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Letter to the Editor

Comorbidities of diabetic patients may strongly influence the impact of diabetic neuropathy on COVID-19 outcome

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With interest we read the article by Tuan *et al*. about a retrospective, longitudinal cohort study on the influence of diabetic neuropathy on the severity and outcome of COVID-19 [1]. Utilizing electronic health records from 55 health care organizations sourced from the US TriNetX research network database, 16511 patients with diabetes and diabetic neuropathy, 16511 patients with diabetes but without diabetic neuropathy, and 80672 patients without diabetes and diabetic neuropathy were included [1]. It was found that patients with diabetic neuropathy had a greater risk of developing severe COVID-19–related complications than those without diabetic neuropathy [1]. The study is appealing but raises concerns that require further discussion.

A limitation of the study is that the upper cut off for age was not provided. According to the method section, age ranged from 18 years to older [1]. Therefore, it is conceivable that elderly patients with diabetes were included in the cohorts as well. Because the prevalence of neuropathy increases with age in general, it is possible that elderly patients had neuropathy due to causes other than diabetes as well. We should be informed how the authors ensured that only patients with diabetic neuropathy but not patients with neuropathy due to other causes were included.

A further limitation of the study is that comorbidities were not included in the evaluation [1]. Because neuropathy has a wide range of aetiologies, which may overlap or co-occur, it is crucial to know which diseases other than diabetes were additionally diagnosed in the included patients. Of particular interest in this respect are immunologic, metabolic, inflammatory, infections, endocrine, vitamin deficiency, neoplastic, paraneoplastic, and genetic disorders, which may manifest with neuropathy [2].

Another limitation of the study is that socio-economic data, such as educational status, rural residency, and employment status, were not included in the evaluation. Socio-economic parameters could affect the risk of severe COVID-19 outcome.

A further strong limitation of the study is also that the current medication the patients were regularly taking was not included. Because several drugs have a strong neurotoxic potential, it is crucial to know the current medication, to assess if a supposedly diabetic neuropathy was in fact drug-induced.

A subtype of diabetic neuropathy not included in the evaluation was small fiber neuropathy (SFN) [3]. SFN due to diabetes may be present long before large fiber diabetic neuropathy becomes evident. Nonetheless, diabetic SFN may strongly influence the outcome as it involves affection of autonomic fibers.

Diabetes can be also complicated by neuralgic amyotrophy (Parsonage Turner syndrome) [4]. Because ICD-10 codes were used for data extraction, we should know if the code G54.5 was included in the evaluation or not.

Overall, the study carries obvious limitations that require re-evaluation and discussion. Clarifying these weaknesses would strengthen the conclusions and could improve the study. As long as comorbidities, differential causes of neuropathy, and the current medication were not considered in the evaluation, final conclusions about the influence of diabetic neuropathy on the outcome SARS-CoV-2 patients is not reliable.

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