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Strategies to combat chronic critical illness

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Abstract

Purpose of review—The population of chronically critically ill patients is growing as advances in intensive care management improve survival from the acute phase of critical illness. These patients are characterized by complex medical needs and heavy resource utilization. This article reviews evidence supporting a comprehensive approach to the prevention and management of chronic critical illness (CCI).

Recent findings—The most efficient approach to weaning patients with CCI at long-term acute care hospitals is daily unassisted breathing trials through a tracheostomy collar. However, a substantial number of patients transferred to long-term acute care hospitals pass their spontaneous weaning trials. Transfer to long-term acute care hospitals is associated with higher acute care costs and payments, but lower costs through the entire episode of illness. Universal decontamination is more effective than targeted decontamination or screening and isolation for preventing nosocomial bloodstream infections.

Summary—Combating CCI begins with prevention in the acute phase of illness. Management strategies include a spectrum of ventilatory, nutritional, and rehabilitation support. Further patient-centered outcome-based research in this specific population is needed to continue to help guide optimal care.

Keywords

chronic critical illness; intensive care; multiorgan failure; prognosis; prolonged mechanical ventilation

INTRODUCTION

Chronic critical illness (CCI) is defining an increasing number of patients who are receiving treatment in the ICU. CCI is a disease state ultimately resulting from our advanced therapies for acute critical illness, leaving some patients with persistent multisystem organ dysfunction [1]. For most patients, this may not be a preventable state, but reflects advances in acute resuscitation and support in critical illness, where short-term mortality continues to decrease and high morbidity states are increasingly prevalent. For other patients, iatrogenic

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Conflicts of interest

There are no conflicts of interest.

complications and failure to prevent them can contribute to CCI. This article will review important strategies to decrease the incidence of CCI and reduce the burden of CCI for patients who are affected (Table 1).

WHAT IS CHRONIC CRITICAL ILLNESS?

Patients with CCI are a population who have survived acute critical illness or injury, but have persistent organ dysfunction leading to prolonged intensive care needs. They are a heterogeneous group of patients for which a universal definition has not yet been agreed upon. Many definitions include the need for prolonged mechanical ventilation (PMV). This has many advantages as PMV is a common requirement for the CCI patient, is easy to track in cohorts, and is of interest to hospital administration and payers as these are patients with substantial hospital costs [2,3]. The actual period that defines PMV is debatable. A consensus conference determined that at least 21 days of mechanical ventilation qualifies as PMV, whereas a current Medicare definition uses 96 h [4–6]. One group uses the term prolonged acute mechanical ventilation (PAMV) to represent patients who require at least 96 h of ventilation [7]. But CCI is a syndrome that, in addition to PMV, usually includes profound weakness, malnutrition, anasarca, prolonged brain dysfunction, and extreme symptom burden. Not all patients ventilated for 96 h have yet developed this phenotype. Placement of a tracheostomy for PMV may be an appropriate inclusion criterion for CCI as tracheostomy placement indicates the care team feels the patient is not going to die or be liberated from mechanical ventilation in the near future [1]. A useful administrative definition was validated that combines tracheostomy placement for PMV and ICU length of stay of at least 21 days [8]. For the clinician, a precise definition is less important than recognition of the physical syndrome with adjustment of practices to meet the unique needs of the CCI patient.

KEY POINTS

- CCI is a difficult-to-define yet increasing syndrome in critical care, and physicians must be prepared to manage this complex patient population.
- Prevention strategies for CCI are anchored in systematic evidence-based practices in the acute setting for ventilator management, limitation of sedation, mobility, and infection prevention.
- A multifaceted, multidisciplinary approach encompassing ventilator, nutritional, and rehabilitation support is required to care for chronically critically ill patients with a focus on patient-centered care.
- Future studies should focus on comparing specific strategies and protocols tailored to the unique physiology of CCI.

