OPEN

Clusters Across Multiple Domains of Health-Related Quality of Life Reveal Complex Patient Outcomes After Subarachnoid Hemorrhage

Julianne Murphy, MS[1]
Hye Jung Shin, BA[2]
Hanyin Wang, BS[3]
Yuan Luo, PhD[3]
Babak Jahromi, MD, PhD[4]
Thomas P. Bleck, MD[5]
David Cella, PhD[6]
Andrew M. Naidech, MD, MSPH[2,3,5]

OBJECTIVES: Patients with aneurysmal subarachnoid hemorrhage (ruptured brain aneurysm) often have reduced health-related quality of life at follow-up in multiple domains (e.g., cognitive function and social function). We tested the hypothesis that there are distinct patterns of patient outcomes across domains of health-related quality of life, "complex patient outcomes," in survivors of subarachnoid hemorrhage.

DESIGN: Patients with subarachnoid hemorrhage were prospectively identified. Clinical data were prospectively recorded. Health-related quality of life was prospectively assessed at 3-month follow-up using the National Institutes of Health Patient Reported Outcomes Measurement Information System and neuro-quality of life in the domains of mobility, cognitive function, satisfaction with social roles, and depression. We used k-means clustering to analyze prospectively recorded health-related quality of life data, identifying clusters of complex patient outcomes. Decision tree analysis identified index hospital stay factors predictive of a patient having a particular complex patient outcome at follow-up.

SETTING: Academic medical center.

PATIENTS: One hundred three survivors of subarachnoid hemorrhage.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: We analyzed 103 patients, of whom 75 (72.8%) were female, and mean age was 53.6 ± 13.4 years. There were three complex patient outcomes: health-related quality of life greater than 1 SD better than the U.S. mean across all domains ($n = 23$, 22.3%), health-related quality of life greater than 1 SD worse than U.S. mean across all domains ($n = 26$, 25.2%), and satisfaction with social roles greater than 0.5 SD worse than U.S. mean with cognitive function, depression, and mobility scores near the U.S. mean ($n = 54$, 52.4%). In decision tree analysis, hospital disposition and Hunt and Hess Grade were associated with complex patient outcome.

CONCLUSIONS: Complex patient outcomes across multiple domains of health-related quality of life at follow-up after subarachnoid hemorrhage are distinct and may be predictable.

KEY WORDS: outcomes research; quality of life; subarachnoid hemorrhage

Subarachnoid hemorrhage (SAH), ruptured brain aneurysm, occurs in nearly 50,000 Americans yearly (1). As techniques for early aneurysm obliteration have advanced, patient survival has improved. Survivors of SAH are typically seen in outpatient follow-up clinics for continuing patient care. Comprehensive follow-up clinics are recommended for survivors of SAH to assess and manage multiple, complex patient needs that are difficult to

DOI: 10.1097/CCE.0000000000000533

predict and likely to benefit from established clinical interventions (2–5).

Patient outcomes are typically assessed at follow-up several months after SAH onset. The typical outcome is a single, ordinal scale, such as the modified Rankin Scale (mRS) or Glasgow Outcomes Scale (6, 7). The mRS is heavily focused on mobility and is less discriminating for other domains of health-related quality of life (HRQoL), such as cognitive function (8). However, patients often have complex patient outcomes with varying degrees of abnormal HRQoL across multiple domains (9, 10). Reductions in HRQoL other than mobility remain difficult to predict (11, 12), making patient outcomes assessment and management reactive, rather than proactive.

It is not known whether scores between HRQoL diverge across domains, for example, when cognitive function differs from mobility. Identifying discrete clusters of scores of HRQoL across multiple domains could identify complex patients more effectively than a global outcome measure. Without a method to identify patterns of complex patient outcomes, the number of potential combinations to consider (i.e., every score of HRQoL independently of every other score) would be unwieldy. We tested the hypothesis that there are discrete clusters across multiple domains of HRQoL in survivors of SAH that represent complex patient outcomes, as opposed to the simple rubric of "good" or "poor" outcome.

MATERIALS AND METHODS

Patient Population

We conducted a retrospective analysis of prospectively collected patient data. Patients were enrolled from July 2010 to February 2021. Patients with SAH were identified at admission, and demographic data were collected. Patients with mild cognitive impairment or dementia were excluded due to the uncommon nature of dementia and depression in patients with SAH; our database only prospectively documents dementia for patients with intracerebral hemorrhage where it is more common. For patients with SAH, disease severity was documented with the Hunt and Hess Scale, an ordinal scale from 1 (minimal symptoms) to 5 (deeply comatose). Radiographic severity of SAH was evaluated with the modified Fisher scale that accounted for thick subarachnoid blood and bilateral intraventricular hemorrhage (13). Additional categorical variables of interest collected during the index hospital stay included interventions for management (i.e., angioplasty or intra-arterial vasodilator), external ventricular drainage for hydrocephalus, the parent artery of the ruptured aneurysm, aneurysm obliteration, global cerebral edema at admission CT (14), seizure, prophylactic levetiracetam, the presence of a visible cerebral infarction indicating delayed cerebral ischemia (the end point as per guidelines from the Neurocritical Care Society) (15), and the total number of cerebral infarctions (single or multiple) (16). Patients were cared for by a team that included fellowship-trained cerebrovascular neurosurgeons and neurointensivists (A.M.N. was present during the entire study period). We noted the patient's disposition from the index hospital stay as home (potentially including outpatient rehabilitation), acute inpatient rehabilitation, acute care, or nursing facility.

