found with those who were frail. The rate of all-cause mortality was higher in PwMS who were frail without depression (HR 1.34, 95%CI 1.09-1.65), those fit with depression (HR 1.19, 95%CI 1.08-1.32), and those frail with depression (HR 2.02, 95%CI 1.35-3.01). In women, 38% of the mortality outcome was attributable to the joint effect of the two conditions (AP 0.38, 95%CI 0.07-0.68).

Conclusions: Depression is associated with increased risk of macrovascular disease and both frailty and depression are associated with increased risk of all-cause mortality. The effect is synergistic in women. Further studies should evaluate whether effectively treating depression and enhanced management of frailty are associated with reduced vascular risk and mortality.

Disclosure

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Walking fatigability manifests globally in several gait domains in people with multiple sclerosis during a prolonged walking

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Background: Spatial-temporal gait parameters are often investigated in people with Multiple Sclerosis (pwMS) during prolonged walking, such as the 6-minute walking test (6MWT). However, no distinctions were made between pwMS presenting (WF) and not presenting (NWF) walking fatigability, a motor symptom defined as a decrease of 10% in the distance walked from the last to the first minute in the 6MWT. Investigating the gait pattern over the 6MWT in WF through spatial-temporal gait parameters can help to explain why pwMS slow down over prolonged walking.

Objectives: This study investigated spatial-temporal gait parameters in WF, NWF, and healthy controls (HC) over the 6MWT.

Methods: Fifty-six (22 WF- Expanded Disability Status Scale (EDSS) 4.8±1.1; 15 NWF- EDSS 4.9±1.3 and 19 HC) participants were included and instructed to perform the 6MWT in a 25-30 m corridor while wearing six wearable sensors (OPAL, V.1, Mobility Lab, APDM) which obtained the spatial-temporal gait parameters (cadence, gait speed, double support time, step duration, and stride length). Each minute's average was calculated for each variable. The distance walked in each minute, and the total distance of the 6MWT was recorded. The distance walking index (DWI), to determine walking-fatigability, was calculated from the distance walked in each minute. Group*minutes comparisons were accomplished through a two-way ANOVA with repeated measures to minutes factor.

Results: WF (306±127m) and NWF (354±137m) walked less far in the 6MWT than HC (584±69m) and presented gait impairments every minute ($p<0.05$). The DWI_{6-1} of the WF (-14.9±4.2%) group was different from both NWF (-2.1±5.6%) and HC (-0.4±5.3%) groups ($p<0.001$), with no difference between NWF and HC ($p>0.05$). Only the WF group presented a significant gradual deterioration in spatial (cadence and stride length), temporal (double support time and step duration), and spatial-temporal (gait speed) gait parameters ($p<0.001$) over the 6MWT, while the NFW and HC groups remained stable ($p>0.05$).

Conclusion: Spatial-temporal gait parameters deteriorated during the 6MWT only in WF despite the same level of disability among MS groups. This result suggests that tailored interventions are required to reduce walking fatigability. The symptom of slowing down is caused by a combination of changes in pace (cadence, stride length, and gait speed), stability (double support), and rhythm (step duration) gait domains. The performance decline may be related to worsening MS symptoms (e.g., spasticity and pain) and a lower capacity of the central nervous system to program and execute movement towards the end of the 6MWT.

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