Quality of life in patients with TIA and minor ischemic stroke

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ABSTRACT

Objective: We investigated health-related quality of life (HRQOL) in patients with TIA and minor ischemic stroke (MIS) using Neuro-QOL, a validated, patient-reported outcome measurement system.

Methods: Consecutive patients with TIA or MIS who had (1) modified Rankin Scale (mRS) score of 0 or 1 at baseline, (2) initial NIH Stroke Scale score of ≤ 5 , (3) no acute reperfusion treatment, and (4) 3-month follow-up, were recruited. Recurrent stroke, disability by mRS and Barthel Index, and Neuro-QOL scores in 5 prespecified domains were prospectively recorded. We assessed the proportion of patients with impaired HRQOL, defined as T scores more than 0.5 SD worse than the general population average, and identified predictors of impaired HRQOL using logistic regression.

Results: Among 332 patients who met study criteria (mean age 65.7 years, 52.4% male), 47 (14.2%) had recurrent stroke within 90 days and 41 (12.3%) were disabled (mRS >1 or Barthel Index <95) at 3 months. Any HRQOL impairment was noted in 119 patients (35.8%). In multivariate analysis, age (adjusted odds ratio [OR] 1.02, 95% confidence interval [CI] 1.01–1.04), initial NIH Stroke Scale score (adjusted OR 1.39, 95% CI 1.17–1.64), recurrent stroke (adjusted OR 2.10, 95% CI 1.06–4.13), and proxy reporting (adjusted OR 3.94, 95% CI 1.54–10.10) were independent predictors of impaired HRQOL at 3 months.

Conclusions: Impairment in HRQOL is common at 3 months after MIS and TIA. Predictors of impaired HRQOL include age, index stroke severity, and recurrent stroke. Future studies should include HRQOL measures in outcome assessment, as these may be more sensitive to mild deficits than traditional disability scales. *Neurology*® 2015;85:1957–1963

GLOSSARY

BI = Barthel Index; **CI** = confidence interval; **DWI** = diffusion-weighted imaging; **HRQOL** = health-related quality of life; **MIS** = minor ischemic stroke; **mRS** = modified Rankin Scale; **NIHSS** = NIH Stroke Scale; **OR** = odds ratio.

Patients with TIA and minor ischemic stroke (MIS) account for the majority of stroke patients who present for emergency care in the United States.¹ Mild symptoms on presentation is a common reason for exclusion from IV tissue plasminogen activator administration.² Acute ischemic stroke leads to decreases in health-related quality of life (HRQOL), even among those who have no or minimal poststroke disability.³ Although the outcomes of most patients with minor symptoms, defined by a low NIH Stroke Scale (NIHSS) score, are favorable, approximately 25% of such patients become disabled.²

Stroke outcomes traditionally have utilized disability scales of functional status, which often fail to represent the full effect of disease and treatment. The modified Rankin Scale (mRS) and Barthel Index (BI) are the most frequently used tools to measure disability and handicap after stroke.⁴ With National Institute of Neurological Disorders and Stroke funding to address these limitations, Neuro-QOL was developed as a clinically robust and validated patient-reported HRQOL assessment tool for adults and children with neurologic disorders.^{5,6} We sought to (1) compare Neuro-QOL assessments with traditional measures using the mRS and BI, and (2) identify predictors of impaired HRQOL after TIA and MIS.

Supplemental data
at Neurology.org

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Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

METHODS Standard protocol approvals, registrations, and patient consents. The study was approved by the local institutional review board. Consecutive patients aged 18 years or older with a confirmed acute ischemic stroke or TIA over a period of 12 months (August 1, 2012 through July 31, 2013) were enrolled in the Northwestern University Brain Attack Registry. Written informed consent was obtained from the patient or their legally authorized representative.