Ethical Approval

Patient identification and data collection methods were approved by the Northwestern University Institutional Review Board (IRB) with the approval number STU00011825. Informed consent was obtained from patients or a legally authorized representative if the patient was unable to consent (e.g., aphasia). The IRB approved a waiver of consent for patients who could not consent and had no identifiable legally authorized representative, and for patients who died (such patients have no HRQoL to report).

Outcomes Assessment

The mRS at 3-month follow-up was assessed for this specific research study using a validated questionnaire (17). Upon obtaining informed consent, patient e-mail addresses were recorded, and an automated e-mail was sent. Failure to respond by e-mail initiated up to three follow-up attempts by telephone if the contact information was not found to be invalid (i.e., telephone disconnected). For each patient's successful 3-month follow-up, we used the National Institutes of Health Patient Reported Outcomes Measurement Information System and Neuro-quality of life (QOL) instruments to prospectively assess HRQoL outcomes (18). Neuro-QOL was validated for report by proxy (e.g., a family member) as part of its development (19). We obtained Neuro-QOL mobility, cognitive function Version 2.0

(earlier data obtained with cognitive function—general concerns Version 1.1 were converted to cognitive function Version 2.0 via an automated calculator at www.healthmeasures.net), social roles and activities, and depression. Cognitive function was measured using a Short Form, and a Computer Adaptive Test was administered to measure depression, mobility, and social roles and activity. All methods result in a raw score, and a T score normalized to the U.S. general population at 50 ± 10 (additional information available at http://www.nihpromis.org/ and http://www.neuro-qol.org/).

The four HRQoL measures assessed were lower extremity function (mobility), cognitive function, ability to participate in social roles and activities, and depression. The cluster analysis did not include patients with missing HRQoL outcomes; we chose these four domains of HRQoL because they were a priori less likely to be correlated, were obtained throughout the study period, and are well described in survivors of SAH (8, 20–22). Mobility measures lower extremity function inclusive of bodily movement, ambulation, balance, and endurance. Cognitive function measures memory, attention, decision-making, and the application of these abilities to daily tasks. Social roles and activities measure an individual's participation in work, family, friend, and leisure activities. Depression measures an individual's overall mood, positive effect, information-processing deficits, self-views, and social cognition.

Statistical Analysis

Baseline patient demographics and clinical characteristics were summarized with percentages for categorical variables and mean ± SD for normally distributed continuous data (e.g., age). Categorical data were tested for an association with cluster membership using chi-square statistics or Fisher exact tests when there were fewer than five observations per cell. Continuous data were tested for an association with cluster membership using analysis of variance or the Kruskal-Wallis *H* test for nonnormally distributed data (e.g., mRS). Dunn test with Bonferroni correction was used for pairwise comparison testing of a difference in mRS between clusters.

We used unsupervised k-means cluster analysis to detect complex patient outcomes across multiple domains of HRQoL (23). The algorithm used Minkowski-based Euclidean distance metrics to generate mutually exclusive clusters. The HRQoL domains of depression, mobility, satisfaction with social roles and activities, and cognitive function were used by the clustering algorithm. The k-means algorithm required the prespecification of the total number of clusters, and we tested solutions with one to 10 clusters. We determined the optimal number of clusters using the average silhouette method calculation and from elbow method heuristics. Clustering is represented by a visibly apparent decrease in the sums of squares of the error by number of clusters. We repeated the analysis with other clustering techniques including k-means clustering with angular cosine distances, Gaussian mixture models, agglomerative hierarchical clustering with Ward linkage, and divisive hierarchical clustering, and found similar results. Each cluster represents a complex patient outcome, that is, a group of scores across multiple domains of HRQoL.

To determine which factors from a patient's index hospitalization were associated with a patient belonging to any individual cluster, we used decision trees, with cluster membership (i.e., complex patient outcome) as the dependent variable. The initial decision tree was overgrown and then pruned back using the optimal cost-complexity parameter to reduce overfitting. Linear methods were not appropriate for this task because the outcome was not ordered (i.e., clusters two and four were not clearly superior to each other).

Statistical analysis was conducted using freely available software (R Version 4.0.2 and R Studio, PBC, Boston, MA) (24, 25).

