World Medical and Health Policy

A Call for the World Health Organization to Create International Classification of Disease Diagnostic Codes for Post-Intensive Care Syndrome in the Age of COVID-19

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Post-intensive care syndrome (PICS), a condition found in survivors of critical illness, is characterized by persistent physical, cognitive, and psychological sequelae that impact the quality of life after discharge from an intensive care unit (ICU). At present, there are no International Classification of Disease (ICD) billing codes for this condition. Without financial alignment, clinicians cannot diagnose PICS, hindering tracking of its prevalence and impeding policy development for this condition. Clinicians should be screening for PICS in all survivors of critical illness, particularly those with acute respiratory distress syndrome (ARDS). Results from single-center studies suggest over 75 percent of ARDS survivors develop PICS. With nearly 5 percent of patients with COVID-19 requiring ICU admission for ARDS, it is important for clinicians to be able to diagnose PICS in survivors, and researchers to be able to track it. Member states should impress upon the World Health Organization to create ICD-10 codes for PICS.

KEY WORDS: post-intensive care syndrome, acute respiratory distress syndrome, COVID-19, cognitive impairment, anxiety, depression, ICD-10, World Health Organization

Introduction

Increasingly, clinicians have begun to recognize a cluster of concerning symptoms in patients who survive an intensive care unit (ICU) admission. Despite overcoming the stressors of critical illness, survivors are often left living with physical, cognitive, and psychological sequelae experienced weeks to months after their discharge. These aftereffects profoundly impact survivors' quality of life long after their discharges from ICUs (Mikkelsen et al., 2012; Sidiras et al., 2019). Dr. Derek C. Angus, an internationally-recognized sepsis researcher, described these sequelae as "a hidden public health disaster" (Angus, 2010, p. 1833).

In 2010, at a stakeholder's conference convened by the Society of Critical Care Medicine (SCCM), the symptom cluster was named post-intensive care syndrome (PICS) (Needham et al., 2012). The SCCM defined PICS as "new or worsening impairment of cognition, mental health, or physical function after critical illness and persisting beyond the acute care hospitalization" (Needham et al., 2012, p. 505). The prevalence of PICS is poorly understood because, at present, the International

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Classification of Diseases-10 (ICD-10) diagnostic codes do not exist for this condition. The lack of ICD-10 codes is hindering epidemiologic investigation of this condition. Without these codes, it is difficult to determine which survivors developed this condition and to track their clinical course.

Critical care and primary care clinicians and researchers worldwide recognize the existence of this condition, and are growing increasingly concerned inadequate attention is being directed to timely identification of PICS and rehabilitative efforts to address long-term impairments after critical illness (Busico et al., 2019; Colbenson, Johnson, & Wilson, 2019; Inoue et al., 2019). In 2014, a second SCCM stakeholders conference was held to pinpoint strategies and resources for raising awareness and education, to understand and address barriers to clinical practice, and to identify research gaps and resources (Elliot et al., 2014). This condition has received significantly more attention in the literature, but a gap persists between research and adoption of best practices aimed at assessment and treatment of this condition after discharge from the ICU.

Etiology

The etiology of PICS is believed to be multifactorial and is associated with certain inflammatory conditions like sepsis (Angus, 2010; Iwashyna, Ely, Smith, & Langa, 2010) and acute respiratory distress syndrome (ARDS) (Herridge et al., 2003; Mikkelsen et al., 2009; Rothenhäusler, Ehrentraut, Stoll, Schelling, & Kapfhammer, 2001). Notably, the COVID-19 virus is known to trigger COVID-19 ARDS, an atypical ARDS that like the traditional condition results in patients needing mechanical ventilation and other ICU-level care (Gattinoni et al., 2020; Gibson, Qin, & Puah, 2020; Li & Ma, 2020). Protracted admissions in ICU settings, mechanical ventilation requirements, the administration of steroid and sedative medications, use of restraints, poor glycemic control, prolonged immobility, and pre-existing comorbid conditions have all been associated with the development of PICS (Karnatovskaia et al., 2019; Needham et al., 2012; Sivanathan et al., 2019). Certain populations such as older adults, people of a minority race and/or with a mental illness, and survivors with a history of transplantation, neurological, and hepatic diseases are at the greatest risk of developing this condition (Needham et al., 2012; Riegel et al., 2019).