Selection of cohort. MIS was defined as sudden-onset neurologic deficits lasting >24 hours without alternative diagnosis, initial NIHSS score ≤ 5 , and/or confirmation of acute ischemic stroke on diffusion-weighted imaging (DWI); presence of DWI abnormality regardless of symptom duration indicated MIS.⁷ TIA was defined as sudden-onset neurologic deficits lasting <24 hours without alternative diagnosis and no acute lesion on DWI. In patients in whom DWI was not performed ($n = 14$), the diagnosis was made clinically based on the duration of symptoms. Diagnosis was made by a board-certified vascular neurologist at our institution in each case. Consecutive patients with the following criteria were included: (1) MIS or TIA as previously defined; (2) absence of acute reperfusion treatment; (3) mRS score 0 or 1 at baseline; and (4) with complete follow-up data at 3 months (figure 1).

Index evaluation of subjects. Demographics, baseline (pre-stroke) disability using the mRS, insurance status, presenting

NIHSS score, risk factors and comorbidities, and hospital course and treatments were collected prospectively. Hypertension, diabetes mellitus, dyslipidemia, prior stroke, atrial fibrillation or flutter, and cardiac disease (history or angina, myocardial infarction, coronary bypass or intervention, or congestive heart failure) were defined by documented history, active medications, or clinical or laboratory findings at presentation. Reperfusion therapy was defined as receipt of IV or intra-arterial tissue plasminogen activator and/or mechanical thrombectomy. Board-certified neurologists prospectively reviewed clinical and radiographic data to determine TOAST (Trial of Org 10172 in Acute Stroke Treatment) subtype⁸ for each confirmed case; adjudication was made by consensus to avoid interrater reliability concerns.⁹ Baseline imaging was independently reviewed by one investigator (S.P.) for presence of DWI lesion along with location and vascular territory, blinded to outcome data. We prospectively monitored for poststroke in-hospital medical complications. In-hospital recurrent stroke was diagnosed as new or worsening initial neurologic symptoms lasting >24 hours without alternative diagnosis. Recurrent stroke after hospitalization was recorded based on a validated questionnaire of reported symptoms of stroke and review of medical records for confirmation.

Outcomes. Three-month outcomes were assessed prospectively using functional outcome scales and domain-specific HRQOL scores. The functional outcome scales included the mRS and the BI. The mRS is a disability scale ranging from no symptoms (0) to dead (6), and BI is an ordinal measure of activities of daily living performance with scores ranging from complete bedridden dependence (0) to full independence (100).¹⁰ We obtained mRS and BI data by telephone interview, a validated method for assessment.^{11,12} We used previously published definitions of favorable outcome (BI of 95 or 100 and mRS score 0 or 1) at the 3-month time point.¹³

At 3-month follow-up, patients or their proxies completed a series of domain-specific HRQOL assessments using the following 5 Neuro-QOL instruments (SF version 1.0): upper extremity function (fine motor activity, reaching activities), lower extremity function (mobility including walking on stairs or uneven surfaces), satisfaction with social roles and activities, applied cognition–executive function (planning, organizing, calculating, working with memory and learning), and applied cognition–general concerns (perceived difficulties with abilities such as memory, attention, and decision-making). Neuro-QOL results were expressed as T scores referenced to general United States population (with enrichment from a clinical neurologic sample) demographics with mean 50 and SD 10 (additional information available at www.neuroqol.org).^{5,6,14}

Statistical analysis. Data are expressed as number (percent), mean (SD), or median (interquartile range) as appropriate. We calculated the proportions of patients with disability (defined by mRS score >1 or BI <95) and impaired HRQOL in any of the 5 Neuro-QOL domains. We defined impaired HRQOL as T scores <45 for any Neuro-QOL domain, which is >0.5 SD from the population mean and considered a conservative estimate of the minimal clinically important difference.¹⁵

We assessed for differences in baseline demographic, clinical, and hospital course variables and disability measures among those with and without impaired HRQOL at 3 months using Pearson χ^2 tests for categorical variables (Fisher exact test when appropriate), t tests for normally distributed continuous variables, and Mann–Whitney U tests for ordinal variables and

Figure 1 Flowchart for study inclusion

IS = ischemic stroke; MIS = minor ischemic stroke; NIHSS = NIH Stroke Scale.