Data Availability

The data used in this study are not publicly available. Data access requests to reproduce the analysis should be communicated to the corresponding author.

RESULTS

Four hundred ninety-seven patients with SAH were screened for inclusion. One hundred twenty-seven patients were assessed at 3-month follow-up, of whom 116 reported HRQoL outcomes. The final analysis was performed in 103 patients (see the Consolidated Standards of Reporting Trials diagram; **Fig. 1**). Details of patient demographics are reported in **Table 1**.

Scores clustered across multiple domains of HRQoL corresponding to distinct complex patient outcomes. **Figure 2** depicts the T scores for each complex patient

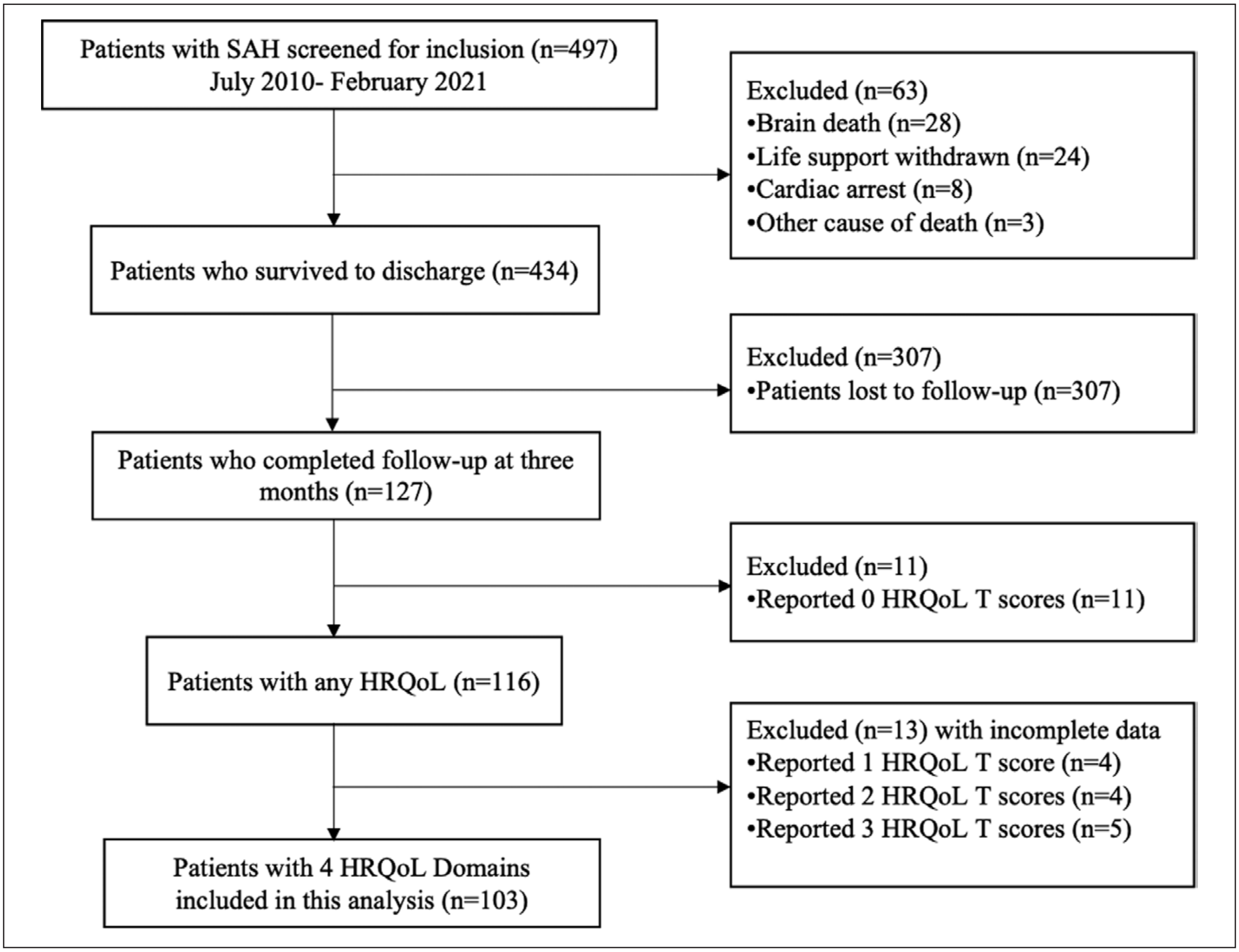

Figure 1. Consolidated Standards of Reporting Trials diagram of patient flow.

outcome across domains of HRQoL. In unsupervised cluster analysis, both the silhouette and elbow methods suggested the optimal number of clusters (k) was 3 (**Supplementary eFig. 1**, http://links.lww.com/CCX/A784, and **Supplementary eFig. 2**, http://links.lww.com/CCX/A785). The patients in cluster 1 reported HRQoL scores more than 1 SD better than the U.S. mean for all domains (best HRQoL). Cluster 2 included patients whose HRQoL scores were above the U.S. mean for mobility, near the U.S. mean for cognitive function and depression, and worse than the U.S. mean for social roles and activities. The patients in cluster 3 reported HRQoL scores more than 1 SD worse than the U.S. mean in mobility, social roles and activities, cognitive function, and depression (worst HRQoL). In other words, cluster 1 had the best outcomes and cluster 3 had the worst outcomes, whereas cluster 2 was distinguished by above-average mobility and below-average social roles and activities. Cluster analysis with additional techniques found larger cluster solutions with lower quality (**Supplementary eTable 1**, http://links.lww.com/CCX/A786).

