Treatment of the Post-ICU Patient in an Outpatient Setting

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The care of a patient in the intensive care unit extends well beyond his or her hospitalization. Evaluation of a patient after leaving the intensive care unit involves a review of the hospital stay, including principal diagnosis, exposure to medications, period spent in the intensive care unit, and history of prolonged mechanical ventilation. Fatigue should prompt evaluation for possible anemia, nutritional deficits, sleep disturbance, muscular deconditioning, and neurologic impairment. Other common problems include poor appetite with possible weight loss, falls, and sexual dysfunction. Psychological morbidities, posttraumatic stress disorder, anxiety disorder, and depression also often occur in the post–intensive care unit patient. These conditions are more common among patients with a history of delirium, prolonged sedation, mechanical ventilation, and acute respiratory distress syndrome. The physician should gain an understanding of the patient's altered quality of life, including employment status, and the state of his or her relationships with loved ones or the primary caregiver. As in many aspects of medicine, a multidisciplinary treatment approach is most beneficial to the post–intensive care unit patient. **(*Am Fam Physician*. 2009;79(6):459-464.**

ILLUSTRATION BY RENEE L. CANNON

Since the inception of modern critical care medicine in the latter half of the 20th century, the focus has been on decreasing short-term mortality during hospitalization. Before the 1990s, little attention was given to the post–intensive care unit (ICU) course, and long-term follow-up studies were rare. More recently, the critical care community has begun to recognize the need for more detailed analyses of the chronic issues that confront patients in the months to years following an ICU stay. In addition to monitoring patients for well-known complications, such as myocardial infarction, pneumonia, and stroke, physicians should be aware of a subset of well-established disease processes specifically associated with the post-ICU course *(Table 1)*. As studies on the long-term characteristics of post-ICU patients emerge, the results will influence the outpatient care of previously critically ill patients, as well as the care they received in the ICU.[1]

Clinical Presentation and Treatment

PHYSICAL CONSIDERATIONS

Hospitalization in the ICU usually involves immobilization for several days and, possibly, mechanical ventilation. Alternative forms of nutrition also may be required. Patients often have multiorgan failure or sepsis. Although no specific guidelines are available to distinguish the different populations of ICU patients from one another, certain problems that can develop in these patients should be understood to ensure proper follow-up after discharge.

Anemia. Post-ICU patients often have chronic anemia following discharge. Between 11.0 and 12.7 percent of patients will require transfusion after leaving the ICU.[2,3] While in the ICU, many patients receive myelotoxic drugs, which can inhibit erythrocyte production. Moreover, some cases of anemia result from poor nutritional intake. Other risk factors for developing anemia after leaving the ICU include a history of sepsis,

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
Post-ICU patients should be monitored for the development of anemia, particularly those who are older, are women, have a history of sepsis, or have a malignancy.	C	2, 3
Post-ICU patients at higher risk of posttraumatic stress disorder include those who are younger, have received sedatives, have been on prolonged mechanical ventilation, and have a history of acute lung injury or traumatic brain injury.	C	19-23
Patients who experienced delirium during ICU hospitalization should be assessed for anxiety.	C	30, 31

ICU = intensive care unit.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.xml.

Table 1. Common Complications in Patients Following ICU Hospitalization

Complication(s)	*Possible causes*	*Evaluation*
Weakness	Anemia, critical illness myopathy or polyneuropathy, muscle atrophy, inadequate nutrition, drug therapy	CBC, iron panel, serum chemistries, serial body weight measurement, physical therapy, neurology consultation
Fatigue	Anemia, insomnia, depression, muscle atrophy, poor nutrition, drug therapy	CBC, iron panel, serum chemistries, serial body weight measurements, physical therapy, sleep/depression questionnaire
Shortness of breath	Pulmonary fibrosis or scarring after acute lung injury, anemia, neuropathy, muscle atrophy, psychological factors, worsening pre-ICU pulmonary or cardiovascular disease	Imaging study (e.g., chest radiography, chest computed tomography) if warranted, CBC, iron panel, reticulocyte count, pulmonary function tests, electrocardiography, echocardiography
Mobility issues	Critical illness myopathy or polyneuropathy, joint pain, joint stiffness, muscle weakness	Physical therapy, neurology consultation
Stridor	Tracheal stenosis	Magnetic resonance imaging of neck or upper endoscopy
Reduced appetite	Altered taste, swallowing difficulties, weakness of pharyngeal muscles, psychological condition precluding patients from feeding themselves	Swallowing study
Peripheral neuropathy, numbness, paresthesia	Critical illness polyneuropathy, iatrogenic cause (e.g., needle injury)	Neurology consultation, electromyography/nerve conduction velocity studies
Hair loss	Telogen effluvium secondary to severe weight loss or major illness	Thyroid-stimulating hormone, CBC, ferritin, and antinuclear antibody testing to rule out other causes
Amenorrhea	Hypothalamic amenorrhea secondary to severe weight loss or major illness	Monitor levels of gonadotropin-releasing hormone, luteinizing hormone, follicle-stimulating hormone, estrogen, and human chorionic gonadotropin
Depressed mood	PTSD, major depressive disorder, familial anxiety or depression, frustration about slow recovery, drug therapy	Depression screening tool (e.g., Center for Epidemiologic Studies Depression Scale, Geriatric Depression Scale)
Anxiety	Generalized anxiety disorder, PTSD	Generalized Anxiety Disorder seven-item scale
Insomnia	PTSD, depression, anxiety disorders	Sleep/depression questionnaire
Impaired memory, poor concentration, nightmares, hallucinations, distressing flashbacks, hyperarousal	PTSD	Clinician-Administered PTSD Scale