Table 1 Overall domain-specific scores and proportions with impaired quality of life and within strata of index stroke diagnosis: MIS vs TIA

	Upper extremity function	Lower extremity function	General concerns	Executive function	Social satisfaction
Overall cohort (n = 332)					
Mean (SD) T score	51.4 (5.7)	49.6 (8.1)	55 (6.0)	53.1 (7.0)	53.2 (7.3)
T score <45, n (%)	55 (16.6)	77 (23.2)	24 (7.2)	31 (9.3)	43 (13.0)
T score <40, n (%)	38 (11.4)	23 (6.9)	8 (2.4)	17 (5.1)	8 (2.4)
MIS (n = 257)					
Mean (SD) T score	51.1 (6.1)	49.0 (8.5)	54.9 (6.2)	52.9 (7.5)	52.4 (7.4)
T score <45, n (%)	49 (19.1)	65 (25.3)	22 (8.6)	29 (11.3)	40 (15.6)
T score <40, n (%)	19 (7.4)	37 (14.4)	8 (3.1)	16 (6.2)	8 (3.1)
TIA (n = 75)					
Mean (SD) T score	52.6 (4.1)	50.0 (6.3)	55.5 (5.1)	53.6 (4.9)	56.2 (5.9)
T score <45, n (%)	6 (8.0)	12 (16.0)	2 (2.7)	2 (2.7)	3 (4.0)
T score <40, n (%)	4 (5.3)	1 (1.3)	0 (0)	1 (1.3)	0 (0)

Abbreviation: MIS = minor ischemic stroke.

nonnormally distributed continuous variables. Normality was assessed by Kolmogorov-Smirnov test.

We developed multivariate models to identify predictors of 3-month impaired HRQOL including those variables that showed univariate association ($p < 0.05$). We used stepwise backward variable removal for final model development. Odds ratios (OR) and 95% confidence intervals (CIs) were estimated. The Hosmer-Lemeshow test was used to assess fitness of the final model. We performed sensitivity analysis assessing only baseline and hospital factors (i.e., removing posthospital

factors such as recurrent stroke) associated with impaired HRQOL. Lastly, stratified univariate analyses in MIS vs TIA patients were performed. Standard statistical software was used (IBM SPSS version 22, Armonk, NY). Statistical significance was considered to be p value < 0.05 . Because of the exploratory nature of this project, no adjustment was made for multiple comparisons.

RESULTS Among 332 patients (mean age 65.7 ± 15.3 years; 52.4% male; 68.1% white; 6.9% Hispanic; 29.2% TIA) included for analysis, 47 (14.2%) had recurrent stroke within 3 months and 41 (12.3%) were disabled (either mRS score > 1 or BI < 95) at 3 months. Three-month outcome data were provided by proxies for 29 patients (8.7%). Any HRQOL impairment (T score < 45 in any of 5 domains) was noted in 119 patients (35.8%), with 27.1% among those with no disability and 97.6% with disability ($p < 0.001$). Using a more conservative threshold (T scores < 40 or 1 SD), 52 (15.7%) had impaired HRQOL in at least 1 of 5 domains with a majority of impairments reported in lower extremity and upper extremity function (table 1). Stratified analysis by index stroke (MIS vs TIA) showed more impairments in patients with MIS compared to TIA (39.7% vs 22.7%, $p < 0.001$). Mean T scores were lower in those with 3-month disability vs those without ($p < 0.001$ for all 5 domains), with absolute differences ranging from 8 to 15 points (figure 2).

On univariate analysis, age, medical risk factors (diabetes, hypertension, and cardiac disease), initial NIHSS score at time of index presentation, presence of acute infarction of DWI, index diagnosis of MIS (vs TIA), recurrent stroke, and proxy reporting (vs patient) were associated with impaired HRQOL at

Figure 2 Comparison of mean T scores in domains of Neuro-QOL between patients with and without disability at 3 months

For each domain-specific comparison, p values < 0.001 .