COST AND OUTCOMES

Of mechanically ventilated patients in the ICUs, 5–10% develop CCI depending on the definition [2]. This total number of CCI patients is projected to more than double in the next decade, resulting in up to 605 898 cases in 2020 [9]. Hospital operating costs for CCI patients amount to over \$12.6 billion annually, with substantial additional costs associated with care following hospital discharge [3,10]. Another important but difficult to quantify cost of CCI is caregiver/family cost. Indirect costs such as transportation, hotels, and food along with lost days of work should not be overlooked. One-year survival for CCI is between 40 and 50% based upon inclusive cohort studies [11,12[■],13]. Because of persistent physical limitations and high care needs, patients who survive their acute hospitalization spend much of their time in other institutions including long-term acute care (LTAC) hospitals or other designated weaning facilities, inpatient rehabilitation facilities, or skilled nursing facilities (SNFs). Patients experience a median of four transfers of care, and they spend over 70% of their days alive during the year in institutionalized care. Only 10% of CCI patients are alive and functionally independent at home after 1 year [14].

PREVENTION AND MANAGEMENT OF CHRONIC CRITICAL ILLNESS

A comprehensive, multidisciplinary approach is required in the prevention and management of CCI.

Mechanical ventilation

The acute respiratory distress syndrome (ARDS) and its associated causes are the most common conditions associated with CCI. Evidence-based management strategies including protective lung ventilation [15] and conservative fluid management [16] are associated with not only improved survival but also fewer ventilator days and ICU days for survivors. Strategies that reduce the incidence of ARDS, such as sepsis bundles and restrictions on transfusions, can also reduce ICU stays [17]. Combining daily awakening trials with daily spontaneous breathing trials (SBTs) is another management principle that both improves survival and reduces ICU stays [18].

Liberating the CCI patient from mechanical ventilation is a special challenge, but the approach is not very different from managing the acutely ill patient. The focus should be on reversing underlying causes of hypoxemia and ventilator failure while daily SBTs are attempted. A recent randomized controlled trial published by Jubran *et al.* [19[■]] compared a pressure support-based weaning protocol with daily unassisted breathing trials through tracheostomy collars in CCI patients at an LTAC hospital. Initially, patients were screened with a SBT. Patients who failed the SBT within 120 h were randomized to pressure support ventilation with systematic reductions as tolerated versus increasing tracheostomy collar time during the day with full ventilator support at night. Thirty-two percent of patients passed the SBT, suggesting that adequate attempts to wean a substantial number of patients at the referring acute care ICUs were lacking. Eligible patients randomized to the tracheostomy collar group weaned in 15 days compared with 19 days in the pressure support group ($P = 0.004$). Mortality did not differ between the groups, with enrolled mortality 46% at 6 months and 55% at 1 year [19[■]]. Most of the difference was accounted for by the

subgroup who failed their SBT between 12 and 120 h. The optimal approach for weaning patients who fail their SBT in less than 12 h is not made clear by this study, but, given their lower physiologic reserve, a more aggressive search for reversible causes of failure is indicated.

ICU-acquired weakness

ICU-acquired weakness (ICUAW) is a well-recognized complication of critical illness that is thought to stem from both muscle and nerve abnormalities –critical illness polyneuropathy (CIP) and critical illness myopathy (CIM) [20,21]. While its role in long-term functional disability has not been adequately defined, it clearly contributes to disability in the CCI patient. In one study of patients requiring at least 28 days of ventilation, neurophysiologic evidence of chronic partial denervation of muscle consistent with previous CIP can be found up to 5 years after ICU discharge in more than 90% of patients [22]. Several risk factors that are common in CCI contribute to ICUAW, including prolonged immobility, hyperglycemia, systemic inflammation, and multiple organ dysfunction [20,23]. Mitochondrial dysfunction contributing to diaphragmatic weakness and functional limitation has been proposed as one pathophysiologic explanation for ICUAW [24]. The role of systemic corticosteroids in ICUAW remains unclear, but exposure should be minimized until future studies provide clarification [21]. Tight glycemic control as a means to combat ICUAW is controversial, but insulin therapy to main glucose levels between 150 and 180 mg/dl is recommended in both the acute and chronic phases of critical illness [21,25[■]]. Another proposed intervention to reduce ICUAW is early and continued mobility in the ICU. Recent literature has shown that early mobility is safe, and decreases ICU and possibly hospital length of stay without increasing costs [26,27[■]]. Coordination between nurses and physical and respiratory therapists is the key to initiate a successful mobility program for critically ill patients. The benefit of continued mobility for CCI patients is yet to be studied, though intuitively it has been felt to be beneficial. This has long been a cornerstone of the multidisciplinary rehabilitation approach to care that characterizes the long term acute care hospital (LTACH) model.