Complex patient outcomes had a different mRS at follow-up (overall $p < 0.001$). After correction for multiple comparisons, clusters 1 (the complex patient outcome with the best HRQoL across domains) and 2 were significantly different from each other ($p = 0.012$). Clusters 1 and 2 were each significantly different from cluster 3 (the complex patient outcome with the worst HRQoL across domains) ($p < 0.001$).

Patients were not evenly distributed between complex patient outcomes (i.e., different clusters of scores of HRQoL). **Table 2** displays the patient characteristics stratified by complex patient outcome. Of the 103 patients, 23 (22.3%) were assigned to cluster 1, 54 (52.4%) to cluster 2, and 26 (25.2%) to cluster 3.

TABLE 1.
Demographics of 103 Patients

Variable	*n* (%) or mean ± SD
Age	53.6 ± 13.4
Sex	
Female	75 (72.8)
Ethnicity	
Asian	7 (6.9)
Black or African American	11 (10.8)
Native Pacific Islander	3 (2.9)
White	81 (79.4)
Hispanic	
Hispanic or Latino	20 (19.4)
CT score	
No blood	6 (6.2)
Thin SAH	20 (20.6)
Thin SAH and bilateral IVH	1 (1.0)
Thick SAH	62 (63.9)
Thick SAH and bilateral IVH	8 (8.2)
Hunt and Hess Grade	
Minimal symptoms	15 (14.6)
Severe headache	55 (53.4)
Lethargy	17 (16.5)
Hemiparesis or stupor	9 (8.7)
Coma, posturing	7 (6.8)
Disposition	
Home	73 (70.9)
Rehab	18 (17.5)
Acute care	6 (5.8)
Nursing facility	6 (5.8)
Aneurysm location	
Anterior cerebral/communicating artery	24 (28.6)
Internal carotid or posterior communicating artery	32 (38.1)
Vertebral, basilar or posterior circulation	6 (7.1)
Middle cerebral artery	22 (26.2)
Aneurysm obliteration	
Clip	34 (34.0)
Coil	49 (49.0)
No repair	17 (17.0)
External ventricular drain	47 (45.6)
Global cerebral edema on admit CT	8 (7.8)

(*Continued*)

TABLE 1. (*Continued*).
Demographics of 103 Patients

Variable	*n* (%) or mean ± SD
Seizure	9 (8.7)
Prophylactic levetiracetam	59 (57.3)
Delayed cerebral ischemia	25 (24.3)
Management interventions	29 (28.2)

IVH = intraventricular hemorrhage, SAH = subarachnoid hemorrhage.
The total number of patients may not equal 103 due to missing data. Percentages are based on available data.

Complex patient outcomes were significantly associated with the initial Hunt and Hess Score ($p = 0.027$), aneurysm obliteration ($p = 0.007$), the use of an external ventricular drain for hydrocephalus ($p = 0.006$), and the patient's disposition from the index hospital stay ($p < 0.001$).

In decision tree analysis of data collected during the index hospital stay, Hunt and Hess Grade and hospital disposition were associated with complex patient outcome at follow-up. The decision tree was moderately predictive (area under the curve = 0.63) of complex patient outcome one through three (the optimal number of clusters of scores of HRQoL).

DISCUSSION

We found distinct complex patient outcomes across several domains of HRQoL in survivors of SAH. Complex patient outcomes where multiple domains of HRQoL are affected might be conceptualized as one of several outcomes representing distinct, complex needs for patient management at follow-up. These results underscore the multidimensional nature of QoL outcomes in patients with SAH.

Our exploratory analysis examined four different domains of HRQoL that are known to be affected after SAH (12). Dozens of domains of HRQoL are assessable, requiring some a priori choices about which domains of HRQoL were most likely to be affected. Abnormalities in cognitive function, social roles and activities, anxiety, fatigue, and depression are well described in survivors of SAH (8, 20–22). It is possible that additional complex patient outcomes would be described if additional domains of HRQoL were collected.

