Long-Term Outcome After Stroke
Evaluating Health-Related Quality of Life Using Utility Measurements

Caroline Haacke, MD; Astrid Althaus, MA; Annika Spottke, MD; Uwe Siebert, MD, MPH; Tobias Back, MD; Richard Dodel, MD

Background and Purpose—As stroke mortality rates decline, individuals are increasingly likely to live with their residual impairments and disabilities. Therefore, the quality of poststroke life is 1 of the pivotal topics that have to be considered beneath the functional outcome. However, data on health-related quality of life (HRQoL) have been infrequently used in stroke trials. The purpose of this study was to examine the long-term outcome (4 years after stroke) of HRQoL and to identify the determinants of HRQoL in stroke survivors.

Methods—Seventy-seven patients were included who were admitted to the Department of Neurology, Philipps-University Marburg, after experiencing an ischemic stroke, a transient ischemic attack, or a hemorrhagic stroke. All patients were examined by a physician, and assessment was performed using a standardized questionnaire. HRQoL was assessed using the German version of the EuroQoL Index (EQ-5D) and the Health Utility Index 2 and 3 (HUI2/3).

Results—Four years after stroke, besides physical functioning, neuropsychological sequelae such as depression and cognitive impairment contributed to a reduced HRQoL. In addition, the incidence of incontinence proved to be an important factor for HRQoL. Explained variances in regression analysis models were high ($R^2$ for HUI and 0.633 for EQ-5D—visual analogue scale) and were based on a few important determinants, including physical state, depression, cognitive impairment, and incontinence.

Conclusion—Our results underscore the importance of nonmotor symptoms on HRQoL in patients with stroke. (Stroke. 2006;37:193-198.)

Key Words: multivariate ▪ quality of life ▪ stroke ▪ stroke outcome

In developed countries, stroke is the third common cause of death after heart disease and cancer. As stroke mortality rates decline, individuals are increasingly likely to live with their residual impairments, which can pose a considerable impact for survivors’ subsequent well-being. Therefore, the quality of life (QoL) and life satisfaction are pivotal where the impact is often lifelong and multidimensional.

The Barthel index (BI) and the modified Rankin scale (mRS) are the most frequent outcome measures used in stroke research focusing on stroke-related disability. However, stroke patients have a broad range of symptoms beyond the mere motor dysfunction, and those scales fall short in appropriately assessing the entire range of stroke sequelae. Therefore, a more comprehensive assessment of the burden of the disease is necessary. The concept of health-related QoL (HRQoL) is a multidimensional approach to quantify the patients’ burden of disease. Data on HRQoL have only infrequently been used in stroke trials. To assess HRQoL, a multitude of generic and specific HRQoL instruments have been developed. Generic HRQoL instruments can be applied across a wide range of populations and interventions, whereas specific HRQoL instruments are designed to assess HRQoL only of particular subpopulations. Generic HRQoL instruments can be further classified into health profiles, which describe HRQoL in terms of various dimensions including physical, functional, psychological and social health, and utility measurements, which are preference-based measures. Utility measurements summarize HRQoL in a single value or index, mostly ranging from 0 (for dead) to 1 (for complete health).

The factors that contribute to the reduced HRQoL were not systematically investigated in long-term stroke survivors, and only very few studies have used preference-based measures to assess HRQoL. Therefore, the aim of our study was to identify HRQoL in stroke survivors via preference-based measures. We used the German version of the EuroQoL

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From the Department of Neurology (C.H., T.B.), Philipps-University Marburg, Germany; the Department of Neurology (A.A., A.S., R.D.), University of Bonn, Germany; MGH Institute for Technology Assessment and the Department of Radiology (U.S.), Harvard Medical School, Boston, Mass; the Department of Public Health, Medical Decision Making and Health Technology Assessment (U.S.), University for Health Sciences, Medical Informatics and Technology, Hall, Austria; and Department of Neurology (T.B.), University of Mannheim, Germany.

