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Long-term outcomes from critical care

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Abstract
With the improved survival of critical care patients, a cohort of chronically critically ill patients has emerged. These patients have a higher 5-year morbidity and mortality and greater utilization of healthcare resources. This well-documented deterioration in physical, cognitive and/or psychological health in critical care survivors is known as post intensive care syndrome (PICS) which has personal and socioeconomic implications not only for the patient, but also for their families, care givers and society. Greater awareness of the impact of critical illness on quality of life has led to the emergence of research focused on overall patient outcomes rather than crude survival. National guidelines state personal rehabilitation programmes involving a multidisciplinary team should be commenced within 4 days of admission and continued after discharge to the ward. Once discharged home specialist ICU follow-up clinics are key in identifying any long-term complications of critical care admission and should focus on all aspects of the PICS. COVID-19 has highlighted PICS on a national level with patients experiencing multiple long-term complications of critical illness, some as yet unknown.

Keywords Cognitive morbidity; critical illness; mortality; physical morbidity; psychological morbidity; quality of life; rehabilitation

Introduction
Over 150,000 patients are admitted to critical care each year in the UK, and in the 5 years after admission this group have a higher morbidity and mortality compared with age-matched controls.1 The purpose of critical care is to support individuals through their acute illness to allow them to return to their pre-admission lifestyle and functional status. However, leaving critical care is only the start of the recovery process which may take months or years of rehabilitation with some symptoms persisting at 5 years.2

With advances in critical care, a group of chronically critically ill patients have emerged who would historically not have survived the acute episode. This group tend to have longer critical care and hospital length of stay (LOS), with serious lasting physical, cognitive and psychological problems and a greater dependence and healthcare utilization following discharge from hospital.1,3 This well-documented deterioration in physical, cognitive and or psychological health in critical care survivors is known as post intensive care syndrome (PICS).4 It is thought up to half of all patients in critical care will experience PICS, with some recovering quickly and others having long-term sequelae.

PICS has personal and socioeconomic implications not only for the patient but for their families, care givers and society.

The ongoing COVID-19 pandemic has highlighted PICS and the complex rehabilitation needs for people with severe illness and long ICU stays. It has also highlighted gaps in funding and provision of many services essential to this.

Physical
Physical complications following an episode of critical illness are often under recognized by healthcare professionals and under reported by patients.

After what may be considered a short ICU admission (greater than 4 days), national guidelines for the provision of critical care recommend the patient has access to an intensive care follow-up programme 2–3 months post discharge.5 Critical care follow-up clinics form part of a series of national recommendations to monitor and support patients return to their pre-admission health. However, within the financial constraints placed upon the modern day NHS this is not always feasible and the availability of allied health professionals such as clinical psychologists and occupational therapists can be lacking in areas.

Airway
Laryngeal pathology is common after prolonged intubation. Inflammation from the endotracheal tube (ETT) can cause vocal cord damage and the formation of scar tissue can lead to vocal changes, stridor and susceptibility to upper airway obstruction.

Tracheal stenosis may occur in up to 30% patients who undergo tracheostomy insertion. This is often related to pressure damage from the tracheostomy tube cuff distal to the stoma. Laser treatment and tracheal stenting at a later date may be required in severe cases.6

Tracheomalacia occurs following ischaemic injury to the tracheal wall causing damage to the cartilage that provides the structural integrity of the trachea. Potential risk factors include recurrent infection, prolonged invasive ventilatory support or tracheostomy with their associated mucosal friction and inflammation. Symptoms are often absent but may develop due to tracheal collapse on expiration and can include stridor, persistent cough, sputum retention and exertional dyspnoea. Respiratory failure of unknown cause after de-cannulation or extubation should lead to a high index of suspicion of tracheomalacia.

Respiratory
Long-term respiratory dysfunction has been reported in a significant proportion of patients requiring invasive ventilation during their critical care stay. Prolonged exertional dyspnoea and failure to return to pre-admission baseline is seen in a number of patient groups. This often reflects severity of illness, number of organ failure and the degree of pre-morbid comorbidities.