Symptomatology

Cognitive and psychological sequelae of PICS include anxiety, depression, agitation, insomnia, nightmares, social disengagement, impaired ability to complete activities of daily living, and cognitive impairment (Iwashyna et al., 2010; Karnatovskaia et al., 2019; Mikkelsen et al., 2009; Needham et al., 2012; Sidiras et al., 2019). Depression alone can have serious implications on long-term health. One study reported depression after critical illness is associated with a 47 percent increased risk of dying within the first 2 years following discharge from an ICU (Hatch et al., 2018). Cognitive impairment is an umbrella term that encompasses

impaired attention, memory, processing speed, executive function, and visuospatial ability (Mikkelsen et al., 2009; Needham et al., 2012). A study of ARDS patients 12 months after recovery from critical illness found 55 percent ($n = 41$) tested positive for some degree of cognitive impairment (Mikkelsen et al., 2012).

In addition, survivors report muscle weakness, impaired handgrip, and nerve pain 6 months after discharge (Iwashyna et al., 2010; Sidiras et al., 2019). This symptomatology is likely attributable in part to mitochondrial dysfunction after critical illness, as well as treatment effects, prolonged immobility, and disruption of the circadian rhythm (Needham et al., 2012; Owen et al., 2019). The ICU length of stay may play a role in the number or severity of symptoms. Survivors of severe sepsis without a prior history of functional limitations are reported to develop on average, 1.57 new limitations (Iwashyna et al., 2010). Patients with mild/moderate limitations before sepsis had an increase of 1.5 additional limitations after sepsis, and they persisted for up to 8 years of follow-up (Iwashyna et al., 2010). By contrast, no significant changes were noted in non-sepsis general hospitalizations.

Implications

PICS can impact survivors' ability to work and their quality of life (Herridge et al., 2003; Norman et al., 2016; Wintermann, Petrowski, Weidner, Strauß, & Rosendahl, 2019). A study of 34 survivors of critical illness reported that 44.1 percent ($n = 15$) remained hospitalized for 3 months after discharge from the ICU, and of the remaining 19 respondents, only 1 (5.3 percent) was able to return to their previous employment (Heydon, Wibrow, Jacques, Sonawane, & Anstey, 2019). Sixteen of the 18 survivors (88.9 percent) who were unable to return to work indicated this was related to their critical illness (Heydon et al., 2019). In a 2019 systematic review with meta-analysis, the estimates across studies for return to employment among those employed before critical illness were 33 percent (95% confidence interval [CI], 21%–48%), 55 percent (95% CI, 45%–64%), and 56 percent (95% CI, 45%–66%) at 3, 6, and 12 months, respectively (McPeake et al., 2019). A second systematic review and meta-analysis reported similar results at the 3- and 12-month marks, and found the return to work prevalence from 42 to 60 months was 68 percent (95% CI, 51%–85%) (Kamdar et al., 2020). Impairments that prevent survivors from returning to work include decreased pulmonary function, reduced strength of respiratory and extremity muscles, reduced 6-minute walk test distance, and limited ability to perform activities of daily living (ADLs), instrumental ADLs, and drive (Ohtake et al., 2018). Survivors' inability to return back to their careers can lead to a serious role crisis (Sidiras, et al., 2019).

Additionally, an inability to work can be financially devastating for survivors and their families. In the Heydon et al. (2019) study, 35.3 percent of respondents of a 3-month survey ($n = 12$) indicated they were having financial difficulties as a result of their illness (Heydon et al., 2019). In another study, 34 percent of ARDS survivors reported receiving new disability payments 2 years after their hospitalization (Hopkins et al., 2005). The economic impact of PICS has not been quantified

but is likely tremendous given the reports from single-center studies of survivors who develop this condition.

