The Contribution of Vascular Risk Factors in Prevalence of Fatigue Four Years Following Stroke: Results from a Population-Based Study

Susan Mahon, BHSC Honours,* Alice Theadom, PHD,* Suzanne Barker-Collo, PHD,† Steve Taylor, MSC,‡ Rita Krishnamurthi, PHD,* Kelly Jones, PHD,* Emma Witt, MSC,† and Valery Feigin, MD,PHD,FAAN*

Background: Fatigue is a debilitating symptom after stroke, which may persist for many years. Survivors of stroke commonly have comorbid medical conditions such as hypertension and diabetes mellitus that may produce fatigue by themselves. The contribution of vascular and other risk factors on long-term poststroke fatigue (PSF) has not been sufficiently investigated at a population-based level. *Methods:* Adults (N = 256) with stroke, who consented into the Auckland Regional Stroke Outcomes Study (ARCOS-IV), completed assessments including the Fatigue Severity Scale (FFS) at 4 years poststroke. A mean score greater than 4 was indicative of fatigue. A multiple regression model identified baseline associations (reported as adjusted odds ratio [AOR] with 95% confidence intervals [CI]) with long-term fatigue. *Results:* Fatigue was present in 141 stroke survivors (55%) 4 years after stroke, with a mean FSS score of 5.2 ± 1.3. Having hypertension (AOR = 2.05, 95% CI: 1.05-3.99, $P < .05$), diabetes mellitus (AOR = 2.15, 95% CI: 1.09-4.25, $P < .05$), and arrhythmia (AOR = 3.01, 95% CI: 1.46-6.20, $P < .01$) at the time of stroke were associated with increased PSF at 4 years. Nonvascular risk factors including female sex (AOR = 1.99, 95% CI: 1.06-03.70, $P < .05$) and depression (AOR = 1.18, 95% CI: 1.01-1.39, $P < .05$) were related to PSF. *Conclusions:* PSF was prevalent in the majority of survivors, with comorbid vascular factors significantly contributing to persistent fatigue. The implications of these findings are important as potentially

From the *National Institute for Stroke and Applied Neurosciences, Faculty of Health and Environmental Studies, Auckland University of Technology, Auckland, New Zealand; †Department of Psychology, University of Auckland, Auckland, New Zealand; and ‡Department of Biostatistics and Epidemiology, Faculty of Health and Environmental Studies, Auckland University of Technology, Auckland, New Zealand.

Received December 27, 2017; revision received February 20, 2018; accepted March 26, 2018.

Grant support: This study has been supported by Health Research Council of New Zealand (HRC 10/458) and the Neurological Foundation of New Zealand (1423-GS).

Conflict of interest: The authors declare that they have no conflict of interest.

Author contributions: S.M. interpreted the data and wrote the first draft of the manuscript, S.T. analyzed the data, S.M. and E.W. managed the study, S.M. acquired the data and revised the manuscript, V.F. conceived and designed the ARCOS IV study, R.K., S.B.C., A.T., K.J., E.W., and V.F. interpreted the data and revised the manuscript.

Address correspondence to Susan Mahon, BHSC Honours, National Institute for Stroke and Applied Neurosciences, School of Rehabilitation and Occupation Studies, School of Public Health and Psychosocial Studies, Faculty of Health and Environmental Studies, Auckland University of Technology, North Shore Campus, AR418, 90 Akoranga Dr, Northcote 0627, Private Bag 92006, Auckland 1142, New Zealand. E-mail: susan.mahon@aut.ac.nz.

1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.03.020

modifiable factors can be targeted and treated from acute onset. Additional research examining PSF predictors in other populations and trialing targeted interventions to control predictors of PSF are warranted. **Key Words:** Cerebrovascular disease—fatigue—vascular risk factors—long term—prevalence.

