

## ORIGINAL REPORT

## VISUAL PROBLEMS ARE ASSOCIATED WITH LONG-TERM FATIGUE AFTER STROKE

Synne G. PEDERSEN, PhD<sup>1</sup>, Mari T. LØKHOLM, CAND. PSYCHOL<sup>1</sup>, Oddgeir FRIBORG, PhD<sup>2</sup>, Marianne B. HALVORSEN, PhD<sup>3</sup>, Marit KIRKEVOLD, PhD<sup>4</sup>, Guri HEIBERG, PhD<sup>1</sup> and Audny ANKE, PhD<sup>1,4,5</sup>  
 From the <sup>1</sup>Department of Rehabilitation, University Hospital of North Norway, <sup>2</sup>Faculty of Health Sciences, Department of Psychology, UiT – The Arctic University of Norway, <sup>3</sup>Department of Pediatric Rehabilitation, University Hospital of North Norway, Tromsø, <sup>4</sup>Institute of Health and Society, Research Centre for Habilitation and Rehabilitation Model and Services (CHARM), Faculty of Medicine, University of Oslo, Oslo and <sup>5</sup>Faculty of Health Sciences, Department of Clinical Medicine, UiT – The Arctic University of Norway, Tromsø, Norway

**Objective:** Post-stroke fatigue may be associated with functioning even in patients with mild stroke. In order to guide rehabilitation, the aim of this study was to investigate the independent contribution of 12 function-related domains to severe long-term fatigue.

**Design:** Observational follow-up study.

**Subjects:** A total of 144 stroke survivors (mean age 67.3, standard deviation (SD) 10.9 years) were included.

**Methods:** Fatigue 3–4 years post-stroke was measured with the Fatigue Severity Scale (cut-off  $\geq 5$ ). Independent variables were the multidimensional Stroke-Specific Quality of Life scale with 12 domains, demographics, and baseline stroke characteristics.

**Results:** Most of the participants had mild and moderate stroke. Thirty-five percent ( $n = 51$ ) reported severe fatigue 3–4 years after stroke. Those living with a significant other, and working participants reported significantly less fatigue. All domains of the Stroke-Specific Quality of Life scale were significantly associated with the Fatigue Severity Scale. Adjusted for age, sex, marital status, and work status, the domains “energy”, “mood”, and, unexpectedly, the domain “vision”, were all variables independently associated with severe long-term fatigue.

**Conclusion:** Stroke survivors with prominent self-reported visual problems were more likely to experience fatigue. This finding should be verified in further studies. Visual examination and visual rehabilitation may reduce fatigue in selected stroke survivors.

**Key words:** fatigue; health-related quality of life; stroke; visual disorder.

Accepted Dec 20, 2022

J Rehabil Med 2023; 55: jrm00374

DOI: 10.2340/jrm.v55.4813

Correspondence address: Synne Garder Pedersen, Department

## LAY ABSTRACT

Post-stroke fatigue presumes worse outcomes for rehabilitation and recovery after stroke. More knowledge of how specific long-term consequences relate to fatigue is needed to guide care and rehabilitation. The aim of this study is to investigate whether specific areas of function are related to fatigue 3–4 years after stroke. In total, 144 stroke survivors with predominantly initial mild and moderate stroke severity were included. Self-reported questionnaires with 12 function-related areas from a stroke-specific health-related quality of life measurement were tested in relation to a fatigue scale. This study found severe fatigue in 35% of participants. All functional areas were related to fatigue. When corrected for age, sex, and marital status the domains “energy”, “mood”, and “vision” were of particular importance for severe fatigue. The results of this study indicate that stroke survivors with prominent visual problems may especially be at risk of severe fatigue.

of Rehabilitation, University Hospital of North Norway, Sykehusveien 38, 9038 Tromsø, Norway. Email: synne.garder.pedersen@unn.no; synnegp@hotmail.com

Post-stroke fatigue (PSF) is a common and long-lasting sequela of stroke (1–4). PSF may persist among 40–74% of patients 2–3 years after (5–9), and 37% 6 years after stroke (1). Even after mild stroke PSF can be a major symptom; however, this is easily obscured by other symptoms (2, 10–12). Therefore, more evidence about how specific long-term functional consequences relate to severe fatigue is needed in order to guide care and rehabilitation (1, 13). The current study is an observational follow-up study of fatigue and multidimensional health-related quality of life (HRQoL), measured with the Stroke-Specific Quality of Life (SS-QOL) scale (14).

The relationship between HRQoL and PSF seems to be consistently negatively correlated (1, 3, 4, 9, 13, 15), and thus mapping of HRQoL may be considered complementary to the assessment of fatigue (3). A limitation with the available studies on HRQoL is the generic quality of

most measures (13), or studies yielding single global scores (15). In contrast, Elf et al. (1) investigated the impact of stroke 6 years later using the HRQoL measure Stroke Impact Scale (SIS) and observed higher odds of PSF among persons with worse SIS-domains scores related to; participation, mobility, communication, emotion, memory/thinking, and strength. The activities of daily life (ADL) domain scores and hand function were, however, less affected. This suggests that PSF is associated with functional impairments across several domains. Psychological factors may also contribute to long-term PSF (16), and prior studies have shown overlaps with PSF and symptoms of anxiety and depression (1, 5–9).