CBC = complete blood count; ICU = intensive care unit; PTSD = posttraumatic stress disorder.

malignancy, female sex, and older age.[2] Many of these cases will be detected during the ICU stay. However, the threshold for performing a complete blood count, iron panel (iron, ferritin, total iron-binding capacity, transferrin), and reticulocyte count should be very low in the outpatient setting, particularly when patients have dyspnea or generalized fatigue.

Myopathy. Post-ICU patients are often limited by muscular deconditioning that occurs with prolonged immobilization. The net reduction of the myosin:actin ratio after an ICU stay is referred to as critical illness myopathy. After prolonged periods of immobility, patients lose their lean body mass at a rate of 2 percent per day.[4] In addition to generalized weakness, patients often have decreased mobility because of poor balance control, fear of falling, and joint stiffness. In one study, patients with prolonged ICU stays, poor premorbid health, and longer duration of mechanical ventilation were most likely to have trouble climbing stairs eight weeks after discharge from the ICU.[5] Prolonged length of stay and hours of mechanical ventilation were also predictive of decreased mobility outdoors. Complications of this deconditioning can persist up to 12 months after discharge.[6,7]

During follow-up, it is crucial to identify patients who would benefit from physical rehabilitation beyond basic patient education. Graded exercise programs speed recovery back to prehospitalization abilities. The results of one randomized trial demonstrated that a six-week self-help rehabilitation program was effective in aiding physical recovery and reducing the incidence of depression compared with routine clinic appointments.[8]

Neuropathy. In addition to critical illness myopathy, critical illness polyneuropathy has been reported in ICU patients. It most commonly affects patients with sepsis and multiorgan failure.[9] Severe neurogenic atrophy and axonal degeneration can lead to acute denervation of sensory and motor nerves, with particular involvement of the lower limbs and respiratory muscles.[10] Although several pathogenetic mechanisms have been proposed, the etiology remains unclear. This type of neuropathy typically resolves within three years after discharge. Long-term treatment consists of extensive rehabilitation. Neuropathic pain medications, such as capsaicin cream (Zostrix), gabapentin (Neurontin) and other anticonvulsants, selective serotonin reuptake inhibitors (SSRIs), and venlafaxine (Effexor), may also be considered. However, no studies have examined their effects on critical illness polyneuropathy.

Metabolic Bone Disease. In addition to muscular deconditioning leading to weakness, it is important to consider metabolic bone disease in post-ICU patients. Many of these patients are exposed to bone-demineralizing drugs, such as steroids *(Table 2)*; experience limited weight-bearing for prolonged periods, leading to bone hyperresorption; or develop vitamin D deficiency because of poor nutrition, lack of sunlight, and renal and hepatic dysfunction. In one review, 92 percent of the chronically critically ill patients studied had bone hyperresorption and 42 percent had vitamin D deficiency.[11] This bone loss can lead to osteoporosis with vertebral and hip fractures. Although there is no evidence suggesting that post-ICU patients should be screened differently than other populations, physicians should review U.S. Preventive Services Task Force recommendations on osteoporosis screening and should consider prolonged immobility to be a pertinent risk factor in women older than 60 years. For patients meeting T-score and clinical criteria, the preventive use of bisphosphonates may be beneficial.

Tracheoarterial Fistula and Tracheal Stenosis. Many ICU patients require tracheostomy for airway management. Complications, such as tracheoarterial fistulas or tracheal stenosis, are exceedingly rare.[12,13] Although younger age and repeated intubations are risk factors for complications, there is no established association between complications and duration of tracheostomy.[14] These complications should be considered in patients of any age with dyspnea or stridor and a compatible history. If complications are suspected, bronchoscopy or computed tomography should be performed.