The first 2 authors contributed equally to this work.
Correspondence to PD Dr Richard Dodel, Department of Neurology, University of Bonn, Sigmund-Freudstr. 25, 53111 Bonn, Germany. E-mail richard.dodel@ukb.uni-bonn.de
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Index (EQ-5D) and Health Utility Index 2 and 3 (HUI2/3) to quantify HRQoL.

**Patients and Methods**

The study included all patients who were admitted to the Department of Neurology, Philipps-University Marburg, between January 1 and March 31, 1999, after experiencing an ischemic stroke, a transient ischemic attack (TIA), or a hemorrhagic stroke. The diagnosis that was assigned to patients was based on the discharge diagnosis. A total of 152 patients met the inclusion criteria of the study. After 4 years, 151 patients could be located; 50 patients were deceased by the time of enquiry; and 24 patients refused to participate in the study; the mean age of these patients was 74.6 years, and the median age was 77.0 years.

Seventy-seven patients were examined by 1 experienced physician, and assessment of HRQoL and other clinical characteristics was performed using a standardized questionnaire. One examination lasted 1 to 1.5 hours. The examination consisted of 2 parts; in the first part, the patients’ social, economic, and health-related situation was assessed by means of a standardized interview. Subsequently, to the face-to-face interview, HRQoL questionnaires were completed by the patients. The physician was present during the entire examination. Data of patients who were not able to fill out the QoL questionnaires without any help because of dementia or aphasia were excluded from QoL analyses.

**Instruments**

Disability was evaluated using the BI and the mRS. The BI measures the degree of autonomy in daily living activities and gives a score ranging from 0 (total independence) to 100 (total dependence). The BI mean scores were categorized as follows: BI <30 was classified as needing “institutional care”; 30 to 70 was classified as “help needed”; and patients having a BI >70 were classified as being “functionally independent.”

The mRS assesses the patients’ ability to perform the activities they carried out previously and any assistance in doing so. It ranges from 0 (no symptoms at all) to 6 (dead). Patients scoring 0 to 2 on the mRS were classified as independent; patients scoring 3 to 6 were categorized as experiencing severe disability or death.

Depression was scored using the Hospital Anxiety Depression Scale (HADS) German version. HADS total scores were categorized as follows: HADS 0 to 7 normal; HADS 8 to 10 marginal; HADS 11 to 21 pathological.

Cognitive impairment was assessed by the mini mental state examination (MMSE). The MMSE total scores were categorized as follows: 27 to 30 normal; 21 to 26 mild cognitive impairment; 10 to 20 moderate cognitive impairment; and <10 severe cognitive impairment.

We used the HUI 2/3 to quantify HRQoL. The HUI2 and HUI3 overall scores are defined as perfect health equal to 1.00 and being dead equal to 0; negative scores imply health states considered worse than death. The HUI2 overall score includes sensation, mobility, emotion, cognition, self-care, and pain. HUI3 includes vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain. We decided to use both scales because of the different dimensions included in these scales, which can be affected by stroke. The 2 systems are independent but complementary. The widespread use of HUI facilitates the interpretation of results and permits comparisons of disease and treatment outcomes and also comparisons of long-term sequelae.

In addition, HRQoL was evaluated using the EQ-5D. This instrument comprises a 5-domain health self-classification system (mobility, self-care, daily activities, pain, and anxiety/depression), with 3 degrees of severity and a visual analogue scale (VAS), described as a “feeling thermometer” rated from 0 to 100, anchored by worst and best imaginable health state. The EQ-5D allows to calculate a preference-based summary index based on time tradeoff techniques in which the value 0 represents death and 1 represents perfect health. We chose utility measurements (ie, preference-based measures) to identify determinants of HRQoL in stroke survivors because they are appropriate to compare QoL across different neurologic diseases as well as across different populations and instruments.

**Statistical Analysis**

Results are presented as means±SD and median or proportions (%) as appropriate.

Comparisons between groups were assessed using parametric and nonparametric tests (ANOVAs; t tests, Wilcoxon, Kruskall–Wallis tests).