Reductions in several domains of HRQoL may not have a specifically identifiable cause. Fatigue, anxiety,

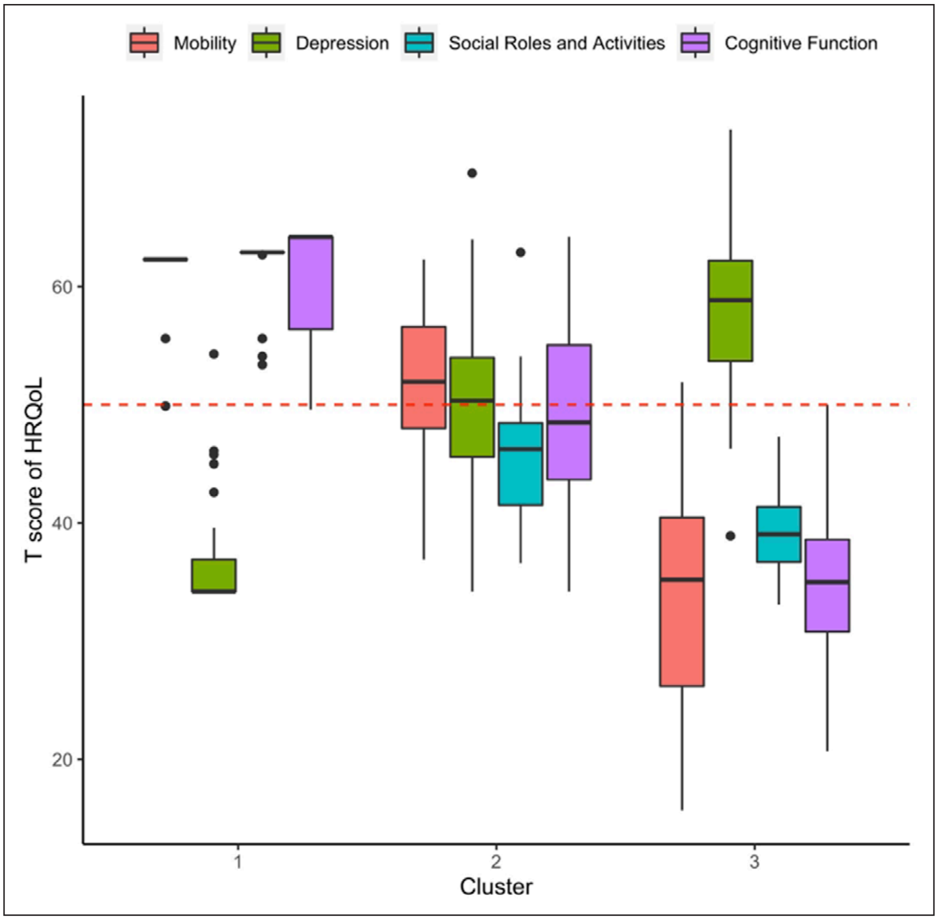

Figure 2. Boxplots of three clusters across scores for depression, mobility, satisfaction with social roles and activities, and cognitive function. *Clusters* represent complex patient outcomes across multiple domains of health-related quality of life. Patients in cluster 1 had scores greater than 1 SD better than the U.S. population mean (50, *horizontal line*). Patients in cluster 2 had scores for satisfaction with social roles greater than 0.5 SD worse than U.S. mean with cognitive function, depression, and mobility scores near the U.S. mean. Patients in cluster 3 had scores greater than 1 SD worse than the U.S. population mean (high depression scores indicate more symptoms).

and depression are correlated with each other as part of the "postintensive care syndrome" (26), which could affect survivors of SAH as much as survivors of other conditions that require extended critical care. In our data, Hunt and Hess Grade, an external ventricular drain for hydrocephalus, aneurysm obliteration, and hospital disposition were associated with scores of HRQoL at 3-month follow-up. However, the mechanisms are not defined, and the moderate performance of our decision tree demonstrates that predicting complex patient outcomes is an important goal requiring further study.

Predicting complex patient outcomes across multiple domains of HRQoL could help make follow-up care more proactive. For example, a prediction that a patient is likely to have normal mobility, reduced cognitive function, and increased depression could be useful to proactively plan for appropriate evaluations that may be different from a patient likely to only have reduced mobility. Predictions of complex patient outcomes over multiple domains of QoL could help to plan for efficient and effective care before patient follow-up (e.g., proactive planning for neurocognitive evaluations).

Complex patient outcomes could elucidate the interpretation of patient outcomes data, particularly when HRQoL scores are similar. A magnitude of difference of 0.5 SD between groups is generally considered significant (27, 28), and the differences between scores we found of HRQoL for the complex patient outcomes were generally greater than 1 SD. The majority of patients in this analysis reported near-average scores across all four domains, underscoring the typically moderate correlation between scores of HRQoL (9). We found scores across multiple domains of HRQoL in all the clusters defined by the algorithm.

