## Immobile ALS patients or those at risk of venous thromboembolism require a comprehensive examination and low-dose heparinisation

**Dear Editor,**

We were interested to read the article by Hamad et al. on a review and meta-analysis of the prevalence and risk factors for venous thromboembolism (VTE) in 26788 patients with amyotrophic lateral sclerosis (ALS) recruited from eight studies [1]. The pooled annual incidence of VTE across all studies was 22 per 1,000 person-years [1]. Risk factors for VTE were a history of VTE, non-invasive ventilation, immobility and impaired functional status [1]. A multiregression analysis showed no association between age and VTE risk [1]. It was concluded that ALS patients have an increased risk of VTE compared to age-matched controls [1]. The study is appealing, but some points should be discussed.

The first point is that the risk and prevalence of VTE strongly depends on the mobility of ALS patients, whether immobile patients receive low-dose heparin as antithrombotic prophylaxis and whether the heparin dosage is sufficient in relation to the patient's degree of mobility and weight.

The second issue is that coagulation status was not included in the analysis [1]. As the prevalence of VTE may be highly dependent on whether there is a congenital or acquired coagulopathy or platelet dysfunction or thrombocytopenia or thrombocytosis, it is crucial to know how many of the included patients had such a coagulopathy. VTE can only be attributed to ALS if coagulopathies are recorded and excluded from the analysis.

The third point is that VTE can also be associated with infection [2]. Since ALS patients often develop broncho-pulmonary infections due to dysphagia and aspiration, we should know how many patients with VTE were suffering from acute infection at the time of VTE onset.

The fourth point is that VTE prevalence was not related to disease severity [1]. ALS patients with impaired mobility or muscular respiratory insufficiency may have a higher risk of VTE than patients with normal or only mildly impaired respiratory function.

The fifth point is that the incidence rate varied considerably between the eight studies (19-111) [1]. This high variability suggests that the results are extremely heterogeneous, probably multicausal and possibly unreliable. What was the reason for this extreme variability? Did the different studies include patients with varying degrees of disease severity?

The sixth point is that ALS patients develop pulmonary embolism (PE) with varying frequency [3]. As it may be another cause of morbidity or mortality in these patients, we should know the rate of PE in the cohort studied.

In conclusion, this interesting study has limitations that put the results and their interpretation into perspective. Addressing these limitations could strengthen the conclusions and reinforce the message of the study. All open questions need to be clarified before readers can uncritically accept the conclusions of the study. VTE in ALS patients is likely to be multicausal, and before attributing it to ALS alone, other explanations must be thoroughly ruled out. Immobile ALS patients or those at risk of VTE must be prophylactically anticoagulated with low-dose heparin.

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