation for recommendations for psychotropic management and psychotherapy (protocol driven by monitors and clinical staff)	Psychiatry outpatient consultation for recommendations for psychotropic management and psychotherapy (protocol driven by monitors and clinical staff)
Outpatient treatment goals	Outpatient treatment goals