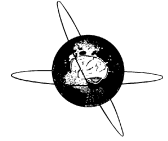




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## Letter to the Editor

## Myopathy in acute and long-term COVID-19



We read with great interest the recent paper “Electrodiagnostic findings in COVID-19 patients: a single center experience” by Hameed and colleagues (Hameed et al., 2021).

The study investigated the acute neuromuscular manifestations of the new coronavirus disease 2019 (COVID-19). Hameed and colleagues report 18 patients examined with nerve conduction studies (NCS) and electromyography (EMG) in a 1-year period. Of these, 11 patients required intubation. Electrodiagnostic findings showed myopathy in 82% of the patient's required intubation, and in 5 patients, there was concurrent axonal neuropathy. Myopathy was seen in 3 of the 7 patients who did not require intubation. The authors conclude that myopathic EMG changes are commonly seen in critically ill COVID-19 patients, especially with a prolonged hospital stay.

The high incidence of myopathy in this study did not surprise us. Unfortunately, Hameed and colleagues could not support their data with muscle biopsy, and the question of whether critical illness myopathy (CIM) associated with COVID-19 is different than the other etiologies could not be answered in this study. However, there is increasing evidence that skeletal muscles are particularly affected in COVID-19, and most possibly, Hameed and colleagues (Hameed et al., 2021) could show not only typical CIM pathological features as reported in non-COVID-19 patients, but also, additional features correlated with COVID-19.

Two recent studies investigated skeletal muscle in autopsy specimens from patients with COVID-19 (Aschman et al., 2021; Suh et al., 2021). Aschman and colleagues showed signs of muscle inflammation, ranging from mild to severe inflammatory myopathy in 60% of the patients who died with severe COVID-19, and the inflammation was more pronounced in skeletal muscle compared to cardiac muscle. Suh and colleagues investigated psoas muscle and femoral nerve sampled from 35 consecutive autopsies of patients who died with COVID-19, and showed necrotizing myopathy in 28%, myositis in 22% and neuritis in 28% of the autopsies providing evidence that muscle and nerve biopsies document a variety of pathologic changes in patients dying of COVID-19. Severe Acute Respiratory Syndrome 2 (SARS-CoV-2) immunostaining of skeletal muscle was negative in both autopsy studies, possibly due to post-mortem changes with a post-mortem interval of around 6 days. We believe further studies in muscle biopsies performed during the first days of acute infection not only in critically ill patients but also in patient with mild and moderate COVID-19 are warranted to eliminate this possibility. Accordingly, exploring the extent and characteristics of muscle involvement in acute COVID-19 may provide an important milestone in understanding the mechanisms of muscular complaints in long-term COVID-19 as well.

While the number and severity of acute disease are decreasing, a worrying number of reports demonstrate long-term health issues after COVID-19, also in non-hospitalized patients. In large cohorts of long-term COVID-19 patients at 4–6 months follow-up, fatigue (up to 68%) is reported as one of the most common symptoms (Nasserie et al., 2021). In a recent study, Agergaard and colleagues showed that in patients with long-term muscular complaints or fatigue after mild or moderate SARS-CoV-2 infection, myopathy was a common finding (Agergaard et al., 2021). Their study could not provide definite evidence for a causal link between acute infection and long-term myalgia, fatigue and myopathy but it supports the findings from the two recent autopsy studies (Aschman et al., 2021; Suh et al., 2021).

Hameed and colleagues defined neuropathy and myopathy on the basis of NCS and EMG findings. In each patient, a large number of nerves and muscles have been examined. It was indicated that in some of the patients, low compound muscle action potential (CMAP) amplitudes were noted. While this is an expected finding in all patients with CIM, information about CMAP duration and F-wave results would be valuable. Overall, it would be desirable to see all the NCS and EMG findings in a Table.

In conclusion, Hameed and colleagues' study emphasizes once more the burden of CIM in COVID-19 related critically ill patients, as had been indicated in the first CIM case report as a consequence of COVID-19 in the beginning of the pandemic (Tankisi et al., 2020). At that time, there was no evidence for whether COVID-19 associated CIM is different than other etiologies, but the recent histopathological reports suggest that CIM as a consequence of COVID-19 may be a distinct entity.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## References

- Agergaard J, Leth S, Pedersen TH, Harbo T, Blicher JU, Karlsson P, Østergaard L, Andersen H, Tankisi H. Myopathic changes in patients with long-term fatigue after COVID-19. *Clin Neurophysiol* 2021;132(8):1974–81.
- Aschman T, Schneider J, Greuel S, Meinhardt J, Streit S, Goebel H-H, Büttnerova I, Elezkurtaj S, Scheibe F, Radke J, Meisel C, Drosten C, Radbruch H, Heppner FL, Corman VM, Stenzel W. Association Between SARS-CoV-2 Infection and Immune-Mediated Myopathy in Patients Who Have Died. *JAMA Neurol* 2021;78(8):948. <https://doi.org/10.1001/jamaneurol.2021.2004>.
- Nasserie T, Hittle M, Goodman SN. Assessment of the Frequency and Variety of Persistent Symptoms Among Patients With COVID-19: A Systematic Review. *JAMA Netw Open*. 2021;4(5):e2111417. <https://doi.org/10.1001/jamanetworkopen.2021.11417>.
- Hameed S, Khan AF, Khan S. Electrodiagnostic findings in COVID-19 patients: a single center experience. *Clin Neurophysiol* 2021;132(12):3019–24.

Suh J, Mukerji SS, Collens SI, Padera RF, Pinkus GS, Amato AA, Solomon IH. Skeletal Muscle and Peripheral Nerve Histopathology in COVID-19. *Neurology* 2021;97(8):e849–58.

Tankisi H, Tankisi A, Harbo T, Markvardsen LK, Andersen H, Pedersen TH. Critical illness myopathy as a consequence of Covid-19 infection. *Clin Neurophysiol* 2020;131(8):1931–2.

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