3 months (table 2). Stroke symptom type (motor, sensory, visual, or language/speech), sex, race, ethnicity, prior stroke, atrial fibrillation, current smoking, chronic kidney disease, insurance status, living situation at baseline, baseline mRS score, and in-hospital medical complications were not associated with impaired HRQOL. Stratified analyses in MIS vs TIA patients showed similar results in the MIS subgroup, while the findings were not significant among TIA patients except for age (tables e-1 and e-2 on the *Neurology*[®] Web site at Neurology.org).

In multivariate analysis that included age, diabetes, hypertension, cardiac disease, initial NIHSS score, index MIS (vs TIA), recurrent stroke, and proxy reporting, independent predictors of impaired HRQOL at 3 months were age, initial NIHSS score, recurrent stroke, and proxy reporting (table 3). When limiting to only baseline and hospital predictors, age (adjusted OR 1.01, 95% CI 1.01–1.05), NIHSS

score (adjusted OR 1.43, 95% CI 1.21–1.68), and MIS vs TIA (adjusted OR 1.91, 95% CI 1.01–3.63) were independent predictors of impaired HRQOL at 3 months.

DISCUSSION In this novel study of patient-reported outcomes utilizing the Neuro-QOL tool after MIS and TIA, we observed that (1) more than one-third of patients reported impairments in various domains of HRQOL at 3 months; (2) Neuro-QOL scores correspond well with traditional measures of disability using the mRS and BI, although impaired HRQOL was noted in more than one-quarter of TIA/MIS patients without disability; and (3) age, index stroke severity, and recurrent stroke predict impaired HRQOL.

The mRS has long been utilized in clinical trials as the primary instrument in assessment of functional outcome after stroke and has many advantages,¹⁶

Table 2 Baseline demographics, clinical history, and outcomes among those with normal and impaired QOL at 3 months after TIA or MIS (n = 332)

	Normal QOL at 3 mo (n = 213)	Impaired QOL at 3 mo (n = 119) ^a	p Value
Demographics			
Age (SD), y	63.3 (14.9)	69.9 (15.1)	<0.001
Male, n (%)	118 (55.4)	56 (47.1)	0.145
Race, n (%)			0.525
Caucasian	148 (69.5)	78 (65.5)	
African American	56 (26.3)	35 (29.4)	
Asian	9 (4.2)	5 (4.2)	
Other	0	1 (0.8)	
Hispanic ethnicity, n (%)	12 (5.6)	11 (9.2)	0.214
Medicare or private insurance, n (%)	188 (88.3)	102 (85.7)	0.503
Living with family at baseline, n (%)	164 (77.0)	84 (70.6)	0.199
mRS score at baseline, median (IQR)	0 (0–0)	0 (0–0)	0.211
Comorbid medical conditions, n (%)			
Diabetes mellitus	43 (20.2)	36 (30.3)	0.039
Hypercholesterolemia	164 (77.0)	87 (73.1)	0.429
Atrial fibrillation	25 (11.7)	23 (19.3)	0.059
Cardiac disease	32 (15.0)	29 (24.4)	0.035
Prior stroke	32 (15.0)	28 (23.5)	0.053
Chronic kidney disease	15 (7.0)	16 (13.4)	0.054
Hypertension	154 (72.3)	98 (82.4)	0.040
Smoking within past 6 mo	105 (49.3)	47 (39.5)	0.108
Clinical, hospital, and imaging characteristics			
NIHSS score, median (IQR)	1 (0–2)	2 (1–3)	0.001
Motor symptoms, n (%)	62 (29.1)	35 (29.4)	0.953
Sensory symptoms, n (%)	23 (10.8)	6 (5.0)	0.104
Visual symptoms, n (%)	40 (18.8)	20 (16.8)	0.654

