Clinical Neurology and Neurosurgery 174 (2018) 192–197

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Chronic post-stroke fatigue: It may no longer be about the stroke itself

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ARTICLE INFO

Keywords:
Post-stroke fatigue
Stroke
Outcomes
Quality of life

ABSTRACT

Objective: Post-stroke fatigue (PSF) is a debilitating complication of stroke recovery. Contributing risk factors, whether they are modifiable, and if they change over time remain understudied. We determine factors associated with PSF and how they evolve from the subacute through chronic phases of recovery.

Patients and methods: A consecutive series of patients presenting to our comprehensive stroke center with acute stroke were seen in follow-up within 6 months of infarct and administered the Functional Assessment of Chronic Illness Therapy (FACIT) fatigue scale to evaluate for PSF. It was re-administered > 6 months post-infarct. Demographics, stroke characteristics (NIH Stroke Scale [NIHSS], infarct size and location), medical comorbidities, and outcomes (modified Rankin Scale [mRS]) were also recorded. Regression analyses were used to determine factors associated with FACIT scores and PSF at each time point.

Results: 203 patients were administered the FACIT a mean 1.6 months post-stroke; 128 underwent re-administration (mean 13.9 months post-event). In adjusted models, stroke severity (follow-up NIHSS [$p < 0.001$], mRS [$p = 0.005$]) and posterior circulation localization ($p = 0.012$) were associated with lower FACIT scores (increased fatigue) in the subacute setting, while medical comorbidities (hypertension [$p = 0.024$], obstructive sleep apnea [$p = 0.020$]) and medication use (anticonvulsants [$p = 0.021$]) were associated with lower scores chronically. Baseline depression ($p < 0.001$, $p = 0.029$) was associated with lower scores at both time points.

Conclusion: Early PSF appears to be largely attributable to stroke severity, while chronic fatigue occurs in the setting of medical comorbidities and medication use. This has significant clinical implications when considering management strategies at different stages of recovery.

1. Introduction

Stroke frequently results in a combination of physical, behavioral, cognitive, and psychological impairments [1,2]. Post-stroke fatigue (PSF) is an increasingly recognized, but previously underreported complication that hinders recovery of these deficits [3]. The lack of consensus regarding its definition, poor understanding of its underlying cause, and presence of confounding medical comorbidities can make it challenging to accurately assess, diagnose, and treat [3,4]. Further studies are needed to determine who is at greatest risk for developing PSF, along with when and how it should be treated, in order to best optimize patient outcomes.

Prior studies have defined PSF as a subjective feeling of physical and/or mental exhaustion, or a constant lack of energy that negatively impacts quality of life and causes difficulties in performing everyday activities [3–5]. Unlike normal fatigue [6,7], pathological fatigue following cerebral infarct often does not improve with rest and has been documented to persist chronically in some patients [4,8–10]. Along with being common post-stroke (prevalence ranging from 16% [11] to 92% [8]) and one of the most disabling sequelae [12–15], PSF occurs even in those with good neurological recovery [3,16]. Therefore, it is critical to elucidate the risk factors contributing to PSF to better guide management.

Numerous sociodemographic, psychocognitive, and neurophysiological variables have been associated with PSF including age, sex, stroke severity and location, physical impairment, neuroendocrine changes and inflammatory biomarkers, social support, medication use, sleep patterns, and depression; however, these risk factors are not consistent across all studies [10,11,17,18]. Variability between studies may be due to an inconsistent definition of PSF (only recently reaching consensus as "a self-reported significant fatigue that interferes with daily activities" [10]); the lack of a standardized evaluation measure (there are currently greater than 50 tools in use for assessment [10]); and differences in the timeframe in which PSF was assessed (i.e., acute, subacute, or chronic phase of stroke recovery) [18]. While many studies have examined how the prevalence of PSF evolves over time [8,19], few have evaluated whether potentially modifiable risk factors remain the same at all time points of recovery. Knowing how the risk factors associated

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https://doi.org/10.1016/j.clineuro.2018.09.027
Received 17 June 2018; Received in revised form 24 August 2018; Accepted 16 September 2018
Available online 17 September 2018

with PSF change over the course of post-stroke recovery will help physicians tailor how they address and manage fatigue at different stages. In this study, we determine what factors are associated with PSF and how they differ in the subacute versus chronic phases of recovery.

