

# Fatigue Impact Scale Demonstrates Greater Fatigue in Younger Stroke Survivors

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**ABSTRACT: Background:** Fatigue affects 33-77% of stroke survivors. There is no consensus concerning risk factors for fatigue post-stroke, perhaps reflecting the multifaceted nature of fatigue. We characterized post-stroke fatigue using the Fatigue Impact Scale (FIS), a validated questionnaire capturing physical, cognitive, and psychosocial aspects of fatigue. **Methods:** The Stroke Outcomes Study (SOS) prospectively enrolled ischemic stroke patients from 2001-2002. Measures collected included basic demographics, pre-morbid function (Oxford Handicap Scale, OHS), stroke severity (Stroke Severity Scale, SSS), stroke subtype (Oxfordshire Community Stroke Project Classification, OCSF), and discharge function (OHS; Barthel Index, BI). An interview was performed at 12 months evaluating function (BI; Modified Rankin Score, mRS), quality of life (Reintegration into Normal Living Scale, RNL), depression (Geriatric Depression Scale, GDS), and fatigue (FIS). **Results:** We enrolled 522 ischemic stroke patients and 228 (57.6%) survivors completed one-year follow-up. In total, 36.8% endorsed fatigue (59.5% rated one of worst post-stroke symptoms). Linear regression demonstrated younger age was associated with increased fatigue frequency ( $\beta=-0.20$ ;  $p=0.01$ ), duration ( $\beta=-0.22$ ;  $p<0.01$ ), and disability ( $\beta=-0.24$ ;  $p<0.01$ ). Younger patients were more likely to describe fatigue as one of the worst symptoms post-stroke ( $\beta=-0.24$ ;  $p=0.001$ ). Younger patients experienced greater impact on cognitive ( $\beta=-0.27$ ;  $p<0.05$ ) and psychosocial ( $\beta=-0.27$ ;  $p<0.05$ ) function due to fatigue. Fatigue was correlated with depressive symptoms and diminished quality of life. Fatigue occurred without depression as 49.0% of respondents with fatigue as one of their worst symptoms did not have an elevated GDS. **Conclusions:** Age was the only consistent predictor of fatigue severity at one year. Younger participants experienced increased cognitive and psychosocial fatigue.

**RÉSUMÉ: L'échelle de l'impact de la fatigue démontre la présence d'une fatigue plus importante chez les survivants d'un accident vasculaire cérébral qui sont plus jeunes. Contexte :** Entre 33 et 77% des patients qui survivent à un accident vasculaire cérébral (AVC) éprouvent de la fatigue. Il n'existe pas de consensus concernant les facteurs de risque de la fatigue post AVC, ce qui témoigne peut-être des multiples facettes de la fatigue. Nous avons caractérisé la fatigue post AVC au moyen de l'Échelle des répercussions de la fatigue (ERF), un questionnaire validé qui englobe les aspects physiques, cognitifs et psychosociaux de la fatigue. **Méthode :** Le Stroke Outcomes Study a recruté de façon prospective des patients atteints d'un AVC ischémique en 2001-2002. Les données démographiques, le niveau de fonction pré-morbide (Oxford Handicap Scale, OHS), la sévérité de l'AVC (Stroke Severity Scale, SSS), le sous-type d'AVC (Oxfordshire Community Stroke Project Classification, OCSF) et le niveau de fonctionnement au moment du congé hospitalier (OHS; Indice de Barthel, IB) ont été colligés. Une entrevue a été effectuée 12 mois après l'AVC pour évaluer le fonctionnement (IB; score de Rankin modifié, SRm), la qualité de vie (Indice de réintégration à la vie normale, IRVN), la dépression (échelle de dépression gériatrique, EDG) et la fatigue (ERF). **Résultats :** Nous avons recruté 522 patients atteints d'un AVC ischémique et 228 des patients (57,6%) survivants ont participé au suivi d'un an post AVC. Trente-six pour cent des patients accusaient de la fatigue et 59,5% d'entre eux la considéraient comme l'un des pires symptômes post AVC. L'analyse de régression linéaire a montré une association entre un âge inférieur et une fréquence de la fatigue plus élevée ( $\beta = -0,20$ ;  $p = 0,01$ ), plus prolongée ( $\beta = -0,22$ ;  $p < 0,01$ ) et plus invalidante ( $\beta = -0,24$ ;  $p < 0,01$ ). Les patients plus jeunes étaient plus susceptibles de décrire la fatigue comme l'un des pires symptômes post AVC ( $\beta = -0,24$ ;  $p < 0,05$ ). Les patients plus jeunes accusaient un impact plus considérable de la fatigue sur la fonction cognitive ( $\beta = 0,-27$ ;  $p < 0,05$ ) et sur la fonction psychosociale ( $\beta = -0,27$ ;  $p < 0,05$ ). La fatigue était corrélée aux symptômes dépressifs et altérait leur qualité de vie. La fatigue sans dépression était présente chez 49,0% des répondants dont la fatigue était l'un des pires symptômes bien qu'ils n'avaient pas un score GDS élevé. **Conclusions :** L'âge était le seul facteur de prédiction constant de la sévérité de la fatigue lors du suivi un an après l'AVC : les participants plus jeunes accusaient une fatigue cognitive et psychosociale plus sévère.