Following stroke, different impairments and functional difficulties may occur in a variety of combinations. For example, within motor (17), sensory (18), cognitive (19), visual (20), communicative (21), or emotional (22) areas. Studies have found associations between ADL and fatigue in a long-term perspective (5), although other studies have not established this association (1, 9). Short-term PSF levels were significantly associated with the component of mental HRQoL (13). Studies are inconclusive concerning the relationship between fatigue and cognition post-stroke (23). Furthermore, a possible important clinical association between vision and mental fatigue has been found in a Swedish study (24). More knowledge of how different stroke-related consequences are associated with fatigue are warranted, and we are not aware of any other studies using a multidimensional stroke-specific instrument, also including the domains vision and energy, to assess such associations.

The current study examines: (i) associations between the function-related domains of the SS-QOL scale and fatigue 3–4 years after stroke; and (ii) which of the 12 sub-domains are the most significant factors for severe fatigue, as examined in a logistic regression analysis including crude and adjusted coefficients.

In concordance with the literature, the a priori hypothesis of this study was that the SS-QOL domain “mood”, and the component score of the SS-QOL “cognitive-social-mental” dimension would be positively correlated and associated with fatigue. Furthermore, it was hypothesized that the domains “energy” and “mood” in the SS-QOL would be significant factors in regression analysis for severe fatigue, as the energy-domain covers tiredness and the need for rest after stroke.

## METHODS

### Design

This is an observational study in North Norway with primary data (SS-QOL and fatigue) collected 3–4 years

after stroke. Some of the potential confounding variables were, however, collected at baseline and 12 months post-stroke. The study is registered in ClinicalTrials.gov as “Emotional and cognitive determinants of post-stroke fatigue. A prospective study” (NCT 03639259).

### Participants

Participants were recruited from the Norwegian arm of the study “Rehabilitation, function, and quality of life after stroke in North Norway and Central Denmark – the NorDenStroke study”. Patients with verified cerebral stroke were recruited from stroke units at the University Hospital of North Norway (UNN-HF) between March 2014 and December 2015 (25). Exclusion criteria at baseline were patients with stroke related to brain malignancy, subarachnoid haemorrhage, or brain trauma. Stroke survivors were included if they were: (i) 18 years or older; (ii) diagnosed with stroke according to the International Classification of Diseases, version 10 (ICD-10 I.61 or I.63); (iii) admitted to 1 of the 3 stroke units at UNN-HF, located at either Narvik, Harstad or Tromsø; and (iv) for the current study; completed questionnaires in the NorDenStroke study 1 year after stroke ( $n=217$ ). In a drop-out analysis the 149 participants in the fatigue study were compared with the 68 stroke survivors who did not respond or consent at a follow-up 3–4 years post-stroke, when invited to participate (Fig. 1). The participants who did not respond or consent ( $n=68$ ) were significantly ( $p=0.001$ ) older than those who agreed to the follow-up ( $n=149$ ) (67 vs 72 years), but the groups did not differ in terms of sex, stroke type or stroke severity.

### Data collection procedures

The Regional Committee for Research Ethics in Medicine and Health Sciences in North Norway approved

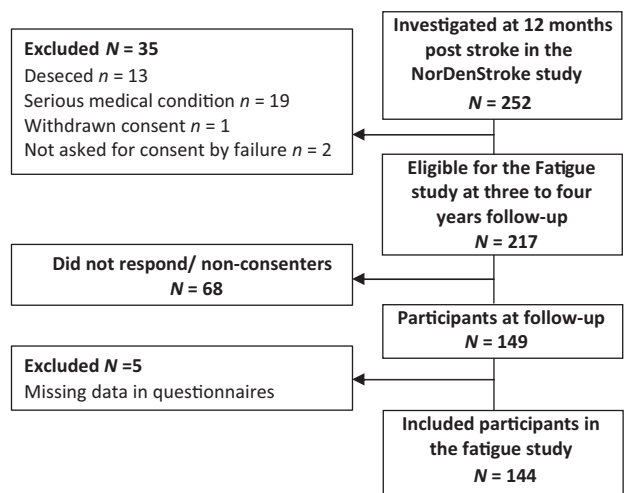


Fig. 1. Study flowchart.

the study. For the current follow-up study at 3–4 years post-stroke, a health professional informed potential participants about the study and asked for written consent. Questionnaires were sent by post. After new written informed consent was obtained, earlier collected information pertaining to stroke-related factors and medical information either from the National Norwegian Stroke Register, or from the patient's medical files were utilized. The latter concerned patients that was not already registered in register ( $n=8$ ). When data were missing in questionnaires, participants received a follow-up by telephone call and were encouraged to answer any missing questions. Through this process, it was established that some participants ( $n=5$ ) were unable to complete the questionnaires due to deteriorating health.

#### *Dependent variable*

Fatigue 3–4 years after stroke was measured with the Norwegian version (26) of the Fatigue Severity Scale (FSS). The FSS has been used extensively to assess fatigue in population-based stroke research (10). Ozyemisci-Taskiran et al. (27) showed that the FSS is a valid and reliable scale to measure fatigue after stroke, with excellent internal consistency (Cronbach's  $\alpha$ : 0.928), and good test–retest reliability (intra-class correlation coefficient (ICC): 0.742). However, the FSS was not found sensitive enough to differentiate fatigue in stroke from the control subjects (patients with other diagnoses) (27). The questionnaire comprises of 9 items probing for fatigue in daily life across domains of daily activity, social participation, sleep, and motivation. Items are graded on a 7-point Likert scale ranging from 1 (no problem) to 7 (a significant problem), with higher scores indicating more fatigue. A global average score is calculated based on all 9 items (25). A cut-off score  $\geq 5$  is recommended for defining cases of severe fatigue (26) and was applied in the current study.