Nutrition and metabolic support

Intensive metabolic support (IMS) is a term coined to describe metabolic control with insulin therapy, early and consistent nutrition support, and nutritional pharmacology in critically ill patients [28]. Although strong evidence is lacking, it is thought that focusing on metabolic support may help reverse the pathophysiology associated with CCI. Malnutrition is reported in up to 43% of critically ill patients, which is associated with increased morbidity and mortality, infection rates, length of ICU stay, poor wound healing, and muscle weakness [29]. Therefore, a thorough nutritional assessment should be performed by a qualified provider to form the optimal nutrition plan including caloric, protein, electrolyte, and vitamin and mineral support.

Data support the use of enteral nutrition in critically ill patients with a functioning gastrointestinal tract. A recent study revealed that nasojejunal versus nasogastric feeds in mechanically ventilated patients did not improve nutritional targets [30[■]]. The timing of enteral and parenteral nutrition therapy has been a topic of recent clinical trials. The ARDS

Clinical Trials Network published the EDEN trial, finding no significant differences in mortality or ventilator-free days between enteric full and trophic feeds for up to 6 days in patients with ARDS [31[■]]. In a follow-up study, they reported that ARDS patients have substantial physical, psychological, and cognitive impairments, reduced quality of life, substantial need for institutional care and impaired return to work, but mean physical function and survival at 12 months were not affected by initial trophic versus full feed [32[■]].

A recent randomized trial has shown that adding parenteral to enteral to accomplish 100% of nutritional goals in mechanically ventilated patients from day 3 to 8 in the ICU showed a decrease in later (days 9–28) nosocomial infections (27 versus 38%, respectively); however, this was not statistically significant. There was no change in time on mechanical ventilation, ICU and hospital length of stay, or ICU and hospital mortality [33[■]]. These studies address early nutrition in the acute phase of critical illness. Data for optimum calorie delivery in CCI patients are lacking, largely because few investigators would consider that underfeeding patients for weeks would be beneficial. However, overfeeding may be more common than underfeeding and is similarly undesirable with increased infectious complications, liver dysfunction, and increased mortality [34]. Therefore clinical trials of effective nutrition assessment and delivery strategies are needed for the CCI population.

Another metabolic complication of CCI is hyper-resorption of the skeleton marked by elevated osteoclast activity. A study by Via *et al.* [35] showed that a single intravenous dose of a bisphosphonate had a measurable transient effect in osteoclast activity in patients with CCI. Studies of longer-term therapy and outcomes are worth exploring further.

Cognitive impairment and mental health

Brain dysfunction is a frequent complication of critical illness, resulting from a myriad of insults such as toxic or metabolic derangements, ischemic or traumatic brain injury, or as side effects of medications, especially sedating agents commonly used in the ICU [36]. It can manifest as coma or delirium, and, when measured in CCI patients after transfer to facilities specializing in CCI, incidence has been shown to be 17–70% initially, whereas long-term occurrence is 40–74% [37–41]. It is known that 20–80% of ICU survivors at 1 year have long-term cognitive impairment, and there may be a relationship between acute delirium and long-term impairment [37]. Most important in management of delirium is to evaluate for a cause that is modifiable in any acute mental changes including infection, hypotension, electrolyte imbalance, hypoxia, and sedating medications [36]. Depression and post-traumatic stress disorder are very common in CCI patients [41,42]. Denehy and Elliott [43] point out the challenges of screening and treating mental health issues such as depression, anxiety, and sleep disturbances in the critically ill. This is obviously an important issue to address in CCI patients and will need the support of the entire care team in management.