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Clinically, fatigue is a common concern cited by patients following a stroke. While there is a popular notion of what constitutes fatigue, a widely accepted operational definition for scientific study is lacking<sup>1</sup>. Fatigue is subjective, an experience that may be conceptualized on a continuum from normal to pathologic<sup>2</sup>. Pathologic fatigue may be differentiated by severity, duration, and functional impairment. The experience of fatigue

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is multifaceted with physical, cognitive, and emotional components<sup>3</sup>. The Fatigue Impact Scale (FIS) is a validated questionnaire that measures the physical, cognitive and psychosocial aspects of fatigue<sup>4</sup>.

Prevalence of post-stroke fatigue ranges from 33-77%<sup>5-8</sup>. Fatigue frequency is significantly higher among stroke survivors compared to elderly control subjects with stroke patients attributing greater physical and psychosocial limitations to their fatigue<sup>6</sup>. Post-stroke fatigue may be the only symptom in patients with excellent neurologic recovery<sup>9</sup> and persist for many years<sup>8</sup>. In addition, post-stroke fatigue has been associated with decreased quality of life<sup>10</sup>, depression<sup>11-13</sup> and increased mortality<sup>11</sup>.

There has been no consensus concerning risk factors for development of post-stroke fatigue<sup>14</sup> perhaps due to heterogeneity in defining fatigue. We quantified the physical, cognitive, and psychosocial aspects of fatigue using the FIS, and identified risk factors for post-stroke fatigue at one year in a prospective cohort study.

## METHODS

### Study Population

The Stroke Outcomes Study (SOS)<sup>15-18</sup> prospectively enrolled all patients who presented to the Halifax Infirmary (Halifax, Nova Scotia) with a diagnosis of stroke from 2001 to 2002. This study was approved by the Capital Health Research Ethics Board and each patient/surrogate decision maker provided written consent for study participation. Patient information was simultaneously entered in a prospective acute stroke registry containing variables documented by the on-call neurology physician and by the stroke team during hospitalization. Information for each patient in the two databases was linked using a unique identifier. The Halifax Infirmary functions as a tertiary care centre affiliated with Dalhousie University serving a population of approximately 900,000<sup>19</sup>. However, it functions as the local emergency department for approximately 200,000 people who live in the districts of Halifax and Halifax West.

Presence of stroke was determined by World Health Organization criteria<sup>20</sup>, and a computed tomogram (CT) scan that excluded stroke mimics. Patients were excluded if they had (1) suffered a transient ischemic attack, subarachnoid hemorrhage, subdural hematoma or cerebral hemorrhage; (2) did not speak English; or (3) had decreased levels of consciousness, dysphasia, or severe cognitive impairment at 12 month follow-up such that they were unable to answer self-rating questionnaires.