#### *Independent variables*

Function-related consequences were collected with the Stroke-Specific Quality of Life (SS-QOL) scale (14) 3–4 years after stroke. The SS-QOL comprehensively indexes a multiple number of HRQoL domains that may be severely affected in a stroke survivor's life. The SS-QOL scale covers 12 functional domains across 49 items and has been validated for use in Norwegian clinical settings (28). The domains are: “work and productivity”, “upper extremity function”, “mobility”, “self-care”, “energy”, “mood”, “social roles”, “family roles”, “vision”, “language”, “thinking”, and “personality”. Each domain is measured by 3–6 six items using a 5-point (1–5) Likert scale (higher scores

indicate better function). An example from the language domain; “Did you have trouble finding the word you wanted to say?” and possible replies: 1: could not do it at all; 2: a lot of trouble; 3: some trouble; 4: a little trouble; 5: no trouble at all. Another example from the energy domain; “I was too tired to do what I wanted to do” and possible replies: 1: strongly agree; 2: moderately agree; 3: neither agree nor disagree; 4: moderately disagree; 5: strongly disagree. All items are answered based on how the respondent has experienced the specific question or statement the past week. An average score for each domain is calculated, which allows for comparisons between domains and is helpful for identifying specific areas that are affected by stroke (14). The overall SS-QOL score is used for providing a simpler summary. The reliability of the SS-QOL specific and overall scores have been documented in numerous studies, confirming an acceptable internal consistency of the domains (14, 28, 29). The test–retest reliability coefficient is documented as generally good (Spearman's  $\rho=0.65–0.99$ ) (28, 29).

#### *Potential confounding variables*

*Demographic data and stroke characteristics.* Information about sex, age, and stroke characteristics were collected through the National Norwegian Stroke Register or medical records at baseline. Marital status (married/cohabitant or single), level of education, living- and working situation were collected through questionnaires at 12 months.

*Pre-stroke fatigue.* Fatigue prior to stroke was assessed with 1 question 3–4 years post-stroke: “Did you have a problem with fatigue before your stroke?” (30) (yes/no).

#### *Statistical analyses*

The Statistical Package of Social Sciences (SPSS) software (IBM Corporation, version 28) were used for all statistical analyses. Descriptive data was presented as means, standard deviations (SDs), or medians and interquartile range (IQR). For correlation-tests, the distributional properties of the SS-QOL subscales were examined visually with normality plots with tests (e.g. Q-Q plots). In addition, z-values for skewness and kurtosis were evaluated according to sample size, and formal normality-test (Shapiro–Wilk test) was used to assess whether assumption of normality was acceptable.

Because the SS-QOL data was non-normally distributed, Spearman's rank-order correlations were used to assess bivariate relationships between the FSS and the 12 domains, the 2 components score, and total score of the SS-QOL scale. Correlations ( $\rho$ ) were defined as low  $<0.3$ , moderate  $0.3–0.5$ , and high  $\geq 0.5$  based on

**Table I.** Demographic and stroke characteristics of patients with or without fatigue

	Total <i>n</i> = 144 (100%)	FSS < 5 <i>n</i> = 93 (65%)	FSS ≥ 5 <i>n</i> = 51 (35%)	<i>p</i>
<i>Baseline</i>				
Age at time of injury, mean ( <i>SD</i> )	67.3 (10.9)	67.3 (9.4)	67.3 (13.2)	0.988
Age, <i>n</i> (%)				
18–55 years	22 (15)	11 (50)	11 (50)	0.066
56–74 years	86 (60)	62 (72)	24 (28)	
> 75 years	36 (25)	20 (56)	16 (44)	
Sex, <i>n</i> (%)				
Female	52 (36)	22 (42)	30 (58)	<0.001
Male	92 (64)	71 (77)	21 (23)	
Stroke type, <i>n</i> (%)				
Ischemic	130 (90)	82 (63)	48 (37)	0.198*
Haemorrhagic	14 (10)	11 (79)	3 (21)	
Scandinavian Stroke Scale (SSS), median [IQR]	47 [14]	48.2 [12]	46.1 [11]	0.151
SSS impairment, <i>n</i> (%)				
Very severe (0–14), severe (15–29) and moderate (30–44)	53 (37)	32 (60)	21 (40)	0.421
Mild (45–58)	91 (63)	61 (67)	30 (33)	
<i>Variables 1-year post stroke</i>				
Education, <i>n</i> (%)				
≤10 years	49 (34)	30 (61)	19 (39)	0.410
> 10 years	82 (57)	56 (68)	26 (32)	
Missing	13 (9)			
Marital status, <i>n</i> (%)				
Married/cohabitant	106 (74)	76 (72)	30 (28)	0.003
Widowed/single	38 (26)	17 (45)	21 (55)	
Work status, <i>n</i> (%)				
Working	21 (15)	18 (86)	3 (14)	0.022*
Retired/sick leave/unemployed	123 (85)	75 (61)	48 (39)	
<i>Variables 3–4 years post-stroke</i>				
Pre-stroke fatigue, <i>n</i> (%)				
No	114 (80)	76 (67)	38 (33)	0.308
Yes	30 (20)	17 (57)	13 (43)	

\*Fisher's exact test.