Nutrition. Nutritional issues related to the ICU hospital course, including appetite, oral intake, and dietary supplements, should also be addressed during outpatient visits. The patient's weight should be monitored closely and compared with preadmission values. Patients may experience changes in taste that affect their appetite. Previous intubation/tracheostomy may lead to swallowing difficulties, as well as weakness and lack of

Table 2. Drugs Used in the ICU Setting That Are Associated with Bone Marrow Suppression

Amphotericin B (Fungizone)*	Phenytoin (Dilantin)
Antivirals	Rifampin (Rifadin)
Dapsone	Steroids
Isoniazid (Nydrazid)	Sulfonamides
Penicillin	Trimethoprim (Primsol)
Phenobarbital	

ICU = intensive care unit.

**—Brand no longer available in the United States.*

coordination of pharyngeal muscles.[6] In cases of prolonged absence of oral intake, the bowel mucosa atrophies. Furthermore, absence of lipids in proximal small bowel prevents cholecystokinin-mediated contraction of the gallbladder, leading to bile stasis and potentially acalculous cholecystitis. During one study that included severely septic ICU patients, a loss of approximately 2 lb, 11 oz (1.21 kg; 13 percent) of total body protein occurred over 21 days.[4] In the first 10 days, 67 percent of the lost protein came from skeletal muscle, but after that it was predominantly from the viscera. The threshold for referral to a nutritionist should be low to ensure proper caloric and vitamin intake.

Sexual Dysfunction. Sexual dysfunction is common among post-ICU patients. Rates of sexual dysfunction range from 16 to 42.6 percent one year after discharge.[15,16] Although these rates may not be higher than in the general population, sexual problems are more likely to be discounted or overlooked in the presence of other comorbidities. Sexual dysfunction can include lack of desire, impotence, and shortness of breath with exertion. Causes that should be considered include surgical disfigurement or psychological concerns about the relapse of illness with sexual activity. During the evaluation, it is important to eliminate other potential etiologies, including chronic medical conditions, medications, and surgery. Furthermore, there is a strong correlation between sexual dysfunction and symptoms of posttraumatic stress disorder (PTSD; $P = .019$).[16] No known studies have examined the effectiveness of commonly used phosphodiesterase-5 selective inhibitors in this subset population.

PSYCHOLOGICAL CONSIDERATIONS

The term *ICU syndrome* is sometimes used to include anxiety, depression, and PTSD, all of which have a higher prevalence in the post-ICU patient. Unfortunately, neither a uniform method for evaluating the different diagnoses nor established follow-up times for evaluation exist.

PTSD. PTSD is the psychiatric condition most extensively studied in the post-ICU patient. Symptoms of PTSD, regardless of inciting trauma, include intrusive phenomena (nightmares, flashbacks), persistent reexperiencing, avoidance of reminders of the event, thoughts or feelings related to trauma, and hyperarousal (insomnia, hypervigilance). These symptoms often lead to sleep alterations, outbursts, and increased startle reaction. The perception of illness and threat to life, rather than the actual severity of the illness, is an accurate predictor of PTSD development.[17-19]

Presence of delirium during intensive care unit hospitalization increases the risk of an anxiety disorder up to two years after discharge.

Three to six months after patients are discharged from the ICU, rates of PTSD symptoms range from 22 to 50 percent; however, fewer patients (1.9 to 25.5 percent) meet diagnostic criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed.[20,21] Younger patients, particularly those who have experienced a traumatic event such as traumatic brain injury, and those on prolonged mechanical ventilation have an increased incidence of PTSD. History of acute respiratory distress syndrome (ARDS) is also a risk factor for PTSD. In one study, investigators found increased prevalence up to eight years after discharge.[22]

In addition to the psychological trauma of having a near-death experience, other factors might also play a role in the development of PTSD. The use of sedatives and neuromuscular blocking agents in the ICU for acute lung injury is associated with subsequent depression and PTSD symptoms six to 41 months after discharge.[23,24] SSRIs should be considered in patients who meet criteria for or show significant symptoms of PTSD.

Depression. Post-ICU patients need to be monitored for signs of major depressive disorder. Rates of depression two to three months following discharge range from 9.8 to 30 percent, although rates tend to be higher in patients with ARDS or acute lung injury.[7,23,25,26] In younger post-ICU patients, inability to return to work and prolonged periods of sedation are significant risk factors for depression. Patients should be monitored closely for signs and symptoms of depression in this setting, and pharmacologic and behavior therapy should be initiated when appropriate.