Our results should be considered to be of a subset of patients who all have "good outcome," in the sense that patients are generally independent of ambulation (mRS ≤ 3). Our cohort excludes patients who are neurologically devastated or dead and, therefore, do not have measurements of HRQoL. The results confirm reductions in multiple domains of HRQoL in patients with "good outcome" (8, 20–22). Although complex patient outcomes may not be as straightforward to order as categories of the mRS or magnitude of T scores of HRQoL, complex patient outcomes are likely to distinguish discrete outcomes that are meaningful for patients and caregivers, reflect a broader measure of a patient's outcome, and have distinct implications

TABLE 2.
Comparison of Patient Characteristics Across Complex Patient Outcomes

Patient Characteristic	Cluster 1 (*n* = 23)	Cluster 2 (*n* = 54)	Cluster 3 (*n* = 26)	*p*
Mobility HRQoL, mean ± SD	61.5 ± 2.9	52.4 ± 6.8	33.6 ± 9.7	< 0.001[a]
Depression HRQoL, mean ± SD	37.2 ± 5.6	49.6 ± 7.7	58.0 ± 7.8	< 0.001[a]
Social roles and activities HRQoL, mean ± SD	61.5 ± 3.2	45.5 ± 5.2	39.4 ± 3.7	< 0.001[a]
Cognitive function HRQoL, mean ± SD	60.4 ± 5.3	49.5 ± 8.1	34.8 ± 7.2	< 0.001[a]
Modified Rankin Scale, median (interquartile range)	0 (0–0)	1 (1–2)	3 (3–4)	< 0.001[a]
Age, *n* (%)	50.4 (13.6)	54.2 (13.9)	55.2 (12.4)	0.4
Sex, *n* (%)				
Female	14 (60.9)	41 (75.9)	20 (76.9)	0.3
Ethnicity, *n* (%)				
Asian	1 (4.3)	4 (7.5)	2 (7.7)	0.4
Black or African American	0 (0.0)	8 (15.1)	3 (11.5)	
Native Pacific Islander	1 (4.3)	2 (3.8)	0 (0.0)	
White	21 (91.3)	39 (73.6)	21 (80.8)	
Hispanic, *n* (%)				
Hispanic or Latino	5 (21.7)	11 (20.4)	4 (15.4)	0.8
CT score, *n* (%)				
No blood	2 (8.7)	3 (6.1)	1 (4.0)	0.6
Thin SAH	7 (30.4)	10 (20.4)	3 (12.0)	
Thin SAH and bilateral IVH	1 (4.3)	0 (0.0)	0 (0.0)	
Thick SAH	12 (52.2)	32 (65.3)	18 (72.0)	
Thick SAH and bilateral IVH	1 (4.3)	4 (8.2)	3 (12.0)	
Hunt and Hess Grade, *n* (%)				
Minimal symptoms	5 (21.7)	8 (14.8)	2 (7.7)	0.027[a]
Severe headache	14 (60.9)	33 (61.1)	8 (30.8)	
Lethargy	3 (13.0)	8 (14.8)	6 (23.1)	
Hemiparesis or stupor	1 (4.3)	3 (5.6)	5 (19.2)	
Coma, posturing	0 (0.0)	2 (3.7)	5 (19.2)	
Disposition, *n* (%)				
Home	21 (91.3)	42 (77.8)	10 (38.5)	< 0.001[a]
Rehabilitation	1 (4.3)	12 (22.2)	5 (19.2)	
Acute care	0 (0.0)	0 (0.0)	6 (23.1)	
Nursing facility	1 (4.3)	0 (0.0)	5 (19.2)	
Aneurysm location, *n* (%)				
Anterior cerebral/communicating artery	5 (33.3)	11 (24.4)	8 (33.3)	1.0
Internal carotid or posterior communicating artery	5 (33.3)	18 (40.0)	9 (37.5)	
Vertebral, basilar, or posterior circulation	1 (6.7)	4 (8.9)	1 (4.2)	
Middle cerebral artery	4 (26.7)	12 (26.7)	6 (25.0)	

(*Continued*)

TABLE 2. (*Continued*).
Comparison of Patient Characteristics Across Complex Patient Outcomes

Patient Characteristic	Cluster 1 (*n* = 23)	Cluster 2 (*n* = 54)	Cluster 3 (*n* = 26)	*p*
Aneurysm obliteration, *n* (%)				
Clip	5 (22.7)	14 (26.9)	15 (57.7)	0.007[a]
Coil	9 (40.9)	30 (57.7)	10 (38.5)	
No repair	8 (36.4)	8 (15.4)	1 (3.8)	
External ventricular drain, *n* (%)	8 (34.8)	20 (37.0)	19 (73.1)	0.006[a]
Global cerebral edema on admit CT, *n* (%)	2 (8.7)	2 (3.7)	4 (15.4)	0.2
Seizure, *n* (%)	1 (4.3)	3 (5.6)	5 (19.2)	0.1
Prophylactic levetiracetam, *n* (%)	11 (47.8)	30 (55.6)	18 (69.2)	0.3
Delayed cerebral ischemia, *n* (%)	5 (21.7)	11 (20.4)	9 (34.6)	0.4
Management interventions, *n* (%)	5 (21.7)	15 (27.8)	9 (34.6)	0.6