A total of 41 variables analyzed by means of Spearman rank correlation (P=0.10; univariate “variable screening”) with regard to their possible impact on HRQoL were selected. In a second step, we performed multivariate regression analysis with forward selection mode to determine independent predictors of HRQoL using a significance level of α=0.05.

**Results**

A total of 77 patients completed the 4-year follow-up, with 34 patients experiencing ischemic infarct, 5 patients experiencing...
hemorrhage, and 38 patients with diagnosed TIA at time of discharge. Twenty of these patients experienced additional infarct(s) before or after the TIA and were therefore considered stroke patients in further analyses (Table 1). The number of sustained strokes correlated with all 4 HRQoL measures. Correlation coefficients varied from $-0.390$ to $-0.462$ ($P=0.01$).

Four years after the stroke event, 16% of the patients experiencing TIA ($n=11$), 47% of the patients experiencing infarct ($n=35$), and 57% of the patients experiencing hemorrhage ($n=7$) were dead. Table 1 shows the clinical and sociodemographic characteristics of the study population.

According to the BI at time of examination, 61 patients were classified as “functionally independent.” Nine patients were labeled “help needed,” and 7 patients were classified “institutional care needed.” The mRS category “independence” comprised 47 patients; 30 patients are included in the mRS category “severe disability” (Table 1).

### Univariate Analysis

HRQoL of survivors at 4 years was evaluated using HUI2/3, EQ-5D index, and EQ-5D-VAS. The HRQoL scores were compared depending on different variables including diagnosis, gender, age, HADS classifications, BI, mRS, and cognitive impairment (MMSE). The results are summarized in Table 2. Mean scores of HUI2 and HUI3 depending on diagnosis are depicted in Figure 1. Significant mean score differences were found between the different groups of diagnoses, the age groups,
the HADS classifications (anxiety and depression), and between the MMSE categorization.

EQ-5D Index scores and EQ-5D VAS scores depending on diagnosis are presented in Figure 2. Patients experiencing TIA without any additional strokes scored best on all 4 HRQoL measures, followed by patients with infarct and patients with hemorrhage. Mean score differences proved significant for both measures ($P<0.01$).

The differential evaluations for age categories showed that the HRQoL outcomes decreased significantly with increasing patient age.

Mean score differences between the different MMSE categories were also significant for all 4 HRQoL measures and deteriorated with declining MMSE scores.

HRQoL increased with decreasing scores on the HADS (depression and anxiety).

Married patients scored higher on all HRQoL measures than single living patients/divorced or widowed patients but mean score differences were not significant.

Patients who had to change domicile because of sequelae of stroke had significant worse mean scores for all 4 HRQoL measures than patients who did not have to change their domicile.

Multivariate Analyses
Table 3 shows the variables that turned significant in bivariate analyses and were finally included in the regression models. The variance explained by the predictors vary across the different models from $R^2=0.802$ (HUI3) to $R^2=0.633$ (VAS).

The MMSE score was a significant predictor for HUI2 and HUI3. Clinical condition assessed by the Rankin scale predicted HUIs but not EQ-5D. On the other hand, clinical condition evaluated by the BI was a significant predictor for EQ-5D index. Anal incontinence was a predictor for all 4 HRQoL measures. Depression measured by the HADS also predicted the outcome of all 4 HRQoL measures.

Discussion
In the present study, the long-term outcome of HRQoL in stroke survivors was assessed 4 years after the stroke event. We show that HRQoL depends on several clinical and demographic factors. The HRQoL decreased with increasing patient age consistently for all evaluated HRQoL measures, which is in accordance with previous evaluations of HRQoL in healthy populations. The subgroup analyses for age categories showed that younger and older patients differ in severity of the deterioration of the HRQoL, probably because of increasing disability and health problems in old age. Similarly, Ahlsio et al reported that in their study, age and initial function are prognostically important factors for HRQoL outcomes. However, considered in a regression model, in combination with other variables, the predictor age loses its independent impact on HRQoL.