The financial burden of mild cognitive impairment alone is estimated at $15,022 per patient per year, and $34,515 for severe cognitive impairment (Rockwood et al., 2002). Cognitive impairment is just one domain of PICS. Cognitive impairment plus comorbid depression is associated with a fourfold increase (odds ratio [OR] = 3.02) in activities of daily living limitations, and increased odds of hospitalization (OR = 1.53) and nursing home admission (OR = 3.34) (Xiang & An, 2015). This has serious financial implications for survivors, insurers, and health-care systems.

Some survivors do not recover to their previous state of health, despite extensive rehabilitation. One study reported persistently low quality of life 3 and 6 months post-discharge (Sidiras et al., 2019). Three months post-discharge, patients reported decreased physical abilities and energy levels, and unusual emotional reactions ($p < .05$). In addition to these sequelae, patients reported greater pain, sleep disturbances, and social isolation 6 months after their discharge (Sidiras et al., 2019). Another multicenter study reported 64 percent of participants exhibited symptoms consistent with PICS at 3 months and 56 percent at 12 months after discharge (Marra et al., 2018).

Impact on Children and Families

PICS is not exclusive to adults but may be present in over one-third of pediatric patients (PICS-P) surviving ICU admissions (Bronner, Knoester, Bos, Last, & Grootenhuis, 2008; Pinto, Rhinesmith, Kim, Ladner, & Pollack, 2017). Subclinical PTSD was reported in 36.5 percent ($n = 10$) of pediatric critical illness survivors, and PTSD in 17.9 percent ($n = 5$) (Bronner et al., 2008). PICS-P may impact children's ability to achieve important growth and development milestones. Additionally, families are known to experience depression, anxiety, and post-traumatic stress disorder symptomatology that matches with that seen in patients after discharge from ICUs (Azoulay et al., 2005; Petrinec & Martin, 2018). The family condition has been labeled PICS-F (see Table 1). One study completed 90 days after ICU discharge, found 47 percent ($n = 66$) of family members exhibited signs of post-traumatic stress syndrome, 39 percent ($n = 55$) showed signs of anxiety, and 29 percent ($n = 41$) demonstrated signs of depression. No significant differences were found between relatives of survivors and non-survivors of critical illness (Matt, Schwarzkopf, Reinhart, Konig, & Hartog, 2017). A previous history of anxiety, depression, and post-traumatic stress disorder may predict symptom

Table 1. Comparison of Three Classifications of Post-Intensive Care Syndrome (PICS)

Conditions	Description
PICS	Post-intensive care syndrome seen in *adult* survivors of critical illness
PICS-P	Post-intensive care syndrome seen in *pediatric* survivors of critical illness
PICS-F	Post-intensive care syndrome seen in *family members* of adult or pediatric survivors of critical illness

severity and prevalence in family members with PICS-F (Petrinec & Martin, 2018). Bronner et al. (2008) found maternal PTSD was the strongest predictor for child PTSD.

The Case for ICD-10 Codes

The absence of ICD-10 diagnostic codes for PICS, PICS-P, and PICS-F makes investigating the epidemiology of these conditions on national and international scales impossible. Without diagnostic codes, providers are forced to code individual manifestations (e.g., anxiety, depression, insomnia), which makes tracking the prevalence of PICS on a large scale impossible. The results of the single- and few multicenter studies that have been published are alarming. A study of 55 consecutive survivors of ARDS reported 100 percent of survivors exhibited neurological or behavioral decline that impacted their quality of life after discharge (Hopkins et al., 1999). Another study of 43 survivors from two academic medical ICUs found 83.7 percent ($n = 36$) exhibited symptoms consistent with PICS (95% CI, 69.3%–93.2%) (Maley et al., 2016). Being able to diagnose and code patients with PICS, PICS-P, or PICS-F is an initial step in building the science, and will enable the development of evidence-based treatment interventions. An understanding of predictors would enable clinicians to better screen for the PICS conditions, and target preventative interventions toward those likely to develop one.