Nosocomial infections

Chronic critical illness patients have a host of indwelling devices (urinary catheters, endotracheal or tracheostomy tubes, nasogastric tubes, intravenous catheters) often for a prolonged time that put them at a daily risk for nosocomial infections. Additionally, they

reside in environments in which frequent multidrug-resistant organisms (MDROs) exist. One study of LTACH admissions found 69% of patients were colonized with at least one MDRO [44]. Diminished immunological and physiologic reserve following severe sepsis, referred to as ‘immune exhaustion’, is another proposed mechanism that puts CCI patients at risk [45]. Additionally, many CCI patients have pre-existing comorbid conditions such as hepatic failure, renal failure, or malignancy that predispose them to decreased immune function [46].

It is important to continue prevention strategies for nosocomial infections throughout the CCI patient’s hospitalization. The infection with the highest associated mortality rate is catheter-associated bloodstream infections (CABSI). Systematic prevention strategies are well proven and should be in place in both the acute ICU and LTAC settings [47]. Similar systematic prevention strategies for ventilator-associated pneumonia are also important to reduce morbidity and length of stay [48]. Catheter-associated urinary tract infections (CAUTIs) are common in CCI as the urinary catheter rate in CCI patients is high. Staff education in basic infection control and minimizing use of urinary catheters have been shown to reduce the rate of CAUTIs in hospitalized patients [46]. In a recent review, Cabrera-Cancio [46] suggests a combination of judicious use of antibiotics (antimicrobial stewardship) to help decrease rates of MDRO and *Clostridium difficile*, surveillance cultures to guide isolation practices, family/patient education, and strict housekeeping protocols to decrease incidence of nosocomial infections in the CCI. A recent cluster randomized trial of ICUs revealed that universal decontamination using 5 days of twice-daily intranasal mupirocin and daily bathing with chlorhexidine-impregnated cloths was more effective than targeted decontamination or screening and isolation of colonized patients in reducing rates of methicillin-resistant *Staphylococcus aureus* clinical isolates and bloodstream infections of any type [49[■]].

PATIENT-CENTERED CARE

Eliciting patient values and preferences, often through early structured conversations with proxy decision makers, remains important to provide a level of care that meets the wishes of patients with CCI. Most patients do not have identified proxy decision makers or signed advance directives [50], which necessitates early and frequent conversations with families and caregivers regarding patient wishes, thresholds for continuation or discontinuation of life-prolonging therapies, open and honest communication about nature and location of eventual discharge (if likely), and preparedness planning for both performing interventions (e.g. hemodialysis and enteral feeding) and potentially stopping them. This occasionally requires the services of consultative palliative care teams for complex clinical and psychosocial situations [51]. CCI patients are a heterogeneous group; thus, being able to distinguish between high and low-risk patients would be helpful both for the care team and family/ decision makers. The ProVent score was developed as a mortality prediction model using four clinical variables (age, platelet count, requirement for vasopressors, and hemodialysis) on day 21 of mechanical ventilation to identify patients at high and low risk of mortality [12[■]], and can be used to guide families and the care team in their discussions. Written information regarding CCI is available for families [52], as are tools to evaluate the satisfaction of communication perceived by families [53]. An innovative decision aid to

assist with communication of prognosis and goals of care is currently being studied in a multicenter randomized trial [54[■]].