FSS: Fatigue Severity Scale; SSS: Scandinavian Stroke Scale.

reasonable conversions to correlation coefficients from the standardized mean differences (Cohen's *d*) (31). Differences between groups (fatigue/non-fatigue) were tested by independent sample *t*-tests and Mann–Whitney *U* tests for continuous normally and non-normally distributed variables, respectively, and by the  $\chi^2$  test for categorical variables. Effect sizes were calculated as standardized mean differences, i.e. Cohen's *d*. Although the interpretation guidelines for power are adjusted in rehabilitation research (32), Cohen's effect sizes were used in this study: a value <0.5 is regarded as small, 0.5–0.8 medium, and >0.8 large effect size (31).

Prior to logistic regression analyses, indices of multicollinearity were assessed with a multiple linear regression (with fatigue as a continuous outcome) with tolerance- and variance inflation factor (VIF) values. The SS-QOL domains "mobility" and "work/productivity" were withdrawn from the logistic analyses due to multicollinearity-issues with most SS-QOL domains (VIF = 6.348 and 7.506). Backward binary logistic regression was applied to investigate which domains of the SS-QOL were significantly associated with fatigue/non-fatigue. Variables from univariate analyses with *p*-values

<0.1 were included in the analyses (age, sex, marital status, and work status). Although age was removed during the backward analysis because of non-significant *p* (>0.05), age was re-added as the last adjustment variable to ensure that results were not age-related. The model fit was investigated with the Hosmer and Lemeshow test to assess whether the agreement between observed and predicted outcomes at each decline of risk, increasing from 0 to 1, is roughly equal. Nagelkerke's  $R^2$  expresses the ratio of sum likelihoods for the intercept only vs the full regression model, thus approximating the well-known R-square index for explained variance.

## RESULTS

Of 149 eligible participants who completed the survey at 3–4 years post-stroke, 5 were excluded due to missing data in the administered questionnaires. The remaining participants (*n* = 144) had no missing data on the survey forms.

The demographic and stroke characteristics of the participants and their relation to FSS are shown in Table I. Thirty-five percent of the participants (*n* = 51) had fatigue 3–4 years after stroke. Ninety percent

**Table II.** Associations of the Stroke-Specific Quality of Life (SS-QOL) scale and fatigue measured with the Fatigue Severity Scale ( $n=144$ )

	Fatigue Severity Scale (FSS)		
	Spearman's rho	95% CI	$p$
SSQOL total	-0.688**	-0.785   -0.567	<0.001
Self-care	-0.360**	-0.497   -0.205	<0.001
Vision	-0.382**	-0.514   -0.228	<0.001
Language	-0.362**	-0.507   -0.201	<0.001
Mobility	-0.458**	-0.591   -0.302	<0.001
Work/productivity	-0.417**	-0.555   -0.262	<0.001
Upper extremity function	-0.486**	-0.614   -0.344	<0.001
Thinking	-0.474**	-0.591   -0.339	<0.001
Personality	-0.504**	-0.627   -0.365	<0.001
Family roles	-0.567**	-0.682   -0.434	<0.001
Mood	-0.643**	-0.745   -0.512	<0.001
Social roles	-0.584**	-0.688   -0.453	<0.001
Energy	-0.634**	-0.747   -0.506	<0.001
Component scores			
Physical Health (PH) <sup>a</sup>	-0.504**	-0.629   -0.360	<0.001
Cognitive-Social-Mental (CSM) <sup>b</sup>	-0.675**	-0.779   -0.552	<0.001

<sup>a</sup>Self-care, mobility, work/productivity, upper extremity function.

<sup>b</sup>Thinking, personality, family roles, mood, social roles, energy.

CI: confidence intervals.

Spearman's  $r$  was bootstrapped (1,000 samples) to ensure robust 95% confidence intervals (95% CI).

( $n=130$ ) of the participants had an ischemic stroke, and 63% ( $n=91$ ) had mild stroke impairment measured with the Scandinavian Stroke Scale at baseline (Table I). Age was not significantly associated with fatigue, although there was a tendency towards more fatigue in the youngest and oldest age group in this population. Participants were predominantly men (64%); however, female sex was significantly associated with fatigue ( $p \leq 0.001$ ). Those living with a significant other, as well as working participants at 12 months post-stroke, reported significantly less fatigue at follow-up than

those who were unmarried, or lived alone ( $p=0.003$ ) and non-working participants ( $p=0.022$ ).

As shown in Table II, the SS-QOL total scale, the 12 domains, and the 2 SS-QOL component scores (25) were all significantly correlated with fatigue ( $\rho > 0.3$ ). Seven of the sub-domains were moderately correlated with the FSS ( $\rho 0.3-0.5$ ). Five of the sub-domains, the total SS-QOL scale and the 2 dimensions of SS-QOL had all high correlations with the FSS ( $\rho > 0.5$ ) (Table II). There was a statistically significant difference in the means between groups defined as non-fatigued (FSS <5) and fatigued (FSS  $\geq 5$ ) in all aspects of the SS-QOL scale, where all domains, total-score, and component-scores of the SS-QOL scale were generally lower in the fatigued group (Table III).