### Acute Stroke

The prospective acute stroke registry recorded measures collected during initial hospitalization including age, sex, medical history including previous stroke, functional ability prior to admission using the Oxford Handicap Scale (OHS)<sup>21</sup>, the six simple variables previously shown to be predictive of stroke outcome (age, pre-stroke functional status, living alone pre-stroke, orientation, ability to lift both arms off the bed, and walk unaided)<sup>15,17,18,22,23</sup>, stroke severity using the Stroke Severity Scale (SSS)<sup>24</sup>, lesion location (derived from best imaging information available during the hospitalization or from the initial clinical examination), and ischemic stroke subtype using

**Table 1: Description of acute stroke registry and 12 month follow-up measures**

| Measure  | Description and Coding   |
|--|--|
| OHS <sup>21</sup>                              | Functional status pre-stroke and at time of discharge. No symptoms (0) to severe handicap (5)  |
| Six Simple Variables <sup>15,17,18,22,23</sup> | Recorded at presentation. Age, pre-stroke function, marital status, orientation (time, place, person), able to lift both arms off the bed, able to walk without help from another person |
| SSS <sup>24</sup>                              | Neurologic symptoms, signs, and number of impaired functional domains at admission. Categorical groups of mild (1-4 = 1), moderate (5-7 = 2), severe (8-10 = 3)                          |
| OCSF Event Type <sup>25</sup>                  | Derived using findings from CT and neurological examination: Lacunar (LACS), Total anterior circulation (TACS), Partial anterior circulation (PACS), Posterior circulation (POCS) stroke |
| Lesion Location                                | Coded according to imaging findings or neurological signs and symptoms: right hemisphere, left hemisphere, other   |
| BI <sup>26</sup>                               | Activities of daily living within 7 days of admission, at discharge, and at 12 months. Maximally dependent (0) to independent (100)  |
| mRS <sup>27,28</sup>                           | Disability 12 months. No symptoms (0) to severe disability (5)   |
| RNL <sup>29</sup>                              | Quality of life 12 months. Reintegration: none (0) to complete (22)  |
| GDS <sup>30</sup>                              | Symptoms of depression 12 months. Depression was defined as a score of $\geq 11$ . The item "do you feel full of energy?" was excluded   |

the Oxfordshire Community Stroke Project Classification (OCSF)<sup>25</sup>. At discharge, functional capacity was scored using the Barthel Index (BI)<sup>26</sup> and OHS. (Table 1)

### 12 Month Follow-Up

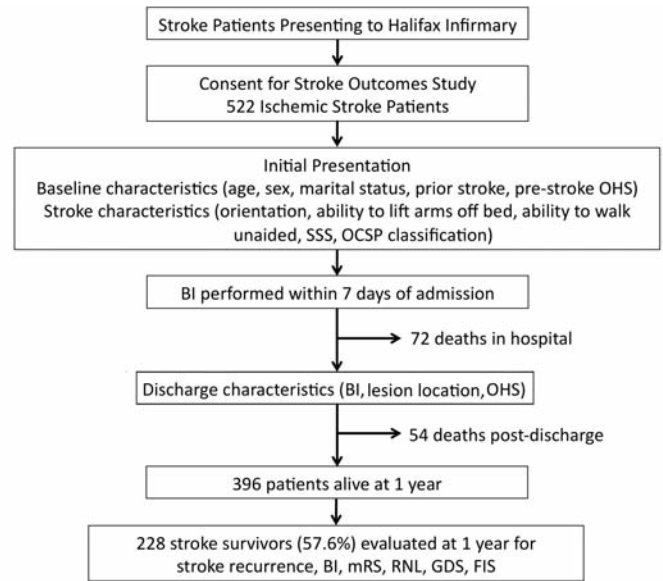
An interview was performed at 12 months by a trained stroke assessor. Vital status at 12 months was determined by contacting next of kin if the patient could not be reached for an interview. Information was obtained on stroke recurrence along with whether investigations had been performed to confirm a new stroke. Functional ability was determined by the BI and modified Rankin Score (mRS)<sup>27,28</sup>. Quality of life was measured using the Reintegration into Normal Living (RNL) scale<sup>29</sup>. Depression was measured by self-report using the Geriatric Depression Scale (GDS)<sup>30</sup> with depression defined as a score of  $\geq 11$ .