2. Materials and methods

2.1. Study population

This prospective study was approved by the Johns Hopkins University School of Medicine Institutional Review Board. The cohort included a consecutive series of adults (≥18 years of age) seen within 6 months of hospital discharge for acute stroke (including both ischemic and hemorrhagic) between 2014 and 2017. At their clinic visit, patients self-administered the Functional Assessment of Chronic Illness Therapy (FACIT), a 13-item self-report questionnaire with scores ranging from 0 to 52 used to evaluate for fatigue [20]. Lower scores indicate more severe fatigue. The FACIT was chosen given ease of administration and evaluation of additional areas of interest such as sleep, functional abilities, participant frustration, and social withdrawal. The tool was re-administered > 6 months post-event to evaluate for persistent, chronic PSF through one of two methods: 1) self-administration in clinic during patients' second follow-up, or 2) interviewer-administration via telephone for those who did not return to clinic [21,22]. A maximum of 4 telephone calls were made to reach each patient, and a voice message was left on the last attempt. Along with FACIT administration, electronic medical records were reviewed for pre-determined, potential confounders including: patient demographics (age, sex, race, education, occupation, marital status, social support, mean income by zip code); medical comorbidities and medications (body mass index [BMI]; history of: coronary artery disease [CAD], congestive heart failure [CHF], diabetes, hypertension, cancer, chronic obstructive pulmonary disease [COPD], dementia, obstructive sleep apnea [OSA], anemia, depression, anxiety, prior stroke, pre-stroke fatigue, tobacco use, alcohol use; use of: selective serotonin reuptake inhibitors [SSRIs], sedatives, anticonvulsants, beta blockers); laboratory tests (white blood cell [WBC] count, hematocrit, erythrocyte sedimentation rate, hemoglobin, sodium, blood urea nitrogen, creatinine, glucose); stroke characteristics (National Institutes of Health Stroke Scale [NIHSS] [23] on admission and at follow-up, Cardiovascular Health Study [CHS] [24] white matter rating, Trial of Org 10172 in Acute Stroke Treatment [TOAST] [25] classification; infarct location, localization, laterality, volume); and outcome (modified Rankin Scale [mRS] [26] at follow-up). Variables were chosen based on their significance in prior studies [10,11,17,18].

2.2. Statistical analysis

Stata SE version 13 (College Station, Texas) was used to evaluate differences in the factors associated with FACIT scores and PSF at each phase of stroke recovery (i.e., subacute [< 6 months] versus chronic [> 6 months]). Fatigue was evaluated as both a continuous and dichotomous variable: any fatigue (FACIT < 41), severe fatigue (FACIT < 31). Univariate regression analyses were performed with FACIT score as the dependent variable for each time point. Covariates significant in univariate analysis ($p < 0.050$) were entered, along with age, sex, and race, into multivariable regression analyses with FACIT score or fatigue as the dependent variable for each time point.

3. Results

3.1. Final included cohort

Two hundred five patients were identified and enrolled at their follow-up clinic visit a mean 1.6 months (SD 0.8) post-infarct. Patients with more than one hospital admission (n = 2) were included only once using their most recent stroke occurrence, leaving 203 patients included

Table 1
Patient characteristics of those reached for evaluation of chronic fatigue versus those lost to follow-up.

