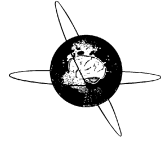




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Editorial

Critical illness myopathy and polyneuropathy in Covid-19: Is it a distinct entity?



See Article, pages 1733–1740

Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2), causing the new coronavirus disease 2019 (COVID-19), continues to spread and have serious health and socioeconomic consequences worldwide. Among neurological manifestations, stroke (Siepmann et al., 2021), Guillain Barre Syndrome (Arnaud et al., 2020; Uncini et al., 2021), epilepsy (Canham et al., 2020; Mithani et al., 2021) and encephalopathy (Vellieux et al., 2020; Niguet et al., 2021) have been described during the acute infection. Additionally, in many patients, intensive care unit (ICU) treatment and long-term ventilatory support are required, increasing the risk of critical illness myopathy (CIM) and polyneuropathy (CIP). CIM and CIP have been reported as a consequence of Covid-19 (Tankisi et al., 2020a; Cabanes-Martinez et al., 2020; Bax et al., 2021), however, it is not known whether the clinical and electrophysiological features in Covid-19-related CIM and CIP differ from non-Covid-19 patients.

In the current issue of *Clinical Neurophysiology*, Frithiof and colleagues reported 11 patients with CIM or CIP of 111 COVID-19 patients admitted to the ICU between March 2020 and June 2020 (Frithiof et al., 2021). This corresponds to an incidence of 10%, which is lower than the earlier reports. Different studies have indicated that approximately 50% of patients under mechanical ventilation for more than 7 days develop CIM, CIP or both (Koch et al., 2011; Z'Graggen and Tankisi, 2020). As the authors have also appreciated, a false low incidence of CIM and CIP in this study is possible, because referrals to electrophysiological studies were strictly selected to ICU patients with quadriplegia. Of the 11 patients, 4 had CIM and 7 showed CIP. None of the patients showed signs of both myopathy and neuropathy, which is otherwise a frequently reported condition (Tankisi et al., 2020b).

The diagnosis of CIM and CIP are currently made by conventional nerve conduction studies (NCS) and electromyography (EMG), and muscle biopsy showing preferential myosin loss (Swash and de Carvalho, 2020). Frithiof and co-workers performed a detailed NCS protocol whereas motor unit potential (MUP) analysis could not be done in most patients due to lack of cooperation. CIM diagnosis cannot be excluded in these patients which may be a reason for the low incidence of CIM in this cohort. One area not sufficiently covered by this study are potential alterations in compound muscle action potential (CMAP) duration. The authors addressed the highly significant group difference in patients with

and without CIM, however the duration and shape of CMAPs in individual patients would have been of interest, and synchronous and smooth long duration CMAPs could be interpreted in favor of CIM, particularly in patients where MUP analysis was not possible. Since most patients in ICU are sedated and mechanically ventilated, other approaches for performing MUP analysis should be tried. Passive movements of the joints and scratching the foot sole with the naked end of a cotton swab can almost always enable recruitment of MUPs (Tankisi et al., 2021).

There is agreement in literature that CIM is more common than CIP and has better prognosis in patients with different etiologies (Koch et al., 2011; Z'Graggen and Tankisi, 2020; Tankisi et al., 2020b). Frithiof and co-workers found more frequent CIP among COVID-19 patients compared with a non-COVID-19 cohort. Higher incidence of CIP may be a specific finding for Covid-19, however, a false high incidence is possible since abnormal sensory NCS may sometimes be unreliable in ICU due to edema, positioning of the patient or noise from equipment (Tankisi et al., 2020c).

Frithiof and colleagues showed high neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP) levels in the early phase of ICU care in Covid-19 patients who later developed CIM or CIP, suggesting these as potential blood biomarkers. This finding is in contrast to a previous study suggesting that early diagnosis of ICU-acquired weakness (ICUAW) is not possible using plasma NfL levels (Wieske et al., 2014). Further studies are needed to determine whether the potential of NfL and GFAP as early predictive biomarkers is limited to Covid-19 related ICUAW.

In general, the existing methods for the diagnosis of CIM and CIP detect mostly advanced changes, leaving patients, especially in the early stages, at risk of being missed. So, novel methodologies for early diagnosis are needed. In a recent study, a newer method, muscle velocity recovery cycles (MVRCs) was suggested as a tool for early detection of evolving CIM. MVRCs could detect alterations in muscle fiber membrane properties in patients with ICUAW not yet fulfilling the diagnostic criteria for CIM. In contrast to MUP analysis, this method does not require patient's cooperation. The MVRCs are measured by direct muscle stimulation and EMG needle recording, and the method is fast and easy to perform (Z'Graggen and Bostock, 2009; Witt et al., 2020). The utility of MVRCs has been shown in different conditions such as muscle channelopathies (Tan et al., 2018, 2020) and neurogenic muscles (Witt et al., 2019). How-

ever, the method has not become established as a diagnostic tool in the clinic yet probably because at present specialist equipment is required.

Overall, Frithiof and co-workers' study highlights the need for large-scale longitudinal studies to determine the incidence and pathogenesis of CIM and CIP and to explore methodologies for earlier and more accurate diagnosis. This disabling and under-recognized condition deserves special attention in the context of a growing awareness of short- and long-term complications of Covid-19. Accordingly, further studies in larger cohorts of Covid-19 are essential to determine whether CIM and CIP related to Covid-19 are distinct entities.

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Accepted 7 April 2021

Available online 20 April 2021