Fatigue presence and severity was measured by self-report using the FIS<sup>4</sup>, previously validated in patients with multiple sclerosis<sup>31</sup> and used in previous studies of post-stroke fatigue<sup>6</sup>. Fatigue was defined as a lack of energy in physical, social, or cognitive tasks. Fatigue frequency was quantified as days per month: 0, 1 to 4, 5 to 9, 10 to 19, 20 to 29, or everyday. Fatigue duration was measured in hours per day: 0, <6, 6 to 12, or 13 to 24. Fatigue was compared relative to other stroke-related symptoms with breakdown into not a symptom, least severe

symptom, one of less severe symptoms, one of worst symptoms, or worst symptom. The impact of fatigue on daily life was measured on a scale of 0-10 representing no disabling effect to severely disabling effect. Subjects who reported fatigue were also asked to rate the extent to which fatigue had affected their functioning in cognitive (10 items), physical (10 items), and psychosocial (20 items) domains (0 = no problem to 4 = extreme problem; maximum impact score = 160).

**Statistical Analysis**

Comparison between groups was made with the Student's t test (continuous variables) or the chi-square statistic (categorical variables). Linear regression analysis was performed using fatigue measures as the dependent variable. Independent variables were entered in several steps. These included baseline characteristics (age, sex, marital status, history of stroke, and pre-stroke function according to the OHS), stroke characteristics (stroke localization, orientation, lift both arms off the bed post-stroke, walk post-stroke, stroke severity according to the SSS, and function according to BI performed within the first seven days after admission), function at discharge from hospital (OHS



**Figure:** Flow diagram of study participation. Barthel Index (BI); Fatigue Impact Scale (FIS); Geriatric Depression Scale (GDS); Modified Rankin Score (mRS); Oxford Community Stroke Project Classification (OCSF); Oxford Handicap Scale (OHS); Reintegration into Normal Living (RNL) Scale; Stroke Severity Scale (SSS)

**Table 2: Demographics and stroke characteristics of those who completed the FIS at 12 months versus those who survived to hospital discharge but did not complete the FIS**

|               | FIS               |                     |                  |
|---------------|-------------------|---------------------|------------------|
|               | Complete<br>n=228 | Incomplete<br>n=222 |                  |
| Age (years)   | 68.4 ± 13.4       | 70.6 ± 14.6         | t=1.7; p=0.09    |
| Sex (% male)  | 53.1%             | 54.1%               | χ²=0.04; p=0.8   |
| Prior Stroke  | 26.9%             | 29.4%               | χ²=0.4; p=0.6    |
| Pre-OHS       | 0.7 ± 1.1         | 1.2 ± 1.5           | t=4.3; p<0.001   |
| Married       | 76.8%             | 70.6%               | χ²=2.2; p=0.1    |
| First SSS     | 1.9 ± 0.6         | 2.2 ± 0.6           | t=3.9; p<0.001   |
| First BI      | 65.7 ± 32.9       | 43.0 ± 35.9         | t=-6.9; p<0.001  |
| OCSF          |                   |                     | χ²=19.3; p=0.001 |
| LACS          | 34.6%             | 19.8%               |                  |
| TACS          | 5.7%              | 13.5%               |                  |
| PACS          | 33.3%             | 40.5%               |                  |
| POCS          | 21.5%             | 23.4%               |                  |
| Uncertain     | 4.8%              | 2.7%                |                  |
| Discharge OHS | 2.2 ± 1.2         | 3.2 ± 1.1           | t=8.7; p<0.001   |
| Discharge BI  | 79.7 ± 25.4       | 55.3 ± 35.1         | t=-8.4; p<0.001  |

± Standard Deviation

and BI), and whether there was recurrent stroke. All statistics were performed in SPSS version 19.0.

**RESULTS**

In total, there were 522 ischemic stroke patients who provided consent for inclusion in the stroke outcomes study. Of 126 deaths, 72 occurred in hospital, 37 within the first six months after stroke, and 17 from six to twelve months post-stroke. Follow-up including the FIS at one-year, was completed by 228 survivors (57.6%) of the initial cohort (Figure 1).

**Baseline Characteristics**

The demographics and stroke characteristics of patients who returned for follow-up at 12 months versus those who survived to hospital discharge but did not complete the FIS are summarized in Table 2. Those who did not return for follow-up demonstrated greater pre-stroke disability according to the OHS, received a higher stroke severity score, and experienced more profound post-stroke disability according to BI and OHS. There was a significant effect of stroke subtype with a higher frequency of total anterior circulation stroke (TACS) among those who did not follow-up and a higher frequency of lacunar stroke (LACS) among those who completed the FIS.