Logistic regression analysis showed that the hypothesized associated domains "energy" and "mood", together with the domain "vision", were independent variables associated with severe fatigue at long-term follow-up. In the overall model (without division of groups within the vision-domain), vision had an odds ratio (OR)=4.44 ( $p=0.037$ , 95% CI 1.06–17.68). To explore the vision-domain further, it was divided into 3 groups. Within those reporting severe fatigue,  $n=26$  had no visual problems (score 5/5),  $n=11$  had some visual problems (score between 4.5 and 5, indicating easy problems in 1 of the items of vision), and  $n=14$  reported pronounced visual problems (score <4.5, indicating more complex problems across items, or large impairment in 1 item). The latter group explained severe fatigue (OR 4.1, CI 1.08–15.82,  $p=0.038$ ). Among the demographic adjustment-variables those who were unmarried, or living alone, were more likely to report severe fatigue (OR 0.2,  $p=0.006$ ). Nagelkerke's  $R^2=0.53$ . Age did

**Table III.** Comparison of Stroke-Specific Quality of Life (SS-QOL) scale scores between groups defined as non-fatigued and fatigued

SSQOL index scores	FSS < 5	FSS $\geq 5$	Mann-Whitney $U$ test $p$ -value	Cohen's $d$
	$N=93$ Mean (SD)	$N=51$ Mean (SD)		
SSQOL total	4.54 (0.515)	3.77 (0.703)	<0.001	1.249
Self-care	4.84 (0.466)	4.57 (0.742)	<0.001	0.435
Vision	4.91 (0.206)	4.57 (0.636)	<0.001	0.719
Language	4.78 (0.366)	4.44 (0.676)	<0.001	0.625
Mobility	4.67 (0.611)	4.08 (0.853)	<0.001	0.795
Work/productivity	4.72 (0.607)	4.18 (0.914)	<0.001	0.696
Upper extremity function	4.78 (0.476)	4.17 (0.921)	<0.001	0.832
Thinking	4.07 (1.141)	3.17 (1.193)	<0.001	0.771
Personality	4.27 (1.070)	3.37 (1.230)	<0.001	0.780
Family roles	4.54 (0.875)	3.36 (1.293)	<0.001	1.068
Mood	4.34 (0.999)	2.96 (1.175)	<0.001	1.265
Social roles	4.25 (0.903)	3.28 (1.027)	<0.001	1.003
Energy	3.96 (1.233)	2.38 (1.233)	<0.001	1.281
Component scores				
Physical Health (PH)	4.75 (.489)	4.25 (.790)	<0.001	0.761
Cognitive-Social-Mental (CSM)	4.22 (.826)	3.13 (.940)	<0.001	1.231

FSS: Fatigue Severity Scale.

**Table IV.** Binary logistic prediction model with non-fatigue and fatigue ( $n = 144$ ) as outcome at 3–4 years post-stroke

	OR	95% CI	$p$ -value
<i>Demographic adjustment-variables</i>			
Age	1.01	0.97–1.05	0.504
Female sex	2.59	0.99–6.80	0.052
Not married or cohabitant	4.32	1.51–12.30	0.006
<i>Domains of the SS-QOL scale</i>			
SS-QOL Energy	1.57	1.05–2.35	0.029
SS-QOL Mood	1.97	1.27–3.06	0.002
<i>SS-QOL Vision</i>			
Some problems with vision	2.34	0.48–11.33	0.292
Pronounced visual problems	4.14	1.08–15.82	0.038

SS-QOL: Stroke-Specific Quality of Life scale.

not significantly adjust these outcomes (Table IV). The domains “mobility” and “work/productivity” were initially withdrawn from the logistic analyses due to multicollinearity issues.

## DISCUSSION

The aims of this study were: to explore relationships between sociodemographic and stroke characteristics and long-term fatigue; to examine associations between the 12 domains and 2 components of the SS-QOL scale and fatigue; and to assess whether any of the 12 domains of the SS-QOL scale were independent variables associated with severe fatigue long-term post-stroke. The study found fatigue in 35% of participants 3–4 years after stroke. Fatigue was significantly associated with all domains, as well as both the physical health (PH) component and the cognitive-social-mental (CSM) component in the SS-QOL scale in univariate analysis (lower SS-QOL scores, higher FSS scores). Female sex and not being married or having a cohabitant, was also significantly associated with higher scores on the FSS. Concordant with the study hypothesis, the domains “energy” and “mood” were both strong correlates, and independent variables associated with severe fatigue long-term post-stroke. Unexpectedly, the domain vision was also an independently associated variable for fatigue, and additional analyses showed that the group with prominent vision problems especially were more likely to report severe fatigue. The participants in this study had a mean age of 67 years at stroke onset, and some of the participants may have had pre-existing age-related visual deficits. However, age did not affect the results in the analyses.

The proportion of PSF (35%) in the current study is lower than a comparable study (9) with approximately the same time of assessment (58%), but in line with another study with a 6-year follow-up in which 37% of the participants reported the presence of PSF (1). However, both of these studies used a diagnostic FSS cut-off  $\geq 4$ , whereas the current study used a cut-off  $\geq 5$ .

It has been argued that using a cut-off  $\geq 4$  might lead to an overestimation of fatigue (26). In a large, population-based study ( $n = 1,893$ ), almost half of the participants scored  $\geq 4$  on the FSS. Consequently, a cut-off  $\geq 5$  has been suggested for defining fatigue (26). Exact comparisons with other studies are difficult due to the unequal times of assessment, use of other fatigue-scales and the representativeness of the participants. Nevertheless, the prevalence in the current study is fairly equal to comparable studies after stroke. Since PSF is a negative prognostic factor for rehabilitation and recovery after stroke (1, 20), it has been suggested that PSF should be routinely assessed, and the symptoms addressed during the recovery process (11).