Variables	Entire Cohort (N = 203)	Reached for Chronic FACIT (N = 128)	Not Reached for Chronic FACIT (N = 75)	P-value
Demographics				
Age, mean years (SD)	65.2 (15.7)	64.0 (15.6)	67.1 (15.7)	0.180
Sex, n male (%)	102 (50)	68 (53)	34 (45)	0.284
Race, n non-black (%)	154 (76)	100 (78)	54 (72)	0.325
Education, n college degree or higher (%)	29 (14)	26 (20)	3 (4)	0.011*
Employed, n (%)	85 (42)	62 (48)	23 (31)	0.048*
Married, n (%)	93 (46)	65 (51)	28 (37)	0.042*
Lives with others, n (%)	165 (81)	104 (81)	61 (81)	0.923
Income, mean for zip code (SD)	72834.0 (25836.3)	75533.4 (29744.3)	68164.9 (16244.9)	0.051
Medical Characteristics				
BMI, mean kg/m^2 (SD)	29.9 (7.1)	30.8 (7.6)	28.5 (6.1)	0.027*
CAD, n (%)	44 (22)	20 (16)	24 (32)	0.006*
CHF, n (%)	24 (12)	17 (13)	7 (9)	0.400
Diabetes, n (%)	89 (44)	54 (42)	35 (47)	0.535
Hypertension, n (%)	179 (88)	113 (88)	66 (88)	0.952
Cancer, n (%)	21 (10)	15 (12)	6 (8)	0.401
COPD, n (%)	25 (12)	14 (11)	11 (15)	0.435
Dementia, n (%)	16 (8)	3 (2)	13 (17)	< 0.001*
OSA, n (%)	19 (9)	13 (10)	6 (8)	0.611
Anemia, n (%)	20 (10)	9 (7)	11 (15)	0.078
Depression, n (%)	42 (21)	24 (19)	18 (24)	0.373
Anxiety, n (%)	20 (10)	12 (9)	8 (11)	0.766
Prior stroke, n (%)	42 (21)	19 (15)	23 (31)	0.007*
Pre-stroke fatigue, n (%)	5 (2)	4 (3)	1 (1)	0.427
Tobacco use, n (%)	120 (59)	71 (55)	49 (65)	0.168
Alcohol use, n (%)	91 (45)	54 (42)	37 (49)	0.323
WBC count, 10^3/μL (SD)	9.0 (3.2)	8.8 (3.2)	9.3 (3.1)	0.275
Use of SSRIs, n (%)	88 (43)	55 (43)	33 (44)	0.924
Use of sedatives, n (%)	17 (8)	11 (9)	6 (8)	0.883
Use of anticonvulsants, n (%)	32 (16)	18 (14)	14 (19)	0.385
Use of beta blockers, n (%)	84 (41)	44 (34)	40 (53)	0.008*
Stroke Characteristics				
NIHSS on admission, mean (SD)	4.6 (4.8)	4.0 (4.9)	5.5 (4.5)	0.046*
NIHSS at follow-up, mean (SD)	2.2 (3.2)	1.3 (2.0)	3.7 (4.2)	< 0.001*
mRS at follow-up, mean (SD)	1.7 (1.5)	1.4 (1.2)	2.1 (1.7)	0.002*
CHS score, mean (SD)	3.7 (2.3)	4.0 (2.2)	3.2 (2.2)	0.015*
Stroke etiology (TOAST), n (%)				0.517
Large artery atherosclerosis	49 (24)	32 (25)	17 (23)	
Cardioembolism	49 (24)	26 (20)	23 (31)	
Small vessel occlusion	52 (26)	33 (26)	19 (25)	
Stroke of other determined etiology	33 (16)	23 (18)	10 (13)	
Stroke of undetermined etiology	20 (10)	14 (11)	6 (8)	
Localization, n (%)				0.366
Anterior circulation	135 (67)	87 (68)	48 (64)	
Posterior circulation	61 (30)	35 (27)	26 (35)	
Both	6 (3)	5 (4)	1 (1)	
Affected hemisphere, n (%)				0.831
Left only	88 (43)	54 (42)	34 (45)	
Right only	93 (46)	61 (48)	32 (43)	
Both	21 (10)	13 (10)	8 (11)	

(continued on next page)

Table 1 (*continued*)

Variables	Entire Cohort (N = 203)	Reached for Chronic FACIT (N = 128)	Not Reached for Chronic FACIT (N = 75)	P-value
Infarct volume, mean cc (SD)	16.8 (31.4)	16.5 (31.7)	17.3 (31.2)	0.860
Time from stroke to 1st FACIT, mean days (SD)	48.4 (24.2)	47.5 (24.4)	49.8 (24.0)	0.521
Time from stroke to 2nd FACIT, mean days (SD)	422.9 (216.3)			

* Statistically significant.

in the final analysis. One hundred twenty-eight of these patients (63%) were reached (n = 30 in-person, n = 98 via telephone) and successfully completed re-administration of the FACIT a mean 13.9 months (SD 7.1) post-event. Patients failed to complete re-administration for the following reasons: did not respond to calls and voice message (n = 38), were deceased (n = 13), refused to take or finish the FACIT (n = 10), moved with no known phone number (n = 5), had an invalid phone number listed in the electronic medical record (n = 4), were cognitively impaired (n = 3; i.e., aphasia, dementia), or did not speak English (n = 2).

Characteristics of the cohort are displayed in Table 1. The average age at time of stroke was 65.2 years (SD 15.7). Fifty percent were male, 24% were black, 46% were actively married, and 42% were working at the time of follow-up. The mean infarct volume was 16.8 cc (SD 31.4), and the average presenting NIHSS was 4.6 (SD 4.8). The mean follow-up NIHSS and mRS scores were 2.2 (SD 3.2) and 1.7 (SD 1.5), respectively. Compared to patients who were lost for chronic evaluation, those reached were more likely to have a higher level of education (20% versus 4%, p = 0.011) and to be actively working (48% versus 31%, p = 0.048) and married (51% versus 37%, p = 0.042). In addition, those reached had similar but lower NIHSS scores on admission (4.0 versus 5.5, p = 0.046) and at follow-up (1.3 versus 3.7, p < 0.001) along with better follow-up mRS scores (1.4 versus 2.1, p = 0.002).