VENUES OF CARE

Management of CCI is complex and requires a fully integrated interdisciplinary team (Fig. 1), but this rehabilitation approach can be implemented in sites other than an acute ICU for stable patients. Deciding if, where, and when to transfer care of a CCI patient is a regular challenge for the critical care team, assuming transfer options are available. LTAC hospitals are an option in some regions in the US [55,56[■]]. Kahn *et al.* describe outcomes of Medicare beneficiaries with CCI who are discharged to LTACs. Out of 234 799 CCI patients, 48 416 (20.6%) were discharged to an LTACH. In an adjusted analysis, no association was found between LTACs and 1-year survival. The 180-day hospitalization-related costs were lower for patients who spent time in an LTAC, but actual Medicare payments were higher. A similar finding was noted in a large centers for Medicare and Medicaid services (CMS)-funded study [10]. The authors conclude that LTAC transfer shows a potential for cost-saving if payment models are re-evaluated by policy makers [57[■]]. There is significant regional variation in LTAC availability in the US, and there is also variability in utilization of LTACs in regions where they are available [58[■]]. Free standing weaning facilities are less common outside the US, although this model is being explored in a number of European countries with projections of cost-savings [59–61]. Other options include keeping CCI patients in the acute care ICU with specialized consultation [62], or transferring to a step-down unit or a hospital-based respiratory care unit (RCU). The best option will vary by patient and family circumstances and local resources.

CONCLUSION AND FUTURE DIRECTIONS

Combating CCI begins with prevention efforts, including systematic application of evidence-based practices in acute critical care settings, such as early goal-directed therapy, lung protective ventilation, daily awakening and SBTs, early mobility, and prevention of nosocomial infections. Management of CCI requires ventilator, nutrition, and rehabilitation strategies tailored to the unique physiology of CCI. Research is needed to better define physiologic differences so that CCI-specific clinical protocols can be developed and compared [63]. Further innovations to improve shared decision-making for CCI patients and their families are also needed.

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- ■ of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 518).

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FIGURE 1.
The chronic critical illness 'core' team.

Table 1**Management of chronic critical illness**

Type of support	Management principles	Barriers/challenges	Potential future research
Mechanical ventilation	Prevents CCI with lung protective ventilation, conservative fluid management, daily awakening, and SBTs Weaning with SBTs and rests with full ventilator support	Patients cared for in a variety of settings (ICUs, LTACHs) with various weaning strategies	Identifying risk factors for requirement of PMV
Functional recovery	Prevent hyperglycemia with insulin infusions if necessary Early mobility is safe and effective in critical illness	Early mobility must be accepted and promoted by all facets of the critical care team to be feasible	Effect of aggressive mobility on long-term functional outcomes
Nutritional and metabolic support	Both underfeeding and overfeeding have been linked with detrimental results in CCI EN over PN currently favored	Favored route, EN, often difficult to provide 100% nutrition needs with unclear long term effects in CCI Difficult to calculate nutrition and metabolic needs in the CCI population	Long-term effects of different feeding strategies Identify other nutritional supplements for improved functional outcomes
Cognitive and mental health	Minimize sedating medications while preventing/treating delirium and pain	Distinguishing agitation, delirium and pain is difficult and there are no proven therapies for delirium	Identifying long-term cognitive effects of CCI Develop targeted therapies directed at brain dysfunction in CCI
Nosocomial infection	Adhering to prevention strategies with VAP bundle sets and CVC insertion checklists Remove/reduce use of indwelling devices Consider nasal and skin decontamination in addition to isolation	CCI patients are medically complex, requiring many interventions putting them at risk for infection	Establishing uniform isolation and decontamination practices for CCI Identifying strategies to decrease antibiotic use in CCI patients Determine if rates of infection change between type of care facility (LTACH versus ICU)
Patient-centered care	Solicitation of patient values and preferences, starting at admission Frequent communication with decision makers, using multiple modalities for education Incorporation of consultative palliative care (and other complementary) services when complex needs arise	Caregivers and decision makers are often intermittently available, necessitating need for scheduled, regular conferences for information updates and decision making	Understanding how decision makers' values and preferences change throughout the ICU stay Investigate best practices for providing information and giving recommendations for care that are feasible and acceptable to caregivers

CCI, chronic critical illness; CVC, central venous catheter; EN, enteral nutrition; LTACH, long term acute care hospital; PMV, prolonged mechanical ventilation; PN, parenteral nutrition; VAP, ventilator associated pneumonia.