Continued

Table 2 Continued

	Normal QOL at 3 mo (n = 213)	Impaired QOL at 3 mo (n = 119) ^a	p Value
Language/speech symptoms, n (%)	120 (56.3)	75 (63.0)	0.235
In-hospital medical complications, n (%)	32 (15.0)	26 (21.8)	0.116
DWI abnormality, n (%) ^b	150 (72.1)	95 (86.4)	0.005
Index MIS (vs TIA)	155 (72.8)	102 (85.7)	0.006
TOAST subtype, n (%)			0.314
Cardioembolic	37 (17.4)	25 (40.3)	
Large artery atherosclerosis	36 (16.9)	24 (20.2)	
Small artery disease	31 (14.6)	21 (17.6)	
Other	31 (14.6)	9 (7.6)	
Cryptogenic	79 (36.6)	40 (33.6)	
3-mo data, n (%)			
Proxy (vs patient) report at 3 mo	7 (3.3)	22 (18.5)	<0.001
Interval inpatient rehabilitation	40 (18.8)	70 (58.8)	<0.001
Recurrent stroke within 3 mo	23 (10.8)	24 (20.2)	0.019
mRS score 0–1 at 3 mo	212 (99.5)	87 (73.1)	<0.001
BI 95–100 at 3 mo	213 (100)	85 (71.4)	<0.001

Abbreviations: BI = Barthel Index; DWI = diffusion-weighted imaging; IQR = interquartile range; MIS = minor ischemic stroke; mRS = modified Rankin Scale; NIHSS = NIH Stroke Scale; QOL = quality of life; TOAST = Trial of Org 10172 in Acute Stroke Treatment.

^a Impaired HRQOL was defined as T scores <45 for any Neuro-QOL domain: upper extremity function, lower extremity function, applied cognition-executive function, applied cognition-general concerns, and social satisfaction.

^b DWI was not performed in 14 patients.

including a high interrater reliability,¹⁷ use of validated questionnaires,^{18,19} and inclusion as the standard outcome in high-profile stroke trials.¹² The mRS aligns closely with HRQOL in stroke survivors²⁰ and with Neuro-QOL scores in hemorrhagic stroke patients, with each step change in mRS associated with approximately 7-point change in mobility T scores.¹⁴ However, Neuro-QOL scores provide context regarding the reasons for poor outcomes (i.e., poor mobility vs inability to manage one's own affairs), a shortcoming of the mRS. It may also overcome ceiling effects that are known to limit the mRS. Stewart and Cramer²¹ previously observed that, of 21 patients

with radiographically confirmed strokes with no disability based on mRS and NIHSS, 71% reported difficulty with hand movements by the Stroke Impact Score or reduced arm use by the Motor Activity Log score. Thus, when placed in this context, our finding that HRQOL impairments are noted even in those without disability by the mRS or BI is not surprising.

HRQOL has been evaluated in multiple populations and has been found to be important in patients with ischemic stroke and TIA.^{3,22,23} While no formal comparison has been conducted between Neuro-QOL and other stroke-specific QOL measures such as the Stroke Impact Score, some advantages of Neuro-QOL might include (1) domain selection based on the outcomes most likely to be affected by the disease (i.e., upper and lower extremity function, cognition, and executive function), (2) continuous normalized scores that simplify analysis and interpretation, and (3) the ability to compare scores across different diseases (i.e., executive function in stroke vs executive function in multiple sclerosis).

In patients with 3-month disability, mean T scores were the lowest (worst) for lower extremity function, underscoring the importance of mobility on disability. Indeed, nearly one-quarter of patients reported impairment in lower extremity function. Besides motor complaints, several studies have noted that cognitive and

Table 3 Multivariate model of independent predictors of impaired health-related quality of life at 3 months following TIA or MIS^a

	Adjusted OR	95% CI
Age (per y)	1.02	1.01–1.04
NIHSS score (per point up to 5)	1.39	1.17–1.64
Recurrent stroke	2.10	1.06–4.13
Proxy reporting	3.94	1.54–10.10

Abbreviations: CI = confidence interval; MIS = minor ischemic stroke; NIHSS = NIH Stroke Scale; OR = odds ratio.

^a Adjusted for age, diabetes, hypertension, cardiac disease, initial NIHSS score, index MIS (vs TIA), recurrent stroke, and proxy (vs patient) reporting; Hosmer-Lemeshow test showed good fit ($p = 0.738$).

communication problems in addition to fatigue occur after TIA.^{24–27} Our findings are consistent with these studies in that 7% to 13% of TIA and MIS patients had self-reported impairments in executive function, general concerns, and social satisfaction.