**Fatigue Description**

In total, 84 respondents (36.8%) indicated that they experienced fatigue at least once per month. Among those who experienced fatigue, the median frequency was everyday with a median duration of less than six hours per day. Fatigue was the worst or one of the worst symptoms for 59.5% of those who

**Table 3: Rank of fatigue as a symptom at one year among stroke survivors experiencing fatigue**

| Fatigue as a Symptom | Participants |       |
|----------------------|--------------|-------|
| Not a problem        | 5            | 6.0%  |
| Least severe         | 11           | 13.1% |
| One of less severe   | 18           | 21.4% |
| One of worst         | 34           | 40.5% |
| Worst                | 16           | 19.0% |

experienced fatigue (Table 3). Individuals with post-stroke fatigue reported the following FIS scores (mean  $\pm$  standard deviation) for cognitive (0-40), psychosocial (0-80), and physical (0-40) aspects of fatigue respectively:  $9.9 \pm 9.2$ ,  $20.2 \pm 17.8$ , and  $13.8 \pm 8.7$ .

#### Predictors of Fatigue

Linear regression analysis was performed to determine which factors present during hospitalization for acute stroke in the 228 respondents predicted fatigue at one year, quantified in terms of frequency (days/month), duration (hours/day), attributed disability (scale of 0 to 10), or rank as a symptom (not a symptom to worst symptom) (Table 4). Younger age at the time of stroke was the only consistent significant predictor of increased fatigue measures at one year. Younger age predicted increased fatigue frequency ( $\beta=-0.20$ ;  $p=0.01$ ), fatigue duration ( $\beta=-0.22$ ,  $p=0.003$ ), disability attributed to fatigue ( $\beta=-0.24$ ,  $p=0.002$ ), and ranking of fatigue as the worst or one of the worst symptoms post-stroke ( $\beta=-0.24$ ,  $p=0.001$ ).

Among those patients with fatigue at one year, linear regression analysis was performed to determine which factors present during hospitalization for acute stroke predicted the cognitive, psychosocial, and physical components of fatigue (Table 5). Higher pre-stroke disability predicted higher levels of cognitive ( $\beta=0.29$ ,  $p=0.03$ ), psychosocial ( $\beta=0.33$ ,  $p=0.02$ ), and physical ( $\beta=0.34$ ,  $p=0.01$ ) fatigue. Younger age predicted increased cognitive ( $\beta=-0.27$ ,  $p=0.04$ ) and psychosocial ( $\beta=-0.27$ ,  $p=0.04$ ) fatigue.

#### Correlates of Fatigue

At one year, the mean GDS among all respondents was 7.5. Severe fatigue was observed in the absence of significant depressive symptoms as 49.0% (24/49) of respondents who reported fatigue as their worst or one of their worst symptoms did not report elevated GDS ( $\geq 11$ ). However, fatigue was related to depressive symptoms overall as the GDS score was positively correlated with increased fatigue frequency ( $r=0.3$ ,  $p<0.001$ ), fatigue duration ( $r=0.4$ ,  $p<0.001$ ), disability attributed to fatigue ( $r=0.5$ ,  $p<0.001$ ), and fatigue that was ranked as one of the worst

symptoms post-stroke ( $r=0.4$ ,  $p<0.001$ ) (Table 6). The impact of fatigue was also seen on subjective ratings of quality of life, measured by the RNL scale, as the RNL was negatively associated with increased fatigue frequency ( $r=-0.2$ ,  $p=0.01$ ), fatigue duration ( $r=-0.3$ ,  $p<0.001$ ), disability attributed to fatigue ( $r=-0.3$ ,  $p<0.001$ ), and fatigue that was ranked as one of the worst post-stroke symptoms ( $r=-0.2$ ,  $p=0.003$ ). However, there was no relationship between fatigue and functional disability measured by BI or mRS at one year.