The clinical condition as assessed by the Rankin scale constitutes a significant predictor for the HUIs. They seem, besides assessing HRQoL, also to be sensitive at assessing the objective clinical status as evaluated by the physician. Furthermore, anal incontinence as a symbol of severe handicap was the predictor that had a considerable effect on all 4 HRQoL measures. mRS scores, BI scores, and incontinence constituted the physical aspects that most affected HRQoL in the studied population.
TABLE 3. Results From the Multivariate Regression Models Estimating the Influence of Potential Predictors on HRQoL

<table>
<thead>
<tr>
<th></th>
<th>HUI 2 B (P)</th>
<th>HUI 3 B (P)</th>
<th>EQ-5D Index B (P)</th>
<th>VAS B (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>0.408 (0.133)</td>
<td>0.051 (0.911)</td>
<td>−0.389 (0.312)</td>
<td>48.493 (0.136)</td>
</tr>
<tr>
<td>Age at beginning of disease</td>
<td>−0.001 (0.667)</td>
<td>−0.003 (0.439)</td>
<td>0.005 (0.086)</td>
<td>0.085 (0.721)</td>
</tr>
<tr>
<td>Smoker</td>
<td>−0.044 (0.131)</td>
<td>−0.020 (0.682)</td>
<td>−0.067 (0.110)</td>
<td>−2.388 (0.487)</td>
</tr>
<tr>
<td>Income</td>
<td>−0.026 (0.382)</td>
<td>−0.021 (0.666)</td>
<td>−0.009 (0.837)</td>
<td>−0.578 (0.870)</td>
</tr>
<tr>
<td>MMSE</td>
<td>0.016* (0.012)</td>
<td>0.026* (0.017)</td>
<td>0.014 (0.110)</td>
<td>0.449 (0.547)</td>
</tr>
<tr>
<td>HADS anxiety</td>
<td>−0.006 (0.448)</td>
<td>0.006 (0.653)</td>
<td>0.013 (0.242)</td>
<td>−0.316 (0.729)</td>
</tr>
<tr>
<td>HADS depression</td>
<td>−0.011* (0.049)</td>
<td>−0.030** (0.002)</td>
<td>−0.020* (0.012)</td>
<td>−1.756** (0.009)</td>
</tr>
<tr>
<td>mRS</td>
<td>−0.056* (0.023)</td>
<td>−0.134** (0.002)</td>
<td>−0.024 (0.487)</td>
<td>0.042 (0.988)</td>
</tr>
<tr>
<td>BI</td>
<td>0.003 (0.127)</td>
<td>0.001 (0.735)</td>
<td>0.010* (0.000)</td>
<td>0.379 (0.064)</td>
</tr>
<tr>
<td>Employment</td>
<td>0.018 (0.809)</td>
<td>0.148 (0.238)</td>
<td>−0.084 (0.427)</td>
<td>−10.321 (0.247)</td>
</tr>
<tr>
<td>Passing water</td>
<td>−0.018 (0.660)</td>
<td>−0.053 (0.451)</td>
<td>0.040 (0.510)</td>
<td>4.568 (0.366)</td>
</tr>
<tr>
<td>Anal incontinence</td>
<td>−0.179** (0.002)</td>
<td>−0.291** (0.002)</td>
<td>−0.219** (0.006)</td>
<td>−18.467** (0.005)</td>
</tr>
<tr>
<td>Sleep</td>
<td>0.018 (0.711)</td>
<td>0.041 (0.610)</td>
<td>−0.019 (0.786)</td>
<td>0.584 (0.919)</td>
</tr>
<tr>
<td>Heart</td>
<td>0.010 (0.798)</td>
<td>0.002 (0.972)</td>
<td>0.049 (0.366)</td>
<td>7.425 (0.105)</td>
</tr>
<tr>
<td>Lung</td>
<td>−0.026 (0.550)</td>
<td>−0.059 (0.425)</td>
<td>−0.069 (0.270)</td>
<td>−12.824* (0.017)</td>
</tr>
<tr>
<td>$R^2$</td>
<td>0.791</td>
<td>0.802</td>
<td>0.751</td>
<td>0.633</td>
</tr>
</tbody>
</table>

Significance *P<0.05; **P<0.01. The following variables did not turn significant in Spearman rank correlation (P<0.10; univariate variable screening) and were not included in multivariate regression models: gender, BMI, diagnoses, blood pressure (systolic/diastolic), change of domicile, help needed in everyday life, physiotherapy, physical functioning, pain, general perception of health, vitality, social functioning, emotional functioning, mental well-being, vision, hearing, speech, ambulation, dexterity, emotion, cognition, pain, sensation, mobility, self-care, death. Age turned significant but was not considered in further analyses in favor of “age at beginning of disease”.

