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Posttraumatic Stress Disorder in Critical Illness Survivors: Too Many Questions Remain

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As critical illness-related mortality has decreased, interest has increased in the mental health of critical illness survivors in order to better understand their quality of survivorship. Over the last decade, an increasing number of studies have identified that critical illness survivors have high rates of psychiatric disorders such as posttraumatic stress disorder (PTSD) (1, 2). A 2008 systematic review of studies of general intensive care unit (ICU) survivors found that approximately one-fifth had either substantial PTSD symptoms or clinician-diagnosed PTSD, benzodiazepine sedation was associated with increased risk of post-ICU PTSD, and post-ICU PTSD was associated with worse health-related quality of life (HRQOL) (2).

Since this review was published, the literature on PTSD in critical illness survivors has expanded substantially. In recent years, several cohort studies have published their findings on the prevalence of, and potential risk factors for, PTSD in critical illness survivors (3–5). Also, a common PTSD screening questionnaire, the Impact of Events Scale-Revised (IES-R), has been validated in this population (6). Furthermore, promising interventions with the goal of preventing post-ICU PTSD have been developed and studied (7, 8).

With this backdrop in mind, in the current issue of *Critical Care Medicine*, Parker et al. present the findings of a meta-analysis of the prevalence of PTSD in general critical illness survivors (9). They also conducted a systematic review of potential risk factors and interventions for PTSD in this population. Synthesizing data from over 3,400 patients who were followed in 40 studies, Parker et al. found that the point prevalence of substantial PTSD symptoms following critical illness ranged from 4 to 62% across all studies. Since the IES was the most common instrument utilized to assess post-ICU PTSD (16 studies), a meta-analysis of post-ICU substantial PTSD symptoms as ascertained by the IES identified that the pooled prevalence of post-ICU substantial PTSD symptoms was 25%-44% at 1-6 months post-ICU (depending on whether an IES cutoff score of 35 or 20 was used) and 17%-34% at 7-12 months post-ICU.

Importantly, Parker et al. replicated the results of prior work in this area (2), finding that early post-ICU memories of in-ICU frightening or psychotic experiences were associated with increased risk of post-ICU PTSD in over 80% of the studies that examined this factor. They also found that pre-ICU psychopathology was associated with increased risk of post-ICU PTSD in over half of studies examining this characteristic, also in line with previous work (2). Furthermore, Parker et al. found that nearly half of the studies examining benzodiazepine sedation as a potential risk factor for post-ICU PTSD identified an association with increased risk. Yet, as Parker et al. acknowledge, it remains unclear whether the association between benzodiazepine sedation and post-ICU PTSD is truly causal, or if receipt of higher doses of benzodiazepines is a marker for predisposing psychiatric illness manifesting increased anxiety in the ICU. In addition, studies have identified that substantial acute stress symptoms (i.e., substantial PTSD symptoms occurring < 1 month after exposure to a traumatic stressor) are a potent, independent risk factor for increased PTSD severity following critical illness (4), a potential risk factor not discussed by Parker et al. As with prior work (2), Parker et al. also found that studies examining relationships between post-ICU PTSD and post-ICU HRQOL identified an association with worse HRQOL among critical illness survivors with substantial PTSD symptoms.

Notably, the increase in studies of interventions targeting post-ICU PTSD has allowed Parker et al. to conduct a systematic review of this literature. Of the interventions studied, which included ICU diaries (7, 8), enhanced post-ICU care coordination in ICU follow-up clinics, and a self-help rehabilitation manual, ICU diaries appeared to show the greatest promise for reducing, and potentially preventing, PTSD symptoms in critical illness survivors. However, there remain too few randomized controlled trials (RCTs) of ICU diaries to draw definitive conclusions regarding their effectiveness, a point highlighted by a recent Cochrane Collaborative systematic review (10). Also, as of yet there have been no published trials of ICU diaries conducted in the United States. Since ICU diaries are a relatively low cost intervention with the potential for substantial patient benefit, additional studies are greatly needed. In addition to ICU diaries, interventions that combine identifying critical illness survivors with substantial acute stress symptoms prior to hospital discharge with increasing their exposure to evidence-based therapies early in recovery need study, as these types of interventions have been found to significantly reduce PTSD symptoms in survivors of traumatic injury (including trauma ICU survivors) (11).

Due to variability in the methods used to ascertain post-ICU PTSD and potential risk factors, Parker et al. could not conduct a meta-analysis of the prevalence of PTSD or of data on its potential risk factors across all 40 studies. There also remain too few RCTs of interventions for post-ICU PTSD to conduct a meta-analysis in this area.

Despite these limitations, Parker et al.'s meta-analysis and systematic review definitively reinforces that substantial PTSD symptoms are alarmingly common in critical illness survivors, and they are associated with worse HRQOL. This point is sobering when considering that millions of patients survive ICU stays for critical illnesses annually (2), and when taken together with the growing literature on persistent cognitive dysfunction in critical illness survivors (12, 13). Moreover, as societies have become increasingly concerned with the financial costs of health care and long-term solvency of publicly-funded

healthcare systems, evidence has mounted that psychiatric disorders are independently associated with increased acute care service utilization (14). Notably, a recent study has shown that PTSD symptoms are independently associated with increased acute care service utilization among medical-surgical ICU survivors over the course of the year post-ICU (15). Therefore, Parker et al.'s work comes at a crucial point in time. It serves as an important reminder that we have a long way to go to definitively understand the risk factors for psychiatric disorders such as PTSD in critical illness survivors, and that more work in the development of interventions to reduce psychiatric morbidity in this patient population is desperately needed.

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