As expected, the SS-QOL domains “energy” and “mood” were strong correlates and significantly associated with severe fatigue. It has been argued that the energy-domain in the SS-QOL scale measures aspects of fatigue, and a previous study found that this domain had the largest impact of all domains in the SS-QOL scale on the participants 1 year post-stroke in 2 cohorts in different countries (25). The SS-QOL is 1 of the few multidimensional stroke-specific HRQoL instruments that includes an energy domain. No studies were found for comparison in relation to fatigue. The current study shows that the SS-QOL energy domain can be used as an indication of fatigue in future studies. The relationship between mood and fatigue found in the current study supports previous research highlighting the connection between PSF and mood problems both early and late after stroke (1, 9, 33). In the current study, the odds for PSF were higher in stroke survivors with a higher perceived impact in the mood domain (OR 1.97,  $p = 0.002$ ). This finding is in line with the study of Elf et al. (1), in which the emotion domain in the SIS scale showed similar results.

In the current study, the vision domain was an independent variable associated with severe fatigue, and the group of stroke survivors with prominent self-reported vision problems were more likely to report severe fatigue (OR 4.14). The vision domain in the SS-QOL scale has 3 graded questions: (a) Did you have trouble seeing the television well enough to enjoy a show? (b) Did you have trouble reaching for things because of poor eyesight? (c) Did you have trouble seeing things off to one side? The 3 questions do not cover the multiple problems stroke survivors might experience related to visual consequences, but do include elements that might impact function, everyday activities, and social interaction. To our knowledge, no other stroke-specific HRQoL multidimensional instrument has a vision-domain included in the measure. However, the SS-QOL scale does not include problems with reading, which is a major problem after an acquired brain injury (35). Hence, the SS-QOL may not include an important group

of patients with visual problems. The current study found 1 study by Elf et al. (1) that investigated stroke-specific HRQoL and fatigue with the Stroke Impact Scale. This instrument does not include a vision domain, and comparisons with other studies using self-reported stroke-specific measures are therefore not possible in relation to vision and fatigue. Nevertheless, the findings of the current study are in line with a study ( $n=328$ ) by Sand et al. (34), which found that participants who reported a vision problem more often experienced fatigue approximately 6 months after their stroke. This study used a generic self-reported questionnaire (15D) with a graded question on vision that included both sight and walking ability. Another study (36) found an association between binocular visual dysfunction and fatigue. The latter study had few stroke survivors included ( $n=29$ ), and follow-up between 3 and 6 months after the stroke. A study by Berthold-Lindstedt et al. (24), on patients with acquired brain injury found a statistically significant association between visual deficits (structured visual interview) and self-reported moderate-to-severe mental fatigue measured with the Mental Fatigue Scale. The prevalence of mental fatigue among stroke patients in this study was 36.8%.

Post-stroke visual impairments are common, and approximately 30% of stroke survivors report visual deficits in different studies (20, 33). Nevertheless, vision impairment is one of the most overlooked and under-treated conditions of elderly patients and those with acquired brain injuries, including stroke (24, 35, 37). The visual system is complex, involving several parts of the brain, and is a central sensory-motor modality for fine- and gross-motor functioning as well as social interaction (20, 24). Therefore, patients might not relate their symptoms to visual impairments (24, 38), but rather to the everyday impairments in function or social interactions. Following a stroke, common visual consequences are symptoms of hemianopsia, visual neglect, diplopia, reduced visual perception, oculomotor dysfunction, and double vision (20, 35). Although partial or complete recovery of visual impairments can occur, many patients develop permanent disability (20). Decreased visual function constitutes reduced postural stability, increases the risk of falls, has a negative impact on quality of life (39, 40), and may also affect the association between vision impairment and disabilities in activities of daily living (ADL) (20).

#### *Strengths and limitations of the study*

High-quality data from stroke registries, combined with questionnaires with a high completeness rate in the data, minimize the risk of information bias, representing a strength of this study. There are few studies on fatigue and associated factors long-term after stroke. Furthermore,

studies specifically investigating associations between visual impairments and fatigue in stroke populations are scarce, and amongst conducted studies participants have different primary diagnoses (24). Hence, a further strength of this study is that the population consists only of stroke survivors. Self-reported data is valuable for providing a wide range of responses, and for obtaining the individual's own perspectives, views, and opinions. However, a limitation concerning questionnaires is the non-response bias, which may be the case in this study as those who had a more severe stroke were less likely to respond in the primary study that this current study recruited from. For this reason, interpretation of results is relevant to stroke survivors with mild and moderate stroke, but extends less well to populations with more severe strokes. For the current study, a non-response bias regarding older age is relevant, since non-responders were older than responders. Although age was not significantly associated with fatigue in the current study, there was a tendency towards more fatigue in the youngest and oldest age group in this population. Thus, a higher response rate among the oldest participants might have impacted the results. Another limitation is that the visual problems were patient-reported, and not verified by visual examinations.

## CONCLUSION

This study showed that the SSQOL domains energy, mood and vision contributed to severe fatigue. Visual disorders were found to have an independent impact on severe long-term fatigue post-stroke. Both visual disturbances and fatigue are common after stroke. However, this should be investigated further in additional studies and with larger populations. These findings emphasize the importance of a thorough visual examination with follow-up, as well as visual rehabilitation, which might, in turn, reduce the burden of fatigue in stroke survivors.