Several hypotheses might explain disability after MIS. First, the index stroke may cause unmeasured (especially cognitive) and underappreciated deficits. Second, an early recurrent stroke may occur. Third, medical complications, medical treatments, and poststroke care (i.e., rehabilitation) may influence disability in long-term follow-up; for example, patients may report fatigue from β -blockers²⁸ or psychological impairments from being placed on anticoagulation.²⁹ A prior study found that infarct growth on early brain MRI predicts disability after MIS, suggesting that the index stroke may be the key predictor.^{30,31} However, a recent analysis from the CHANCE trial found that recurrent stroke has a major role in determining HRQOL after TIA and MIS.³² Our observation that both index stroke severity and recurrent stroke were independent predictors of impaired HRQOL is consistent with these prior studies.

We used T scores <45, or approximately 0.5 SD from the population mean, as the cutoff for impairment in Neuro-QOL. This difference is likely to be a meaningful one. A thorough analysis of the distribution of effect sizes computed from estimated minimal clinically important difference from 33 studies performed by Norman et al.³³ demonstrated that when patients with a chronic disease are asked to identify minimal important change, the estimates fall very close to 0.5 SD. We also relied on telephone interviews. Neuro-QOL may be administered via face-to-face interviews, by telephone, or online self-administration. A recent study by Bjorner et al.³⁴ noted that score validity and reliability are not affected by mode of administration (i.e., telephone, computer, pen and paper, handheld devices) for PROMIS (Patient Reported Outcomes Measurement Information System) measures. Neuro-QOL measures were developed in conjunction with PROMIS measures by the same group of coinvestigators using similar development protocols.

While our study has several strengths including its prospective design and longitudinal follow-up at 3 months, there are also several limitations. First, as a report from a single urban academic medical center, our results may not be generalizable to all settings. Replication of our findings in multicenter cohorts and different settings is needed. Second, our rate of disability (12.3%) after MIS and TIA likely is an underestimate compared to prior studies suggesting 25% have disability since we included patients within all presenting time windows (i.e., not only reperfusion or hyperacute windows) and only those who survived to 3-month follow-up. Third, Neuro-QOL measures are patient-reported outcomes; objective

measures of cognition and psychological function after TIA and MIS were not performed in this study; therefore, we cannot comment on the degree of cognitive impairment and psychological dysfunction. Fourth, we did not assess other measures of HRQOL such as fatigue, language function, or depression. Fifth, we are unable to report changes in T scores pre- and poststroke. Prestroke measures of HRQOL were not collected since these are cumbersome to perform and not validated in hospitalized patients. Lastly, HRQOL assessment requires active participation by the patient and therefore may be suspect to inaccuracy if patients lose interest or become fatigued during the assessment.

Neuro-QOL provides researchers and clinicians with a novel tool for assessment of HRQOL. Impairment in HRQOL is common at 3 months after MIS and TIA, even in patients without disability by traditional outcome scales such as the mRS. Predictors of impaired HRQOL include age, index stroke severity, and recurrent stroke. Future studies should include Neuro-QOL measures in outcome assessment after TIA and MIS, as these may be complementary to traditional disability scales for the detection of mild deficits.

AUTHOR CONTRIBUTIONS

Dr. Sangha: acquisition of data, analysis and interpretation, writing the paper. Dr. Caprio: analysis, drafting of manuscript, and critical revision of manuscript. Dr. Askew: analysis and interpretation, critical revision of manuscript. Mr. Corado: acquisition of data. Dr. Bernstein: acquisition of data, critical revision of the manuscript for important intellectual content. Dr. Curran: acquisition of data. Dr. Ruff: acquisition of data. Dr. Cella: critical revision of the manuscript for important intellectual content. Dr. Naidech: critical revision of the manuscript for important intellectual content. Dr. Prabhakaran: study concept and design, analysis and interpretation, critical revision of the manuscript for important intellectual content.

STUDY FUNDING

No targeted funding reported.