Introduction

Long-term poststroke fatigue (PSF) has been described as a chronic, debilitating, persistent, and profound sense of tiredness resulting from physical and mental exertion[1] that is not ameliorated by rest.[2] While 11% of the general population are reported to be affected by fatigue, rates are much higher among survivors of stroke (up to 79%).[3,4] While a third of stroke patients with fatigue will recover within the first 3 months, extreme tiredness can persist for months or even years,[5,6] with up to 73% reporting subjective fatigue up to 6 years after stroke.[7] Around 40% of all patients report PSF as one of the most difficult symptoms to cope with when facing life after stroke.[8] Persisting fatigue can significantly impair emotional and psychological well-being, interfering with the capacity to work, and negatively affect sexual intimacy and engagement in rehabilitation.[1,9,10] Furthermore, PSF is also associated with admission to private hospital[11] and increased risk of mortality.[12]

While PSF at the acute stage after stroke may be triggered by biological factors (eg, location of the lesion and severity), delayed PSF is thought to be associated more with psychological (anxiety and depression) and behavioral factors (lack of physical activity and coping strategies).[13] Increasing age (>75 years) and female sex have been associated with higher levels of fatigue.[14,15] Individuals who suffer from stroke commonly have comorbid medical conditions such as hypertension, hyperlipidemia, diabetes mellitus, and arrhythmia that may produce fatigue by themselves.[16,17] The contribution of these comorbidities on PSF is not known as there is a paucity of data to support this.

Quantitative research on PSF is poor,[13] and while fatigue has been extensively validated in normal aging,[18] longitudinal data within the population of patients with stroke are limited. Moreover, despite being in the top 10 priorities for research on life after stroke,[8] fatigue following stroke onset is rarely addressed by health professionals in terms of long-term management and prevention. To design effective interventions and management strategies, it is crucial to understand risk factors associated with the development of PSF to improve overall outcomes for stroke survivors and their families. The present study aimed to examine associations between PSF and baseline vascular and other clinical risk factors in a population-based cohort of 4-year stroke survivors.

Methods

This cohort study comprised patients with first-ever stroke who had previously consented into a prospective population-based stroke incidence study, the Auckland Regional Stroke Outcomes Study (ARCOS-IV). Full methods for ARCOS-IV have been described previously.[19] In brief, potential participants were all ARCOS-IV participants with stroke consenting to involvement in future research. Stroke was classified using World Health Organization standard diagnostic criteria[20] and were divided into pathological types (ischemic stroke [IS], primary intracerebral hemorrhage, subarachnoid hemorrhage, undetermined) according to standard clinical and computed tomography, magnetic resonance imaging, or necropsy findings (97% cases were identified according to these criteria). Study neurologists used medical history, clinical and diagnostic findings (carotid ultrasound, echocardiography, electrocardiography, transesophageal echocardiography, cerebral arterial angiography), hospital discharge summaries, or necropsy results, when available. IS cases were subclassified using Oxfordshire Community Stroke Project classification[21] as lacunar infarct, partial anterior circulation infarct, posterior circulation infarct, and total anterior circulation infarct, and also into 5 causal subtypes (atherothrombotic, embolic, lacunar, and other determined and undetermined cause) based on the Trial of ORG 10172 in Acute Stroke Treatment (TOAST)[22] criteria. Medical risk factors were obtained via hospital medical records at the time of stroke, which included high blood pressure, hyperlipidemia, diabetes mellitus, and arrhythmia. Other baseline assessments were carried out by ARCOS-IV staff within 2 weeks of the incident stroke.

Procedure

Attempts were made to contact all potential participants who had previously given consent to be contacted about future stroke research at their 12-month follow-up assessment (N = 499, see Fig 1). From a potential sample of 499 participants, 75 had died and 31 could not be contacted. Of the remaining 393, 83 declined to take part in the study, and 51 had been admitted to private hospital and/or too unwell to participate. Two hundred fifty-six participants completed face-to-face assessments (including the Fatigue Severity Scale [FFS]) conducted at the participants' primary place of residence that took approximately 60 minutes to complete. In addition to the measure of fatigue, questions were asked about changes in general health and sociodemographic information since the last assessment at 12 months. Demographic variables were extracted from baseline data (see Table 1).

Ethical approval was obtained from the New Zealand Northern Y Regional Ethics Committee (NTX/10/90/