Anxiety Disorders. Anxiety disorders can slow the recovery of post-ICU patients. Rates of anxiety disorders in these patients have been as high as 25 percent two years after discharge.[26] Patients who had delirium during their ICU stay have shown decreased ability to remember facts about their stay at 18 to 24 months.[27] Studies confirm the association between delirium during hospitalization and amnesia.[28,29] The absence of factual memories about the hospitalization is associated with higher rates of anxiety and PTSD.[30] More progressive treatment for anxiety disorders in these patients includes tours of the ICU several months following discharge and psychotherapy focused on recalling factual memories.

Cognitive Impairment. Patients in the ICU are exposed to many different medications that can impair their memory recall, including opiates, benzodiazepines,

propofol (Diprivan), adrenaline, and steroids. Furthermore, depending on the severity of their illness, patients can experience transient hypoxemic episodes that may lead to memory impairment. Multiple studies have linked ICU hospitalization with impairments in memory, attention, and concentration up to nine to 12 months following discharge.[24,26,31] Thirty percent of post-ICU patients who had ARDS were still globally impaired at one year, and 78 percent were impaired in one or more domains.[26] These cognitive difficulties can have a major impact on quality of life after ICU hospitalization and may explain the relatively slow return to work in patients who were previously employed.

Sleep Disturbance. As a result of any of the previously mentioned psychological conditions, or independently, the ICU stay may lead to sleep disturbances, which can also contribute to ongoing fatigue.[7] Sleep disturbances are common in this patient group, and special attention should be made to patients following ARDS and use of mechanical ventilation, because these are likely independent risk factors.[32]

SOCIAL CONSIDERATIONS

Social considerations must be examined in post-ICU patients. Some patients respond to severe illness with avoidant behavior. Compared with men, women have a greater tendency toward social isolation after mechanical ventilation.[32] Forty-five percent of patients at six months reported going out less often.[6] Physicians should inquire about the patient's immediate family, specifically how they are coping with the patient's illness. PTSD symptoms have been found to be present in approximately 33 percent of family members of ICU survivors.[33] Risk factors for the development of PTSD among family members include the feeling that medical information was incomplete and that they did not sufficiently contribute to the medical decision making.[33] In response to a critical illness, the family may experience anxiety and depression that manifests as overprotective behavior. These feelings, coupled with unrealistic expectations that the patient may have of his or her capabilities, can lead to frustration and conflict.[30]

End-of-Life Issues

For years after discharge, post-ICU patients have higher mortality rates. Therefore, it is important for the primary care physician to address end-of-life issues with the patient, if not previously addressed. This should include ensuring that the patient has a documented health care proxy, in case the patient is unable to make decisions competently, and a living will.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Navy or the U.S. Naval Service at large.

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Author disclosure: Nothing to disclose.

REFERENCES

1. Angus DC, Carlet J. Surviving intensive care: a report from the 2002 Brussels Roundtable. *Intensive Care Med.* 2003;29(3):368-377.
2. Marque S, Cariou A, Chiche JD, et al. Risk factors for post-ICU red blood cell transfusion: a prospective study. *Crit Care.* 2006;10(5):R129.
3. Vincent JL, Baron JF, Reinhart K, et al., for the ABC Investigators. Anemia and blood transfusion in critically ill patients. *JAMA.* 2002;288(12):1499-1507.
4. Plank LD, Connolly AB, Hill GL. Sequential changes in the metabolic response in severely septic patients during the first 23 days after the onset of peritonitis. *Ann Surg.* 1998;228(2):146-158.
5. Jones C, Griffiths RD. Identifying post intensive care patients who may need physical rehabilitation. *Clin Intensive Care.* 2000;11(1):35-38.
6. Griffiths RD, Jones C. Recovery from intensive care. *BMJ.* 1999;319 (7207):427-429.
7. Eddleston JM, White P, Guthrie E. Survival, morbidity, and quality of life after discharge from intensive care. *Crit Care Med.* 2000;28(7): 2293-2299.
8. Jones C, Skirrow P, Griffiths RD, et al. Rehabilitation after critical illness: a randomized, controlled trial. *Crit Care Med.* 2003;31(10):2456-2461.
9. Bolton CF. Critical illness polyneuropathy and myopathy [published correction appears in *Crit Care Med.* 2002;39(4):953]. *Crit Care Med.* 2001;29(12):2388-2390.
10. Hund E. Neurological complications of sepsis: critical illness polyneuropathy and myopathy. *J Neurol.* 2001;248(11):929-934.
11. Nierman DM, Mechanick JI. Bone hyperresorption is prevalent in chronically critically ill patients. *Chest.* 1998;114(4):1122-1128.
12. Scalise P, Prunk SR, Healy D, Votto J. The incidence of tracheoarterial fistula in patients with chronic tracheostomy tubes: a retrospective study of 544 patients in a long-term care facility. *Chest.* 2005;128(6):3906-3909.
13. Koitschev A, Simon C, Blumenstock G, Mach H, Graumueller S. Surgical technique affects the risk for tracheostoma-related complications in post-ICU patients. *Acta Otolaryngol.* 2006;126(12):1303-1308.
14. Griffiths RD, Jones C. *Physical and Psychological Recovery. Intensive Care Aftercare.* Oxford, United Kingdom: Butterworth-Heinemann; 2002:125-130.
15. Quinlan J, Waldmann C, Fawcett D. Sexual dysfunction after intensive care [published correction appears in *Br J Anaesth.* 1999;82(1):159]. *Br J Anaesth.* 1998;81(5):809.