DISCLOSURE

R. Sangha, F. Caprio, R. Askew, and C. Corado report no disclosures relevant to the manuscript. R. Bernstein reports disclosures of consultant, research funding, and speakers bureau from the following companies: Medtronic, Boehringer Ingelheim, Pfizer/Bristol-Myers alliance. Y. Curran and I. Ruff report no disclosures relevant to the manuscript. D. Cella reports disclosures of receiving research funding from the National Institute of Neurologic Disorders and Stroke (NINDS) contract HHSN271201200036C for funding of QOL research, multiple NIH grants, Pfizer, Novartis, Biogen Idec, Clovis, and Bayer. Industry relationships that involve consulting include Pfizer, Novartis, Clovis, Astellas, Biogen Idec, Daiichi Sankyo, Inc., AstraZeneca, Genentech, and Bayer. A. Naidech reports disclosures of receiving salary support from the NINDS contract HHSN271201200036C and unrelated funding from Gaymar Inc. S. Prabhakaran reports disclosures of receiving funding from NINDS (U10NS08660, R01NS084288) and PCORI (AD-1310-07237). Go to Neurology.org for full disclosures.

Received February 25, 2015. Accepted in final form June 29, 2015.

REFERENCES

1. Reeves M, Khoury J, Alwell K, et al. Distribution of National Institutes of Health Stroke Scale in the Cincinnati/Northern Kentucky Stroke Study. *Stroke* 2013;44:3211–3213.