IVH = intraventricular hemorrhage, HRQoL = health-related quality of life, SAH = subarachnoid hemorrhage.
The number of patients may not equal the total number of patients in each cluster due to missing data. Percentages are based on available data.
[a]$p < 0.05$.

for patient management (e.g., evaluation of reduced cognitive function as opposed to worse social function and depression). The analysis of clusters across domains of HRQoL permits a comprehensive assessment of patient outcome, and a potential improvement over a single, global outcome or consideration of individual domains of HRQoL.

This study has several limitations. These data are from a single center and identifying HRQoL clusters with distinct patterns in other datasets would be of interest. Our analysis did not include baseline mRS, limiting comparison with the reported mRS at 3-month follow-up. Baseline mRS was not collected because our patients with SAH were typically normal prior to the onset of SAH, in distinction to patients with intracerebral hemorrhage who may have dementia at baseline (e.g., from cerebral amyloid angiopathy) (29). Although the analysis is subject to the limitations of the k-means clustering algorithm that assumes spherical and equally sized clusters, an analysis of other clustering techniques revealed k-means with Euclidean distance metrics as the optimal solution. Other clustering algorithms had similar results, and all of these clustering techniques required complete data. How to predict which patients would fall into which clusters based on a patient's index hospitalization is not clear—Hunt and Hess Grade, aneurysm obliteration, and an external ventricular drain are crude measures—representing a topic for future research. Cluster 1, the patients with the best outcomes, more commonly had no aneurysm repair and thin SAH, consistent with the syndrome of "perimesencephalic" hemorrhage and a normal HRQoL at follow-up (30). Approximately half the cohort was in one cluster, with smaller proportions having supranormal HRQoL and more severe impairments across multiple domains of HRQoL. Clustering results that may more evenly divide the cohort may also be clinically intuitive (e.g., four clusters) and highlight additional patterns of abnormal HRQoL, such as normal mobility with reduced cognitive function.

Most notably, a large proportion of patients were lost to follow-up (71% of the surviving patients in the cohort). Many patients did not provide HRQoL at follow-up, and we did not assess the same domains over the entire study period, reducing the number of patients that could be included. It is possible that the patients from whom we obtained HRQoL are not representative of the total cohort of patients with SAH. A limitation of HRQoL research is that these data are challenging to obtain. Although we attempted to follow-up with patients by recording e-mail addresses and telephone numbers, we are unable to collect data from patients who do not provide this information. At 3-month follow-up, we are unable to collect information from patients who are dead or disabled. Our cohort represented the best available data at present, and the cohort's size was typical of other SAH patient cohorts assessed at 3-month follow-up (11).

CONCLUSION

In sum, we found that survivors of SAH had identifiable complex patient outcomes across domains of HRQoL. Clusters of scores of HRQoL were associated with severity of neurologic injury. Clustering algorithms provide an intelligible method to conceptualize HRQoL outcomes across multiple domains. Predicting complex patient outcomes could make follow-up patient care more proactive by anticipating patient needs across several domains of HRQoL.

1 Center for Education in Health Sciences, Feinberg School of Medicine of Northwestern University, Chicago, IL.

2 Institute for Public Health and Medicine, Feinberg School of Medicine of Northwestern University, Chicago, IL.

3 Department of Preventive Medicine, Feinberg School of Medicine of Northwestern University, Chicago, IL.

4 Department of Neurological Surgery, Feinberg School of Medicine of Northwestern University, Chicago, IL.

5 Department of Neurology, Feinberg School of Medicine of Northwestern University, Chicago, IL.

6 Department of Medical Social Sciences, Feinberg School of Medicine of Northwestern University, Chicago, IL.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/ccejournal).

Ms. Murphy reports funding from T32 LM012203, Ms. Wang reports funding from UL1 TR001422, Dr. Luo reports funding from R01 LM013337 and GM105688, and Dr. Naidech reports funding from National Institutes of Health R01 NS110779 and U01 NS110772. The remaining authors have disclosed that they do not have any potential conflicts of interest.