The PICS epidemic is likely to worsen with the current COVID-19 viral pandemic, as patients are being admitted to ICUs for an ARDS-like illness, and have protracted ICU admissions that usually involve mechanical ventilation and sedation infusions. The long-term complications of a COVID-19 infection are unknown, but it is reasonable to assume these patients will be at high risk for PICS, given the similarities in severity of illness and treatment course. As of January 1, 2021, there have been over 80 million cases worldwide, and at least 5 percent will require an ICU admission to manage their condition (Centers for Disease Control and Prevention, 2020; Grasselli, Pesenti, & Cecconi, 2020; Johns Hopkins University and Medicine, 2020).

Understanding the prevalence of diseases and conditions like PICS, PICS-P, and PICS-F is needed for allocation of public health funds for screening and treatment, but also for government agencies to determine their research priorities. The lack of ICD-10 codes impedes policy development. To date, PICS, PICS-P, and PICS-F have received minimal research funding globally and remain understudied, despite their reported large personal and economic impact on critical illness survivors and their families. Their burden on international health-care systems is likely great, but currently unrecognized. Most studies of these conditions have been conducted in single centers or systems in a small number of countries, limiting the generalizability of findings. Data from these studies suggest the PICS conditions may be unrealized epidemics, like the vaping-related acute lung injury (VALI) reported in 2019 by world news outlets. Conditions like VALI and PICS can be understudied for a long period of time without ICD-10 codes.

Beyond hindering epidemiological investigations, the absence of ICD-10 codes for PICS is a disincentive to care coordination in outpatient settings, and effective post-acute treatment.

Providers are not incentivized to complete assessments, because, without ICD-10 codes, they cannot bill for them. All providers should have heightened awareness about this condition and should be assessing for manifestations during patient visits after ICU admission. Primary care providers should be able to screen for sequelae of PICS, PICS-P, or PICS-F and diagnose it if ICD-10 codes exist, or be willing to refer patients to a psychiatric provider who could make the diagnosis. One recent study found ICU survivors who exhibit symptoms of PICS have more visits with primary care providers than patients with similar characteristics in the general population (van Beusekom et al., 2019).

At a recent SCCM consensus conference on the prediction and identification of long-term impairments after critical illness, experts made recommendations on screening adults for post-discharge impairments (Mikkelsen et al., 2020). Recommendations included serial assessments within 2–4 weeks of hospital discharge using the Montreal Cognitive Assessment test, Hospital Anxiety and Depression Scale, 6-minute walk, Impact of Events Scale-Revised (IES-R) to assess for PTSD, and/or the EuroQol-5D-5L to assess the quality of life (Mikkelsen et al., 2020). The best tool for studying PTSD symptoms in survivors of critical illness remains a point of dispute in the literature. Besides the IES-R, other tools frequently used for patient assessment include the Clinician-Administered Post-Traumatic Stress Disorder Scale, Post-Traumatic Stress Disorder Checklist—Civilian V5, Post-Traumatic Stress Syndrome 14-Question Inventory, Post-Traumatic Stress Disorder Checklist—Civilian V17, Structured Clinical Interview, the Posttraumatic Stress Diagnostic Scale, the Post-Traumatic Stress Syndrome 10-Question Inventory, the Trauma Screening Questionnaire, and the Davidson Trauma Scale (Righy et al., 2019). Regardless of the tools selected, assessments of survivors of critical illness are important and should be completed by primary care physicians in coordination with psychologists, rehabilitation, and neurology providers (when cognitive impairment is detected). Without ICD-10 codes, it is impossible for providers to adopt the SCCM experts' recommendations, as there is no administrative or financial alignment.

The World Health Organization (WHO) is responsible for managing the International Classification of Diseases—10th edition, used by hospitals in over 100 countries (World Health Organization [WHO], 2019). According to the WHO (2019), 70 percent of the world's health expenditures ($3.5 billion USD) are appropriated using the ICD codes, making them crucial for diagnosis and billing of diseases. It is imperative that member countries petition the WHO to create diagnostic/billing codes for the PICS conditions. These codes are critically important for researchers to develop the science underlying these conditions, for policymakers to recognize funding priorities, and for providers to assess for PICS in adult and pediatric ICU survivors and their family members.

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Notes

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