Regarding HRQoL, patients experiencing TIA achieve high HRQoL scores if there are no additional infarcts. Otherwise, HRQoL seems to be determined by the preceding or after infarct.

Daffertshofer et al. conclude that there is a relevant individual risk of early stroke, death, or disability in TIA patients. In our TIA subsample, 11 patients had experienced strokes before the discharge diagnosis TIA, and 9 patients experienced additional strokes after the discharge diagnosis.

Neuropsychiatric disorders such as depression and dementia after stroke become increasingly important in long-term stroke survivors. A considerable decline in cognitive function has been reported by several studies and can be assessed shortly after the occurrence of stroke. In a recent longitudinal study, ~30% of patients with stroke developed dementia compared with 11% in controls, and stroke increased the risk for dementia by 4 to 12×. Even mild or moderate difficulties with cognitive function limit the survivors’ ability to plan and develop goals in life that are required abilities to achieve life satisfaction. In our study, cognitive impairment is a strong predictor for low HRQoL outcomes.

If untreated, poststroke depression, which occurs in 30% to 40% of stroke patients, can interfere with recovery and adversely affect functional and social outcomes. Of 7 studies examining the independent effect of depression on stroke morbidity, 6 studies reported a strong influence. In our study, a depressive or anxious status is also associated with low HRQoL. Increasing HADS scores are accompanied by decreasing scores on all 4 HRQoL measures.

These results are consistent with previous work that affirms that low scores seem to be closely linked to depression. In our study, poststroke depression measured by the HADS predicted the outcomes of HUI2/3 and EQ-5D index/EQ-5D-VAS. Although its prevalence peaks 3 to 6 months after stroke onset, even 4 years after the incidence, still a substantial number of patients did experience depressive episodes and subsequently a considerably reduced HRQoL. A further analysis of those patients detected that ~81% of the patients in this study did not receive an adequate treatment. Interestingly, anxiety seems to play an ancillary role in patients after stroke in contrast to depression; anxiety did not contribute to the results in the regression model. Although physical symptoms in contrast to a report by King also contribute to HRQoL, our results clearly show that depression may have a more pronounced impact on HRQoL and well-being of the patients.
were independent in ADL had significantly better HRQoL than patients who were dependent.21

This study has several limitations. First, we considered a rather small sample size, which reduces the generalizability of the results. Some patients refused to participate in the study or were excluded from the study because of dementia or aphasia. As described above, patients who refused to join the study had similar sociodemographic and clinical characteristics to patients who participated. Therefore, we do not have any evidence that the inclusion of these patients in our analyses would have changed our results regarding HRQoL.

Data of demented or aphasic patients were excluded from HRQoL analyses because most of the questionnaires we used to assess HRQoL are not validated for proxy assessments and the comparability between patients and proxy assessment is difficult. Otherwise, our results show that HRQoL scores deteriorated with declining MMSE scores. Therefore, we assume that the patients excluded because of dementia or aphasia probably would have shown very low HRQoL scores and might have changed our results in terms of lower HRQoL scores. Further on, patients died during the 4-year follow-up; we may have lost the information on patients with severely reduced HRQoL. We analyzed predictors of HRQoL, which must not be interpreted in a causal manner.

In conclusion, a substantial proportion of stroke survivors have very poor HRQoL. In our study, besides physical and cognitive functioning, depression proved to be an important factor for life-satisfaction in terms of HRQoL. It seems important to detect and treat depression to increase the psychological well-being of stroke patients. However, other important factors such as incontinence must be also considered.

References

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