2. Smith EE, Fonarow GC, Reeves MJ, et al. Outcomes in mild or rapidly improving stroke not treated with intravenous recombinant tissue-type plasminogen activator: findings from Get With the Guidelines–Stroke. *Stroke* 2011; 42:3110–3115.
3. Lai SM, Studenski S, Duncan PW, Perera S. Persisting consequences of stroke measured by the Stroke Impact Scale. *Stroke* 2002;33:1840–1844.
4. D'Olhaberriague L, Litvan I, Mitsias P, Mansbach HH. A reappraisal of reliability and validity studies in stroke. *Stroke* 1996;27:2331–2336.
5. Cella D, Lai JS, Nowinski CJ, et al. Neuro-QOL: brief measures of health-related quality of life for clinical research in neurology. *Neurology* 2012;78:1860–1867.
6. Cella D, Nowinski C, Peterman A, et al. The neurology quality-of-life measurement initiative. *Arch Phys Med Rehabil* 2011;92(suppl):S28–S36.
7. Sacco RL, Kasner SE, Broderick JP, et al. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2013;44:2064–2089.
8. Adams HP Jr, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute IS: definitions for use in a multicenter clinical trial. *Trial of Org 10172 in Acute Stroke Treatment (TOAST)*. *Stroke* 1993;24:35–41.
9. Goldstein LB, Jones MR, Matchar DB, et al. Improving the reliability of stroke subgroup classification using the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria. *Stroke* 2001;32:1091–1098.
10. Granger CV, Devis LS, Peters MC, Sherwood CC, Barrett JE. Stroke rehabilitation: analysis of repeated Barthel Index measures. *Arch Phys Med Rehabil* 1979;60:14–17.
11. Bruno A, Akinwuntan AE, Lin C, et al. Simplified modified Rankin Scale questionnaire: reproducibility over the telephone and validation with quality of life. *Stroke* 2011; 42:2276–2279.
12. Janssen PM, Visser NA, Dorhout Mees SM, Klijn CJ, Algra A, Rinkel GJ. Comparison of telephone and face-to-face assessment of the modified Rankin Scale. *Cerebrovasc Dis* 2010;29:137–139.
13. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med* 1995; 333:1581–1587.
14. Naidech AM, Beaumont JL, Berman M, et al. Web-based assessment of outcomes after subarachnoid and intracerebral hemorrhage: a new patient centered option for outcomes assessment. *Neurocrit Care* 2015;23:22–27.
15. Sloan J, Cella D, Hays R. Clinical significance of patient-reported questionnaire data: another step toward consensus. *J Clin Epidemiol* 2005;58:1217–1219.
16. Weimar C, Kurth T, Kraywinkel K, et al. Assessment of functioning and disability after ischemic stroke. *Stroke* 2002;33:2053–2059.
17. Banks JL, Marotta CA. Outcomes validity and reliability of the modified Rankin Scale: implications for stroke clinical trials: a literature review and synthesis. *Stroke* 2007; 38:1091–1096.
18. Saver JL, Filip B, Hamilton S, et al. Improving the reliability of stroke disability grading in clinical trials and clinical practice: the Rankin Focused Assessment (RFA). *Stroke* 2010;41:992–995.
19. Wilson JTL, Hareendran A, Grant M, et al. Improving the assessment of outcomes in stroke: use of a structured interview to assign grade on the modified Rankin Scale. *Stroke* 2002;33:2243–2246.
20. Ali M, Fulton R, Quinn T, Brady M, Collaboration V. How well do standard stroke outcome measures reflect quality of life? A retrospective analysis of clinical trial data. *Stroke* 2013;44:3161–3165.
21. Stewart JC, Cramer SC. Patient-reported measures provide unique insights into motor function after stroke. *Stroke* 2013;44:1111–1116.
22. Bushnell CD, Reeves MJ, Zhao X, et al. Sex differences in quality of life after ischemic stroke. *Neurology* 2014;82: 922–931.
23. Verbraak ME, Hoeksma AF, Lindeboom R, Kwa VI. Subtle problems in activities of daily living after a transient ischemic attack or an apparently fully recovered non-disabling stroke. *J Stroke Cerebrovasc Dis* 2012;21:124–130.
24. Fens M, van Heugten CM, Beusmans GH, et al. Not as transient: patients with transient ischaemic attack or minor stroke experience cognitive and communication problems: an exploratory study. *Eur J Gen Pract* 2013;19:11–16.
25. Muus I, Petzold M, Ringsberg KC. Health-related quality of life among Danish patients 3 and 12 months after TIA or mild stroke. *Scand J Caring Sci* 2010;24:211–218.
26. Franzen-Dahlin A, Laska AC. Gender differences in quality of life after stroke and TIA: a cross-sectional survey of out-patients. *J Clin Nurs* 2012;21:2386–2391.
27. Moran GM, Fletcher B, Feltham MG, Calvert M, Sackley C, Marshall T. Fatigue, psychological and cognitive impairment following transient ischaemic attack and minor stroke: a systematic review. *Eur J Neurol* 2014;21:1258–1267.
28. Ko DT, Hebert PR, Coffey CS, Sedrkyan A, Curtis JP, Krumholz HM. β -Blocker therapy and symptoms of depression, fatigue, and sexual dysfunction. *JAMA* 2002; 288:351–357.
29. Corbi ISA, Dantas RAS, Pelegrino FM, Carvalho ARS. Health related quality of life of patients undergoing oral anticoagulation therapy. *Rev Lat Am Enfermagem* 2011; 19:865–873.
30. Khatri P, Conaway MR, Johnston KC; Acute Stroke Accurate Prediction Study (ASAP) Investigators. Ninety-day outcome rates of a prospective cohort of consecutive patients with mild ischemic stroke. *Stroke* 2012;43:560–562.
31. Courtis SB, Hill MD, Eliasziw M, Fischer K, Demchuk AM; VISION Study Group. Final 2 year results of the Vascular Imaging of Acute Stroke for Identifying Predictors of Clinical Outcome and Recurrent Ischemic Events (VISION) Study. *BMC Cardiovasc Dis* 2011;11:18.
32. Wang YL, Pan YS, Zhao XQ, et al; CHANCE investigators. Recurrent stroke was associated with poor quality of life in patients with transient ischemic attack or minor stroke: finding from the CHANCE trial. *CNS Neurosci Ther* 2014;20:1029–1035.
33. Norman GR, Sloan JA, Wyrrich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. *Med Care* 2003;41:582–592.
34. Bjorner JB, Rose M, Gandek B, Stone AA, Junghaenel DU, Ware JE Jr. Method of administration of PROMIS scales did not significantly impact score level, reliability, or validity. *J Clin Epidemiol* 2014;67:108–113.