3.2. Factors associated with PSF

Factors associated with FACIT scores in the subacute and chronic settings are displayed in Table 2. When fatigue was evaluated as a continuous variable, markers of stroke severity (admission NIHSS [p = 0.016], follow-up NIHSS [p < 0.001], mRS [p < 0.001]), WBC count (p < 0.001, a potential acute phase reactant [27]), and localization within the posterior circulation (p = 0.034) were associated with lower FACIT scores in the subacute period. Female sex (p = 0.033), medical comorbidities (hypertension [p = 0.040], OSA [p = 0.010]), and medication use (anticonvulsants [p = 0.025], beta blockers [p = 0.043]) were significant predictors of lower FACIT scores in the chronic setting. Baseline depression (p < 0.001, p = 0.004) and anxiety (p = 0.025, p = 0.046) were significant at both time points. Those with a greater number of medical comorbidities were more likely to have lower FACIT scores at both time points (p < 0.01). In multivariable modeling, stroke characteristics including follow-up NIHSS (p < 0.001), mRS (p = 0.005), and posterior circulation localization (p = 0.012) remained significantly associated with lower FACIT scores in the subacute phase of recovery. These variables were not significantly associated with chronic fatigue. With adjustment, female sex (p = 0.028), time from stroke to second FACIT (p = 0.032), use of anticonvulsants (p = 0.021), hypertension (p = 0.024), and OSA (p = 0.020) instead remained significant predictors of lower FACIT scores in the chronic period. Baseline depression continued to be significantly associated with lower FACIT scores at both time points (p < 0.001, p = 0.029).

Results remained consistent when fatigue was evaluated as a dichotomous variable (Table 3). The likelihood of severe PSF in the subacute setting increased with greater stroke severity (follow-up NIHSS [OR 1.267, 95% CI 1.041–1.542] and mRS [OR 1.467, 95% CI 1.018–2.112]), while the likelihood of severe, chronic PSF increased with the presence of medical comorbidities including OSA (OR 5.055, 95% CI 1.246–20.507). In addition, baseline depression increased the likelihood of any and severe fatigue in both the subacute (OR 4.348, 95% CI 1.629–11.602; OR 5.623, 95% CI 2.113–14.968) and chronic (OR 5.412, 95% CI 1.451–20.183; OR 3.394, 95% CI 1.084–10.633) phases of recovery.

Table 2
Univariate linear regression associations with increased FACIT scores (less severe fatigue) for each time point.

Variables	Subacute		Chronic	
	Regression Coefficient[a]	P-value	Regression Coefficient[a]	P-value
Demographics				
Age (years)	−0.081	0.166	−0.048	0.530
Sex (male)	2.129	0.243	5.011	0.033*
Race (black)	1.477	0.489	3.361	0.239
Education	1.962	0.242	3.262	0.128
Occupation	3.072	0.081	2.492	0.268
Married	−0.996	0.415	−1.205	0.423
Support system	0.782	0.744	0.292	0.925
Mean income ($)	1.99e-06	0.956	1.81e-06	0.964
Medical Characteristics				
BMI (kg/m^2)	−0.041	0.748	−0.272	0.080
CAD	−1.288	0.561	0.598	0.854
CHF	−1.587	0.575	2.335	0.503
Diabetes	−4.777	0.009*	−2.308	0.335
Hypertension	−4.225	0.134	−7.500	0.040*
Cancer	3.359	0.262	0.628	0.864
COPD	−2.533	0.362	−3.949	0.297
Dementia	1.014	0.765	−5.576	0.476
OSA	−5.974	0.056	−9.914	0.010*
Anemia	−4.094	0.181	−7.889	0.087
Depression	−10.463	< 0.001*	−8.702	0.004*
Anxiety	−6.812	0.025*	−8.032	0.046*
Prior stroke	−2.928	0.193	0.960	0.773
Pre-stroke fatigue	−8.141	0.166	−10.782	0.111
Tobacco use	−2.485	0.180	−0.304	0.898
Alcohol use	0.406	0.825	0.959	0.689
WBC count (10^3/μL)	−1.019	< 0.001*	−0.087	0.813
Use of SSRIs	−3.498	0.057	−0.381	0.874
Use of sedatives	−5.200	0.114	0.010	0.998
Use of anticonvulsants	−4.604	0.065	−7.565	0.025*
Use of beta blockers	−2.458	0.184	−5.008	0.043*
Number of comorbidities	−2.267	< 0.001*	−2.597	0.002*
Stroke Characteristics				
NIHSS on admission	−0.469	0.016*	−0.098	0.693
NIHSS on follow-up	−1.617	< 0.001*	−1.165	0.055
mRS on follow-up	−3.408	< 0.001*	−1.512	0.129
CHS score	−0.334	0.434	0.291	0.605
Stroke etiology (TOAST)	0.612	0.392	−0.618	0.492
Localization	3.797	0.034*	−0.021	0.993
Affected hemisphere	−2.279	0.098	−1.779	0.319
Infarct volume (cc)	−0.046	0.112	0.052	0.167
Time from stroke to 1st FACIT (days)	−0.024	0.531	−0.095	0.050
Time from stroke to 2nd FACIT (days)			−0.012	0.025*