16. Griffiths J, Gager M, Alder N, Fawcett D, Waldmann C, Quinlan J. A self-report-based study of the incidence and associations of sexual dysfunction in survivors of intensive care treatment. *Intensive Care Med*. 2006;32(3):445-451.
17. Jeavons S. Predicting who suffers psychological trauma in the first year after a road accident. *Behav Res Ther*. 2000;38(5):499-508.
18. Schnyder U, Moergeli H, Klaghofer R, Buddeberg C. Incidence and prediction of posttraumatic stress disorder symptoms in severely injured accident victims. *Am J Psychiatry*. 2001;158(4):594-599.
19. Alexander DA. Psychological aspects of trauma. In: Greaves I, Porter KM, Burke D, eds. *Key Topics in Trauma*. Oxford, United Kingdom: BIOS Scientific Publishers; 1997:249-257.
20. Cuthbertson BH, Hull A, Strachan M, Scott J. Post-traumatic stress disorder after critical illness requiring general intensive care. *Intensive Care Med*. 2004;30(3):450-455.
21. Shalev AY, Peri T, Canetti L, Schreiber S. Predictors of PTSD in injured trauma survivors: a prospective study. *Am J Psychiatry*. 1996;153(2):219-225.
22. Kapfhammer HP, Rothenhäusler HB, Krauseneck T, Stoll C, Schelling G. Posttraumatic stress disorder and health-related quality of life in long-term survivors of acute respiratory distress syndrome. *Am J Psychiatry*. 2004;161(1):45-52.
23. Nelson BJ, Weinert CR, Bury CL, Marinelli WA, Gross CR. Intensive care unit drug use and subsequent quality of life in acute lung injury patients. *Crit Care Med*. 2000;28(11):3626-3630.
24. Richter JC, Waydhas C, Pajonk FG. Incidence of posttraumatic stress disorder after prolonged surgical intensive care unit treatment. *Psychosomatics*. 2006;47(3):223-230.
25. Griffiths RD, Jones C. Filling the intensive care memory gap? *Intensive Care Med*. 2001;27(2):344-346.
26. Hopkins RO, Weaver LK, Pope D, Orme JF, Bigler ED, Larson-Lohr V. Neuropsychological sequelae and impaired health status in survivors of severe acute respiratory distress syndrome. *Am J Respir Crit Care Med*. 1999;160(1):50-56.
27. Roberts B, Rickard CM, Rajbhandari D, et al. Multicentre study of delirium in ICU patients using a simple screening tool. *Aust Crit Care*. 2005;18(1):6-14.
28. Marshall MC, Soucy MD. Delirium in the intensive care unit. *Crit Care Nurs Q*. 2003;26(3):172-178.
29. Ely EW, Gautam S, Margolin R, et al. The impact of delirium in the intensive care unit on hospital length of stay. *Intensive Care Med*. 2001;27(12):1892-1900.
30. Jones C, Griffiths RD, Macmillan RR, Palmer TE. Psychological problems occurring after intensive care. *Br J Intensive Care*. 1994;2:46-53.
31. Jones C, Griffiths RD, Humphris G. Disturbed memory and amnesia related to intensive care. *Memory*. 2000;8(2):79-94.
32. Combes A, Costa MA, Trouillet JL, et al. Morbidity, mortality, and quality-of-life outcomes of patients requiring >or= 14 days of mechanical ventilation. *Crit Care Med*. 2003;31(5):1373-1381.
33. Azoulay E, Pochard F, Kentish-Barnes N, et al., for the FAMIREA Study Group. Risk of post-traumatic stress symptoms in family members of intensive care unit patients. *Am J Respir Crit Care Med*. 2005; 171(9):987-994.