## ACKNOWLEDGEMENTS

This study was made possible by the Dam Foundation. The publication charge for this article has been funded by a grant from the publication fund of UIT – The Arctic University of Norway.

*Funding/financial support: Dam Foundation*

*Ethics clearance.* The Regional Committee for Research Ethics in Medicine and Health Sciences in North Norway approved the study (Institutional Protocol Number 2017/1966).

*The authors have no conflicts of interest to declare.*

## REFERENCES

- Elf M, Eriksson G, Johansson S, von Koch L, Ytterberg C. Self-reported fatigue and associated factors six years after stroke. *PLoS One* 2016; 11: 1–9. DOI: 10.1371/journal.pone.0161942
- Paciaroni M, Acciarresi M. Poststroke fatigue. *Stroke* 2019; 50: 1927–1933. DOI: 10.1161/STROKEAHA.119.023552
- Hinkle JL, Becker KJ, Kim JS, Choi-Kwon S, Saban KL, McNair N, et al. Poststroke fatigue: emerging evidence and approaches to management: a scientific statement for healthcare professionals from the American Heart Association. *Stroke* 2017; 48: 159–170. DOI: 10.1161/STR.000000000000132
- Ramirez-Moreno JM, Munoz-Vega P, Alberca SB, Peral-Pacheco D. Health-related quality of life and fatigue after transient ischemic attack and minor stroke. *J Stroke Cerebrovasc Dis* 2019; 28: 276–284. DOI: 10.1016/j.jstrokecerebrovasdis.2018.09.046
- Glader EL, Stegmayr B, Asplund K. Poststroke fatigue: a 2-year follow-up study of stroke patients in Sweden. *Stroke* 2002; 33: 1327–1333. DOI: 10.1161/01.str.0000014248.28711.d6
- Naess H, Lunde L, Brogger J, Waje-Andreassen U. Fatigue among stroke patients on long-term follow-up. The Bergen Stroke Study. *J Neurol Sci* 2012; 312: 138–141. DOI: 10.1016/j.jns.2011.08.002
- Snaphaan L, van der Werf S, de Leeuw FE. Time course and risk factors of post-stroke fatigue: a prospective cohort study. *Eur J Neurol* 2011; 18: 611–617. DOI: 10.1111/j.1468-1331.2010.03217.x
- van der Werf SP, van den Broek HL, Anten HW, Bleijenberg G. Experience of severe fatigue long after stroke and its relation to depressive symptoms and disease characteristics. *Eur J Neurol* 2001; 45: 28–33. DOI: 10.1159/000052085
- van de Port IG, Kwakkel G, Schepers VP, Heinemans CT, Lindeman E. Is fatigue an independent factor associated with activities of daily living, instrumental activities of daily living and health-related quality of life in chronic stroke? *Cerebrovasc Dis* 2007; 23: 40–45. DOI: 10.1159/000095757
- Cumming TB, Packer M, Kramer SF, English C. The prevalence of fatigue after stroke: a systematic review and meta-analysis. *Int J Stroke* 2016; 11: 968–977. DOI: 10.1177/1747493016669861
- Vitturi BK, Mitre LP, Kim AIH, Gagliardi RJ. Prevalence and predictors of fatigue and neuropsychiatric symptoms in patients with minor ischemic stroke. *J Stroke Cerebrovasc Dis* 2021; 30: 1–7. DOI: 10.1016/j.jstrokecerebrovasdis.2021.105964
- Pedersen SG, Anke A, Aadal L, Pallesen H, Moe S, Arntzen C. Experiences of quality of life the first year after stroke in Denmark and Norway. A qualitative analysis. *Int J Qual Stud Health Well-being* 2019; 14: 1–14. DOI: 10.1080/17482631.2019.1659540
- Almhdawi KA, Jaber HB, Khalil HW, Kanaan SF, Shyyab AA, Mansour ZM, et al. Post-stroke fatigue level is significantly associated with mental health component of health-related quality of life: a cross-sectional study. *Qual Life Res* 2021; 30: 1165–1172. DOI: 10.1007/s11136-020-02714-z
- Williams LS, Weinberger M, Harris LE, Clark DO, Biller J. Development of a stroke-specific quality of life scale. *Stroke* 1999; 30: 1362–1369. DOI: 10.1161/01.STR.30.7.1362
- Chen YK, Qu JF, Xiao WM, Li WY, Weng HY, Li W, et al. Poststroke fatigue: risk factors and its effect on functional status and health-related quality of life. *Int J Stroke* 2015; 10: 506–512. DOI: 10.1111/ijss.12409
- Wu S, Mead G, Macleod M, Chalder T. Model of understanding fatigue after stroke. *Stroke* 2015; 46: 893–898. DOI: 10.1161/STROKEAHA.114.006647
- Wist S, Clivaz J, Sattelmayer M. Muscle strengthening for hemiparesis after stroke: a meta-analysis. *Ann Phys Rehabil Med* 2016; 59: 114–124. DOI: 10.1016/j.rehab.2016.02.001
- Bolognini N, Russo C, Edwards DJ. The sensory side of post-stroke motor rehabilitation. *Restor Neurol Neurosci* 2016; 34: 571–586. DOI: 10.3233/RNN-150606
- de Haan EH, Nys GM, Van Zandvoort MJ. Cognitive function following stroke and vascular cognitive impairment. *Curr Opin Neurol* 2006; 19: 559–564. DOI: 10.1097/01.wco.0000247612.21235.d9
- Sand KM, Midelfart A, Thomassen L, Melms A, Wilhelm H, Hoff JM. Visual impairment in stroke patients – a review. *Acta Neurol Scand Suppl* 2013; Suppl 127: 52–56. DOI: 10.1111/ane.12050
- Borthwick S. Communication impairment in patients following stroke. *Nurs Stand* 2012; 26: 35–41. DOI: 10.7748/ns2012.01.26.19.35.c8879
- Kim JS. Post-stroke mood and emotional disturbances: pharmacological therapy based on mechanisms. *J Stroke* 2016; 18: 244–255. DOI: 10.5853/jos.2016.01144
- Lagogianni C, Thomas S, Lincoln N. Examining the relationship between fatigue and cognition after stroke: a systematic review. *Neuropsychol Rehabil* 2018; 28: 57–116. DOI: 10.1080/09602011.2015.1127820
- Berthold-Lindstedt M, Johansson J, Ygge J, Borg K. Vision-related symptoms after acquired brain injury and the association with mental fatigue, anxiety and depression. *J Rehabil Med* 2019; 51: 499–505. DOI: 10.2340/16501977-2570
- Pedersen SG, Friberg O, Heiberg GA, Arntzen C, Stabel HH, Thrane G, et al. Stroke-specific quality of life one-year post-stroke in two Scandinavian country-regions with different organisation of rehabilitation services: a prospective study. *Disabil Rehabil* 2021; 43: 3810–3820. DOI: 10.1080/09638288.2020.1753830
- Lerdal A, Wahl A, Rustoen T, Hanestad BR, Mow T. Fatigue in the general population: a translation and test of the psychometric properties of the Norwegian version of the fatigue severity scale. *Scand J Public Health* 2005; 33: 123–130. DOI: 10.1080/14034940410028406
- Ozyemisci-Taskiran O, Batur EB, Yuksel S, Cengiz M, Karatas GK. Validity and reliability of fatigue severity scale in stroke. *Topics in Stroke Rehabilitation* 2019; 26: 122–127. DOI: 10.1080/10749357.2018.1550957
- Pedersen SG, Heiberg GA, Nielsen JF, Friberg O, Stabel HH, Anke A, et al. Validity, reliability and Norwegian adaptation of the Stroke-Specific Quality of Life (SS-QOL) scale. *SAGE Open Med* 2018; 6: 1–10. DOI: 10.1177/2050312117752031
- Muus I, Williams LS, Ringsberg KC. Validation of the Stroke Specific Quality of Life Scale (SS-QOL): test of reliability and validity of the Danish version (SS-QOL-DK). *Clin Rehabil* 2007; 21: 620–627. DOI: 10.1177/0269215507075504
- Duncan F, Lewis SJ, Greig CA, Dennis MS, Sharpe M, MacLulich AM, et al. Exploratory longitudinal cohort study of associations of fatigue after stroke. *Stroke* 2015; 46: 1052–1058. DOI: 10.1161/STROKEAHA.114.008079
- Cohen J. *Statistical power analysis for the behavioral sciences*. 2nd edn. New York: Routledge, 1988.
- Kinney AR, Eakman AM, Graham JE. Novel effect size interpretation guidelines and an evaluation of statistical power in rehabilitation research. *Arch Phys Med Rehabil* 2020; 101: 2219–2226. DOI: 10.1016/j.apmr.2020.02.017
- Wu S, Barugh A, Macleod M, Mead G. Psychological associations of poststroke fatigue: a systematic review and meta-analysis. *Stroke* 2014; 45: 1778–1783. DOI: 10.1161/STROKEAHA.113.004584
- Sand KM, Wilhelmsen G, Naess H, Midelfart A, Thomassen L, Hoff JM. Vision problems in ischaemic stroke patients: effects on life quality and disability. *Eur J Neurol* 2016; 23: 1–7. DOI: 10.1111/ene.12848