#### DISCUSSION

Post-stroke fatigue has been described as a highly prevalent but largely overlooked issue in stroke care<sup>2</sup>. A recent review of post-stroke fatigue concluded that understanding of this phenomenon is still in the foundation stage<sup>14</sup>. In this study of risk factors for post-stroke fatigue using a multidimensional fatigue scale, we demonstrated that the only consistent predictor of fatigue among a number of stroke-related variables is younger age at the time of stroke. Younger age predicted a higher frequency and duration of fatigue episodes at one year. As well, younger age was predictive of increased impairments attributed to fatigue and the belief that fatigue was one of the worst symptoms post-stroke. The heightened burden of fatigue among

**Table 4: Linear regression analysis for predictors of fatigue at one year**

|                   | Fatigue         |                    |                    |                    |
|-------------------|-----------------|--------------------|--------------------|--------------------|
|                   | Frequency       | Duration           | Disability         | Symptom Rank       |
| <b>Predictors</b> |                 |                    |                    |                    |
| Age               | $\beta=-0.20^*$ | $\beta=-0.22^{**}$ | $\beta=-0.24^{**}$ | $\beta=-0.24^{**}$ |
| Sex               | $\beta=-0.02$   | $\beta=-0.04$      | $\beta=-0.07$      | $\beta=-0.03$      |
| Prior Stroke      | $\beta=0.10$    | $\beta=0.19^{**}$  | $\beta=0.10$       | $\beta=0.09$       |
| Pre-OHS           | $\beta=-0.002$  | $\beta=0.12$       | $\beta=0.15$       | $\beta=0.03$       |
| Marital Status    | $\beta=0.03$    | $\beta=-0.07$      | $\beta=0.04$       | $\beta=0.007$      |
| Orientation       | $\beta=0.03$    | $\beta=0.04$       | $\beta=0.08$       | $\beta=0.05$       |
| Lift Arms         | $\beta=0.06$    | $\beta=-0.12$      | $\beta=0.02$       | $\beta=0.02$       |
| Walk              | $\beta=-0.08$   | $\beta=-0.15$      | $\beta=-0.03$      | $\beta=-0.13$      |
| First SSS         | $\beta=0.04$    | $\beta=-0.003$     | $\beta=0.07$       | $\beta=0.03$       |
| First BI          | $\beta=-0.04$   | $\beta=-0.04$      | $\beta=-0.12$      | $\beta=-0.05$      |
| Localization      | $\beta=-0.003$  | $\beta=0.05$       | $\beta=0.009$      | $\beta=0.009$      |
| Discharge OHS     | $\beta=0.04$    | $\beta=-0.10$      | $\beta=-0.01$      | $\beta=0.01$       |
| Discharge BI      | $\beta=0.16$    | $\beta=0.15$       | $\beta=0.20$       | $\beta=0.18$       |
| Stroke Recurrence | $\beta=0.01$    | $\beta=0.09$       | $\beta=0.04$       | $\beta=0.04$       |

$p<0.05^*$ ;  $p<0.01^{**}$ ;  $p<0.001^{***}$

**Table 5: Linear regression analysis of predictors of fatigue subtypes among stroke survivors experiencing fatigue**

| Predictors        | Fatigue         |                 |                |
|-------------------|-----------------|-----------------|----------------|
|                   | Cognitive       | Psychosocial    | Physical       |
| Age               | $\beta=-0.27^*$ | $\beta=-0.27^*$ | $\beta=-0.15$  |
| Sex               | $\beta=-0.12$   | $\beta=-0.15$   | $\beta=-0.14$  |
| Prior Stroke      | $\beta=-0.02$   | $\beta=-0.04$   | $\beta=-0.02$  |
| Pre-OHS           | $\beta=0.29^*$  | $\beta=0.33^*$  | $\beta=0.34^*$ |
| Marital Status    | $\beta=0.14$    | $\beta=0.15$    | $\beta=-0.03$  |
| First SSS         | $\beta=0.30^*$  | $\beta=0.18$    | $\beta=0.24$   |
| First BI          | $\beta=0.30$    | $\beta=0.34$    | $\beta=0.40$   |
| Localization      | $\beta=0.08$    | $\beta=0.03$    | $\beta=-0.01$  |
| Discharge OHS     | $\beta=0.07$    | $\beta=0.18$    | $\beta=0.12$   |
| Discharge BI      | $\beta=-0.12$   | $\beta=-0.13$   | $\beta=-0.19$  |
| Stroke Recurrence | $\beta=-0.006$  | $\beta=-0.07$   | $\beta=0.07$   |

$p<0.05^*$ ;  $p<0.01^{**}$ ;  $p<0.001^{***}$

the young may be attributed to greater cognitive and psychosocial fatigue, as physical fatigue remained constant with age.

