Received: 8 August 2022 | Accepted: 11 August 2022

DOI: 10.1111/ene.15525

european journal of neurology
the official journal of the european academy of neurology

LETTER TO THE EDITOR

Reply to "Post-COVID myopathy"

We read with interest the letter by Finsterer and Scorza [1] that commented on our recent article "Myopathy as a cause of fatigue in long-term post-COVID-19 symptoms: Evidence of skeletal muscle histopathology" [2].

In their letter, Finsterer and Scorza point out that there was no information on the medication the patients were taking for COVID-19. We agree that certain types of medication, such as steroids, chloroquine, tocilizumab, remdesivir, and statins, can be myotoxic. As we described in our article [2], one patient who was hospitalized for 10 days was treated with remdesevir, dexamethasone, and oxygen in the acute phase. None of the other patients were taking any myotoxic medication in the acute phase or during the long-term post-COVID-19 period. Accordingly, none of our patients had rhabdomyolysis during the acute phase. Moreover, none of our patients were critically ill which are otherwise conditions that may be associated with critical illness myopathy [3] and rhabdomyolysis [4].

Finsterer and Scorza also propose that post-COVID syndrome is frequently characterized by depression, physical inactivity, easy fatigability, and tiredness. It is our understanding that fatigue is meant as early fatigability and tiredness, and as we indicated throughout our article [2], fatigue was the main symptom in all our patients. None of the 14 patients we tested showed signs of depression. Although we did not test all patients, neither electromyography (EMG) nor histopathological changes can be explained by depression.

Finsterer and Scorza questioned whether the clinical, electromyographic, or biopsy findings were attributable to non-use of the muscles. We discussed this in our article [2], and proposed that although immobilization might have caused the type 2 atrophy in some patients, none of our patients were critically ill or confined to bed, and type 1 atrophy cannot be explained by immobilization.

We agree with Finsterer and Scorza that myastenia gravis (MG) should be considered as a differential diagnosis. None of our patients had a history of MG or any other neuromuscular disorder. Thus, none of the patients had any ocular or bulbar symptoms or deficits. Furthermore, MG could not explain the histopathological findings, and therefore we did not perform systematically antibody tests for establishing a diagnosis of MG. We did antibody testing against acetylcholine receptors in 13 patients, and against muscle-specific tyrosine kinase (MuSK) in 8 patients, and all were negative. We also agree that fatigue in post-COVID patients may be caused by cerebral involvement. None of our patients had acute or chronic clinical central nervous system involvement. We want to stress that all our patients had mild or moderate acute infection only, and we did not expect to find cerebral pathology in magnetic resonance imaging that could explain long-term fatigue. We only examined the peripheral nerve system aspects of fatigue and exercise intolerance, and we agree that further studies examining other aspects are necessary.

We thank Finsterer and Scorza for pointing out the discrepancy between the abstract and Figure 1 in the number of cases with muscle weakness. Seven of 16 patients (44%) had muscle weakness. Regarding their criticism of the lack of reference limits in Figure 1, this information was presented in the figure legend [2].

Finsterer and Scorza challenge the laboratory test results presented in our article [2]. Creatinine kinase was just above the upper limit of normal, and all other patients had normal routine blood tests including lactic dehydrogenase levels. However, we did not perform biochemical investigations of respiratory chain complex functions in any of the patients. We agree that this would be interesting to know and may follow in subsequent presentations from our group.

Finsterer and Scorza question the results of the interference pattern analysis which were described in our article. In all patients with myopathic motor unit potential (MUP) analysis, interference pattern was also myopathic, with full pattern and low amplitude. None had reduced pattern.

In conclusion, we want to emphasize that the wide variety of histological changes and EMG findings in our present study [2] in line with our previous study which showed high incidence of myopathic EMG [5] suggest that skeletal muscles may be a target in COVID-19 causing symptoms related to striated muscles.

AUTHOR CONTRIBUTIONS

Eva K Hejbøl: Writing – review and editing (equal). **Thomas Harbo:** Writing – review and editing (equal). **Jane Agergaard:** Writing – review and editing (equal). **Lars J Østergaard:** Writing – review and editing (equal). **Henning Andersen:** Writing – review and editing (equal). **Henrik Daa Schrøder:** Writing – review and editing (equal). **Hatice Tankisi:** Conceptualization (lead); writing – original draft (lead).

KEYWORDS

electromyography, fatigue, long-term COVID, myopathy, post-COVID syndrome, muscle biopsy

FUNDING INFORMATION

Danmarks Frie Forskningsfond, Grant/Award Number: 9039-00272B; Novo Nordisk Fonden, Grant/Award Number: NNF21OC0066984

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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