35. Berthold-Lindstedt M, Ygge J, Borg K. Visual dysfunction is underestimated in patients with acquired brain injury. *J Rehabil Med* 2017; 49: 327–332. DOI: 10.2340/16501977-2218
36. Schow T, Teasdale TW, Quas KJ, Rasmussen MA. Problems with balance and binocular visual dysfunction are associated with post-stroke fatigue. *Topics in Stroke Rehabilitation* 2017; 24: 41–49. DOI: 10.1080/10749357.2016.1188475
37. Wolter M, Preda S. Visual deficits following stroke: maximizing participation in rehabilitation. *Top Stroke Rehabil* 2006; 13: 12–21. DOI: 10.1310/3JRY-B168-5N49-XQWA
38. Berthold-Lindstedt M, Johansson J, Ygge J, Borg K. How to assess visual function in acquired brain injury – asking is not enough. *Brain Behav* 2021; 11: 1–8. DOI: 10.1002/brb3.1958
39. Corriveau H, Hebert R, Raiche M, Prince F. Evaluation of postural stability in the elderly with stroke. *Arch Phys Med Rehabil* 2004; 85: 1095–1101. DOI: 10.1016/j.apmr.2003.09.023
40. Papageorgiou E, Hardiess G, Schaeffel F, Wiethoelter H, Karnath HO, Mallot H, et al. Assessment of vision-related quality of life in patients with homonymous visual field defects. *Graefes Arch Clin Exp Ophthalmol* 2007; 245: 1749–1758. DOI: 10.1007/s00417-007-0644-z