[a] Negative coefficients indicate increasing fatigue.
* Statistically significant in univariate analysis.

Table 3
Multivariable logistic regression model of factors associated with any (FACIT < 41) and severe (FACIT ≤ 30) post-stroke fatigue at each time point.

		Any Fatigue		Severe Fatigue	
	Variables	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval
Subacute	Age (years)	1.006	0.981—1.031	1.000	0.972—1.030
	Race (black)	0.321*	0.125—0.823	0.478	0.172—1.328
	Sex (male)	0.708	0.341—1.471	0.756	0.331—1.724
	NIHSS on admission	1.039	0.960—1.126	1.014	0.929—1.107
	NIHSS at follow-up	1.308*	1.066—1.605	1.267*	1.041—1.542
	mRS at follow-up	1.142	0.815—1.601	1.467*	1.018—2.112
	Localization	0.606	0.297—1.235	0.581	0.268—1.259
	WBC count (10^3/μL)	1.044	0.925—1.178	1.099	0.968—1.249
	Diabetes	1.490	0.724—3.067	1.538	0.691—3.421
	Depression	4.348*	1.629—11.602	5.623*	2.113—14.968
	Anxiety	1.249	0.357—4.368	0.950	0.246—3.671
Chronic	Age (years)	0.992	0.963—1.022	0.968*	0.936—1.000
	Race (black)	0.523	0.182—1.504	0.361	0.111—1.171
	Sex (male)	0.323*	0.136—0.763	0.292*	0.113—0.755
	Hypertension	4.002	0.942—16.998	4.227	0.872—20.494
	OSA	2.161	0.544—8.582	5.055*	1.246—20.507
	Use of anticonvulsants	2.552	0.749—8.698	2.644	0.818—8.550
	Use of beta blockers	1.798	0.726—4.454	1.839	0.706—4.790
	Depression	5.412*	1.451—20.183	3.394*	1.084—10.633
	Anxiety	0.389	0.074—2.055	1.216	0.254—5.824
	Time from stroke to 2nd FACIT	1.002*	1.000—1.004	1.002	1.000—1.004

* Statistically significant in multivariable logistic regression analysis.

4. Discussion

Our findings suggest that distinct factors underlie the development and persistence of PSF throughout each phase of stroke recovery. Indicators of stroke severity including degree of neurological impairment (measured by NIHSS) and functional disability (measured by mRS), along with posterior circulation localization, are most significantly associated with lower FACIT scores in the earliest stages, weeks to months after infarct. These variables all capture the amount of neuronal injury that occurs as a result of the stroke. Our results are consistent with the idea that recovering from neurologic impairment requires energy and effort that can be physically, cognitively, and emotionally exhausting. They are also in line with previous studies reporting a significant relationship between PSF and NIHSS [14,28,29] as well as functional disability [9,28–34] in the acute to subacute setting. In addition, one prior study found stroke localization (as classified by the Oxfordshire Community Stroke Project) to be a marginally predictive factor of early PSF [35].