For information regarding this article, E-mail: juliannemurphy2023@u.northwestern.edu

REFERENCES

1. Virani SS, Alonso A, Aparicio HJ, et al; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee: Heart disease and stroke statistics-2021 update: A report from the American Heart Association. *Circulation* 2021; 143:e254–e743
2. Why patients with aSAH need multidisciplinary follow-up. *Lancet Neurol* 2011; 10:289
3. Mocco J, Ransom ER, Komotar RJ, et al: Long-term domain-specific improvement following poor grade aneurysmal subarachnoid hemorrhage. *J Neurol* 2006; 253:1278–1284
4. Springer MV, Schmidt JM, Wartenberg KE, et al: Predictors of global cognitive impairment 1 year after subarachnoid hemorrhage. *Neurosurgery* 2009; 65:1043–1050
5. Chahal N, Barker-Collo S, Feigin V: Cognitive and functional outcomes of 5-year subarachnoid haemorrhage survivors: Comparison to matched healthy controls. *Neuroepidemiology* 2011; 37:31–38
6. Rankin J: Cerebral vascular accidents in patients over the age of 60. II. Prognosis. *Scott Med J* 1957; 2:200–215
7. 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
8. Naidech AM, Beaumont JL, Berman M, et al: Dichotomous "good outcome" indicates mobility more than cognitive or social quality of life. *Crit Care Med* 2015; 43:1654–1659
9. Katzan IL, Schuster A, Newey C, et al: Patient-reported outcomes across cerebrovascular event types: More similar than different. *Neurology* 2018; 91:e2182–e2191
10. Katzan IL, Fan Y, Uchino K, et al: The PROMIS physical function scale: A promising scale for use in patients with ischemic stroke. *Neurology* 2016; 86:1801–1807
11. Mayer SA, Kreiter KT, Copeland D, et al: Global and domain-specific cognitive impairment and outcome after subarachnoid hemorrhage. *Neurology* 2002; 59:1750–1758
12. Kreiter KT, Copeland D, Bernardini GL, et al: Predictors of cognitive dysfunction after subarachnoid hemorrhage. *Stroke* 2002; 33:200–208
13. Claassen J, Bernardini GL, Kreiter K, et al: Effect of cisternal and ventricular blood on risk of delayed cerebral ischemia after subarachnoid hemorrhage: The Fisher scale revisited. *Stroke* 2001; 32:2012–2020
14. Claassen J, Carhuapoma JR, Kreiter KT, et al: Global cerebral edema after subarachnoid hemorrhage: Frequency, predictors, and impact on outcome. *Stroke* 2002; 33:1225–1232
15. Diringer MN, Bleck TP, Claude Hemphill J III, et al; Neurocritical Care Society: Critical care management of patients following aneurysmal subarachnoid hemorrhage: Recommendations from the Neurocritical Care Society's Multidisciplinary Consensus Conference. *Neurocrit Care* 2011; 15:211–240
16. Rabinstein AA, Weigand S, Atkinson JL, et al: Patterns of cerebral infarction in aneurysmal subarachnoid hemorrhage. *Stroke* 2005; 36:992–997
17. Saver JL, Filip B, Hamilton S, et al; FAST-MAG Investigators and Coordinators: Improving the reliability of stroke disability grading in clinical trials and clinical practice: The Rankin Focused Assessment (RFA). *Stroke* 2010; 41:992–995
18. Cella D, Riley W, Stone A, et al: The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. *J Clin Epidemiol* 2010; 63:1179–1194
19. 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
20. Katzan IL, Thompson NR, Lapin B, et al: Added value of patient-reported outcome measures in stroke clinical practice. *J Am Heart Assoc* 2017; 6:e005356

21. Lin C, Lee J, Chatterjee N, et al: Predicting domain-specific health-related quality of life using acute infarct volume. *Stroke* 2017; 48:1925–1931
22. Naidech AM, Kreiter KT, Janjua N, et al: Phenytoin exposure is associated with functional and cognitive disability after subarachnoid hemorrhage. *Stroke* 2005; 36:583–587
23. Everitt BS, Landau S, Leese M, et al: Cluster Analysis. Hoboken, NJ, Wiley, 2011
24. R Core Team: R: A Language and Environment for Statistical Computing. Vienna, Austria, R Foundation for Statistical Computing, 2020
25. R Studio Team: RStudio: Integrated development for R. Boston, MA, PBC, 2020
26. Mikkelsen ME, Still M, Anderson BJ, et al: Society of Critical Care Medicine's international consensus conference on prediction and identification of long-term impairments after critical illness. *Crit Care Med* 2020; 48:1670–1679
27. Bath PM, Lees KR, Schellinger PD, et al; European Stroke Organisation Outcomes Working Group: Statistical analysis of the primary outcome in acute stroke trials. *Stroke* 2012; 43:1171–1178
28. Bath PM, Gray LJ, Collier T, et al: Can we improve the statistical analysis of stroke trials? Statistical reanalysis of functional outcomes in stroke trials. *Stroke* 2007; 38:1911–1915
29. Naidech AM, Beaumont J, Muldoon K, et al: Prophylactic seizure medication and health-related quality of life after intracerebral hemorrhage. *Crit Care Med* 2018; 46:1480–1485
30. Konczalla J, Schmitz J, Kashefiolasl S, et al: Non-aneurysmal subarachnoid hemorrhage in 173 patients: A prospective study of long-term outcome. *Eur J Neurol* 2015; 22:1329–1336