In high-risk patients with severe acute respiratory distress syndrome (ARDS), respiratory function can be impaired for 2–5 years following hospital discharge with some evidence of prolonged impairment in functional status extending beyond 5 years.7 Thoracic computed tomographic imaging of survivors of ARDS commonly shows minor fibrotic changes in non-dependant areas of the lung.8 This structural change is reflected in
pulmonary function tests with abnormal lung volumes and reduced 6 minute walk tests, 70% of which remain abnormal at 1 year.7

In addition to parenchymal damage, respiratory impairment can be related to diaphragmatic and respiratory muscle weakness associated with ICU-acquired weakness.

Cardiovascular

Arterial line placement for monitoring and blood sampling is both common and often prolonged during an ICU admission. The most common site of arterial catheter placement is the radial artery. Complications in the short term can include limb ischaemia occurring due to embolic phenomenon from line placement in end arteries, e.g. commonly the brachial artery, requiring embolectomy. Rarer sequelae include pseudoaneurysms and cosmetic scarring at insertion sites along with numbness, neuropathic pain and local tenderness. These are of particular relevance when occurring in the dominant upper limb of the patient.

Central venous catheters can be associated with serious complications such as catheter-related blood stream infection, sepsis and ensuing organ dysfunction, in addition to infections local to the catheter site such as endocarditis.

Repeated central venous catheter placement may predispose to venous stenosis and/or thrombosis. The resultant impaired venous drainage can cause limb oedema and further vessel stenosis leading to potential difficulty with future line placement. These are particularly important if vascular access is required, or the formation of an arteriovenous fistula anticipated, for long-term dialysis.

Gastrointestinal

Weight loss and muscle wasting are common during a period of critical illness despite the provision of early nutritional support. Problems during admission with abnormal functional swallowing, ileus and malabsorption can persist after discharge from ICU and enteral feed or calorie supplementation may be required for a prolonged period of time after hospital discharge.

Patients can also be troubled with anorexia, nausea and altered taste that can make eating unappealing and onerous, affecting the individual’s ability to sustain adequate nutritional intake. The symptoms generally resolve with time but can be quite distressing and have a negative impact on quality of life.

Genitourinary

Sexual dysfunction is a frequent problem after a critical illness and is under-reported due to the sensitive nature of the issue. This clearly impacts on patients and the intimacy of their relationships to differing degrees but can contribute to ongoing psychological difficulties associated with recovery. The cause of this can be multifactorial and is often related to medications started during admission, surgery or procedures during treatment and the psychological impact of the acute events. National guidelines stipulate patients should be questioned about return of sexual health during follow-up clinics, and referral to specialist healthcare services as required.5,9

Patients with acute kidney injury (AKI) requiring renal replacement therapy (RRT) are known to have higher in-hospital mortality and morbidity. Schiødt et al. reported an overall in-hospital mortality in this group of 47% with mortality rates at 10 years as high as 80%.6 AKI in ICU is also a risk factor for the development of chronic renal impairment at a later date.

Musculoskeletal

Loss of muscle mass in critical illness

In critically ill patients, over 15–20% of total muscle mass can be lost by the end of the first week of the ICU admission, with a greater proportion of muscle lost by those with escalating organ failure. Patients with greater pre-existing muscle reserve will have a better outcome but will never return to age-matched base line or premorbid state. This is because muscle repaired following critical illness may not be of comparable quality, with higher fat and water content. Even with multimodal therapy to restore or increase muscle bulk, aerobic capacity may still fail to recover to the individual’s baseline status.

Despite early proactive physiotherapy, flexion contractures can occur and are common in patients who have a prolonged stay or those with neuromuscular diseases. This impacts on future rehabilitation potential and ability to return to work.

Intensive care unit acquired weakness

ICU acquired weakness (ICU-AW) is the most common form of physical impairment seen in ICU survivors.10 It is a group of disorders which encompasses patients with ill-defined weakness and poor mobility along with those with critical illness myopathy (CIM), polyneuropathy (CIP), and combined CIM/CIP. Clinically, patients demonstrate global limb weakness, more pronounced in the proximal muscle groups, e.g. shoulders and hips and it also affects respiratory muscles which can impede weaning from mechanical ventilation.10 This is often seen in patients who have had a protracted stay, requiring prolonged sedation and liberal use of neuromuscular blockers, all reflecting increased illness severity. It continues to be an important contributor to reduced quality of life in patients with severe ARDS who were followed up for 5 years.7 Muscle weakness and functional impairment were frequently observed at 1 year, and recovery from physical dysfunction was incomplete even 5 years after discharge.