While stroke-related characteristics appear to be significant factors for the development of PSF in the subacute period, we demonstrate that their effects are diminished in the chronic phase of recovery; instead, persistence of fatigue is significantly associated with variables unrelated to the stroke itself including female sex, use of anticonvulsants, and underlying medical comorbidities such as OSA and hypertension. Our findings seem to be at odds with prior work showing that higher NIHSS scores and poor functional outcomes also predict PSF in the chronic setting, [36–39] though are in line with the finding that degree of ambulatory activity is not associated with PSF [40]. Our results also seem to refute the hypothesis that those with better recovery who attempt to be more active perceive greater fatigue as their level of required exertion increases. We found no relationship with stroke severity or degree of recovery (favorable or poor) to PSF in our population. A potential explanation for these discrepancies is the difference in patient characteristics and measures chosen for evaluation. Both the NIHSS scores and functional outcomes of our patients at follow-up were relatively good (mean NIHSS 2.2 and mRS 1.7 – slight disability; unable to carry out all pre-stroke activities but able to look after self without daily help [26]). As a result, for our cohort, poor overall health may have acted as a confounding variable in the chronic period, overshadowing neurological and functional impairment due to the stroke itself and driving the increased likelihood of chronic fatigue. Those with more medical comorbidities were also more likely to have lower FACIT scores and more fatigue in the subacute setting, confirming the need for management at all time points; however, early on the co-existing effect of stroke severity appeared to drive degree of fatigue and this effect diminished over time. The group reached by phone had lower NIHSS scores at their follow-up appointment than those not reached, which may have amplified findings; however, both groups had relatively mild stroke severity at follow-up (mean NIHSS 1.3–3.7).

Based on our results, we propose that neural recovery is no longer the driving force for patients with lasting fatigue, and identifying potentially modifiable comorbidities may instead lead to more effective therapies. Not all medical comorbidities were associated with chronic post-stroke fatigue, though most trended toward statistical significance. One explanation may be that similar potentially fatiguing medications are used to treat many of the conditions (e.g., beta blockers). The idea of medical comorbidities confounding stroke morbidity is not a new concept and is consistent with prior reports suggesting an association between chronic PSF and sleep disorders [36,41–43] as well as medications [41]. In this study, we were unable to determine the effect of specific medications or factors such as CPAP compliance. This may be an important focus of future research.

It is important to note that an underlying mood disorder such as depression or anxiety was associated with fatigue for all time points, though other medical comorbidities remained significant in both the acute and chronic phases even when treating and subsequently adjusting for depression. It is not well understood whether PSF and post-stroke mood changes are distinct processes or share a similar temporal relationship [8]. Consistent with prior studies [3,12,18,44], we found that PSF was still present even when depression was controlled for, suggesting that fatigue and mood are separate entities and supporting the idea that both sequelae should be independently addressed as a part of stroke recovery. Our study supports a previously proposed conceptual model for PSF suggesting that stroke characteristics contribute to early fatigue, while psychosocial factors drive persistent fatigue [10]. Our data further add to this model by demonstrating that chronic medical problems and medications help to perpetuate fatigue long-term in addition to psychosocial factors such as depression. As persistent fatigue is largely attributable to medical comorbidities rather than the stroke itself, physicians should aim to aggressively modify and manage

these conditions to improve their patients' chronic fatigue, and in turn, their function and quality of life.

Our study is not without limitations. Our cohort is taken from a single, urban, academic, comprehensive stroke center with relatively good outcomes (low NIHSS, mRS). Therefore, findings may not be generalizable to all stroke populations. Furthermore, the characteristics of those reached for chronic evaluation of fatigue and those lost to follow-up did have several significant differences. Patients who were reached tended to have fewer medical comorbidities and less severe strokes along with better sociodemographic conditions. As such, one would not expect them to experience PSF to the same degree as those lost to follow-up. However, PSF was still present in this group of patients, leading us to believe that our results are valid despite the differences between the two populations. Finally, there may be additional risk factors for PSF that were not analyzed as part of this study.

Despite these limitations, our data highlight the importance of recognizing that the risk factors associated with PSF evolve over time, as well as the need to identify contributing factors other than the stroke itself in patients with persistent fatigue. Prognostication and treatment of PSF at each stage should be individualized. Patients commonly experience fatigue in the subacute period following infarction due to neurologic injury and functional impairment, but this should improve over time as long as their chronic medical problems are addressed. If fatigue persists, it is necessary to screen for and manage other contributing factors.

5. Conclusion

Post-stroke fatigue is common throughout all phases of recovery, but is associated with distinct factors at each time point. While PSF in the subacute period is largely due to characteristics of the stroke itself such as severity and functional impairment, chronic fatigue occurs in the setting of medical comorbidities and medication use. Fatigue that does not improve long-term may be indicative of other underlying factors that need to be modified.

Conflicts of interest

None.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgement

None.

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