Fatigue has important implications. Younger stroke survivors identify post-stroke fatigue as an incapacitating symptom, resulting in “an inability to engage in everyday life”<sup>32</sup>. In a qualitative study of stroke patients less than 55 years, fatigue had financial implications related to inability to re-enter the workforce and impaired ability to perform social roles such as caregiver. Quality of life was significantly lower among young adult stroke patients (15-49 years at stroke onset) who experienced fatigue with impaired physical and social function at a mean follow-up of six years<sup>10</sup>. A qualitative study comparing the perspective of the patient to the health care team in the first year post-stroke indicated that the health care team had a biomedical focus while the patient was also concerned about social and psychological aspects of recovery<sup>33</sup>. In that study, patients identified fatigue as a limiting factor to regaining their former identity, however, health care professionals did not document fatigue as an identified issue in chart notes dating from the same time period as the research interviews.

In one study, young adults, 15-49 years at the time of stroke, had significantly higher fatigue than age-matched controls<sup>13</sup>. In another study in which there was a 33% prevalence of fatigue 1.5

years post-stroke, older age at time of stroke was protective against fatigue<sup>7</sup>. However, there is no consensus concerning the relationship of age to post-stroke fatigue, likely due to heterogeneity in study populations, duration of follow-up, and definitions of fatigue. While several studies report no significant association<sup>6,12</sup>, others demonstrated that fatigue is associated with both older<sup>11</sup> and younger<sup>7</sup> age at stroke onset. The current study lends support to younger age being a risk factor for post-stroke fatigue. As there is no standard definition in the literature for young stroke and aging is a gradual (and variable) process, we did not attempt to describe post-stroke fatigue in our population using an age cut-off.

There are at least 55 different fatigue scales, however, none have been designed specifically for stroke patients<sup>34</sup>. The fatigue severity scale is the most commonly used assessment method in post-stroke fatigue. However, this scale does not differentiate among different aspects of fatigue<sup>14</sup>. Given the heterogeneous nature of fatigue, and the range of impact it can have on various aspects of daily living, we felt that the FIS is a useful tool. It provides a more detailed analysis of fatigue, which could be important for further research on treatment outcomes, as well as the underlying mechanisms.

The Fatigue Impact Scale (FIS) used here was also employed in an earlier study at our centre in which stroke patients (mean age = 66.6 years; mean 212 days post-stroke) were compared with elderly controls (mean age = 73.9 years)<sup>6</sup>. Fatigue was significantly higher in the stroke group (68%) than among the controls (36%). In the current study, 36.8% of stroke patients experienced fatigue at one year; as well, measures of cognitive, physical, and psychosocial fatigue were lower than among the stroke patients studied by Ingles et al<sup>6</sup>.

Lower fatigue measures in the present study may be related to study methodology. In Ingles et al<sup>6</sup>, the FIS was completed between 3 and 13 months (mean 212 days) post-stroke whereas in the present study, follow-up occurred uniformly at 12 months. This suggests that fatigue may be greater earlier in the recovery period. Our study included only ischemic stroke while Ingles et al<sup>6</sup> included intracranial hemorrhage. Participants in Ingles et al<sup>6</sup>

**Table 6: Correlates of Fatigue**

|     | Fatigue       |                |                |               |
|-----|---------------|----------------|----------------|---------------|
|     | Frequency     | Duration       | Disability     | Symptom Rank  |
| GDS | $r=0.3^{***}$ | $r=0.4^{***}$  | $r=0.5^{***}$  | $r=0.4^{***}$ |
| RNL | $r=-0.2^*$    | $r=-0.3^{***}$ | $r=-0.3^{***}$ | $r=-0.2^{**}$ |
| BI  | $r=0.07$      | $r=-0.02$      | $r=-0.03$      | $r=0.05$      |
| mRS | $r=-0.04$     | $r=-0.03$      | $r=0.02$       | $r=-0.07$     |

$p<0.05^*$ ;  $p<0.01^{**}$ ;  $p<0.001^{***}$

demonstrated moderate stroke severity (SSS 5.7), however, in our study participants fell between the categorical groups of mild to moderate using the SSS. In addition, Ingles et al<sup>6</sup> mailed the FIS to participants while the present study required a face-to-face interview; perhaps, fatigue prevented some stroke survivors from attending a scheduled interview. At the interview, a trained stroke assessor provided detailed instruction in completion of the FIS. This face-to-face instruction was unavailable to those who completed the FIS mail-out package. Those who completed participation in either study demonstrated a similar mean age and functional status.