Early mobilization of patients while in ICU is a term used to describe passive and active mobilization within 72 hours of ICU admission, applied to those with most severe respiratory failure. The purpose is to preserve muscle function and limit muscle wastage related to immobility with the intention of reducing the burden related to loss of muscle function. It also encourages the use of minimal sedation which further contributes to a reduction in delirium and ICU acquired weakness.11 The principle of early mobilization in critical care is embedded in critical care units across Europe and the USA.

Contractures

Joint contractures can develop after prolonged immobility, despite rehabilitation. The most commonly affected joints are elbows and ankles with knees and hips also affected. Passive movements as part of daily physiotherapy and the use of splints are aimed at reducing the frequency of severe contractures in
Dermatological

Skin disease can be a primary reason for admission to ICU or can occur as part of multi-organ failure during admission. Pressure damage can result from prolonged mechanical ventilation, immobility, decreased perfusion to skin and vasopressor usage. Necrosis to peripheries and from excessive vasoconstriction can also lead to loss of part or whole digits or limbs.

Any skin damage during the acute phase is further exacerbated by ongoing reduced mobility during the rehabilitation process and discharge from hospital. Poor wound healing and soft tissue infections can be exacerbated by poor nutrition and be accompanied by hair loss and troublesome dry skin for months after discharge from ICU.

Cognitive

Difficulty with memory, concentration, attention and higher functioning are commonly reported following an episode of critical illness. These are necessary for return to independent living, employment and overall quality of life. Studies show cognitive deficits occur in both the young and the elderly and are persistent at 12 months with 34% and 24% patients recording cognitive scores consistent with moderate traumatic brain injury and mild Alzheimer’s disease, respectively. This may be first encountered by secondary healthcare providers, family members, primary care services or highlighted at ICU follow-up clinics.

Although youth does not protect against ICU-acquired cognitive deficits, the elderly are at higher risk. In elderly patients admitted with severe sepsis a fourfold increase in post-ICU moderate to severe cognitive impairment lasting up to 8 years was seen. This has significant implications when considering the aging demographic of patients admitted to critical care.

Studies have suggested increased duration of delirium during the ICU stay is independently associated with both worse global cognition and executive function at 3 months. For those who recover cognitive function, an ongoing elevated long-term risk of cognitive impairment exists, being greatest in the elderly patients and those with mild cognitive impairment pre-admission.

Psychological

Psychological sequelae after critical illness are common and can manifest as depression, anxiety and post-traumatic stress disorder (PTSD). These conditions are directly linked to events during a critical care admission, including episodes of delirium (both hypo and hyperactive), poor sleep hygiene, sedative duration and type with benzodiazepine use being associated with increased delirium risk. Often these symptoms can settle with time but input from clinical psychology may be required. Psychological and emotional dysfunction may be present in both patients and caregivers for up to 5 years after discharge from the ICU, demonstrating a significant impact on quality of life.

Patients can also experience delusional memories which can manifest as hallucinations and nightmares after discharge. Patient diaries involving pictures and written entries by staff and family members/friends are now encouraged to document events during admission. Research has shown that patients and relatives generally find a diary valuable in making sense of their intensive care experiences. In addition, studies have shown that receiving an ICU diary reduces the risk of developing depression, anxiety and PTSD for both patients and relatives.

Rehabilitation after critical illness

All patients at risk of morbidity have their rehabilitation goals agreed within 4 days of admission or prior to discharge from critical care, whichever is sooner. An individualized, structured rehabilitation programme should be commenced as early as clinically possible by allied healthcare professionals who document short-term and medium-term rehabilitation goals and review progress frequently. This rehabilitation programme should involve both patients and family members from the outset and follow them through their journey of recovery from critical care, to the ward and into the community. Information gathered from the multidisciplinary rehabilitation after critical illness (Raci) team should prepare both the patient and family and other caregivers for the challenges ahead. Recovery can be a protracted and frustrating process and patients frequently feel abandoned and anxious when they are stepped down to ward level care and discharged home.

Studies measuring the efficacy or cost effectiveness of Raci teams have been unable to determine a beneficial effect on functional exercise capacity and health-related quality of life interventions initiated after ICU discharge. Patients with intensive nurse-led rehabilitation had the same outcomes as the control groups, but overall felt they had received a better service and had a point of contact for problems after discharge. However valuable patients find the service, in the financially austere climate services such as Raci are vulnerable to funding cuts.

The National Post-Intensive Care Rehabilitation Collaborative has recently released a framework for assessing early rehabilitation needs following critical care. This document aims to provide a unified approach to Raci for COVID-19 patients and ultimately all critical care patients beyond the pandemic. The use of screening tools and rehabilitation prescriptions can be used to identify individual patients specialist needs for inpatient and community rehabilitation.

Patient recovery support groups

ICUsteps is a charity founded in 2005 by ex-patients, their families and ICU staff to help patients recover from critical illness. The groups provide a support network for patients affected by critical illness and promote recognition of the physical and psychological effects.

Although this is run entirely by volunteers, it is a valuable tool to help people come to terms with this life-changing event. They are also advocates for patient diaries during their stay in ICU as they have seen first-hand the impact they can have on recovery.
The true cost of critical illness

Thus far the article has focused on the physical and psychological sequelae of critical illness on the individual. However, the true long-term consequences of critical care are wide reaching affecting the individual, family unit, social and healthcare economics of a country.

There is limited evidence evaluating the long-term socioeconomic impact of critical care on patients and their families. In 2013 Griffiths et al. conducted a prospective UK study to quantify the impact of critical illness among 300 patients who required ventilatory support for greater than 48 hours at 6 and 12 months after critical care discharge. The group used self-reporting questionnaires to compare pre and post critical care health, economics and quality of life. The authors found over 20% of patients still required help with activities of daily living (ADL) at 12 months, with 26% requiring greater than 50 hours per week. In 80% of cases care assistance was provided by family members, resulting in major adjustments to care providers working lives.1

In this study cohort, nearly 50% of patients were retired and 40% employed before critical care admission. Among the latter, 30% suffered a negative impact in their employment status (i.e. early retirement, reduction in hours or unemployment). This persisted at 12 months and was associated with a 33% reduction in family income and an increase in state financial support. In the group of patients requiring care assistance at 12 months, 30–40% had to spend savings, borrow money, re-mortgage or sell their home or look to charity organizations to pay for care provision.

COVID-19

The COVID-19 pandemic brought critical care into national focus with a sudden and rapid rise in the number of people requiring hospitalization and intensive care. The full extent of problems arising from COVID-19 infection remains unclear and are likely to be complex and variable encompassing all organ systems discussed previously. Survivors of previous Coronavirus outbreaks (SARS and MERS) have demonstrated a reduced health-related quality of life at 6 months and beyond, with key areas being impaired exercise tolerance and psychological problems.17,18

Conclusion

In the last 10 years a shift has occurred in critical care philosophy, moving away from the use of the crude binary end point of survival as a measure of the success of critical care. As patients have survived we have learnt the significant and long lasting impact of critical care and the importance of providing meaningful survival with a quality of life that is acceptable for the individual. Observing and working with patients and their families along their path of recovery there has been an evolution in critical care practice, the development of critical care follow-up clinics, the introduction of national guidance for rehabilitation in critical care and rehabilitation after critical illness teams. COVID-19 has further highlighted the sequelae of long-term complications and the need for a robust rehabilitation and mental health service to assist in the journey of critically ill patients.
14 Pandharipande PP, Girard TD, Jackson JC, et al. Long-term cognitive impairment after critical illness. *N Engl J Med* 2013; 369: 1306–16.

15 Responding to COVID and Beyond: framework for assessing early rehabilitation needs following treatment in intensive care. Available from: https://bit.ly/ICSRehab.

16 ICUsteps. The intensive care patient support charity. Available from: http://www.icusteps.org.

17 Wade DT. Rehabilitation after COVID-19: an evidence-based approach. *Clin Med Jul* 2020; 20: 359–65. https://doi.org/10.7861/clinmed.2020-0353.

18 Ahmed H, Patel K, Greenwood D, et al. Long-term clinical outcomes in survivors of coronavirus outbreaks after hospitalisation or ICU admission: a systemic review and meta-analysis of follow-up studies. Medrxiv, 2020; 2020. 04.16.20067975.