The reported prevalence of post-stroke fatigue ranges widely from 33-77%<sup>5-8</sup>. In the largest study of post-stroke fatigue, involving 4023 participants gathered from the Riks Stroke Registry, 39% of stroke survivors reported being always or often fatigued at two-year follow-up (following exclusion of those who were “always depressed”)<sup>11</sup>. Snaphaan et al<sup>7</sup>, in a prospective study using the Checklist Individual Strength, reported that 33% of stroke survivors (including those with depression) experienced fatigue at 1.5 years. While these studies report a prevalence of fatigue similar to our finding of 36.8%, direct comparison is not possible given the methodological differences.

There is no consensus concerning the relationship of factors such as personal demographics and stroke-related characteristics in the development of post-stroke fatigue<sup>14</sup>. Female sex was suggested to lead to increased risk of fatigue in the largest post-stroke fatigue study<sup>11</sup>, however, others have failed to show a significant effect of gender<sup>6,12</sup>. Marital status is one of the predictors of stroke outcome<sup>15,17,18,22,23</sup>, but in one study<sup>35</sup> was not a significant contributor to fatigue. The impact of lesion location is unclear; post-stroke fatigue has been associated with infarcts of the brainstem<sup>13</sup>, basal ganglia<sup>36</sup>, and right hemisphere<sup>37</sup>, but other studies have found no association with lesion location<sup>6,12</sup>. In the present analysis, we did not find any relationship between fatigue and gender, marital status or lesion location.

At one year, fatigue was significantly correlated with increased GDS and decreased quality of life. Depression is commonly associated with fatigue. Fatigue is one of the criteria for diagnosis of depression in the Diagnostic and Statistical Manual of Mental Disorders (4th ed.)<sup>38</sup> and included in many depression scales<sup>39,40</sup>. Post-stroke fatigue is significantly associated with depression<sup>11-13</sup>, however, post-stroke fatigue has been demonstrated in the absence of other features of depression<sup>6,8</sup>. In our study, severe fatigue persisted in the absence of depression as 49.0% of respondents who reported fatigue as their worst or one of their worst symptoms did not report elevated depressive symptoms. As well, our results support previous work demonstrating impaired quality of life in the presence of post-stroke fatigue<sup>10</sup>.

At present, there is no standard treatment for post-stroke fatigue and no effective pharmacologic therapy<sup>41</sup>. Recently, cognitive behavioural therapy alone or in combination with graded activity training was reported to improve fatigue<sup>42,43</sup>. Following 12 weeks of intervention, fatigue improved in both treatment conditions, however, there was greater amelioration of fatigue in the combined cognitive therapy and graded activity training group. The beneficial effect of therapy persisted at six-

month follow-up. As cognitive therapy focused on “pacing and relaxation”, it would be interesting to examine the additional influence of sleep hygiene practices on post-stroke fatigue.

Strengths of this study include prospective design with uniform follow-up provided by a trained stroke assessor at 12 months post-stroke. Participation was good with 57.6% (n=228) of survivors completing the study. Fatigue was quantified using the FIS into psychosocial, cognitive, and physical components allowing greater insight into the patient experience of fatigue. Weaknesses of this study include a selection bias that may have excluded fatigued individuals who did not feel capable of attending a scheduled interview. As well, we did not capture therapies patients may have tried in an attempt to ameliorate post-stroke fatigue.

In summary, younger stroke survivors experienced an increased burden of fatigue, specifically cognitive and psychosocial fatigue, which has important implications on quality of life. This should not be surprising given qualitative research demonstrating the pressure felt by younger stroke survivors to return to previous roles in the work-force and family unit<sup>32</sup>.

Stroke survivors cite fatigue as a significant concern; however, fatigue is not consistently documented by health care professionals<sup>33</sup> and may be under-recognized as a factor that impedes recovery after stroke. This study highlights the importance of addressing cognitive and psychosocial fatigue during stroke rehabilitation. More research is required to better understand the mechanism(s) of post-stroke fatigue and develop interventions for its prevention and treatment.

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